



Prognostic impact of underlying lung disease in pulmonary wedge resection for lung cancer

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Received: 13 September 2018 / Accepted: 1 November 2018 / Published online: 15 November 2018
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Abstract

Background Pulmonary wedge resection is an option for lung cancer patients with limited cardiopulmonary preservation. As the impact of underlying lung status on the prognosis of such patients remains unclear, we assessed this issue.

Methods A total of 149 borderline surgical candidates with localized lung cancer who had undergone wedge resection were retrospectively investigated. Clinical variables related to perioperative morbidity, local control rate, and oncological outcomes based on underlying lung disease were analyzed.

Results According to the risk analysis of postoperative complications, underlying lung disease did not influence the surgical morbidity. Postoperative recurrence occurred in 65 patients (locoregional recurrence in 36, distant metastasis in 12, and both simultaneously in 17). Multivariate analysis revealed that emphysema on computed tomography (CT) [hazard ratio (HR) 0.45; 95% confidence interval (CI) 0.21–0.99] was an independent indicator of locoregional recurrence. Forty-four patients died of lung cancer and 29 of other causes. Multivariate analysis demonstrated that interstitial lung disease on CT (HR 1.98; 95% CI 1.01–3.89) was a predictor of poor prognosis.

Conclusion Pulmonary wedge resection can be safely undergone by lung cancer patients regardless of pulmonary comorbidity, although underlying lung disease may influence the prognosis after wedge resection.

Keywords Lung cancer · Wedge resection · Underlying lung disease · Prognosis

Introduction

Pulmonary wedge resection is a treatment option for high-risk operable patients with early-stage lung cancer, although lobectomy is the standard of care. On the one hand, it has been revealed that wedge resection is associated with fewer perioperative complications and feasible oncologic efficacy, although the incidence rate of local recurrence was reportedly higher than that among patients who underwent standard lobectomy [1, 2]. Other local treatments, such as stereotactic body radiotherapy (SBRT) [3], ablation and cryosurgery [4], and ion beam radiotherapy [5], are recently

indicated in high-risk patients with localized lung cancer, all with acceptable results. Notwithstanding the limitations of these local therapies in respect of pulmonary comorbidity such as pulmonary fibrosis and severe emphysema [6, 7], surgery is frequently indicated in cases of lung cancer with pulmonary fibrosis and/or emphysema. In this regard, it is crucial for clinicians to determine the efficacy of pulmonary wedge resection in the context of pulmonary comorbidity among high-risk patients.

In the present study, to verify this approach we retrospectively reviewed the data of high-risk pulmonary comorbid patients with primary lung cancer who underwent pulmonary wedge resection, focusing on perioperative morbidity, local control rate, and oncological outcomes based on underlying lung disease.

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Materials and methods

Study design and population

A total of 830 patients with primary lung cancer underwent curative surgical resection from January 2005 to December 2012 at Nara Medical University Hospital. Surgeries comprised 8 pneumonectomies, 582 lobectomies, 45 segmentectomies, and 195 wedge resections. Among the 195 patients who underwent wedge resections, 46 had pure ground-glass opacity (GGO) nodules and 149 had part-solid or solid nodules. These 149 patients who underwent wedge resection for part-solid or solid nodules were retrospectively analyzed. The flow chart illustrating the eligibility process is shown in Fig. 1. All of the patients who underwent pulmonary wedge resection were borderline surgical candidates with limited pulmonary reserve, advanced age, or medical comorbidities. The underlying lung where a pulmonary wedge resection was indicated was classified as normal, emphysematous lung, or interstitial lung disease (ILD) according to the findings of computed tomography (CT). The patients'

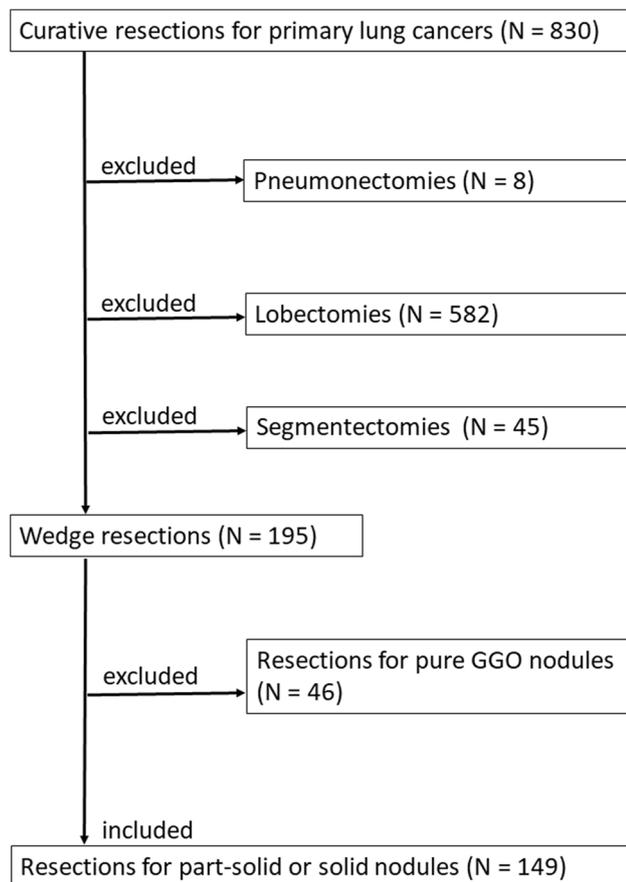


Fig. 1 Flow chart of the eligibility process for the study

characteristics are shown in Table 1. The majority of patients (145 of 149, 97.3%) underwent surgery using the video-assisted thoracoscopic approach. Three patients were converted to thoracotomy because of severe pleuropulmonary adhesions. Median sternotomy was performed in two patients who required simultaneous open-heart surgery. A ring-shaped forceps (P.N.CATCH; Takasago, Tokyo, Japan) was used for every wedge resection procedure. A target nodule was held using the ring forceps and staple lines were placed outside the ring forceps. Although measurement of the margin distance and cytological analysis of the resected margin, as reported previously [8–10], were not carried out in our series, all lesions were excised with pathologically negative resection margins. Most patients did not undergo lymph node sampling during surgery. No patients received preoperative chemotherapy or radiation therapy. The preoperative serum carcinoembryonic antigen (CEA) levels were assessed using enzyme-linked immunosorbent assay kits and classified as elevated or normal according to a cutoff value of 5.0 ng/mL. High-resolution chest computed tomography (HRCT) scans (≤ 2 mm in thickness) were performed to analyze the nodular size and patterns of primary lesions. Pure GGO tumors were not included in the present study. Nodular patterns were divided into solid or part-solid nodule groups according to the presence of GGO on HRCT. Underlying pulmonary disease, such as ILD and emphysema, was also evaluated on the basis of preoperative HRCT findings. HRCT findings were evaluated according to the glossary of the Fleischner Society [11] and confirmed by a board-certified chest radiologist with 16 years of experience. Tumor locations were classified into easily resectable lesions and difficult-to-resect lesions according to a previous report [12]. Patterns of failure were assessed by imaging studies such as CT, magnetic resonance imaging, and/or positron emission tomography. Locoregional recurrence (LR) was defined as disease recurrence at the surgical resection margin, ipsilateral hilum, and/or mediastinum. All other sites of failure, including the supraclavicular fossa and contralateral hilum, were considered sites of distant metastases (DM). Cancer recurrence was evaluated according to the initial relapse pattern (LR, DM, or both simultaneously). Postoperative complications were graded according to the Clavien–Dindo classification [13], grades III to V of which were chosen as complications.

Statistical analysis

Univariate analysis (Chi-squared test) was carried out to investigate the association between operative morbidity and clinical factors. Locoregional recurrence-free survival (LRFS) was estimated as the interval from the date of surgery to the date of LR or last follow-up. Patients who were alive or dead without LR were censored at the date of the

Table 1 Patient characteristics

Variable	All patients (<i>n</i> = 149)	Emphysema (<i>n</i> = 51)	ILD (<i>n</i> = 44)	Normal (<i>n</i> = 54)
Age (years)	74 ± 8 (53–87)*	75 ± 7 (58–87)*	74.5 ± 9 (54–87)*	73 ± 8 (53–86)*
Gender				
Male	116	48	41	27
Female	33	3	3	27
Smoking history				
Current or ex-smoker	121	51	42	28
Non-smoker	28	0	2	26
Preop CEA level				
Normal	98	33	22	43
> 5.0 ng/mL	51	18	22	11
Preop FVC (mL)	2865 ± 759 (980–5300)*	3002 ± 582 (1760–4600)*	3040 ± 834 (1240–5300)*	2593 ± 778 (980–4640)*
Preop FEV1 (mL)	1936 ± 654 (630–4390)*	1724 ± 633 (630–3560)*	2190 ± 676 (900–4390)*	1928 ± 590 (880–3540)*
Preop CT findings				
Whole tumor size (mm)	19 ± 8 (5–42)*	20 ± 7 (10–42)*	21 ± 7 (7–34)*	17 ± 8 (5–36)*
Solid component size (mm)	198 ± 8 (1–42)*	20 ± 8 (3–42)*	20 ± 7 (6–34)*	15 ± 9 (1–36)*
Nodular pattern (solid/part-solid)	127/22	48/3	39/5	40/14
Pulmonary comorbidity (emphysema/ILD/normal)	51/44/54			
Tumor location				
Easy resectable	88	23	28	37
Difficult to resect	61	28	16	17
Surgical approach				
VATS	144	49	44	51
Open	5†	2	0	3
Histology				
Ad	76	23	14	39
Sq	56	23	22	11
Others	17	5	8	4
5Y-OS (%)	52	62	27	65

ILD interstitial lung disease, Preop preoperative, CEA carcinoembryonic antigen, FVC forced vital capacity, FEV1 forced expiratory volume in 1 s, CT computed tomography, VATS video-assisted thoracoscopic surgery, Ad adenocarcinoma, Sq squamous cell carcinoma, 5Y-OS 5-years overall survival

*Mean ± standard deviation (range)

†The open approaches were lateral thoracotomy in three patients and median sternotomy in two patients

last follow-up. Overall survival (OS) was calculated as the interval from the date of surgery to the date of any cause of death or last follow-up. The median follow-up duration was 47 months (range 1–116 months). Survival curves were estimated using the Kaplan–Meier method. Univariate and multivariate Cox proportional hazards models were used to calculate the hazard ratio (HR) and 95% CI to identify independent risk factors for LRFS and OS. Statistical significance was defined as a *P* value of < 0.05, and in multivariate analysis with stepwise variable selection a *P* value of < 0.05 was also used. All statistical analyses were performed using EZR Version 1.32 (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphic user interface for R Version 3.3.2 (The R Foundation for Statistical Computing, Vienna, Austria) [14].

The present study was approved by the institutional review board of our center in February 2014 (No. 793).

Results

Indication for wedge resection

Most patients had heterogeneous backgrounds such as advanced age, medical comorbidities, or other malignancies. The key factors that influenced the decision regarding whether to perform wedge resection are shown in Table 2. Factors associated with cardiopulmonary reserve accounted for about a half of the reasons. The other half included advanced age, other uncontrolled comorbidities,

Table 2 Factors that influenced decisions regarding the wedge resection

Factors	No. of patients
Advanced age	63
Limited pulmonary reserve	63
ILD/emphysema/BA/Others*	32/27/2/2
Cardiovascular disease	31
CAD/Arrhythmia/CHF/GVD/VHD†	13/7/6/3/2
Psychotic and nervous system disease	10
Dementia/stroke/PD/depression/neuropathy	3/2/2/2/1
Multiple neoplasm	30
Multiple lung cancer (metachronous/synchronous)	12 (8/4)
Multiple other neoplasm (metachronous/synchronous)	18 (15/3)
Others‡	14

ILD interstitial lung disease, BA bronchial asthma, CAD coronary artery disease, CHF chronic heart failure, GVD great vessel disease, VHD valvular heart disease

*Other factors were old pulmonary tuberculosis in one patient and nontuberculous mycobacteria in one patient

†Valvular heart disease required a simultaneous operation

‡Other factors were severe obesity in four patients, severe pleuropulmonary adhesion in three patients, false-negative results by intraoperative frozen section diagnosis in two patients, chest wall necrosis due to an overdose of radiation in one patient, progeria in one patient, rheumatoid arthritis in one patient, liver cirrhosis in one patient, and chronic renal failure in one patient

or other uncontrolled malignancies. Fifty-four of 149 patients had multiple factors.

Operative mortality and morbidity

Thirty-six complications were observed in 32 patients (21.5%). Among them, grade IV and V complication of respiratory insufficiency occurred in 2 patients, respectively, whereas grade III complications occurred in 30 patients. The predominant complications were prolonged air leakage in 10 patients (6.7%), respiratory insufficiency in 6 (4.0%), delirium in 8 (5.4%), and surgical site infection in 5 (3.4%). The others were atelectasis in 3 patients (2.0%), pneumonia in 2 (1.3%), atrial arrhythmia in 1 (0.7%), and hypotension 1 (0.7%). The 30-day mortality rate was 0% in the present study group. One in-hospital death occurred in a patient who suffered from prolonged air leakage and pneumonia postoperatively and died of respiratory failure on postoperative day 488. The results of risk analysis of postoperative complications after wedge resection are shown in Table 3. According to the univariate analysis, solid component size on CT ($P=0.002$) was identified as predictors.

Table 3 Risk of postoperative complication (\geq Grade 3) after wedge resection: univariate analysis

Variable	<i>n</i>	Complication	%	<i>P</i> value
Age				
≥ 75	84	19	23	0.841
< 75	65	13	20	
Gender				
Female	33	6	18	0.810
Male	116	26	22	
Smoking history				
Non-smoker	28	5	18	0.799
Current or ex-smoker	121	27	22	
Solid component size on CT				
≤ 20 mm	101	14	14	0.002
> 20 mm	48	18	38	
Nodular pattern on CT				
Part-solid	22	4	18	0.786
Solid	127	28	22	
Pulmonary comorbidity				
Normal	54	8	15	0.110
Emphysema	51	16	31	
ILD	44	8	18	
Tumor location				
Easy resectable	88	15	47	0.155
Difficult to resect	61	17	28	

CT computed tomography, ILD interstitial lung disease

Locoregional recurrence

During the follow-up period, postoperative recurrence developed in 65 patients (43.6%), with LR in 36 patients (24.2%), DM in 12 patients (8.1%), and both simultaneously in 17 patients (11.4%). In total, LR developed in 53 patients (35.6%). Forty patients of the 53 patients with LR included recurrence at the surgical resection margin. Among them, 13 patients had only at the surgical resection margin. The 3-year and 5-year LRFS rate for all 149 patients was 67% and 62%, respectively (Fig. 2a). Table 4 shows the results of risk analysis of LRFS after wedge resection. According to the univariate analysis, the following factors were identified as predictors of LR: gender (HR 2.34; 95% CI 1.05–5.18), solid component size on CT (HR 2.16; 95% CI 1.25–3.72), emphysema on CT (HR 0.72; 95% CI 0.33–1.49), and ILD on CT (HR 2.1; 95% CI 1.15–3.99). Multivariate analysis then revealed that the three factors were independently associated with LRFS [(gender) HR 2.59; 95% CI 1.10–6.11; (solid component size on CT) HR 2.24; 95% CI 1.29–3.88; (emphysema on CT) HR 0.45; 95% CI 0.21–0.99].

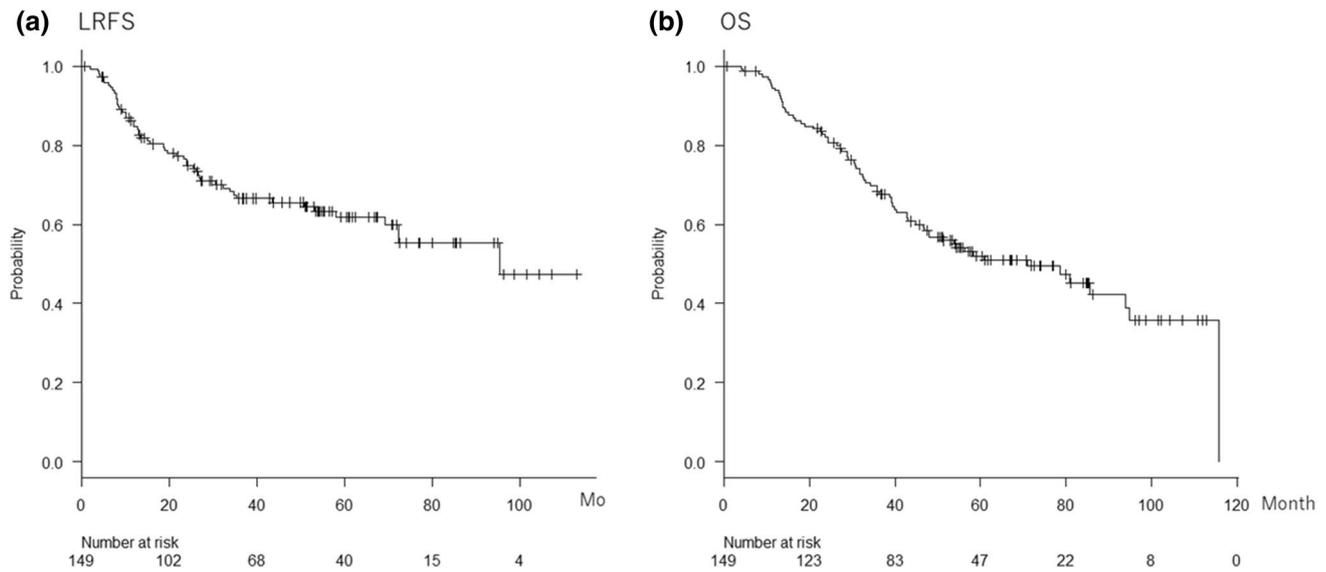


Fig. 2 Kaplan–Meier plot on locoregional recurrence-free survival (a) and overall survival (b) of all patients after wedge resection for lung cancer. *LRFS* locoregional recurrence-free survival, *OS* overall survival

Table 4 Loco-regional recurrence free survival rates after wedge resection: univariate and multivariate analysis

Variable	n	Univariate analysis			Multivariate analysis		
		HR	95% CI	P value	HR	95% CI	P value
Age							
≥75	84	Ref		0.804			
<75	65	1.071	0.624–1.838				
Gender							
Female	33	Ref		0.037	Ref		0.030
Male	116	2.336	1.052–5.813		2.588	1.096–6.110	
Preop CEA level							
Normal	98	Ref		0.291			
>5.0 ng/mL	51	1.352	0.773–2.365				
Smoking history							
Non-smoker	28	Ref		0.101			
Current or ex-smoker	121	1.949	0.879–4.322				
Solid component size on CT							
≤20 mm	101	Ref		0.006	Ref		0.004
>20 mm	48	2.157	1.251–3.720		2.241	1.249–3.881	
Nodular pattern on CT							
Part-solid	22	Ref		0.060			
Solid	127	2.660	0.959–7.378				
Pulmonary comorbidity							
Normal	54	Ref		0.004	Ref		0.004
Emphysema	51	0.716	0.344–1.492		0.453	0.208–0.988	
ILD	44	2.143	1.151–3.991		1.525	0.787–2.955	
Tumor location							
Easy resectable	88	Ref		0.827			
Difficult to resect	61	0.940	0.542–1.632				

HR hazard ratio, *CI* confidence interval, *Ref* reference, *Preop* preoperative, *CEA* carcinoembryonic antigen, *CT* computed tomography, *ILD* interstitial lung disease

Treatment after relapse

Of the 65 patients with recurrence, 28 had ILD, 18 had emphysema, and 19 had no evidence of ILD and emphysema on chest CT. Curative treatments for recurrence were

Table 5 Curative treatments for lung cancer recurrence after wedge resection ($n=33/65$)

Treatment	Non-ILD ($n=24/37$)	ILD ($n=9/28$)
Completion lobectomy	2	0
Thoracic radiotherapy	15	3
Conventional radiotherapy	14	2
Stereotactic radiotherapy	1	1
Concurrent chemo-radiotherapy	1	0
Chemotherapy	6	6
Cytotoxic agents	4	6
EGFR-TKI	2	0

ILD interstitial lung disease, EGFR-TKI epidermal growth factor receptor–tyrosine kinase inhibitor

performed in 33 patients (Table 5). Although the majority of patients received irradiation alone for local treatment of LR, completion lobectomy was performed in two patients. Among patients with DM, systemic chemotherapy was performed in 12. Of these, two patients were treated with an epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI) and 10 were treated with cytotoxic agents. Treatment options after recurrence for patients with ILD were limited compared with the other two groups. Only three out of 28 patients with ILD received thoracic radiotherapy, and no patients were treated with an EGFR-TKI.

Prognosis

During the follow-up period, 44 patients died of lung cancer and 29 of other causes. The 3-year and 5-year OS rate for all 149 patients was 68% and 52%, respectively (Fig. 2b). Table 6 shows the results of risk analysis of OS after wedge resection. According to the univariate analysis, the following factors were identified as predictors of OS: gender (HR 2.70; 95% CI 1.29–5.64), preoperative serum CEA

Table 6 Overall survival rates after wedge resection: univariate and multivariate analysis

Variable	<i>n</i>	Univariate analysis			Multivariate analysis		
		HR	95% CI	<i>P</i> value	HR	95% CI	<i>P</i> value
Age							
≥75	84	Ref		0.502			
<75	65	0.852	0.534–1360				
Gender							
Female	33	Ref		0.008	Ref		0.138
Male	116	2.702	1.294–5.644		2.151	0.781–5.921	
Preop CEA level							
Normal	98	Ref		0.021	Ref		0.262
>5.0 ng/mL	51	1.733	1.085–2.769		1.331	0.807–2.195	
Smoking history							
Non-smoker	28	Ref		0.006	Ref		0.852
Current or ex-smoker	121	1.913	1.202–3.043		0.887	0.253–3.118	
Solid component size on CT							
≤20 mm	101	Ref		0.001	Ref		0.009
>20 mm	48	2.196	1.377–3.501		1.924	1.176–3.148	
Nodular pattern on CT							
Part-solid	22	Ref		0.015	Ref		0.228
Solid	127	3.495	1.274–9.590		1.989	0.651–6.080	
Pulmonary comorbidity							
Normal	54	Ref		0.001	Ref		0.047
Emphysema	51	1.464	0.789–2.718		0.945	0.466–1.915	
ILD	44	2.830	1.580–5.069		1.982	1.010–3.888	
Tumor location							
Easy resectable	88	Ref		0.531			
Difficult to resect	61	0.858	0.532–1.384				

HR hazard ratio, CI confidence interval, Ref reference, Preop preoperative, CEA carcinoembryonic antigen, CT computed tomography, ILD interstitial lung disease

level (HR 1.73; 95% CI 1.09–2.77), smoking history (HR 1.91; 95% CI 1.20–3.04), solid component size on CT (HR 2.20; 95% CI 1.38–3.50), nodular pattern on CT (HR 3.50; 95% CI 1.27–9.59), emphysema on CT (HR 1.46; 95% CI 0.79–2.72), and ILD on CT (HR 2.83; 95% CI 1.58–5.07). Multivariate analysis revealed that the solid component size on CT (HR 1.92; 95% CI 1.18–3.15) and ILD on CT (HR 1.98; 95% CI 1.01–3.89) were significant independent predictors of OS.

Discussion

The current gold standard for early-stage primary lung cancer is surgical resection with lobectomy and lymph node evaluation. However, significant numbers of patients with lung cancer are considered medically inoperable or at high risk for standard surgical resection [15]. Although most patients with early-stage lung cancer are asymptomatic, the estimated 5-year survival of untreated stage I lung cancer is reported to be 10% [15].

A clear definition of “high-risk patient” is difficult to determine in clinical practice. Basically, the optimal surgical intervention is determined according to the routine pulmonary physiologic assessment findings [16]. However, patients with lung cancer have various practical problems other than their cardiopulmonary reserve. These problems include various uncontrolled medical comorbidities, advanced age, personality variations, and other factors. Medical comorbidities and advanced age influence the patient’s surgical risk and life expectancy. Moreover, patients have different levels of operative risk acceptance and aversion. Surgeons make clinical decisions based on all of these factors. In the present study, about half of the factors that influenced the decision regarding the limited procedure were related to no cardiopulmonary comorbidities. In addition, one-third of the patients had multiple risk factors.

Pulmonary wedge resection is a treatment option for high-risk patients with early-stage lung cancer. It has been revealed that high-risk patients can safely undergo wedge resection, although the incidence rate of local recurrence is higher than that of standard lobectomy [1, 2]. Other local treatments such as SBRT, ablation and cryosurgery, and ion beam radiotherapy have recently become available [3–5]. However, these local therapies are limited in terms of pulmonary comorbidity such as pulmonary fibrosis and severe emphysema [6, 7]. Although several studies reported the prognostic impact of coexisting pulmonary disease in patients with lung cancer after surgery, most patients included in these studies were undergoing lobectomy [17–19]. The prognostic impact after pulmonary wedge resection has remained unclear.

According to the previous analyses, coexisting pulmonary disease negatively influenced perioperative morbidity and mortality after major lung cancer resection [17–19]. Most patients in these studies underwent anatomical resection. In the present study, focusing on wedge resection, only tumor size was a predictor of postoperative complication, and the coexisting pulmonary disease did not influence the surgical morbidity. The possible reasons for the result being related to the tumor size were as follows. Larger tumor size might increase the occurrence of air leakage because the parenchyma spared after resection of larger tumors could be thicker than that of smaller lesions, or patients with a larger tumor might be in poorer physical condition than those with a smaller tumor in clinical practice. In addition, exacerbation of ILD, which represents a major concern after surgery for patients with ILD, was not established in our series. According to the results of a Japanese nationwide survey, the risk of acute exacerbation of ILD after lung resection was higher in patients who underwent anatomical resection rather than wedge resection [20].

The incidence of LR in the present series was 35.6% (53/149), which seems to be acceptable, since a review of the studies of pulmonary sublobar resection for primary lung cancer revealed that the locoregional recurrence rate after wedge resection ranged from 14 to 55% [9]. Our series was a heterogeneous cohort in clinical practice and included patients with tumors larger than 2 cm in size, which might influence the high local failure rate of our study. In fact, a solid tumor size of ≥ 2 cm was the risk factor for LR in our analysis. According to previous reports, obtaining adequate margin distance and evaluating the margin cytology could reduce the local failure rate after wedge resection [8, 10, 21]. In addition to the importance of surgical quality of wedge resection in preventing LR, the underlying lung disease may have an impact on LR because emphysema was an indicator of LR in this study. Although emphysematous lung is outstretched and fragile, this pulmonary condition may contribute to obtaining sufficient margin distance in patients with emphysema in comparison with those with a normal lung or ILD. These speculations may be proved by further analyses of margin distance and margin cytology status of the resected lung.

The other local treatment option for lung cancer is radiation therapy, the validity of which has been reported for high-risk patients with early-stage lung cancer [3–5]. In previous series of SBRT for lung cancer, the 3-year OS rate was 56–75% in inoperable patients [3, 4] and 76–95% in operable patients [22, 23]. In our study, the 3-year OS rate was 68% after wedge resection. However, surgical resections provide sufficient specimens for pathological examination in addition to conferring a potentially curative effect. Detailed pathological evaluation of resected specimens positively influences decisions regarding treatment after recurrence.

In the present study, a proportion of patients with EGFR mutation-positive adenocarcinoma were treated with an EGFR-TKI after relapse. Recent progress in molecular biology means that molecular analysis now plays an important role in the therapeutic approach to lung cancer [24]. Furthermore, radiotherapy can be applied after local recurrence. Radiotherapy reportedly plays a role as a salvage option for isolated LR of lung cancer after complete resection [25, 26]. In the present series, the predominant treatment administered after recurrence was radiotherapy. Some patients remained well without distant relapse after radiotherapy for LR. In a recent report, negative margin wedge resection significantly reduced the possibility of death compared with SBRT, while positive margin wedge resection did not show survival benefit [27]. In sum, qualifying wedge resection could be selected as an alternative local treatment option for lung cancer patients who are not fit to undergo anatomical resection.

Although patients with ILD are at increased risk of developing lung cancer [28], therapeutic modalities should be carefully selected in this patient population because of the existing impairments in lung function and the risk of provoking exacerbation of ILD. According to previous reports, major lung resection is associated with increased postoperative morbidity and mortality in patients with ILD [17, 18]. Therefore, sublobar resection is sometimes considered an alternative option to reduce surgical risk. In the present study group, postoperative exacerbation of ILD or severe respiratory insufficiency was rarely observed among patients with ILD. However, the treatment options for patients with ILD after recurrence were limited. High LR rate after wedge resection and the limited treatment options after LR may have contributed to the poor prognosis in patients with ILD. On carrying out wedge resection for lung cancer patients with ILD, surgeons should carefully consider the risk–benefit ratio of the surgical risk and oncological efficacy.

There are several limitations in the present study. First, it was a single-institution study. Second, we did not evaluate margin distances and margin cytology, while every negative margin result was pathologically confirmed. Third, most patients did not undergo lymph node sampling during surgery. These concerns have recently been raised in relation to wedge resection for lung cancer. Finally, our investigation was a retrospective analysis. Nevertheless, the results of our study should provide useful information for physicians who treat lung cancer.

In conclusion, pulmonary wedge resection can be safely undergone regardless of the pulmonary comorbidities and be selected as an alternative local treatment for lung cancer patients not fit to undergo anatomical resection. However, underlying lung disease can influence the outcome after wedge resection. Emphysematous lung had a positive impact on LR and ILD had a negative impact on

OS. When we carry out pulmonary wedge resection for high-risk patients with lung cancer, the impact of their pulmonary comorbidity should be carefully considered.

Acknowledgements We thank Hugh McGonigle, from Edanz Group (<http://www.edanzediting.com/ac>), for editing a draft of the manuscript.

Compliance with ethical standards

Conflict of interest We have no conflict of interest to declare.

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