The Prognosis of Eighth Edition TNM Staging System IB (Invasive Component Size ≤ 2 cm) Non–Small Cell Lung Cancer After Sublobar Resection

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Research

Keywords: Non–small cell lung cancer; Prognosis; Stage IB; Sublobar resection

Posted Date: July 23rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-45285/v1

Abstract

Background. Sublobar resection is sometimes performed as a surgical treatment for small peripheral tumors. However, there is a question about whether sublobar resection is adequate treatment when visceral pleural invasion is diagnosed postoperatively. The purpose of this study was to evaluate the prognosis of patients with small-sized stage IB non–small cell lung cancer (NSCLC) after sublobar resection.

Methods. From January 2010 to December 2018, 227 consecutive patients with eighth edition TNM stage IB NSCLC (per the joint staging system of the International Association for the Study of Lung Cancer and the American Joint Committee on Cancer) underwent curative surgery. The clinicopathological characteristics and prognosis were compared between the sublobar resection group and the lobectomy group. The sublobar resection group included only small-sized (invasive component size ≤ 2 cm) NSCLC.

Results. In all study patients, clinicopathological characteristics between the sublobar resection and lobectomy groups were not different except in maximum standardized uptake value and invasive component size. The 5-year recurrence-free survival rate was 80.7% after sublobar resection and 73.4% after lobectomy (P = .349). The 5-year overall survival rate was 87.3% after sublobar resection and 84.8% after lobectomy (P = .503). In patients with small-sized NSCLC, the clinicopathological characteristics were not different between the sublobar resection group and the lobectomy group. The 5-year recurrence-free survival rate was 80.7% after sublobar resection and 72.3% after lobectomy (P = .417). The 5-year overall survival rate was 87.3% after sublobar resection and 91.2% after lobectomy (P = .956). Sublobar resection was not a risk factor for recurrence in the multivariate analysis.

Conclusions. The prognosis of sublobar resection in patients with small-sized stage IB NSCLC was comparable with lobectomy. Thus, additional completion lobectomy may not be essential in this setting, despite postoperative upstaging from T1 to T2a.

Introduction

The standard surgical treatment of stage I non–small cell lung cancer (NSCLC) is lobectomy [1]. Recently, however, sublobar resection has been increasingly applied for the treatment of stage I NSCLC. In particular, as more people undergo regular checkups, the early detection of lung cancer is increasing, and the detection of less invasive lung cancer is also increasing. The discovery of ground glass opacity (GGO) nodules on chest computed tomography (CT) has also increased, and sublobar resection has been actively performed for the treatment of GGO. In the case of lung cancer presenting as GGO on CT scan, the prognosis of sublobar resection is known to be acceptable. There are many studies that support these results [2-5]. In addition to the increasing frequency of sublobar resection of GGO-dominant tumors, studies have been conducted to demonstrate the efficacy of sublobar resection for solid-dominant tumors of 2 cm or less. Two important randomized controlled trials (JCOG0802 and CALGB140503) of sublobar resection for solid-dominant tumors are being conducted and will produce results in a few years [6-8]. The

results of these studies will clearly demonstrate the efficacy of sublobar resection in small solid-dominant lung cancer.

There are many studies to evaluate the prognosis of sublobar resection for stage IA NSCLC of 2 cm or less [9-11]. However, there have been no studies on the prognosis of sublobar resection in stage IB NSCLC of 2 cm or less. Indeed, patients with clinical stage IA lung cancer of ≤ 2 cm who underwent sublobar resection were sometimes found to have visceral pleural invasion in the postoperative pathological report. If such a result is obtained, it is difficult to determine whether proper treatment was achieved by sublobar resection alone because upstaging had occurred from stage IA to IB. In such cases, the question is whether additional completion lobectomy should be performed immediately.

The eighth edition of the TNM staging system has substantial revisions compared to the seventh edition staging system [12-14]. In particular, the criteria for measuring tumor size were changed to measure the size of invasive components rather than the overall tumor size. Because of these changes in the staging system, it is necessary to apply a new staging system to determine the prognosis of sublobar resection at any stage of NSCLC.

The purpose of this study was to evaluate the prognosis of patients with small-sized (invasive component size ≤ 2 cm) stage IB NSCLC after sublobar resection. In those cases, sublobar resection was performed initially for the treatment of small (invasive component size ≤ 2 cm) tumors, and, postoperatively, histopathological findings revealed the presence of visceral pleural invasion. Through this research, we wanted to find out whether the additional completion lobectomy should be done immediately in such cases.

Patients And Methods

Patients

From January 2010 to December 2018, 1994 patients underwent curative resection of NSCLC at a tertiary hospital in South Korea. Of those patients, 298 patients were diagnosed as having stage IB NSCLC according to the eighth edition of TNM staging system. Patients who underwent neo-adjuvant chemotherapy or adjuvant chemotherapy were excluded from this study. Patients who had residual tumor in the lung or in the resected margins were also excluded. Patients with tumors larger than 2 cm of invasive component size were also excluded. Finally, 227 consecutive patients were reviewed retrospectively. The patients were divided into 2 groups: the sublobar resection group (n = 21) and the lobectomy group (n = 206). The sublobar resection group included only tumors ≤ 2 cm of invasive component size. The clinicopathological characteristics were analyzed in the 2 groups. The comparison of prognosis was conducted in the 2 groups. We also conducted a study comparing the prognosis of sublobar resection and lobectomy in tumors ≤ 2 cm of invasive component size.

Surgical procedures

Patients diagnosed with clinical stage I lung cancer on chest CT scan and combination positron emission tomography (PET) and CT scan were eligible for surgical treatment. The treatment of choice for stage I NSCLC is lobectomy with mediastinal lymph node dissection. However, in patients with GGO or small solid peripheral nodules near the visceral pleura, sublobar 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 cardiopulmonary disease, sublobar resection was usually performed. Sublobar resection consists of wedge resection and segmentectomy. In most cases, a sufficient resection margin was obtained, in which the margin length was greater than the tumor diameter.

Histological evaluation and restaging

All pathology slides and pathology reports were reviewed. Pathology reports included tumor size, tumor location, nodal status, pleural invasion, lymphatic invasion, and vascular invasion. Visceral pleural invasion was defined as a tumor extending beyond the elastic layer. Lymphatic invasion or vascular invasion was defined as tumor cells present in the lymphatic vessel or vascular lumen. TNM staging was based on the eighth edition of the TNM staging system of lung cancer [14]. To reclassify the T category according to the eighth edition, tumor size was remeasured by the pathologist at the greatest diameter of the invasive component on a histopathological preparation [13]. Cases where the invasive component size was $\leq$ 2 cm were defined as small-sized NSCLC.

Statistical analysis

The clinicopathological characteristics of the sublobar resection group and lobectomy group were compared. A Student *t* test or Wilcoxon rank-sum test was used for continuous variables, and the χ^2 test or Fisher exact test was applied for categorical variables. The Kaplan-Meier method was used to analyze data collected from the interval between the time of operation and the time of the last follow-up visit. Recurrence-free survival (RFS) rates and overall survival (OS) rates were estimated by the Kaplan-Meier method. The Cox proportional hazards model was used in a multivariate analysis to determine the risk factor of recurrence and death for all the study patients. The variables with a *P* value < .1 by univariate analysis were entered into a multivariate analysis. A *P* value < .05 was considered statistically significant.

Results

Comparison of sublobar resection and lobectomy in all study patients

Table 1 shows the comparison of clinical and pathological characteristics between the sublobar resection group and the lobectomy group. There was no statistical difference in clinical characteristics between the 2 groups except maximum standardized uptake value (SUVmax) on PET. The mean SUVmax of the lobectomy group was greater than that of the sublobar resection group (7.2 vs 3.5, *P* < .001). In pathological characteristics, most factors were also not different between the 2 groups except tumor size and the presence of visceral pleural invasion. Tumor size and invasive component size were larger in the

lobectomy group. Visceral pleural invasive was present in 100% of the sublobar resection group, but in only 72.3% of the lobectomy group ($P = .006$).

Table 1
The comparison of clinical and pathological characteristics between the sublobar resection group and the lobectomy group in all study patients.

Variables	Sublobar resection group (n = 21)	Lobectomy group (n = 206)	*p* value
Age (± SD)	67.5 (± 10.1)	66.9 (± 10.8)	0.799
Gender	11 (52.4%)	115 (55.8%)	0.820
Male	10 (47.6%)	91 (44.2%)	
Female			
Current or former smoker	9 (42.9%)	96 (46.6%)	0.821
Serum CEA level (ng/mL) (± SD)	4.1 (± 5.7)	3.0 (± 3.3)	0.449
SUVmax (± SD)	3.5 (± 2.4)	7.2 (± 4.2)	< 0.001
Involved lobe	7 (33.3%)	66 (32.0%)	0.402
Right upper	0	23 (11.2%)	
Right middle	7 (33.3%)	49 (23.8%)	
Right lower	3 (14.3%)	42 (20.4%)	
Left upper	4 (19.0%)	26 (12.6%)	
Left lower			
VATS	20 (95.2%)	185 (89.8%)	0.702
Open thoracotomy	1 (4.8%)	21 (10.2%)	

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

Variables	Sublobar resection group (n = 21)	Lobectomy group (n = 206)	*p* value
Surgical procedures	14 (66.7%)	0	< 0.001
Wedge resection	7 (33.3%)	0	
Segmentectomy	0	201 (97.6%)	
Lobectomy	0	5 (2.4%)	
Bilobectomy			
Intraoperative lymph node evaluation	4 (19.0%)	6 (2.9%)	< 0.001
No mediastinal node dissection	5 (23.8%)	162 (78.6%)	
Systematic nodal dissection	12 (57.1%)	38 (18.4%)	
Selective nodal dissection			
Postoperative Complications	1 (4.8%)	43 (20.9%)	0.086
Operative mortality	2 (1.0%)	0	1.000
Postoperative hospital stay (days) (± SD)	6.2 (± 3.2)	8.3 (± 8.8)	0.276
Histology	19 (90.5%)	147 (71.4%)	0.196
Adenocarcinoma	1 (4.8%)	40 (19.4%)	
Squamous cell carcinoma	1 (4.8%)	19 (9.2%)	
Others			
Total tumor size (cm) (± SD)	1.6 (± 0.4)	2.8 (± 0.9)	< 0.001
Invasive component size (cm) (± SD)	1.5 (± 0.3)	2.6 (± 0.9)	< 0.001

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

Variables	Sublobar resection group (n = 21)	Lobectomy group (n = 206)	*p* value
Location	0	24 (11.7%)	0.140
Central	21 (100%)	182 (88.3%)	
Peripheral			
Histological tumor grade	8 (38.1%)	40 (19.4%)	0.138
Well differentiated carcinoma	9 (42.9%)	110 (53.4%)	
Moderately differentiated carcinoma	4 (19.0%)	56 (27.2%)	
Poorly differentiated carcinoma			
Number of dissected lymph nodes (± SD)	6.3 (± 8.9)	14.5 (± 7.5)	< 0.001
Visceral pleural invasion	21 (100%)	149 (72.3%)	0.006
Lymphatic invasion	10 (47.6%)	104 (50.5%)	0.823
Vascular invasion	6 (28.6%)	49 (23.8%)	0.790
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			

The median follow-up period for all study patients was 1348 days (range, 33-3443 days), and 46 patients had recurrence (Table 2). The 5-year RFS rate was 80.7% after sublobar resection and 73.4% after lobectomy (Fig. 1A). The 5-year OS rate was 87.3% after sublobar resection and 84.8% after lobectomy (Fig. 1B). Both RFS and OS were not statistically different between the sublobar resection group and the lobectomy group ($p = .349$ and $p = .503$, respectively). The univariate and multivariate analyses using a Cox proportional hazards model were conducted to find out the risk factor for recurrence (Table 3). Sublobar resection was not a significant risk factor for recurrence in the univariate analysis. Specific variables identified as significant ($P < .1$) by univariate analysis included SUVmax, involved lobes, histological tumor grade, and lymphatic invasion. When these variables were entered into the multivariate model, only histological tumor grade was a significant risk factor for recurrence of all study patients ($P = .017$)

Table 2
Summary of recurrence in all study patients who underwent sublobar resection and lobectomy.

Variables	Sublobar resection group	Lobectomy group	*p* value
Sites of recurrence	3	21	0.654
Locoregional recurrence	0	13	
Distant recurrence	0	9	
Both			
Locoregional = recurrence within ipsilateral hemithorax including pleura and mediastinal lymph nodes			
Both = Locoregional recurrence + Distant recurrence			

Table 3
(A) Univariate analysis and (B) multivariate analysis of risk factors for recurrence in all study patients.

Variables	HR	95% CI	*p* value
Univariate analysis (A)			
Age	0.992	0.965–1.019	0.547
Gender (male)	1.013	0.564–1.820	0.966
Smoker	1.114	0.613–2.024	0.723
Serum CEA level	1.027	0.955–1.105	0.469
SUVmax	1.080	1.018–1.147	0.011
Involved lobe	1	0.381-3.000	0.089
Right upper (reference)	1.069	0.314–1.829	0.899
Right middle	0.758	0.974–4.318	0.537
Right lower	2.051	0.205–1.928	0.059
Left upper	0.628		0.416
Left lower			
VATS	1.261	0.450–3.533	0.659
Sublobar resection	0.575	0.178–1.857	0.355
Intraoperative lymph node evaluation	1	0.215–1.722	0.394
No mediastinal node dissection (reference)	0.608	0.131–1.450	0.349
Systematic nodal dissection	0.436		0.176
Selective nodal dissection			

HR = hazard ratio

CI = confidence interval

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

Variables	HR	95% CI	*p* value
Histology	1	0.419–2.142	0.529
Adenocarcinoma (reference)	0.948	0.658–4.321	0.897
Squamous cell carcinoma	1.686		0.277
Others			
Total tumor size	0.999	0.719–1.388	0.995
Invasive component size	1.054	0.761–1.459	0.753
Central location	0.942	0.371–2.389	0.900
Histological tumor grade	1	0.994–8.283	0.004
Well differentiated carcinoma (reference)	2.869	1.931–17.320	0.051
Moderately differentiated carcinoma	5.783		0.002
Poorly differentiated carcinoma			
Number of dissected lymph nodes	0.999	0.964–1.036	0.960
Visceral pleural invasion	1.293	0.623–2.684	0.491
Lymphatic invasion	2.180	1.183–4.018	0.012
Vascular invasion	1.397	0.720–2.708	0.323
Lymphovascular invasion	2.165	1.163–4.029	0.015
Multivariate analysis (B)			
SUVmax	1.007	0.938–1.083	0.840

HR = hazard ratio

CI = confidence interval

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

Variables	HR	95% CI	*p* value
Lobe	1	0.452–3.573	0.097
Right upper (reference)	1.271	0.274–1.780	0.649
Right middle	0.699	0.999–4.532	0.453
Right lower	2.128	0.193–2.434	0.050
Left upper	0.685		0.558
Left lower			
Histological tumor grade	1	0.882–10.499	0.017
Well differentiated carcinoma (reference)	3.043	1.640-25.043	0.078
Moderately differentiated carcinoma	6.408		0.008
Poorly differentiated carcinoma			
Lymphatic invasion	1.344	0.682–2.651	0.393
HR = hazard ratio			
CI = confidence interval			
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			

Reason for sublobar resection

Table 4 shows the reasons for sublobar resection in 21 patients. Intentional sublobar resection was performed in 10 patients. Of those 10 patients, 8 tumors were part-solid GGOs and 2 tumors were peripheral solid nodules on chest CT. Five patients underwent sublobar resection because of underlying cardiopulmonary disease. Four patients underwent sublobar resection due to previous lung surgery history. One patient had a hematologic malignancy and 1 patient was 86 years old.

Table 4
Reason for sublobar resection (n = 21).

Reasons	N (%)
Intentional sublobar resection	10 (47.6%)
Underlying cardiopulmonary disease	5 (23.8%)
Previous lung operation	4 (19.0%)
Underlying other malignant disease	1 (4.8%)
Old age	1 (4.8%)

Comparison of sublobar resection and lobectomy in small-sized stage IB NSCLC

Of all study patients, 84 patients had small-sized (invasive component size ≤ 2 cm) stage IB NSCLC. We compared the prognosis of sublobar resection and lobectomy in the same size group. Table 5 shows the comparison of clinical and pathological characteristics between the sublobar resection group and the lobectomy group. There was no statistical difference in clinical and pathological characteristics between the 2 groups.

Table 5
The comparison of clinical and pathological characteristics between the sublobar resection group and the lobectomy group in patients with small-sized (≤ 2 cm) stage IB NSCLC.

Variables	Sublobar resection group (n = 21)	Lobectomy group (n = 63)	*p* value
Age (± SD)	67.5 (± 10.1)	64.0 (± 11.3)	0.211
Gender	11 (52.4%)	27 (42.9%)	0.613
Male	10 (47.6%)	36 (57.1%)	
Female			
Current or former smoker	9 (42.9%)	22 (34.9%)	0.604
Serum CEA level (ng/mL) (± SD)	4.1 (± 5.7)	2.4 (± 2.4)	0.216
SUVmax (± SD)	3.5 (± 2.4)	4.6 (± 2.7)	0.121
Involved lobe	7 (33.3%)	18 (28.6%)	0.421
Right upper	0	7 (11.1%)	
Right middle	7 (33.3%)	14 (22.2%)	
Right lower	3 (14.3%)	15 (23.8%)	
Left upper	4 (19.0%)	9 (14.3%)	
Left lower			
VATS	20 (95.2%)	58 (92.1%)	1.000
Open thoracotomy	1 (4.8%)	5 (7.9%)	
Surgical procedures	14 (66.7%)	0	< 0.001
Wedge resection	7 (33.3%)	0	
Segmentectomy	0	62 (98.4%)	
Lobectomy	0	1 (1.6%)	
Bilobectomy			

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

Variables	Sublobar resection group (n = 21)	Lobectomy group (n = 63)	*p* value
Intraoperative lymph node evaluation	4 (19.0%)	2 (3.2%)	< 0.001
No mediastinal node dissection	5 (23.8%)	44 (69.8%)	
Systematic nodal dissection	12 (57.1%)	17 (27.0%)	
Selective nodal dissection			
Postoperative Complications	1 (4.8%)	8 (12.7%)	0.439
Operative mortality	0	0	
Postoperative hospital stay (days) (± SD)	6.2 (± 3.2)	6.2 (± 3.0)	0.959
Histology	19 (90.5%)	56 (88.9%)	1.000
Adenocarcinoma	1 (4.8%)	4 (6.3%)	
Squamous cell carcinoma	1 (4.8%)	3 (4.8%)	
Others			
Total tumor size (± SD)	1.6 (± 0.4)	1.9 (± 0.6)	0.034
Invasive component size (± SD)	1.5 (± 0.3)	1.5 (± 0.3)	0.600
Location	0	3 (4.8%)	0.570
Central	21 (100%)	60 (95.2%)	
Peripheral			
Histological tumor grade	8 (38.1%)	19 (30.2%)	0.741
Well differentiated carcinoma	9 (42.9%)	34 (54.0%)	
Moderately differentiated carcinoma	4 (19.0%)	10 (15.9%)	
Poorly differentiated carcinoma			

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

Variables	Sublobar resection group (n = 21)	Lobectomy group (n = 63)	*p* value
Number of dissected lymph nodes (± SD)	6.3 (± 8.9)	12.6 (± 6.2)	0.001
Visceral pleural invasion	21 (100%)	61 (96.8%)	1.000
Lymphatic invasion	10 (47.6%)	29 (46.0%)	1.000
Vascular invasion	6 (28.6%)	10 (15.9%)	0.213
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			

The median follow-up period for patients with small-sized stage IB NSCLC was 1401 days (range, 335–3443 days), and 18 patients had recurrence (Table 6). The 5-year RFS rate was 80.7% after sublobar resection and 72.3% after lobectomy (Fig. 2A). The 5-year OS rate was 87.3% after sublobar resection and 91.2% after lobectomy (Fig. 2B). There was no difference in RFS and OS between the sublobar resection group and the lobectomy group ($P = .417$ and $P = .956$, respectively). We conducted Cox proportional hazards model to find out the risk factor for recurrence (Table 7). In the univariate analysis, sublobar resection was not a significant risk factor for recurrence in patients with small-sized stage IB NSCLC. SUVmax, histological tumor grade, and lymphatic invasion were significant variables ($P < .1$) in the univariate analysis, and these factors were entered into the multivariate analysis. However, no variables were identified as significant risk factors in the multivariate analysis.

Table 6
Summary of recurrence in patients with small-sized (≤ 2 cm) stage IB NSCLC who underwent sublobar resection and lobectomy.

Variables	Study group	Lobectomy group	P value
Sites of recurrence	5	8	0.824
Locoregional recurrence	0	4	
Distant recurrence	0	1	
Both			
Locoregional = recurrence within ipsilateral hemithorax including pleura and mediastinal lymph nodes			
Both = Locoregional recurrence + Distant recurrence			

Table 7
(A) Univariate analysis and (B) multivariate analysis of risk factors for recurrence in patients with small-sized (≤ 2 cm) stage IB NSCLC.

Variables	HR	95% CI	*p* value
Univariate analysis (A)			
Age	0.983	0.939–1.030	0.479
Gender (male)	1.028	0.382–2.764	0.957
Smoker	1.037	0.352–3.055	0.947
Serum CEA level	1.037	0.929–1.157	0.521
SUVmax	1.254	1.059–1.485	0.009
Lobe	1	0.182–22.141	0.306
Right upper (reference)	2.005	0.490-14.639	0.570
Right middle	2.677	1.099–27.133	0.256
Right lower	5.460	0.424–15.341	0.038
Left upper	2.551		0.306
Left lower			
VATS	1.030	0.136–7.819	0.977
Sublobar resection	0.597	0.170–2.102	0.422
Intraoperative lymph node evaluation	1	0.149–3.139	0.573
No mediastinal node dissection (reference)	0.683	0.077–2.328	0.624
Systematic nodal dissection	0.424		0.324
Selective nodal dissection			

HR = hazard ratio

CI = confidence interval

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

Variables	HR	95% CI	*p* value
Histology	1	0.115–6.466	0.990
Adenocarcinoma (reference)	1.153	0	0.891
Squamous cell carcinoma	0		0.983
Others			
Total tumor size	1.135	0.481–2.677	0.773
Invasive component size	1.942	0.448–8.422	0.375
Central location	3.563	0.455–27.881	0.226
Histological tumor grade	1	0.704–9.862	0.078
Well differentiated carcinoma (reference)	2.635	1.269–29.199	0.150
Moderately differentiated carcinoma	6.087		0.024
Poorly differentiated carcinoma			
Number of dissected lymph nodes	1.003	0.941–1.068	0.932
Lymphatic invasion	3.775	1.216–11.719	0.022
Vascular invasion	0.249	0.033–1.886	0.178
Multivariate analysis			
SUVmax	1.161	0.948–1.423	0.150
Histological tumor grade	1	0.397–10.766	0.347
Well differentiated carcinoma (reference)	2.068	0.577–30.869	0.388
Moderately differentiated carcinoma	4.221		0.156
Poorly differentiated carcinoma			
Lymphatic invasion	1.548	0.394–6.084	0.532
HR = hazard ratio			
CI = confidence interval			
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			

Discussion

Sublobar resection is not usually recommended for the treatment of stage IB NSCLC. However, because visceral pleural invasion is diagnosed only after surgery, it is sometimes diagnosed as postoperative stage IB when sublobar resection was performed for small peripheral nodules. In this study, sublobar resection for small-sized (invasive component size ≤ 2 cm) stage IB NSCLC had comparable prognosis with lobectomy. Firstly, we compared the prognosis between patients with small-sized stage IB NSCLC who underwent sublobar resection and patients with any stage IB NSCLC who underwent lobectomy. All patients were consecutive patients in the same hospital and underwent the same treatment protocols; moreover, both groups were well matched in clinicopathological characteristics except SUVmax and invasive component size. Thus, we then compared the prognosis of sublobar resection and lobectomy in patients with small-sized stage IB NSCLC. In this analysis, all clinicopathological characteristics were well matched and RFS and OS rate were not different in the statistical analysis. Furthermore, sublobar resection was not a risk factor for recurrence in 2 multivariate analyses in this study. Therefore, we concluded that sublobar resection for small-sized stage IB NSCLC had the same prognosis as lobectomy. In other words, these patients may not need an additional completion lobectomy performed immediately.

After implementation of the eighth revision of the TNM classification of NSCLC, the composition of the tumors included in the stage IB classification was changed. Most importantly, the requirement for measuring tumor size was changed. Determination of the T stage in the eighth revision is based only on the maximum dimension of the invasive component and excludes the lepidic component [13, 15]. The size range of the T2a descriptor was also reduced from 3 to 5 cm to 3 to 4 cm. Therefore, the tumor characteristics for the seventh edition stage IB NSCLC were changed in the eighth edition. Because of these changes, we thought that if the stage-based postoperative prognosis is studied, in all cases it is necessary to restudy after applying the eighth edition of TNM staging. This study is also the first to study the prognosis of sublobar resection of stage IB by applying the eighth edition of the TNM staging system.

Sublobar resections are usually performed for small-sized peripheral tumors in our institution. Particularly, patients with GGO tumors (consolidation : tumor ratio < 0.5) were candidates for intentional sublobar resection. Ten patients (47.6%) underwent intentional sublobar resection in this study. On the other hand, 7 patients underwent sublobar resection because of a poor general health condition (underlying cardiopulmonary disease, underlying hematologic malignant disease, and old age). Four patients underwent sublobar resection because of previous contralateral lung surgery. Although the sublobar resection group was not homogenous and the decisions for performing sublobar resection were varied, all study data were collected from consecutive patients who underwent curative surgery at 1 institution and clinicopathological characteristics were not different between the sublobar resection group and the lobectomy group. Thus, the findings of this study are considered meaningful.

The tumors of the sublobar resection group were located near the visceral pleura. Those tumors all invaded the visceral pleura, so their stage was upstaged from clinical T1a-b to pathological T2a. The tumors were all attached to the visceral pleura, making wedge resection and segmentectomy relatively

uncomplicated to perform. It was also easy to ensure sufficient margins after sublobar resection. Studies have shown that the resection margin should be at least the tumor size when sublobar resection is performed [16–18]. In this study, not only was the resection margin longer than the tumor size, but more sufficient lung parenchyma was removed. In the case of tumors adjacent to the visceral pleura, the resection margin can be sufficiently excised even by sublobar resection. Therefore, it may be assumed that sublobar resection might be as effective as lobectomy even for peripheral small-sized stage IB.

There have been few studies analyzing the prognosis of sublobar resection in stage IB NSCLC. This is because, at stage IB, it is generally accepted that lobectomy should be performed. Our previous study reported that sublobar resection for small-sized (≤ 2 cm) NSCLC with visceral pleural invasion or lymphatic invasion had a similar prognosis as lobectomy [19]. Of course, the previous study yielded similar results to the current study; however, the previous study included patients with lymphatic invasion, while the current study included only patients with visceral pleural invasion. Among the cases of visceral pleural and lymphatic invasion, only visceral pleural invasion is the upstaging factor. This is because only visceral pleural invasion can upstage small lung cancers, leading to stage IB. The previous study was based on the seventh edition TNM staging system, while the current study adopted the eighth edition of the TNM staging system. Furthermore, previous studies have included large numbers of patients before 2010; however, this study consists only of data since 2010. This study, which contains relatively new data and adopts the new TNM staging system, is expected to predict more accurate results than previous studies of sublobar resection for small-sized stage IB NSCLC.

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 from which to generalize our results. However, this study examined data from surgical patients treated with a standardized protocol at an 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 also had no problem applying the new staging system using pathology slides. 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, patients with a short follow-up period were included in this study. However, most patients with NSCLC are known to have disease recurrence within a 2-year postoperative period [20], and early recurrence has been shown to be an accurate reflection of long-term outcomes [21].

In conclusion, the prognosis of sublobar resection in patients with small-sized (≤ 2 cm) stage IB NSCLC was comparable with lobectomy. Thus, additional completion lobectomy is not essential in this setting, despite postoperative upstaging from T1 to T2a. Further research through multicenter randomized controlled trials may more accurately depict patient outcomes.

Abbreviations

NSCLC: Non-small cell lung cancer; GGO: ground glass opacity; CT: chest computed tomography; PET: positron emission tomography; RFS: Recurrence-free survival; OS: overall survival; SUVmax: maximum

standardized uptake value

Declarations

Acknowledgements

A native English-speaking professional (BioMed Proofreading, LLC) refined the written content.

Authors' Contributions

(I) Conception and design: Y Moon; (II) Administrative support: SY Choi, MH Moon; (III) Provision of study materials or patients: MH Moon; (IV) Collection and assembly of data: Y Moon, MH Moon; (V) Data analysis and interpretation: Y Moon, SY Choi ; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2019R1G1A1099670)

Availability of data materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Ethics approval and consent to participate

This study was approved by the institutional review board of Seoul St. Mary's Hospital at the Catholic University of Korea and individual consent was waived (Referral number: KC20RASI0020)

Consent for publication

Not applicable

Competing interests

The authors have no conflicts of interest to declare.

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Figures

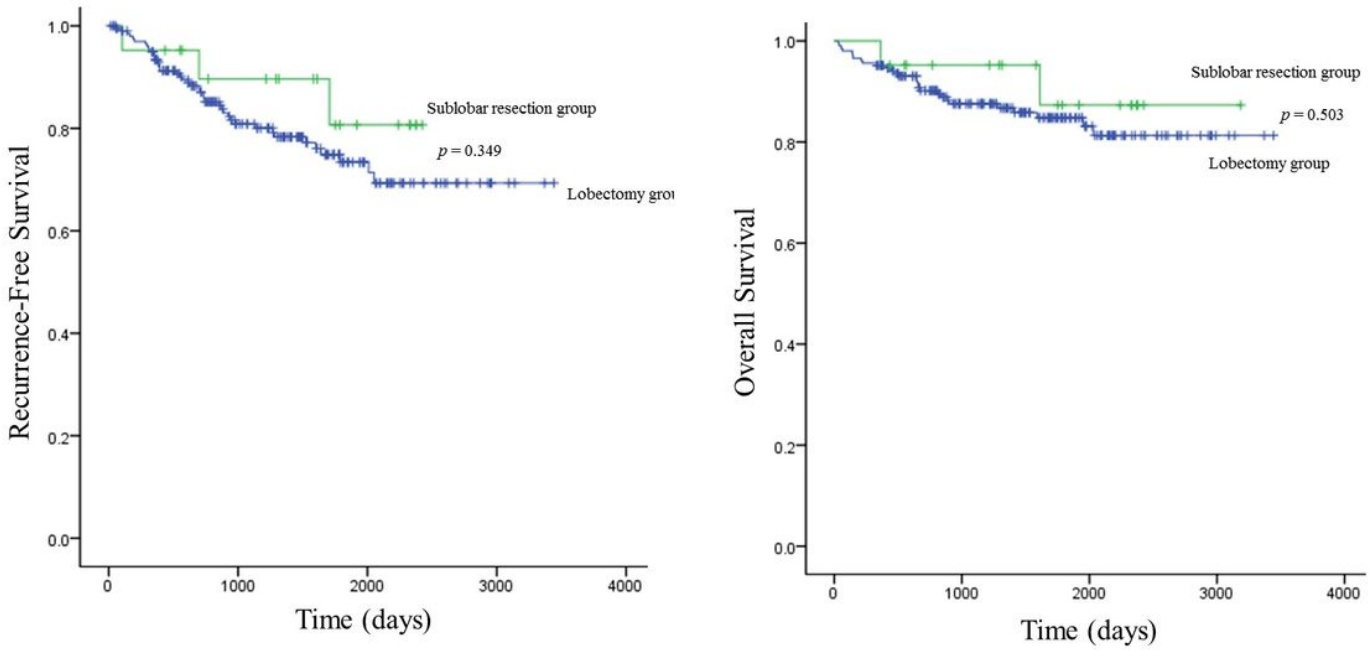

Figure 1

Comparisons of (A) recurrence-free survival and (B) overall survival between the sublobar resection group and the lobectomy group in all study groups.

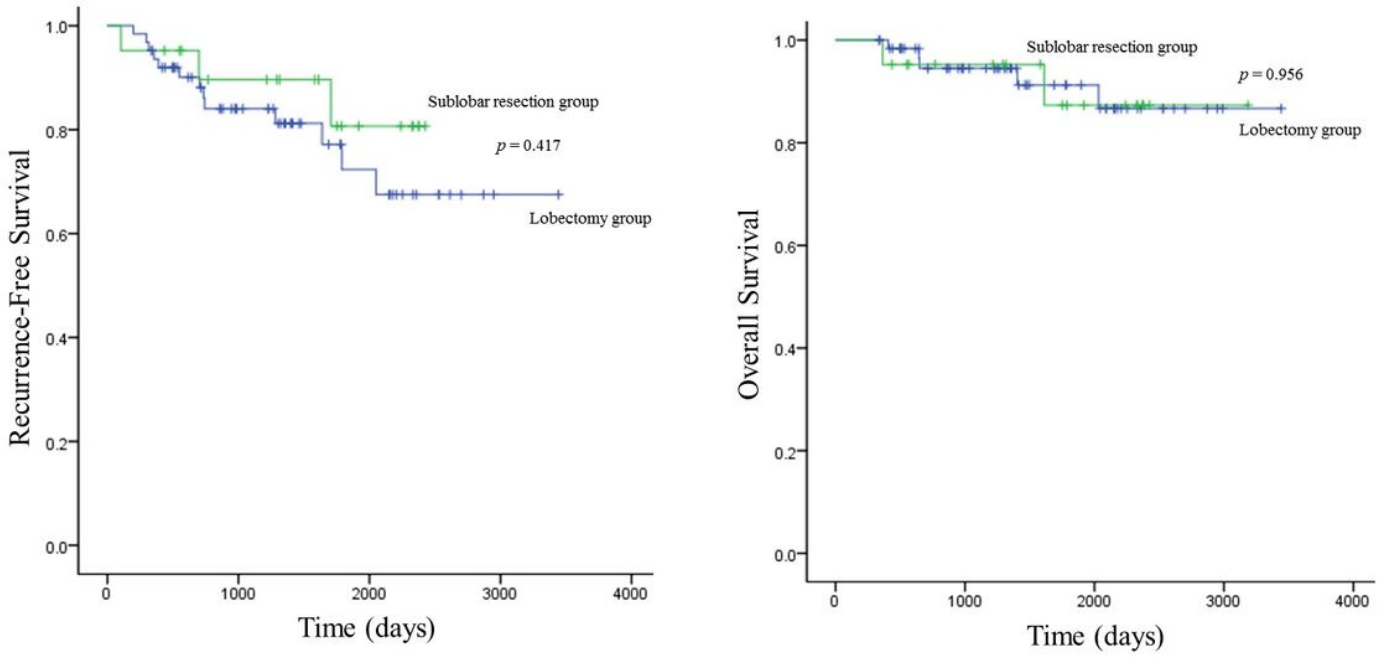

Figure 2

Comparisons of (A) recurrence-free survival and (B) overall survival between the sublobar resection group and the lobectomy group in small-sized (invasive component size ≤ 2 cm) stage IB NSCLC.