Appendix 1

Method

Criteria of intraoperative systemic nodal dissection (SND) and lobe-specific nodal dissection (LSND)

Based on the ESTS guidelines, we defined SND as lymphadenectomy that intraoperatively dissecting all mediastinal lymph nodes systematically within anatomical landmarks (stations 2, 4, 7, 8, and 9 for tumors on the right side; stations 4, 5, 6, 7, 8, and 9 for tumors on the left side). At least three mediastinal nodal stations (always station 7) should be dissected. We defined LNSD as lymphadenectomy dissecting specific lymph node stations based on the lobar location of the primary tumor (stations 2, 4, and 7 for tumors at the right upper and middle lobe; stations 4, 7, 8, and 9 for tumors at the right lower lobe; stations 5, 6, and 7 for tumors at the left upper lobe; stations 7, 8, and 9 for tumors at the left lower lobe). Dissection of the hilar and the intrapulmonary lymph nodes were also required to meet the SND or LSND criteria.

Propensity-score matching

To reduce the selection bias before comparing prognosis between patients undergoing lobectomy and sublobar resection, two propensity-score matched subgroups were generated. This progression was conducted with the "MatchIt" package on R software (26), using a 2:1 nearest neighbor matching algorithm with caliper of 0.2. With respect to the between-group differences of clinical characteristics shown in the original groups, we calculated the propensity score based on age of surgery, sex, age-adjusted Charlson Comorbidity Index, maximum tumor diameter on CT, CEA level and the SUVmax value. An absolute standardized mean difference (ASMD) of 0.1 or less indicated balances in the variables before and after matching (27).

Random survival forests

Two random forests for lung cancer-specific survival (LCSS) and recurrence were developed in the entire study cohort using the randomForestSRC package on R software (28), each was computed with default settings of 1500 trees. Each tree was analyzed utilizing a bootstrap sample of the original data. The risk-adjusted variable importance (VIMP) of each covariate was then calculated by the Breiman-Cutler importance algorithm (29).

References

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- 27. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009;28:3083-107.
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Figure S1 The receiver operating characteristic curve assessing the discriminative power of the SUVmax in predicting aggressive pathology (optimal cut-off point of SUVmax: 2.6 g/dL). AUC, area under the curve; SUV, standardized uptake value.

Parameter	Sufficient surgical margin (n=26)	Insufficient surgical margin (n=15)	P value
Tumor size (cm)	1.6 (1.2, 2.0)	2.1 (1.8, 2.5)	0.04
Lenth of surgical margin (cm)	2.0 (1.8, 2.0)	0.8 (0.5, 1.2)	<0.001
Procedures			0.72
Segmentectomy	15 (57.7)	7 (46.7)	
Wedge resection	11 (42.3)	8 (53.3)	
No. of LN stations sampled	3 (2, 5)	3 (1, 4)	0.26
Tumor recurrence			0.84
Locoregional only	4 (15.4)	4 (26.7)	
Distant	3 (11.5)	1 (6.7)	

Table S1 Comparison of clinical parameters and tumor recurrence according to different margin categories (insufficient vs. sufficient) after sublobar resection

Data are presented as number (%) or median (25th and 75th percentiles). Margin information was available in 65% (41/63) patients undergoing sublobar resection. The length of surgical margin was evaluated macroscopically. A length of 2.0 cm or more than that of the tumor was considered sufficient. LN, lymph node.



Figure S2 Cumulative incidence of (A) LC-CID and (B) CIR curves between WR, SEG and LR after matching. CID, cumulative incidence of death; CI, confidence interval; WR, wedge resection; SEG, segmentectomy; LR, lobar resection; CIR, cumulative incidence of recurrence; LC, lung cancer.

Table S2 Univariable com	peting risks model for	or lung cancer-specific deat	h and tumor recurrence in th	ne entire study cohort
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Covariate	Lung cancer-specific death		Tumor recurrence	
Covariate	HR (95% CI)	P value	HR (95% CI)	P value
Age (per 1-year increase)	1.03 (1.00–1.05)	0.02	0.99 (0.98–1.01)	0.43
Female sex (vs. male)	0.57 (0.35–0.92)	0.02	0.69 (0.50–0.97)	0.03
Smoking status				
Never	Reference		Reference	
Former/current	1.95 (1.22–3.13)	0.006	1.23 (0.88–1.71)	0.22
aCCI				
0–2	Reference		Reference	
>2	1.61 (0.97–2.67)	0.06	0.91 (0.61–1.36)	0.65
FEV1 (per 1 %)	0.99 (0.98–1.01)	0.26	0.99 (0.98–1.00)	0.26
DLCO (per 1%)	1.01 (1.00–1.01)	0.005	1.00 (1.00–1.01)	0.53
CEA level (≥5 <i>v</i> s. <5 ng/mL)	2.22 (1.37–3.61)	<0.001	2.31 (1.64–3.25)	<0.001
CT appearance				
GGO	Reference		Reference	
Pure-solid nodules	3.70 (1.36–10.1)	0.01	2.21 (1.28–3.83)	0.004
Maximum tumor diameter (per 1 cm increase)	1.00 (0.64–1.54)	0.98	1.22 (0.91–1.64)	0.18
SUVmax (per 1 SUV increase)	1.07 (1.02–1.12)	0.002	1.07 (1.03–1.12)	<0.001
Extent of resection				
Lobectomy	Reference		Reference	
Sublobar resection	3.27 (1.90–5.62)	<0.001	1.95 (1.24–3.06)	0.004
Segmentectomy	1.58 (0.58–4.32)	0.37	1.09 (0.51–2.33)	0.82
Wedge resection	4.83 (2.64–8.85)	<0.001	4.04 (2.05–7.97)	<0.001
Pathological stage				
IA	Reference		Reference	
IB	1.35 (0.77–2.37)	0.30	2.01 (1.34–3.03)	<0.001
II	1.65 (0.78–3.49)	0.19	2.53 (1.53–4.20)	< 0.001
III	2.10 (1.06–4.16)	0.03	4.05 (2.56–6.42)	<0.001
Histopathological type				
Adenocarcinoma	Reference		Reference	
Squamous	0.59 (0.18–1.92)	0.38	0.91 (0.46–1.78)	0.78
Others	1.59 (0.46–5.43)	0.46	1.09 (0.40–2.99)	0.86
Histologic grade				
High/intermediate	Reference		Reference	
Low/undifferentiated	1.27 (0.80–2.01)	0.31	1.45 (1.04–2.03)	0.03
Tumor size (per 1 cm increase)	1.02 (0.69–1.51)	0.92	1.16 (0.91–1.47)	0.22
Pleural invasion, present	1.72 (1.08–2.74)	0.02	2.10 (1.51–2.93)	<0.001
Lymphovascular invasion, present	2.18 (1.26–3.76)	0.005	2.24 (1.51–3.31)	<0.001
Receipt of adjuvant chemotherapy, yes	1.33 (0.82–2.17)	0.25	2.25 (1.62–3.13)	<0.001

HR, hazard ratio; CI, confidence interval; aCCI, age-adjusted Charlson Comorbidity Index; FEV1, forced expiratory volume in 1 second; DLCO, diffusion capacity of the lungs for carbon monoxide; CEA, carcinoembryonic antigen; CT, computed tomography; GGO, ground-glass opacity; SUV, standardized uptake value.

Table S3 Multivariable competing risk model	for lung cancer-specific	death and tumor recurren	ce with segmentectomy	and wedge resection
analyzed separately				

O	Lung cancer-speci	Tumor recurrence		
Covariate	HR (95% CI)	P value	HR (95% CI)	P value
Female sex (vs. male)	0.77 (0.46–1.29)	0.32	0.91 (0.64–1.32) 0.63	
CEA level (≥5 <i>v</i> s. <5 ng/mL)	1.73 (1.03–2.91)	0.04	1.85 (1.29–2.66)	<0.001
CT appearance				
GGO	Reference		Reference	
Pure-solid nodules	2.49 (0.93–6.71)	0.07	1.44 (0.83–2.50)	0.20
SUVmax (per 1 SUV increase)	1.04 (0.99–1.10)	0.14	1.05 (1.00–1.10)	0.03
Extent of resection				
Lobectomy	Reference		Reference	
Segmentectomy	2.01 (0.72–5.63)	0.19	1.46 (0.66–3.23)	0.35
Wedge resection	4.17 (2.07–8.36)	<0.001	3.48 (1.91–6.33)	<0.001
Pathological stage				
IA	Reference		Reference	
IB	0.86 (0.36–2.08)	0.74	1.54 (0.83–2.85)	0.17
II	1.49 (0.53–4.17)	0.45	1.81 (0.92–3.55)	0.08
III	1.51 (0.56–4.07)	0.41	2.79 (1.48–5.26)	0.002
Pleural invasion	1.61 (0.75–3.44)	0.22	1.17 (0.71–1.92)	0.53
Lymphovascular invasion	1.66 (0.87–3.19)	0.12	1.33 (0.83–2.11)	0.23
Receipt of adjuvant chemotherapy	0.82 (0.43–1.56)	0.54	1.31 (0.87–1.99)	0.2

The multivariable models were adjusted for variables with a P value <0.1 in the univariable analyses using a backwards selection strategy. HR, hazard ratio; CI, confidence interval; CEA, carcinoembryonic antigen; CT, computed tomography; GGO, ground-glass opacity; SUV, standardized uptake value.

Table S4 Clinicopa	athological chara	cteristics and difference	es between patients	with and without LSND
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Characteristics	LSND criteria not met (n=322)	LSND criteria met (n=204)	ASMD	P value
Age (years)	61.0 (54.0, 67.0)	59.0 (54.0, 64.2)	0.122	0.13
Male sex	173 (53.7)	93 (45.6)	0.163	0.08
Smoking history, yes	138 (42.9)	68 (33.3)	0.202	0.04
CEA level (ng/mL)			0.010	>0.99
<5	257 (79.8)	162 (79.4)		
≥5	65 (20.2)	42 (20.6)		
Tumor location				<0.001
Right upper	88 (27.3)	82 (40.2)	0.262	
Right middle	21 (6.5)	17 (8.3)	0.066	
Right lower	72 (22.4)	18 (8.8)	0.477	
Left upper	48 (14.9)	35 (17.2)	0.060	
Left lower	93 (28.9)	52 (25.5)	0.048	
Maximum tumor diameter (cm)	2.1 (1.7 2.5)	2.0 (1.6, 2.5)	0.130	0.11
GGO component, present	61 (18.9)	37 (18.1)	0.021	0.91
SUVmax (g/dL)	5.1 (3.6, 7.3)	5.0 (3.8, 7.0)	0.036	0.95
Histopathological type				0.18
Adenocarcinoma	287 (89.1)	191 (93.6)	0.184	
Squamous	25 (7.8)	8 (3.9)	0.121	
Others	10 (3.1)	5 (2.4)	0.042	
Low grade/undifferentiated tumor	171 (53.1)	115 (56.4)	0.066	0.52
Tumor size (cm)	2.1 (1.6, 2.5)	2.0 (1.5, 2.5)	0.096	0.29
Pleural invasion, present	103 (32.0)	62 (30.4)	0.035	0.77
Lymphovascular invasion, present	48 (14.9)	32 (15.7)	0.021	0.91
Nodal upstaging	49 (15.2)	48 (23.5)		0.01
pN1	29 (9.0)	20 (9.8)	0.027	
pN2	20 (6.2)	28 (13.7)	0.218	
Adjuvant chemotherapy, yes	92 (28.6)	70 (34.3)	0.121	0.20

Data are presented as number (%) or median (25th and 75th percentiles). LSND, lobe-specific nodal dissection; ASMD, absolute standardized mean difference; CEA, carcinoembryonic antigen; GGO, ground-glass opacity; SUV, standardized uptake value.



Figure S3 Cumulative incidence of (A) LC-CID and (B) CIR curves comparing lymphadenectomy that met the systemic nodal dissection criteria and those that did not in patients undergoing at least lobe-specific nodal dissection. CID, cumulative incidence of death; CI, confidence interval; LSND, lobe-specific nodal dissection; SND, systemic nodal dissection; CIR, cumulative incidence of recurrence; LC, lung cancer.

Table S5 Cox proportional hazard model for recurrence-free s	survival
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Oberneteristics	Univariable	Multivariable		
Characteristics –	HR (95% CI)	P value	HR (95% CI)	P value
Age (per 1-year increase)	1.00 (0.98–1.01)	>0.99	-	_
Female sex (vs. male)	0.74 (0.53–1.02)	0.07	0.95 (0.67–1.34)	0.77
Smoking status				
Never	Reference		-	-
Former/current	1.18 (0.85–1.64)	0.31	-	-
CEA level (≥5 <i>v</i> s. <5 ng/mL)	2.33 (1.64–3.31)	<0.001	1.95 (1.36–2.80)	<0.001
CT appearance				
GGO	Reference		Reference	
Pure-solid nodules	1.87 (1.12–3.09)	0.02	1.43 (0.84–2.44)	0.19
Maximum tumor diameter (per 1 cm increase)	1.42 (1.04–1.93)	0.03	1.41 (0.93–2.14)	0.10
SUVmax (per 1 SUV increase)	1.07 (1.03–1.11)	<0.001	1.05 (1.00–1.10)	0.04
Extent of lymphadenectomy				
LSND criteria not met	Reference		Reference	
LSND criteria met	0.71 (0.49–1.01)	0.06	0.65 (0.46–0.94)	0.02
Histopathological type				
Adenocarcinoma	Reference		-	-
Squamous	0.80 (0.39–1.64)	0.54	-	-
Others	1.54 (0.68–3.49)	0.30	-	-
Tumor size (per 1 cm increase)	1.23 (0.98–1.53)	0.08	-	-
Pleural invasion, present	1.92 (1.39–2.66)	<0.001	1.39 (0.98–1.98)	0.07
Lymphovascular invasion, present	2.47 (1.70–3.61)	<0.001	1.72 (1.13–2.62)	0.01
Pathologic nodal upstaging	2.36 (1.67–3.36)	<0.001	1.64 (1.06–2.51)	0.03
Receipt of adjuvant therapy	2.10 (1.51–2.90)	<0.001	1.21 (0.81–1.81)	0.36

HR, hazard ratio; CI, confidence interval; CEA, carcinoembryonic antigen; CT, computed tomography; GGO, ground-glass opacity; SUV, standardized uptake value; LSND, lobe-specific nodal dissection.