Lobectomy offers improved survival outcomes relative to segmentectomy for >2 but ≤4 cm non–small cell lung cancer tumors

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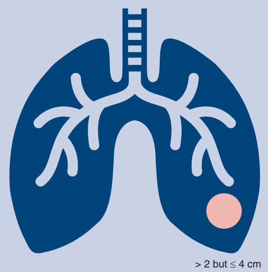
ABSTRACT

Objective: The objective was to compare overall survival (OS) between lobectomy and segmentectomy for patients with non–small cell lung cancers (NSCLCs) > 2 but ≤4 cm.

Methods: The National Cancer Database was queried to identify treatment-naïve patients with NSCLC tumors >2 but ≤4 cm. Eligible patients were diagnosed with pT1 or T2 N0 M0 disease, underwent lobectomy or segmentectomy, and received no adjuvant therapy. OS was compared using the Kaplan-Meier method, and the Cox proportional-hazards model was used to identify prognostic factors for death. Propensity score matching was performed to minimize the effects of potential confounders.

Results: Included were 32,792 patients: lobectomy (n = 31,353) and segmentectomy (n = 1439). Five-year OS was improved following lobectomy over segmentectomy for patients with >2 but ≤4 cm NSCLCs (62.3% vs 52.6%; *P* < .0001). Further stratification demonstrated improved 5-year OS following lobectomy over segmentectomy: >2 but ≤3 cm (64.9% vs 54.3%; *P* < .0001) and >3 but ≤4 cm (56.9% vs 47.6%; *P* = .0003). In patients with a Charlson-Deyo comorbidity index of 0, 5-year OS was greater following lobectomy for >2 but ≤4 cm tumors (67.1% vs 62.1%; *P* = .03). Further stratification demonstrated improved 5-year OS following lobectomy for patients with Charlson-Deyo comorbidity index of 0 and > 3 but ≤4 cm tumors (61.8% vs 54.6%; *P* = .02). Segmentectomy was prognostic for increased risk of death in the year 1 through 5 postoperative period (hazard ratio, 1.35; *P* < .0001). Five-year OS remained greater following lobectomy after propensity score matching (59.6% vs 52.7%; *P* = .02).

Conclusions: Lobectomy is associated with superior 5-year OS compared with segmentectomy and may be preferred for NSCLC tumors >2 but ≤4 cm when feasible. (JTCVS Open 2022;10:356-67)



Overall survival is greater following lobectomy than segmentectomy for tumors >2 but ≤4 cm NSCLC.

CENTRAL MESSAGE

Lobectomy is associated with increased 5-year overall survival than is segmentectomy for patients with non–small cell lung cancer tumors >2 but ≤4 cm and may be preferred in this population.

PERSPECTIVE

There is a paucity of literature comparing lobectomy versus segmentectomy in the treatment of patients with non–small cell lung cancer tumors >2 but ≤4 cm. This study provides critical insight for surgical decision making, demonstrating that lobectomy is associated with superior 5-year overall survival relative to segmentectomy in this patient population.

See Commentary on page 368.

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Abbreviations and Acronyms

CDCI = Charlson-Deyo comorbidity index
NCDB = National Cancer Database
NSCLC = non–small cell lung cancer
OS = overall survival
PUF = participant user file

Video clip is available online.

In 1995, Ginsberg and Rubinstein[1] demonstrated that lobectomy was superior to sublobar resection for T1 N0 M0 non–small cell lung cancer (NSCLC). Relative to lobectomy, sublobar resection was associated with a tripling of locoregional recurrence rate and a 30% increase in overall death rate. These findings effectively established lobectomy as the surgery of choice for early stage NSCLC. In contrast, sublobar resections were relegated to use only for patients who could not tolerate lobectomy, such as those with decreased cardiopulmonary reserve.[2]

In the years following this seminal publication, other reports have suggested that the decision between lobectomy and sublobar resection for early-stage NSCLC may not be so simple; after sublobar resection, patients may experience similar survival outcomes to lobectomy with the added benefit of greater preservation of pulmonary function.[3-8] A meta-analysis of 22 studies from 1994 to 2012 demonstrated similar survival following lobectomy and segmentectomy for patients with stage IA NSCLC tumors ≤2 cm, whereas segmentectomy was associated with worse survival for stage I NSCLC and stage IA NSCLC tumors >2 but <3 cm.[9] The authors acknowledged the need for more robust data from randomized controlled trials to better characterize the utility of segmentectomy for early stage NSCLC but ultimately recommended against its use for NSCLC tumors >2 cm.

Two multicenter randomized Phase 3 trials in Cancer and Leukemia Group B (CALGB)/ALLIANCE 140503 and Japan Clinical Oncology Group (JCOG) 0802/West Japan Oncology Group (WJOG) 4607L are currently investigating outcomes following segmentectomy and sublobar resection compared with lobectomy, but neither study will address NSCLC tumors >2 cm.[10,11] Patients with tumors >4 cm in size, irrespective of the amount of lung resected, may be administered systemic therapy in an adjuvant manner, thereby affecting long-term survival. There is a paucity of surgical data providing a focused evaluation of the viability of segmentectomy relative to lobectomy specifically for early stage NSCLC tumors >2 but ≤4 cm. The hypothesis of this study is that lobectomy will be associated with improved survival outcomes relative to segmentectomy for this patient population. Therefore, the objective of this study was to compare survival outcomes following segmentectomy versus lobectomy for patients with early stage NSCLC tumors >2 but ≤4 cm.

PATIENTS AND METHODS

Data Source

The National Cancer Database (NCDB) compiles de-identified data on demographic characteristics, tumor characteristics, treatment modalities, and clinical outcomes from upward of 34 million patients in the United States.[12] These data are sourced from approximately 1500 Commission on Cancer-accredited treatment facilities nationwide and provide insight into nearly 70% of all patients diagnosed with cancer in the United States each year. This study was approved by the Institutional Review Board at the University of Southern California (HS-16-00906) (effective approval date: December 19, 2016). Informed consent was not required for this study.

Patient Selection

The NCDB participant user file (PUF) (2010-2016) was queried to identify treatment-naïve patients who underwent segmentectomy or lobectomy for a primary NSCLC tumor >2 but ≤4 cm. Pathologic tumor stage was converted from the seventh edition cancer staging system used in the NCDB PUF during the study timeframe to the current eighth edition staging system.[13,14] Based on tumor size and in the absence of additional invasive features, tumors >2 but ≤4 cm are classified T1c (>2 but ≤3 cm) or T2a (>3 but ≤4 cm) in the eighth edition staging system but were previously classified as T1b (>2 but ≤3 cm) or T2a (>3 but ≤5 cm) in the seventh edition staging system; thus, cohort selection relied primarily on tumor descriptor data rather than reported pathologic stage in the NCDB. Patients were further stratified by diagnosis with either >2 but ≤3 cm or >3 but ≤4 cm NSCLC. An upper limit ≤4 cm was selected as NSCLCs of this size are generally treated with segmentectomy or lobectomy without other therapies. Only patients with pathologic N0 and M0 disease were included.

Patients were excluded if T descriptors beyond T2 according to the eighth edition staging system were reported based on pathologic evidence. These include tumor size >5 cm, separate lung tumor nodule(s), or invasion of the chest wall, parietal pleura, parietal pericardium, phrenic nerve, diaphragm, mediastinum, carina, trachea, esophagus, recurrent laryngeal nerve, heart, great vessels, or vertebral body. Other T2 features, including mainstem bronchus involvement, visceral pleura invasion, and association with atelectasis or obstructive pneumonitis extending to the hilar region, were also excluded owing to the possibility of a biologically additive or potentiating detrimental effect (Figure 1). Patients with NSCLC demonstrating middle lobe, overlapping lobe, or not otherwise specified lobe involvement were excluded; patients with middle lobe tumors were excluded given the relatively low rate of segmentectomies expected in this population. An exploratory analysis revealed that segmentectomies for middle lobe lesions constituted only 1% of all segmentectomies (data not shown). Tumors without specified laterality or histology were also excluded. Other exclusion criteria included failure to undergo definitive surgery within 180 days following diagnosis, positive surgical margins or missing margin data, and receipt of additional treatment. The cohort selection process is illustrated in Figure 1.

Variables

Patients were grouped based on receipt of segmentectomy or lobectomy for NSCLC tumor resection. Patients were further subdivided by tumor size (>2 but ≤3 cm vs > 3 but ≤4 cm). Additional covariates of interest included tumor laterality, lobe of tumor involvement, tumor histology, Charlson-Deyo comorbidity index (CDCI), patient demographic

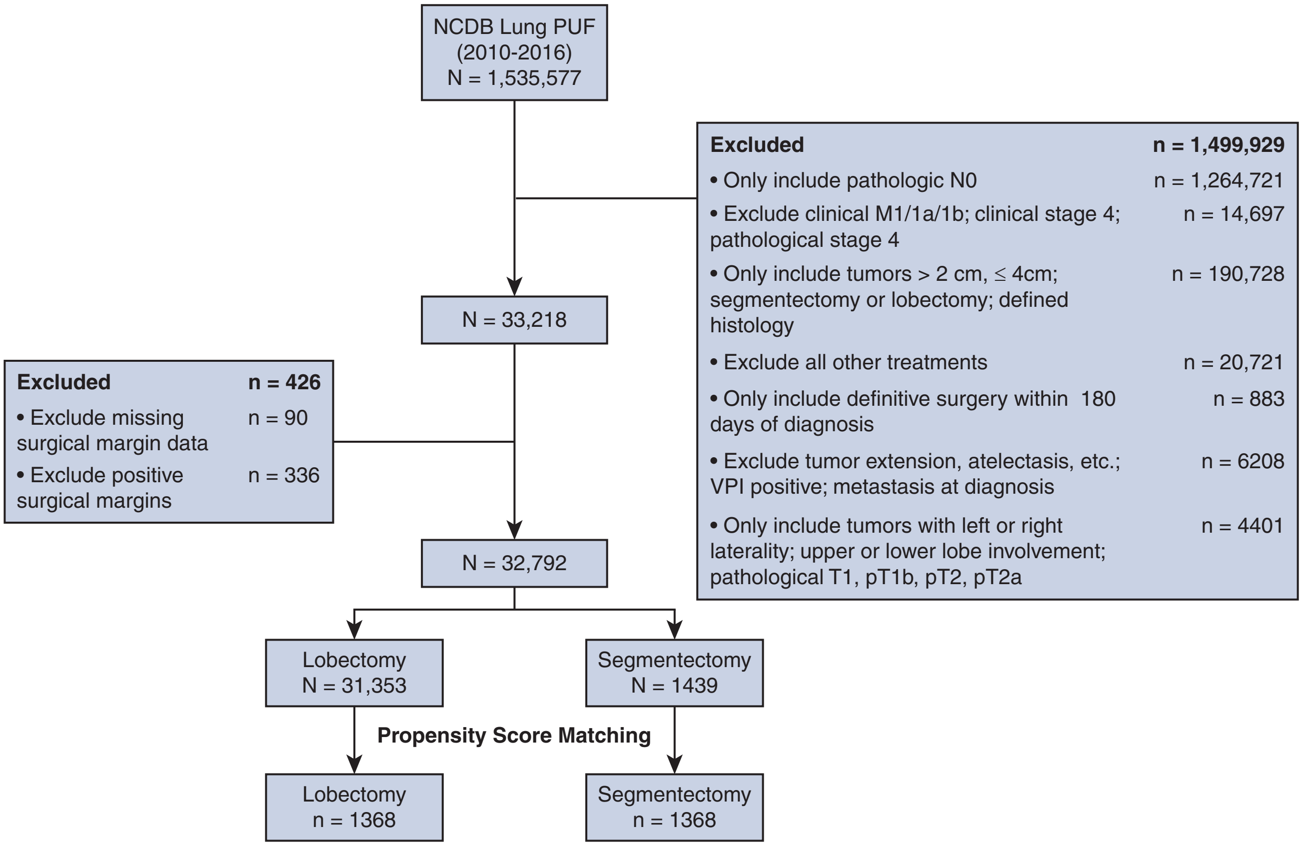


FIGURE 1. Cohort selection diagram. *NCDB*, National Cancer Database; *PUF*, participant user file.

characteristics, and facility type. Before exclusion, patients with positive margins in each resection cohort were noted for descriptive purposes.

Outcomes of Interest

The primary outcome of interest in this study was 5-year overall survival (OS) from the day of surgery. Secondary outcomes of interest were risk of death within 5 years and proportion of positive surgical margins.

Statistical Analysis

Descriptive analyses were performed for resection type, tumor size, tumor histology, tumor laterality, lobe of involvement, CDCI, demographic variables, and facility type. The Kaplan-Meier curve and log-rank test was used to describe 5-year OS from the day of surgery, and the Cox proportional-hazards model was utilized to identify predictors of death within 5 years. Subgroup analyses were performed for the >2 but ≤3 cm and >3 but ≤4 cm cohorts. In an effort to identify patients medically fit for lobectomy or segmentectomy, additional subgroup analyses were performed among patients with CDCI of 0 given the absence of important preoperative data such as pulmonary function testing via the NCDB. Propensity score matching was performed to minimize the effect of potential confounders among patients in the segmentectomy and lobectomy cohorts. Propensity scores were generated by logistic regression, using greedy nearest neighbor 1:1 matching with a caliper of 0.5. The following covariates were used in the propensity score-matching model: Age, tumor size, and exact match for sex, income, education, distance to facility, insurance type, facility type, facility location, CDCI score, and tumor laterality. All statistical analyses were performed with SAS version 9.4 (SAS Institute Inc).

RESULTS

Patient and Tumor Characteristics

A total of 33,218 patients met initial inclusion criteria, of whom 85 out of 31,747 lobectomy patients and 5 out of 1471 segmentectomy patients were excluded due to missing margin data. In addition, 309 of the remaining 31,662 lobectomy patients and 27 of the remaining 1466 segmentectomy patients were excluded due to positive surgical margins. Among the remaining 32,792 patients, 31,353 underwent lobectomy and 1439 underwent segmentectomy. Postoperative 30-day mortality was 2.2% (n = 709) for the overall cohort, 2.2% (n = 685) for patients who underwent lobectomy, and 1.7% (n = 24) for patients who underwent segmentectomy. Cohorts varied significantly by age, race, insurance, income, facility type, area of residence, CDCI score, tumor laterality, lobe of involvement, and tumor size (Table 1). The median age of the segmentectomy cohort was greater than that of the lobectomy cohort. Compared with the lobectomy cohort, greater proportions of patients in the segmentectomy cohort were White, were insured via Medicare, had an income ≥$38,000, received care at an academic or research institution, resided in a metropolitan area, had a CDCI score >0, and were diagnosed with a tumor located in the left lung, involving the lower lobe,

TABLE 1. Patient demographic and tumor characteristics

Variable	Total (N = 32,792)		Lobectomy (n = 31,353)		Segmentectomy (n = 1439)		*P* value
Age (y)	70 (20-90)		70 (20-90)		72 (28-90)		<.0001
Sex							.22
Female	17,010	51.9	16,241	51.8	769	53.4	
Male	15,782	48.1	15,112	48.2	670	46.6	
Race							.03
White	28,934	88.2	27,642	88.2	1292	89.8	
Black	2607	8.0	2520	8.0	87	6.1	
Other	1070	3.3	1022	3.3	48	3.3	
Missing	181	0.6	169	0.5	12	0.83	
Insurance							<.0001
Medicare	21,750	66.3	20,710	66.1	1040	72.3	
Private/MC	8518	26.0	8214	26.2	304	21.1	
Medicaid	1319	4.0	1266	4.0	53	3.7	
Not insured	503	1.5	488	1.6	15	1.0	
Other government	334	1.0	322	1.0	12	0.8	
Missing	368	1.1	353	1.1	15	1.0	
Income							.04
≥$38,000	26,783	81.7	25,579	81.6	1204	83.7	
<$38,000	5840	17.8	5613	17.9	227	15.8	
Missing	169	0.5	161	0.5	8	0.6	
Education							.50
<20.9% NHS	27,276	83.2	26,071	83.2	1205	83.7	
>21% NHS	5366	16.4	5140	16.4	226	15.7	
Missing	150	0.5	142	0.5	8	0.6	
Facility type							<.0001
CCCP	14,148	43.1	13,608	43.4	540	37.5	
Academic/research	12,006	36.6	11,379	36.3	627	43.6	
INCP	4484	13.7	4301	13.7	183	12.7	
CCP	2084	6.4	1997	6.4	87	6.0	
Missing	70	0.2	68	0.2	2	0.1	
Area of residence							.04
Metropolitan	26,204	79.9	25,019	79.8	1185	82.4	
Urban	4964	15.1	4780	15.3	184	12.8	
Rural	683	2.1	652	2.1	31	2.2	
Missing	941	2.9	902	2.9	39	2.7	
Distance to facility							.38
>12.5 miles	17,473	53.3	16,723	53.3	750	52.2	
≤12.5 miles	15,187	46.3	14,505	46.3	682	47.4	
Missing	132	0.4	125	0.4	7	0.5	
Charlson-Deyo comorbidity index							<.0001
0	16,301	49.7	15,674	50.0	627	43.6	
1	10,999	33.5	10,486	33.4	513	35.7	
2	3974	12.1	3757	12.0	217	15.1	
≥3	1518	4.6	1436	4.6	82	5.7	
Tumor laterality							<.0001
Right	18,820	57.4	18,188	58.0	632	43.9	
Left	13,972	42.6	13,165	42.0	807	56.1	
Lobe of involvement							<.0001
Upper lobe	21,181	64.6	20,369	65.0	812	56.4	
Lower lobe	11,611	35.4	10,984	35.0	627	43.6	
Tumor histology							.08
Adenocarcinoma	21,011	64.1	20,126	64.2	885	61.5	

(Continued)

TABLE 1. Continued

Variable	Total (N = 32,792)		Lobectomy (n = 31,353)		Segmentectomy (n = 1439)		*P* value
SCC	10,620	32.4	10,115	32.3	505	35.1	
Other	1161	3.5	1112	3.6	49	3.4	
Tumor size (cm)							<.0001
>2 but ≤3	22,300	68.0	21,212	67.7	1088	75.6	
>3 but ≤4	10,492	32.0	10,141	32.3	351	24.4	

Values are presented as median (range) or n (%). *MC*, Managed care; *NHS*, no high school (did not graduate high school); *CCCP*, comprehensive community cancer program, *INCP*, integrated network cancer program; *CCP*, Community cancer program; *SCC*, squamous cell carcinoma.

and measuring >2 but ≤3 cm in greatest dimension. There were no significant differences with respect to sex, education, distance to facility, or tumor histology.

Comparison of Segmentectomy and Lobectomy

Five-year OS was greater for patients who underwent lobectomy compared with segmentectomy (62.3% vs 52.6%; *P* < .0001) (Figure 2, *A*). Lobectomy was also associated with greater 5-year OS in the >2 but ≤3 cm (64.9% vs 54.3%; *P* < .0001) (Figure 2, *B*) and >3 but ≤4 cm tumor cohorts (56.9% vs 47.6%; *P* = .0003) (Figure 2, *C*). Among patients with CDCI score of 0, those who underwent lobectomy experienced improved 5-year OS compared with segmentectomy (67.1% vs 62.1%; *P* = .03) (Figure 3, *A*). There was no significant difference in 5-year OS between lobectomy and segmentectomy for

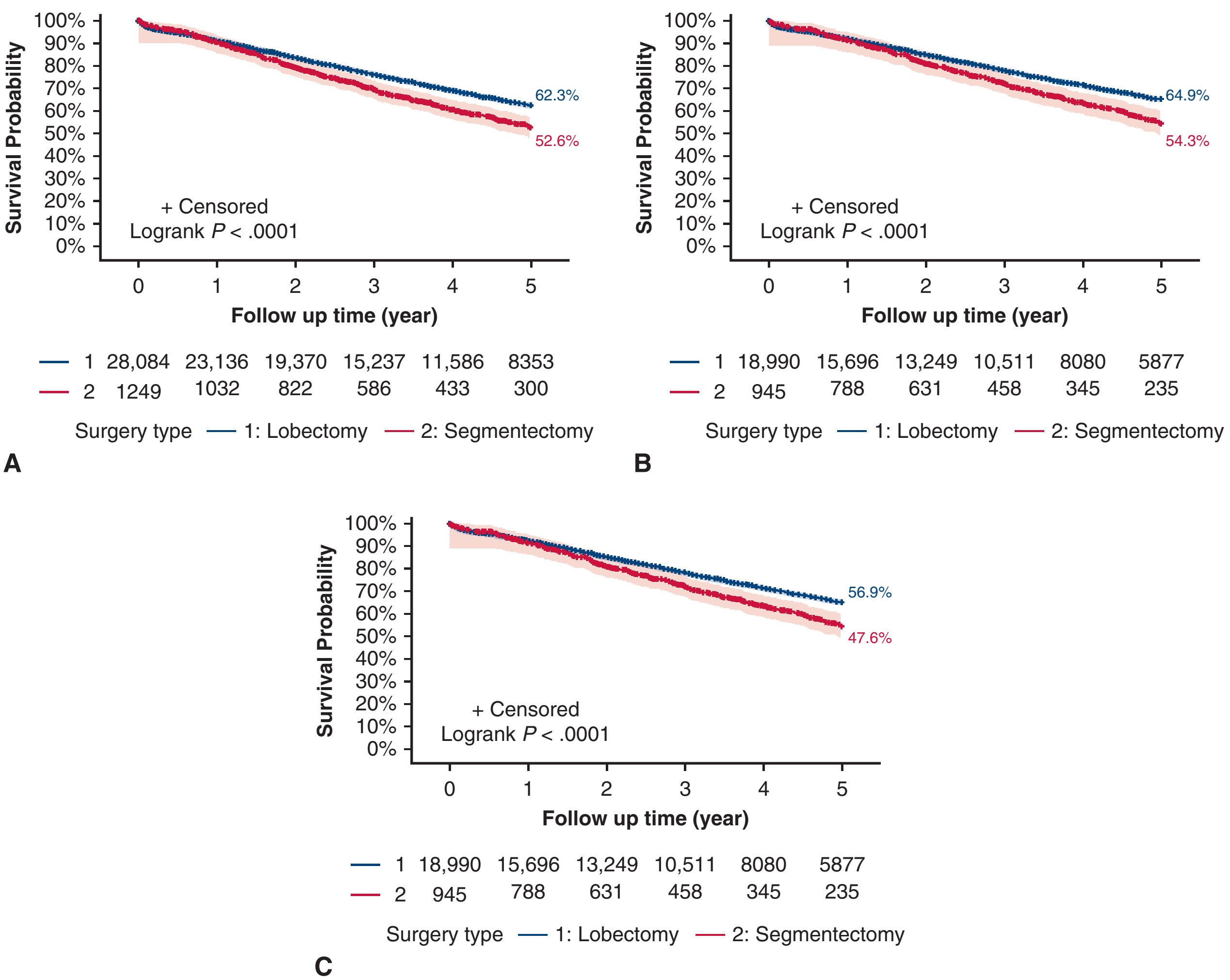


FIGURE 2. Five-year overall survival between lobectomy and segmentectomy cohorts (with number of subjects at risk and 95% Hall-Wellner bands). A, Overall. B, In patients with >2 but ≤3 cm tumors. C, In patients with >3 but ≤4 cm tumors.

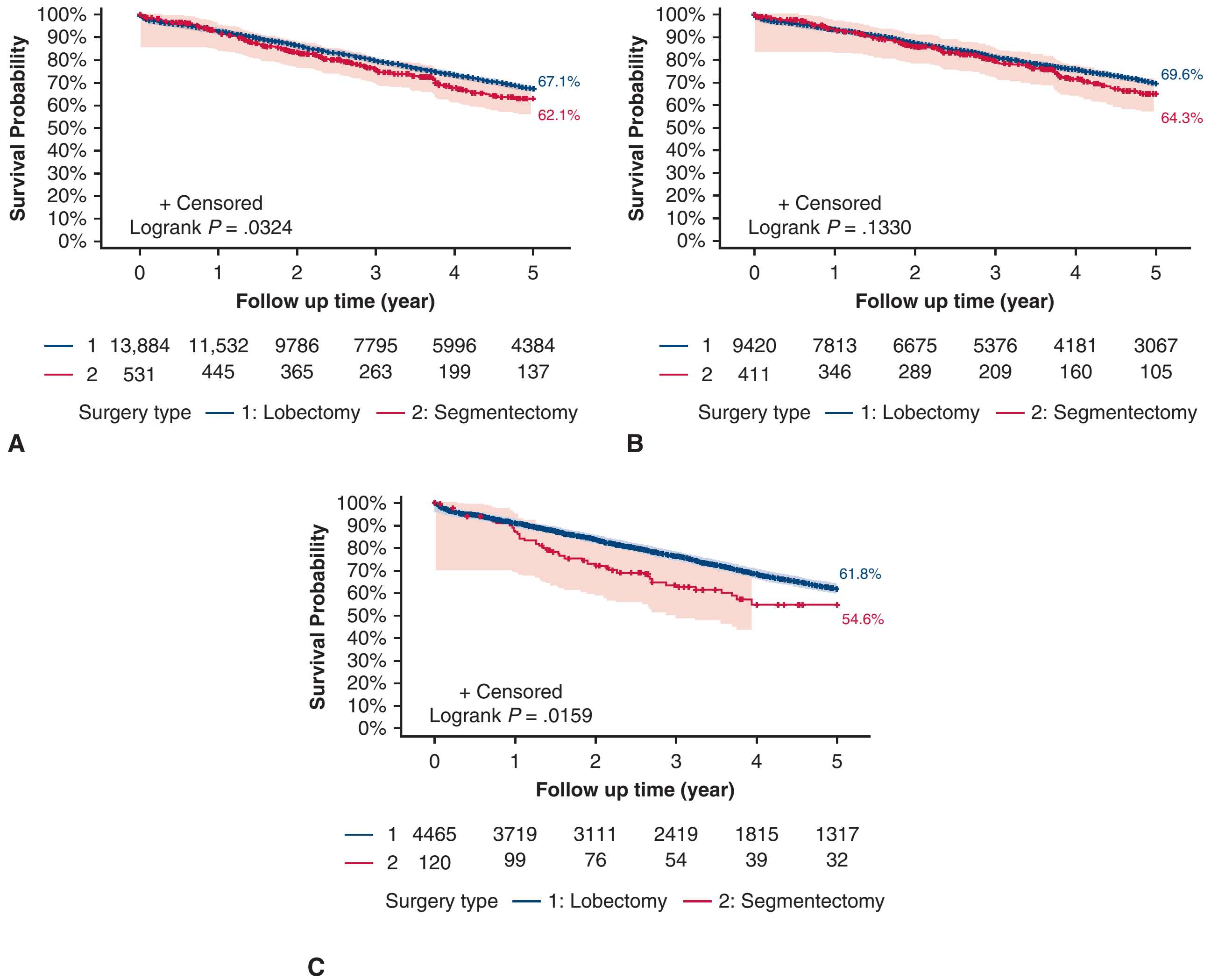


FIGURE 3. A. Five-year overall survival between lobectomy and segmentectomy cohorts in patients with Charlson-Deyo Comorbidity Index (*CDCI*) of 0 (with number of subjects at risk and 95% Hall-Wellner bands). A, Overall. B, In patients with >2 but ≤3 cm tumors. C, In patients with >3 but ≤4 cm tumors.

patients with CDCI score of 0 and > 2 but ≤3 cm tumors (69.6% vs 64.4%; $P = .13$) (Figure 3, *B*). However, 5-year OS was improved following lobectomy for patients with CDCI score of 0 and tumors >3 but ≤4 cm (61.8% vs 54.6%; $P = .02$) (Figure 3, *C*).

Cox Proportional-Hazards Model

A total of 27,901 patients were included in the Cox proportional-hazards model (Table 2). Each additional year of age conferred a 2.9% increase in expected risk of death within 5 years of surgery, and female sex was associated with a lower risk of death. Because the proportional hazard assumption was violated, postoperative follow-up time was approached using 2 distinct intervals: ≤1 year versus > 1 but ≤5 years; this statistical method has been previously demonstrated in the surgical literature.[15] Risk of death in the year 1 through 5 postoperative period was higher for segmentectomy, but no difference was observed during the first postoperative year alone. Relative to Medicaid coverage, private or managed care insurance, Medicare, and other forms of government-sponsored insurance were all associated with decreased risk of death. Lower income was associated with increased risk of death. Compared with patients treated at academic or research institutions, those who underwent surgery at comprehensive community cancer programs, integrated network cancer programs, and community cancer programs experienced elevated risk of death. Patients who resided in urban areas experienced an increased risk of death relative to those who resided in metropolitan settings. Risk of death increased with CDCI score >0. Relative to lesions in the upper lobe, tumors involving the lower lobe were associated

TABLE 2. Cox proportional-hazards model for factors associated with death within 5 years

Variable	Hazard ratio	95% CI	*P* value
Year 1 postsurgery			
Lobectomy*	–	–	–
Segmentectomy	0.85	0.70-1.02	.08
Year 1-5 postsurgery			
Lobectomy*	–	–	–
Segmentectomy	1.35	1.20-1.51	<.0001
Age			
Per year	1.03	1.03-1.03	<.0001
Sex			
Male*	–	–	–
Female	0.71	0.68-0.74	<.0001
Race			
White*	–	–	–
Black	0.97	0.89-1.06	.50
Other	0.73	0.63-0.85	<.0001
Insurance			
Medicaid*	–	–	–
Medicare	0.77	0.69-0.87	<.0001
Private/MC	0.70	0.62-0.79	<.0001
Other government	0.67	0.51-0.88	.004
Not insured	0.93	0.75-1.15	.48
Income			
≥$38,000*	–	–	–
<$38,000	1.09	1.02-1.16	.008
Education			
<20.9% NHS*	–	–	–
>21% NHS	1.07	1.00-1.14	.06
Facility type			
Academic/research*	–	–	–
CCCP	1.14	1.09-1.20	<.0001
INCP	1.10	1.03-1.18	.007
CCP	1.24	1.14-1.36	<.0001
Area of residence			
Metropolitan*	–	–	–
Urban	1.12	1.05-1.20	.0005
Rural	0.88	0.75-1.03	.11
Distance to facility (mi)			
≤12.5*	–	–	–
>12.5	1.04	0.99-1.09	.17
Charlson-Deyo Comorbidity Index			
0*	–	–	–
1	1.20	1.14-1.26	<.0001
2	1.31	1.23-1.40	<.0001
≥3	1.60	1.45-1.76	<.0001
Primary site			
Upper lobe*	–	–	–
Lower lobe	1.06	1.01-1.10	0.02
Tumor laterality			
Right*	–	–	–
Left	1.01	0.96-1.05	0.77
Tumor histology			
Adenocarcinoma*	–	–	–
SCC	1.25	1.19-1.31	<.0001
Other	1.29	1.17-1.44	<.0001
Tumor size (cm)			
>2 but ≤3*	–	–	–
>3 but ≤4	1.20	1.14-1.25	<.0001

MC, Managed care; *NHS*, no high school (did not graduate high school); *CCCP*, comprehensive community cancer program; *INCP*, integrated network cancer program; *CCP*, Community cancer program; *SCC*, squamous cell carcinoma. *Reference category.

with a slightly increased risk of death. Risk of death was greater for squamous cell carcinoma and other histologic subtypes compared with adenocarcinoma. Tumors >3 but ≤4 cm were associated with an increased risk of death compared to tumors >2 but ≤3 cm.

Propensity Score-Matched Analysis

A cohort of 1368 matched pairs was extracted after propensity score matching. Matched pairs had standardized mean differences within 0.1, as shown in the Table E1. In this cohort, sufficient follow-up data were available for only 1205 patients who underwent lobectomy and 1186 patients who underwent segmentectomy. Following propensity score matching, 5-year OS was greater for patients who received lobectomy compared with segmentectomy (59.6% vs 52.7%; log-rank $P = .02$) (Figure 4).

DISCUSSION

The present study demonstrates that lobectomy offers improved 5-year OS compared with segmentectomy for patients with NSCLC tumors >2 cm but ≤4 cm (Figure 5 and Video 1). Five-year OS remained greater following lobectomy than segmentectomy among patients with CDCI score of 0, suggesting that this survival advantage was not solely attributable to differences in baseline health. Propensity score-matched analysis offered further evidence of improved survival following lobectomy relative to segmentectomy. Additionally, segmentectomy was associated with an increased risk of death compared with lobectomy in the year 1 through 5 postoperative period.

Several groups have evaluated sublobar resections for peripheral NSCLCs ≤2 cm and reported that segmentectomies are appropriate for tumors of this size.[6,8,9,16-18] Furthermore, 2 highly anticipated randomized clinical trials in CALGB/ALLIANCE 140503 and JCOG0802/WJOG4607L are currently comparing lobectomy with sublobar resection and segmentectomy for NSCLCs ≤2 cm. Post hoc exploratory analysis for CALGB/ALLIANCE 140503 found no significant mortality

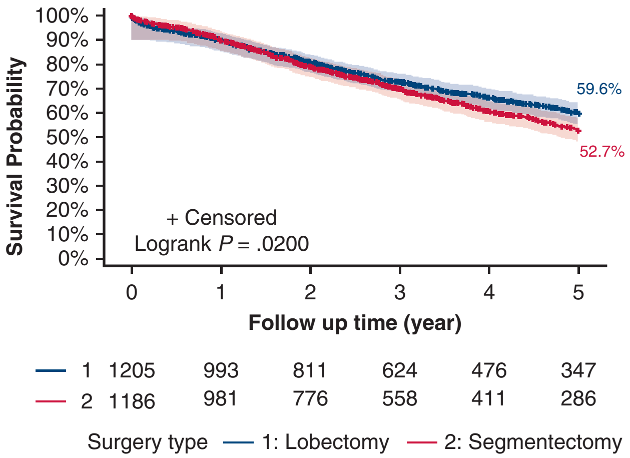
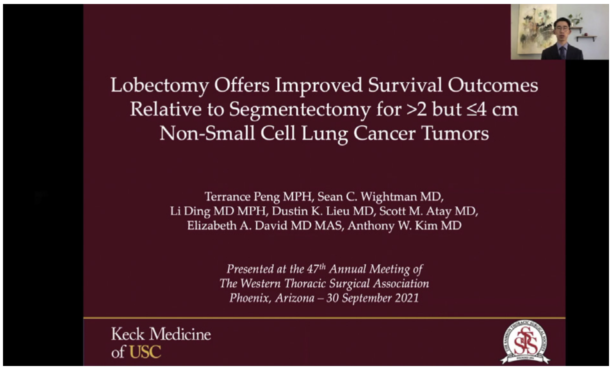


FIGURE 4. Five-year overall survival between lobectomy and segmentectomy after propensity score-matching (with number of subjects at risk and 95% Hall-Wellner bands).

differences between sublobar resection and lobectomy, and preliminary reports from JCOG0802/WJOG4607L showed no differences in most perioperative complications between segmentectomy and lobectomy.[10,11] Although thoracic surgeons eagerly await the results, findings from these studies cannot be used to reliably guide surgical decision making for NSCLC tumors >2 but ≤4 cm. Consequently, the present study is unique in using a large database to investigate outcomes following lobectomy versus segmentectomy for >2 but ≤4 cm NSCLC and demonstrates that the previously reported noninferiority of sublobar resection and segmentectomy to lobectomy cannot be assumed for tumors >2 cm.

Past studies have utilized a tumor size threshold of ≤3 cm, reflective of T1 criteria in previously contemporaneous cancer staging systems.[19,20] In their seminal article, Ginsberg and Rubinstein[1] reported that lobectomy was superior to sublobar resection for small NSCLC tumors,



VIDEO 1. Overall survival is greater following lobectomy than segmentectomy for >2 but ≤4 cm non–small cell lung cancer tumors. Video available at: https://www.jtcvs.org/article/S2666-2736(22)00126-7/fulltext.

including those >2 but ≤3 cm. Fernando and colleagues[21] similarly found lobectomy was associated with greater survival compared with sublobar resection for >2 but ≤3 cm tumors; however, this study included patients who received adjuvant brachytherapy, which was more common in the >2 but ≤3 cm cohort and may have accounted for similar recurrence rates between resections. Neither study specifically investigated segmentectomy nor evaluated tumors >3 cm. The present study supports these conclusions, indicating lobectomy offers improved 5-year OS relative to segmentectomy in patients with >2 but ≤3 cm tumors.

A limitation of large datasets such as the NCDB is that the rationale to proceed with segmentectomy versus lobectomy is unknown. Additionally, it is well known that important variables such as pulmonary function are not reported in the NCDB. Thus, this study uses CDCI score of 0 as a proxy of this measure in an effort to identify patients who were medically fit to undergo either lobectomy or segmentectomy. However, it should be noted that CDCI has been found to significantly underestimate comorbidity for patients with lung cancer.[22] Among patients with CDCI score of 0, there was no difference in 5-year OS between lobectomy and segmentectomy for tumors >2 but ≤3 cm. This finding is consistent with a study from Okada and colleagues[23] that reported similar survival following lobectomy and segmentectomy for tumors ranging 21 to 30 mm. Chan and colleagues[24] also found that anatomic segmentectomy was associated with reduced perioperative complications and similar risk of recurrence relative to lobectomy for patients with clinical T1c N0 M0 (>2 but ≤3 cm) NSCLC. The present study differs in its exclusion of tumors with visceral pleural invasion, which Chan and colleagues[24] observed in greater incidence among patients who underwent segmentectomy. The lack of consensus for >2 but ≤3 cm NSCLC may be partially attributable to inherent differences between segmentectomy and sublobar resection cohorts because wedge and segmental resections have been associated with disparate survival outcomes.[23,25] It is also possible that tumor size alone may not determine whether lobectomy or segmentectomy is more appropriate for >2 but ≤3 cm NSCLC, and differences in 5-year OS may be more dependent on factors not captured in this study, such as baseline pulmonary function or tumor spread through airspaces.

The present study also demonstrates that 5-year OS is greater following lobectomy compared with segmentectomy for resection of >3 but ≤4 cm NSCLC among all patients and those with CDCI score of 0. Okada and colleagues[23] found 5-year survival outcomes were superior following lobectomy to both segmentectomy and wedge resections in their >3 cm tumor cohort. The authors thereby described lobectomy as the most suitable resection for tumors >3 cm, but the absence of a reported mean tumor size or range for this cohort precluded reliable conclusions

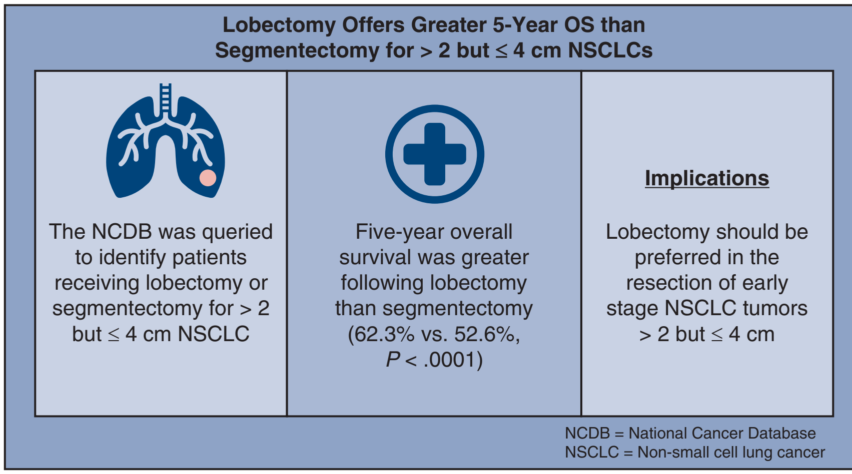


FIGURE 5. Lobectomy offers greater 5-year overall than segmentectomy for >2 but ≤4 cm early-stage non–small cell lung cancer (*NSCLC*). *OS*, Overall survival; *NCDB*, National Cancer Database.

specifically for >3 but ≤4 cm tumors.[23] In their investigation of segmentectomy for stage I NSCLC, Schuchert and colleagues[26] included tumors as large as 11.2 cm but did not separate patients into discrete size cohorts. Mean tumor size was larger in the lobectomy group (3.1 cm) compared with the segmentectomy group (2.3 cm), but no significant differences were noted in overall or recurrence-free survival. Without discrete size cohorts, the authors were similarly unable to draw conclusions specific to >3 but ≤4 cm tumors. As a result, it is possible the observed survival advantage of lobectomy in these studies may have been driven in part by tumors >4 cm. In contrast, the present study is unique in demonstrating that lobectomy may offer superior 5-year OS compared with segmentectomy specifically for tumors in the >2 but ≤3 cm and >3 but ≤4 cm ranges.

These results are consistent with a recent study by Raman and colleagues,[27] which found lobectomy was associated with improved OS compared with segmentectomy for patients with lung adenocarcinoma approximately 10 mm or larger. However, a unique aspect of the present study is the careful selection of a cohort defined by tumor size alone. By excluding patients with tumors exhibiting T2 descriptors other than size and T descriptors beyond T2, the present study reduces the heterogeneity among tumors within the overall cohort, which would ostensibly avoid the potential confounding effects of such additional features on OS; for example, choice of resection and postoperative OS may differ for patients diagnosed with a 3 cm tumor with a T3 descriptor compared with those diagnosed with a tumor of the same size without a T3 descriptor.

This study has several limitations in addition to those aforementioned, including challenges inherent to utilizing retrospective designs and large databases. Selection bias may be substantial in this study, with the vast majority of patients undergoing lobectomy. Factors that would potentially increase the likelihood of recommending segmentectomy include poor pulmonary function tests, other comorbidities, predominantly ground glass lesion, and additional ground glass opacities in other areas of the lung, but the present study is unable to investigate these factors and their potential influence.

Furthermore, the contemporaneous seventh edition staging system of the American Joint Committee on Cancer corresponding to the study period did not distinguish between invasive and noninvasive tumor components, which may similarly influence surgical decision making. In addition, patients in this study were selected based on pathologic rather than clinical criteria. Although selection based on preoperative data would offer greater clinical applicability, pathologic criteria were used in this study in an effort to ensure a more accurately homogenized study cohort, particularly when considering the variety of potential lymph node staging methods and inconsistent clinicopathologic stage alignment. Because pathologic upstaging occurs when tumors are found to be > 4 cm or when lymph node involvement is discovered, the clinical stage becomes less relevant as it pertains to the revised plan of care.

Locoregional recurrence was a key outcome in previous studies, but recurrent disease data are not available via the NCDB.[1,18,28] Although associations between recurrence and surgical margin distance/margin-to-tumor ratios have been described, these data are not reported by the NCDB; consequently, the present study cannot account for the potential influence of these variables on recurrence or survival.[26,29] Similarly, patients with positive surgical margins were excluded given that incomplete resection would likely warrant re-resection or radiation. Thus, the present study was designed to limit the possibility of additional treatments. Moreover, limitations of the NCDB would preclude a sufficiently detailed understanding of the subsequent course of therapy for patients with positive margins and, by extension, a robust analysis of the effects on overall survival. Data pertaining to mode of death and cancer-specific survival are also unavailable through this database, introducing important limitations regarding the specific conclusions that can be drawn from the survival analyses performed in this study. The lack of detailed tumor location data in the NCDB also precluded incorporation of this important variable into the propensity score-matched analysis. Additionally, the NCDB does not report on surgical complications or interventions taking place after the first course of therapy, preventing assessment of the potential influence on survival of such events. The effects of postoperative complications on long-term OS may be significant, but the present study is unable to evaluate these influences given the limited granularity of this large database. Despite these limitations, the present study strives to contribute unique and valuable perspectives to the existing literature through its focused investigation of the >2 but ≤4 cm tumor size range.

Anatomic segmentectomy is defined as the resection of at least 1 pulmonary parenchymal segment with targeted removal of the associated bronchovascular supply, but segmentectomy as a general term may encompass nonanatomic segmentectomies and larger wedge resections.[11,30] Given the possibility that some large wedge and nonanatomic segmental resections are reported as segmentectomies in the NCDB PUF, this study is unable to ensure a specific comparison between anatomic segmentectomy and lobectomy. Moreover, there is insufficient detail available via this data source for the present study to confirm artery, vein, and bronchus were appropriately divided in all patients who underwent segmentectomy.

CONCLUSIONS

This study demonstrates that lobectomy is associated with significantly improved 5-year OS compared with segmentectomy for early-stage NSCLC tumors >2 but ≤4 cm. However, there is no difference in 5-year OS following lobectomy and segmentectomy for patients with CDCI score of 0 and tumors >2 but ≤3 cm, suggesting that the choice between resections may be more nuanced for this size range and more greatly dependent on baseline functional status. Although segmentectomy has been described as a viable resection for tumors ≤2 cm, this study suggests that lobectomy may be preferred in the treatment of early stage NSCLC tumors >2 but ≤4 cm for patients who are able to tolerate this resection; this subject requires further exploration using datasets with greater granularity to appropriately incorporate clinically relevant variables absent in the present study.

Conflict of Interest Statement

Dr David has received honoraria from Medtronic and Astra Zenica unrelated to this work. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: lobectomy, segmentectomy, sublobar resection, non–small cell lung cancer

TABLE E1. Propensity score-matched analysis (1368 matched pairs)

Variable/observations	Mean difference	SD	Standardized difference	Reduction (%)	Variance ratio
Logit propensity score					
All	0.32	0.56	0.57	–	0.93
Region	0.31	0.56	0.56	0.9	0.95
Matched	0.00	0.55	0.00	100.0	1.00
Weighted matched	0.00	0.55	0.00	100.0	1.00
Age					
All	2.35	0.27	0.27	–	0.85
Region	2.31	0.27	0.27	1.7	0.85
Matched	−0.04	−0.01	−0.01	98.1	1.02
Weighted matched	−0.04	−0.01	−0.01	98.1	1.02
Size					
All	−1.34	−0.25	−0.25	–	0.85
Region	−1.31	−0.25	−0.25	1.6	0.86
Matched	−0.01	0.00	0.00	99.4	0.95
Weighted matched	−0.01	0.00	0.00	99.4	0.95