Survival After Sublobar Resection versus Lobectomy for Clinical Stage IA Lung Cancer

An Analysis from the National Cancer Data Base

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Background: Recent data have suggested possible oncologic equivalence of sublobar resection with lobectomy for early-stage non–small-cell lung cancer (NSCLC). Our aim was to evaluate and compare short-term and long-term survival for these surgical approaches.

Methods: This retrospective cohort study utilized the National Cancer Data Base. Patients undergoing lobectomy, segmentectomy, or wedge resection for preoperative clinical T1A N0 NSCLC from 2003 to 2011 were identified. Overall survival (OS) and 30-day mortality were analyzed using multivariable Cox proportional hazards models, logistic regression models, and propensity score matching. Further analysis of survival stratified by tumor size, facility type, number of lymph nodes (LNs) examined, and surgical margins was performed.

Results: A total of 13,606 patients were identified. After propensity score matching, 987 patients remained in each group. Both segmentectomy and wedge resection were associated with significantly worse OS when compared with lobectomy (hazard ratio: 1.70 and 1.45, respectively, both $p < 0.001$), with no difference in 30-day mortality. Median OS for lobectomy, segmentectomy, and wedge resection were 100, 74, and 68 months, respectively ($p < 0.001$). Finally, sublobar resection was associated with increased likelihood of positive surgical margins, lower likelihood of having more than three LNs examined, and significantly lower rates of nodal upstaging.

Conclusion: In this large national-level, clinically diverse sample of clinical T1A NSCLC patients, wedge and segmental resections were shown to have significantly worse OS compared with lobectomy. Further patients undergoing sublobar resection were more likely to have inadequate lymphadenectomy and positive margins. Ongoing prospective study taking into account LN upstaging and margin status is still needed.

Key Words: Non–small-cell lung cancer, Lobectomy, Wedge resection, Segmentectomy, National Cancer Data Base.

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Anatomic surgical resection with a lobectomy and mediastinal lymph node (LN) staging is currently the standard therapy with curative intent for clinical stage IA non–small-cell lung cancer (NSCLC).[1,2] However, preexisting cardiopulmonary disease may make the perceived morbidity and mortality associated with lobectomy prohibitive. In addition, lobectomy leads to significant loss of normal lung parenchyma. Sublobar pulmonary resections, such as wedge resection and anatomical segmentectomy, have lower perioperative morbidity, preserve more pulmonary function, and in many cases allow for greater applicability of minimally invasive techniques. In fact, data from the Surveillance, Epidemiology and End Results (SEER) database indicate that as many as 31% of patients with localized NSCLC do not undergo lobectomy.[3] Several nonrandomized retrospective case series and database analyses have been published comparing lobar and sublobar resections with mixed results, particularly in regards to tumors smaller than 2 cm.[4–12]

As a result, there is ongoing debate in regards to the optimal extent of surgical resection for early-stage lung cancer. Our aim was to examine overall survival (OS) and 30-day survival among patients undergoing lobectomy, segmentectomy, and wedge resection for stage 1 NSCLC 2 cm or smaller, through an analysis of the National Cancer Data Base (NCDB). We hypothesized that patients undergoing lobectomy would have worse operative mortality, and therefore worse 30-day mortality, but better OS.

PATIENT AND METHODS

We performed a retrospective cohort study using the NCDB to compare operative outcomes including mortality

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and long-term survival among patients who underwent lobectomy, segmentectomy, and wedge resection for clinical stage IA NSCLC. The NCDB is a joint endeavor of the Commission on Cancer (CoC) of the American College of Surgeons and the American Cancer Society. It includes registry-level clinical and demographic detail on patients treated at approximately 1500 CoC-approved hospitals across the country. Cases were identified using the NSCLC Participant Use Data file from the NCDB, which contain deidentified patient level data that do not identify hospitals, health care providers, or patients. Institutional review board approval was waived by the Emory University institutional review board.

Patients diagnosed between 2003 and 2011 with clinical stage IA NSCLC who underwent lobectomy, segmentectomy, or wedge resection were included in this analysis. Charlson/Deyo comorbidity scores were not available before 2003; therefore, patients before this time point were excluded. All analyses of OS were limited to patients treated between 2003 and 2006, as long-term survival data are not yet available in the NCDB for cases after 2006. In addition, the following exclusions were made: cases where the diagnosis was at the reporting facility and all treatment was done elsewhere, cancer in situ, palliative care cases, unknown laterality, patients receiving neoadjuvant radiation and those missing 30-day mortality or other secondary outcomes. Only cases with one lifetime cancer or cases where the reported tumor was the first of multiple cancer diagnoses were included to avoid confounding with a prior cancer treatment or diagnosis. The patient selection/exclusion criteria and sample sizes are shown in Supplementary Table 1 (Supplemental Digital Content 1, http://links.lww.com/JTO/A887).

The primary outcome measures were OS, defined as the number of months between surgical resection and the last contact or date of death, and 30-day mortality, defined as death within 30 days of surgery. Secondary outcome measures included surgical margin status, number of regional LN examined (0–3 vs. >3), and regional LN positivity. The following patient demographics, clinical characteristics, and treatment characteristics were included as covariates in the analysis: facility type, sex, race, insurance, income, education, urban/rural, Charlson/Deyo comorbidity score, year of diagnosis, primary site, histology, grade, age, and tumor size. Both income and education were measured as the median household income and percentile of not graduating from high school at the residence area of the patients when diagnosed by matching the zip code and 2000 US Census data. The facility type was determined by the CoC based on services provided and the number of cases.[13] Community cancer programs treat between 100 and 500 cancer cases per year, comprehensive community cancer programs treat more than 500 cancer cases, and academic/research programs (including National Cancer Institute designated cancer centers) treat more than 500 cancer cases in addition to providing postgraduate medical education.

Statistical analysis was conducted using SAS Version 9.3 (Cary, NC), and SAS macros and software developed by the Biostatistics and Bioinformatics Shared Resource at Winship Cancer Insititute.[14] Descriptive statistics were presented as frequencies with percentages or as means with standard deviations for categorical or numerical variables, respectively. The univariate association of each covariate with extent of surgical resection and 30-day mortality were assessed using the χ^2 test for categorical covariates and analysis of variance for numerical covariates. A multivariable logistic regression model for 30-day mortality was fit. The univariate and multivariable association with OS was estimated using Cox proportional hazards models. A backward variable selection method was used in multivariable models to select covariates, applying an α value equal to 0.20 removal criteria. To explore whether the impact of extent of lung resection on OS differed by treatment facility types, tumor size (≤1 vs. 1–2 cm), number of regional LNs examined (≤7 vs. >7), and surgical margin status, an interaction between the stratus variable and extent of surgical resection was introduced into the multivariable model. Kaplan–Meier curves were generated to provide survival estimates for OS. All analyses of OS, as mentioned earlier, were done only on patients diagnosed between 2003 and 2006. All statistical tests were two-sided and used an α value equal to 0.05 level of significance.

A propensity score matching method was also implemented to further eliminate treatment selection bias in the study sample. A nominal logistic regression model predicting extent of surgical resection was used to calculate propensity scores including all covariates. Cases from the three surgical resection groups were matched to each other based on the propensity scores using a nearest neighbor with caliper algorithm.[15] The effectiveness of the matching was evaluated by calculating the pair wise standardized differences of the covariates on the matched sample.[16] A standardized difference of less than 0.1 denoted negligible imbalance and was used to choose the caliper for matching. The treatment effects were recalculated in the matched sample with appropriate methods to account for the matched nature of data, such as stratified logistic or Cox regression.[17] After matching, the baseline covariates, including facility type, sex, race, insurance, income, education, urban/rural, Charlson/Deyo comorbidity score, year of diagnosis, primary site, histology, grade, age, and tumor size, were balanced among the three cohorts.

RESULTS

Twenty-eight thousand two hundred and forty-one patients in the NCDB were identified who underwent surgical resection for stage IA NSCLC and met inclusion criteria. Nineteen thousand seven hundred and eighteen patients underwent lobectomy, 7297 underwent wedge resection, and 1226 underwent segmental resection. Clinical details of the patients at the time of resection are shown in Table 1. When comparing the three cohorts, we identified several differences in baseline patient characteristics. Patients undergoing sublobar resection (wedge resection or segmentectomy) were on average 3 years older and have higher Charlson comorbidity scores. In addition, there was a higher incidence of patients with government, and no insurance in those undergoing sublobar resection. There were slight differences between the groups in regards to gender, race, treatment facility, income, tumor grade, histology, and primary site of tumor as shown in Table 1. No difference was identified in education levels.

TABLE 1. Comparison of Extent of Resection: Lobectomy, Wedge, and Segmental Resection

Covariate	Level	Lobectomy (%), N = 19,718	Wedge Resection (%), N = 7297	Segmental Resection (%), N = 1226	*P* Value
Facility type	Noncomprehensive community cancer program/other	1646 (8.4)	689 (9.4)	69 (5.6)	**<0.001**
	Comprehensive community cancer program	11,206 (56.8)	4018 (55.1)	659 (53.8)	
	Academic/research program (Includes NCI)	6866 (34.8)	2590 (35.5)	498 (40.6)	
Patient age	Mean ± stdandard deviation	65.8 ± 9.9	68.9 ± 9.8	68.7 ± 9.4	**<0.001**
Sex	Male	8001 (40.6)	2937 (40.3)	444 (36.2)	**0.010**
	Female	11,717 (59.4)	4360 (59.8)	782 (63.9)	
Race: White	No	2067 (10.6)	662 (9.2)	108 (8.9)	**<0.001**
	Yes	17,464 (89.4)	6570 (90.9)	1102 (91.1)	
Insurance	Not insured	319 (1.6)	92 (1.3)	12 (1.0)	**<0.001**
	Private insurance	7123 (36.6)	1940 (26.9)	400 (33.0)	
	Government insurance	12,026 (61.8)	5185 (71.8)	800 (66.0)	
Income	<$30,000	2372 (12.8)	908 (13.2)	139 (12.1)	**0.047**
	$30,000–$34,999	3354 (18.1)	1285 (18.6)	214 (18.7)	
	$35,000–$45,999	5321 (28.7)	1938 (28.1)	283 (24.7)	
	$46,000 +	7505 (40.5)	2773 (40.2)	509 (44.5)	
Education	≥29%	2841 (15.3)	1037 (15.0)	158 (13.8)	0.403
	20–28.9%	4463 (24.1)	1711 (24.8)	261 (22.8)	
	14–19.9%	4615 (24.9)	1703 (24.7)	287 (25.1)	
	<14%	6632 (35.8)	2452 (35.5)	439 (38.3)	
Urban/rural	Metro area	15,091 (82.1)	5601 (81.7)	985 (86.6)	**<0.001**
	Urban/rural	3300 (17.9)	1251 (18.3)	153 (13.4)	
Charlson/Deyo score	0	9849 (50.0)	3017 (41.4)	500 (40.8)	**<0.001**
	1	7293 (37.0)	2976 (40.8)	514 (41.9)	
	2+	2576 (13.1)	1304 (17.9)	212 (17.3)	
Primary site	Left upper lobe	5115 (25.9)	2051 (28.1)	385 (31.4)	**<0.001**
	Left lower lobe	2545 (12.9)	1040 (14.3)	215 (17.5)	
	Right upper lobe	7204 (36.5)	2481 (34.0)	320 (26.1)	
	Right middle lobe	1441 (7.3)	348 (4.8)	32 (2.6)	
	Right lower lobe	3132 (15.9)	1219 (16.7)	253 (20.6)	
	Overlapping lesion of lung	73 (0.4)	34 (0.5)	2 (0.2)	
	Lung, NOS; Bronchus, NOS	208 (1.1)	124 (1.7)	19 (1.6)	
Size of tumor (cm)	Mean ± stdandard deviation	1.52 ± 0.39	1.4 ± 0.42	1.46 ± 0.40	**<0.001**
Histology	Adenocarcinomas	13,097 (66.4)	4336 (59.4)	760 (62.0)	**<0.001**
	Adenosquamous carcinomas	419 (2.1)	173 (2.4)	27 (2.2)	
	Large-cell carcinomas	513 (2.6)	216 (3.0)	21 (1.7)	
	Squamous cell carcinomas	3957 (20.1)	1795 (24.6)	289 (23.6)	
	Other tumors[a]	1136 (5.8)	499 (6.8)	90 (7.3)	
	Unknown histology	596 (3.0)	278 (3.8)	39 (3.2)	
Grade	1	4140 (21.0)	1465 (20.1)	255 (20.8)	**<0.001**
	2	8944 (45.4)	3043 (41.7)	556 (45.4)	
	3–4	5262 (26.7)	2036 (27.9)	324 (26.4)	
	Unknown	1372 (7.0)	753 (10.3)	91 (7.4)	
30-Day mortality		1.60%	1.51%	1.55%	0.868
Surgical margins	Negative	19,436 (98.6)	7005 (96.0)	1200 (97.9)	**<0.001**
	Positive	282 (1.4)	292 (4.0)	26 (2.1)	
Regional LN surgery performed	No regional LN surgery	680 (3.5)	3721 (51.1)	258 (21.1)	**<0.001**
	Regional LN surgery	19,029 (96.6)	3560 (48.9)	965 (78.9)	

(*Continued*)

TABLE 1. (*Continued*)

Covariate	Level	Lobectomy (%), N = 19,718	Wedge Resection (%), N = 7297	Segmental Resection (%), N = 1226	*P* Value
Nodal upstaging	No	18,275 (92.7)	7147 (97.9)	1182 (96.4)	**<0.001**
	Yes	1443 (7.3)	150 (2.1)	44 (3.6)	
Number of regional LN examined	0–3	4232 (21.5)	5574 (76.4)	662 (54.0)	**<0.001**
	>3	15,486 (78.5)	1723 (23.6)	564 (46.0)	

Year of diagnosis was included in the model, but not shown here.
[a]Including but not restricted to, spindle cell carcinoma, mucoepidermoid malignancy.
LN, lymph node; NOS, not otherwise specified; NCI, National Cancer Institute.

Further analysis of these socioeconomic differences has previously been reported.[18] In addition, wedge resection and segmentectomy were associated with several secondary outcome measures. Compared with lobectomy, wedge resection was associated with a 2.6% higher incidence of positive surgical margins, a 55% higher incidence of having three or less LN examined, and as a result, a 5% lower incidence of nodal upstaging. Segmentectomy was associated with a similar rate of positive margins when compared with lobectomy but was associated with a 33% higher incidence of having three or less LN examined and a 4% lower incidence of nodal upstaging.

The primary goals of this database analysis were the comparison of 30-day mortality and OS between patients undergoing lobectomy and sublobar resection. Overall, 30-day mortality was quite low at 1.60% for lobectomy, 1.51% for wedge resection, and 1.55% for segmental resection ($p = 0.868$, Table 1). However, on multivariate analysis, the odds of mortality was slightly lower after wedge resection compared with lobectomy (Table 2, OR, 0.72; 95% confidence interval [CI], 0.57–0.90, $p = 0.005$). No difference was noted between segmentectomy and lobectomy. The remainder of the results of the multivariable logistic regression analysis of 30-day mortality is

TABLE 2. Multivariable Association with 30-Day Mortality

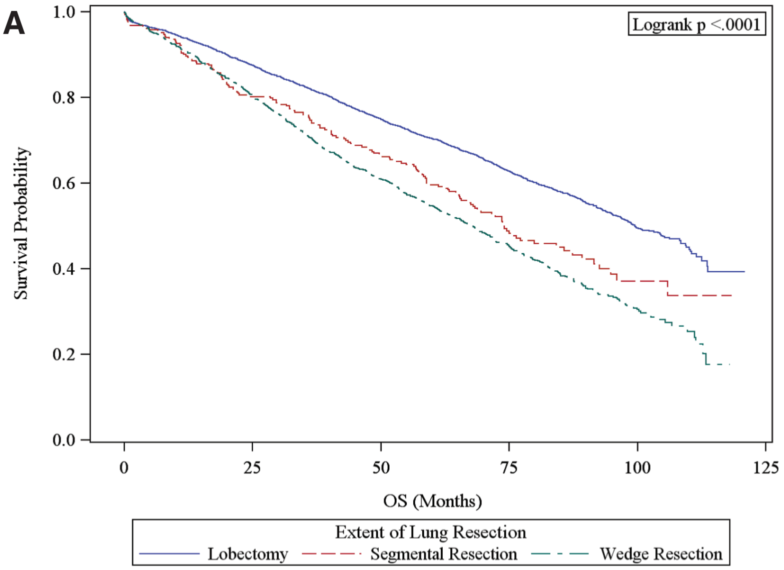
Covariate	Level	Odds Ratio (95% CI)	*P* Value
Extent of lung resection	Segmental resection	0.87 (0.54–1.42)	0.585
	Wedge resection	0.72 (0.57–0.90)	**0.005**
	Lobectomy	—	—
Facility type	Academic/research program (Includes NCI)	0.58 (0.42–0.81)	**0.001**
	Comprehensive community cancer program	0.68 (0.51–0.92)	**0.012**
	Community cancer program/other	—	—
Sex	Male	1.72 (1.41–2.09)	**<0.001**
	Female	—	—
Patient age		1.05 (1.03–1.06)	**<0.001**
Insurance	Not insured	2.05 (0.98–4.27)	0.056
	Private insurance	0.76 (0.57–1.00)	0.054
	Government insurance	—	—
Income	<$30,000	1.27 (0.92–1.73)	0.141
	$30,000–$34,999	1.42 (1.08–1.85)	**0.011**
	$35,000–$45,999	1.32 (1.03–1.68)	**0.027**
	$46,000+	—	—
Charlson/Deyo score	2+	1.44 (1.10–1.88)	**0.007**
	1	1.09 (0.87–1.36)	0.443
	0	—	—
Histology	Unknown histology	1.50 (0.93–2.43)	0.096
	Squamous cell carcinomas	1.56 (1.25–1.94)	**<0.001**
	Other tumors[a]	0.58 (0.28–1.17)	0.129
	Large-cell carcinomas	1.31 (0.76–2.28)	0.332
	Adenosquamous carcinomas	2.22 (1.37–3.59)	**0.001**
	Adenocarcinomas	—	—

[a]Including but not restricted to, spindle cell carcinoma, mucoepidermoid malignancies, neuroendocrine, and mixed malignant tumors.
Year of diagnosis not shown here, but was included in the model and was associated with 30-day mortality.
CI, confidence interval.

shown in Table 2. Male sex, older patient age, lower income, treatment at a noncomprehensive community cancer program, Charlson/Deyo comorbidity score of 2 or higher, older year of diagnosis, and squamous and adenosquamous cell histologies were all associated with higher 30-day mortality.

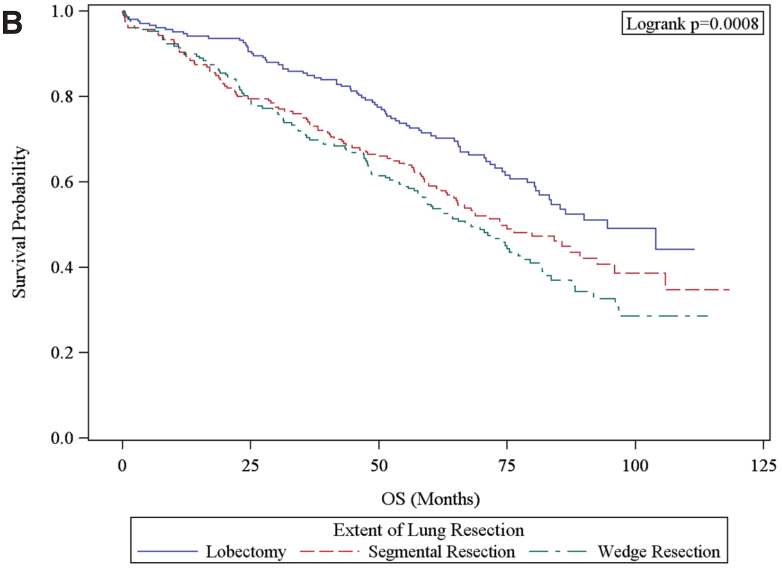
Unadjusted Kaplan–Meier survival curves comparing extent of surgical resection demonstrated significantly improved OS with lobectomy ($p < 0.0001$, Fig. 1*A*). Median OS for lobectomy, segmentectomy, and wedge resection were 99.5 (95% CI, 96.8–105), 74 (95% CI, 65.7–87.4), and 67.9 (95% CI, 63.6–71.3) months, respectively. After controlling for confounding factors, Cox proportional hazard model (Table 3) showed lobectomy was associated with significantly improved OS compared with both wedge resection (hazard

A



Extent of Lung Resection	No. of Subject	Event	Censored	Median Survival (95% CI)	60 mo Survival
Lobectomy	4857	1847 (38%)	3010 (62%)	99.5 (96.8, 105)	70.4% (69.0%, 71.7%)
Segmental Resection	286	147 (51%)	139 (49%)	74 (65.7, 87.4)	59.6% (53.5%, 65.2%)
Wedge Resection	1891	1044 (55%)	847 (45%)	67.9 (63.6, 71.3)	54.6% (52.3%, 56.9%)

B



Extent of Lung Resection	No. of Subject	Event	Censored	Median Survival (95% CI)	60 mo Survival
Lobectomy	209	81 (39%)	128 (61%)	94.5 (80.6, NA)	71.4% (64.4%, 77.3%)
Segmental Resection	209	107 (51%)	102 (49%)	73.7 (63.3, 92.6)	59.1% (51.9%, 65.5%)
Wedge Resection	209	121 (58%)	88 (42%)	67.9 (57.7, 77.1)	54.8% (47.6%, 61.3%)

FIGURE 1. Kaplan–Meier survival curves by extent of surgical resection in (*A*) unadjusted population and (*B*) propensity score matched sample.

TABLE 3. Cox Proportional Hazard Model of Overall Survival

Covariate	Level	Hazard Ratio	*P* Value
Extent of lung resection	Segmental resection	1.33 (1.11–1.60)	**0.002**
	Wedge resection	1.54 (1.42–1.67)	**<0.001**
	Lobectomy	—	—
Facility type	Academic/research program (Includes NCI)	0.86 (0.75–0.99)	**0.041**
	Comprehensive community cancer program	0.92 (0.80–1.05)	0.194
	Community cancer program/other	—	—
Sex	Male	1.24 (1.15–1.33)	**<0.001**
	Female	—	—
Patient age		1.03 (1.02–1.03)	**<0.001**
Insurance	Not insured	0.83 (0.56–1.23)	0.356
	Private insurance	0.83 (0.76–0.92)	**<0.001**
	Govenment insurance	—	—
Income	<$30,000	1.33 (1.18–1.50)	**<0.001**
	$30,000–$34,999	1.30 (1.17–1.44)	**<0.001**
	$35,000–$45,999	1.14 (1.04–1.25)	**0.007**
	$46,000+	—	—
Charlson/Deyo score	2+	1.52 (1.36–1.69)	**<0.001**
	1	1.17 (1.08–1.27)	**<0.001**
	0	—	—
Histology	Unknown histology	1.16 (0.98–1.36)	0.080
	Squamous cell carcinomas	1.06 (0.96–1.16)	0.246
	Other tumors[a]	0.78 (0.59–1.02)	0.074
	Large-cell carcinomas	1.09 (0.90–1.33)	0.366
	Adenosquamous carcinomas	1.18 (0.93–1.50)	0.171
	Adenocarcinomas	—	—
Grade	Unknown, high-grade dysplasia	1.33 (1.12–1.58)	**<0.001**
	3–4	1.57 (1.38–1.79)	**<0.001**
	2	1.43 (1.27–1.62)	**<0.001**
	1	—	—
Size of tumor (cm)		1.21 (1.10–1.34)	**<0.001**

Number of observations in the original data set = 28,241. Number of observations used = 6438. Tumor location was included in the multivariable model but not shown here.
[a]Including but not restricted to, spindle cell carcinoma, mucoepidermoid malignancies, neuroendocrine, and mixed malignant tumors.

ratio [HR] = 1.54, 95% CI, 1.42–1.67, $p < 0.001$) and segmentectomy (HR = 1.33, 95% CI, 1.11–1.60, $p = 0.002$). Other predictors of worse OS included treatment at a noncomprehensive community cancer program, male sex, older age, government insurance, lower income, higher Charlson/Deyo comorbidity score, advanced tumor grade, and larger tumor size.

The interaction between extent of resection with tumor size, treatment facility type, number of LN evaluated, and surgical margin status was then further evaluated (Table 4, Supplementary Figs. 1–4, Supplemental Digital Content 2, http://links.lww.com/JTO/A888). After controlling for confounding variables, the inferiority of sublobar approaches to lobectomy persisted despite the number of LN examined and tumor size (Kaplan–Meier analysis shown in Supplementary Figs. 2 and 3, Supplemental Digital Content 2, http://links.lww.com/JTO/A888). For each subgroup, the HR for long-term survival remained worse after wedge or segmental resection. Although the HR for long-term survival was worse after segmental resection for tumors smaller than 1 cm (1.24), this result was not statistically significant ($p = 0.414$). Given then relatively low sample size of segmentectomies in this cohort (n = 51), it is difficult to draw further conclusions. Furthermore, when comparing stratification levels for these two subgroup analyses, no significant interaction was identified, as evidenced by type 3 p values of 0.203 for tumor size and 0.655 for number of regional LN examined. Furthermore, the interaction of extent of resection with number of LN examined was tested at 3, 5, and 7 LN, with the inferiority of wedge and segmental resections persisting at all levels. In regards to treatment facility type, OS after wedge resection continued to be inferior to lobectomy regardless of treatment facility type. This was confirmed on Kaplan–Meier analysis (Supplementary Fig. 1, Supplemental Digital Content 2, http://links.lww.com/JTO/A888). Similarly, segmentectomy remained inferior to lobectomy at noncomprehensive community programs and academic facilities, as well. However, no difference was identified between segmental resection and lobectomy at comprehensive community programs. Finally, no interaction was identified between extent of resection and surgical margin status. In patients with negative

TABLE 4. Multivariate Association with Long-Term Mortality—Interaction with Facility Type, Tumor Size, and Number of Lymph Nodes Examined

Covariates	Level	Hazard Ratio	HR *P* Value	Type 3 *P* Value[a]
Stratified comparisons by facility type		—	—	**0.035**
Noncomprehensive community cancer program/other	Wedge resection (186) vs. lobectomy (440)	1.34 (1.02–1.76)	**0.032**	—
	Segmental resection (27) vs. lobectomy (440)	2.11 (1.24–3.60)	**0.006**	
Comprehensive community cancer program	Wedge resection (987) vs. lobectomy (2639)	1.47 (1.32–1.64)	**<0.001**	—
	Segmental resection (129) vs. lobectomy (2639)	1.09 (0.82–1.44)	0.561	
Academic/research program	Wedge resection (718) vs. lobectomy (1778)	1.73 (1.51–1.98)	**<0.001**	—
	Segmental resection (130) vs. Lobectomy (1778)	1.51 (1.16–1.96)	**0.002**	
Stratified comparisons by tumor size				0.203
0–1 cm	Wedge resection (439) vs. lobectomy (722)	1.77 (1.45–2.16)	**<0.001**	—
	Segmental resection (51) vs. lobectomy (722)	1.24 (0.74–2.06)	0.414	
1–2 cm	Wedge resection (1452) vs. lobectomy (4135)	1.47 (1.35–1.61)	**<0.001**	—
	Segmental resection (235) vs. lobectomy (4135)	1.32 (1.09–1.60)	**0.004**	
Stratified comparisons by regional LN examined				0.655
0–7	Wedge resection (1739) vs. lobectomy (2881)	1.50 (1.37–1.65)	**<0.001**	—
	Segmental resection (246) vs. lobectomy (2881)	1.27 (1.04–1.55)	**0.020**	
8+	Wedge resection (152) vs. lobectomy (1976)	1.56 (1.21–2.01)	**<0.001**	—
	Segmental resection (40) vs. lobectomy (1976)	1.58 (1.01–2.48)	**0.044**	

Sample size for each subgroup listed in parenthesis.
[a]Type 3 *P* value indicates the significance for the interaction term in the fitted model.
LN, lymph nodes.

surgical margins, OS remained worse after segmentectomy and wedge resection. A difference was not identified in patients with positive margins; however, the sample size in these subgroups was too small to draw reliable conclusions.

To further compare segmentectomy and lobectomy controlling for both surgical margins and adequate lymphadenectomy, we performed a multivariable analysis including only patients with negative margins and more than or equal tofive and seven LNs. After controlling for these factors, we did not identify a difference in OS in patients with negative margins and more than or equal to five LNs examined when comparing segmentectomy (n = 81) with lobectomy (n = 2888) (HR, 1.20; 95% CI, 0.86–1.67; $p = 0.277$). Similarly, we did not identify a difference when only including patients with more than or equal to seven LNs examined (HR = 1.48, 95% CI: 0.98–2.23, $p = 0.063$; segmentectomy n = 44, lobectomy n = 2181). The relatively low number of patients undergoing segmentectomy in this subgroup analysis should be noted.

Finally, to better control for baseline differences between the two cohorts, a propensity score matching method was implemented with results shown in Table 5. A total of 987 patients were matched in each treatment group and were similar in regards to all covariates (standardized difference < 0.1). After matching, there was no difference in 30-day mortality. However, both wedge resection and segmental resection were associated with significantly worse OS, lower likelihood of having more than three LN examined, and as a result significantly lower rate of nodal upstaging. Wedge resection was associated with significantly higher rates of positive surgical margins. Lastly, Kaplan–Meier survival curves in the propensity score matched groups are shown in Figure 1*B* and confirmed significantly improved long-term survival with lobectomy.

DISCUSSION

An anatomical lobectomy with mediastinal LN staging is the current standard surgical therapy for early-stage lung

TABLE 5. Comparison of Primary and Secondary Outcomes by Extent of Resection in Propensity Score Matched Samples

	Extent of Surgical Resection		
Outcome	**Wedge Resection, n = 987**	**Segmentectomy, n = 987**	**Lobectomy, n = 987**
30-Day mortality	0.87 (0.41–1.82), $p = 0.706$	1.13 (0.57–2.27). $p = 0.724$	—
Overall survival[a]	1.70 (1.29–2.26), $\mathbf{p < 0.001}$	1.45 (1.10–1.91), $\mathbf{p = 0.009}$	—
Positive surgical margins	2.02 (1.13–3.63), $\mathbf{p = 0.018}$	1.29 (0.69–2.43), $p = 0.426$	—
> 3 LN examined	0.07 (0.05–0.09), $\mathbf{p < 0.001}$	0.18 (0.14–0.22), $\mathbf{p < 0.001}$	—
Positive regional LN	0.39 (0.24–0.63), $\mathbf{p < 0.001}$	0.59 (0.38–0.89), $\mathbf{p = 0.013}$	—

[a]Overall survival analysis limited to patients treated between 2003 and 2006, n = 209 per group. Overall survival reported as hazard ratio. Remaining variables reported as odds ratio with 95% confidence intervals.
LN, lymph nodes.

cancer. This is based on the randomized trial conducted by the Lung Cancer Study Group (LCSG).[2] However, sublobar resections do offer several potential advantages: preservation of pulmonary function, greater application of minimally invasive surgical techniques, and increased likelihood of curative surgery in the event of a second primary lung cancer. Concerns of long-term oncologic efficacy raised by the LCSG have relegated the utilization of sublobar resection to patients with limited cardiopulmonary reserve. Similar to the results of the LCSG, results of our analysis of the NCDB found significantly worse survival after sublobar resections. Furthermore, propensity score matching was used to account for differences in baseline patient characteristics among the three surgical therapies. Results of this analysis showed no difference in 30-day mortality, with significantly worse OS, lower likelihood of having adequate numbers of LN examined, and lower nodal upstaging rates after both wedge and segmental resections. Furthermore, wedge resection was associated with significantly increased likelihood of having positive surgical margins. However, when comparing only patients with both negative margins and adequate numbers of LNs examined, no difference was identified in OS between segmentectomy and lobectomy. This finding may represent equivalency between segmentectomy and lobectomy in this highly selected subgroup of patients or may be because of underpowering of this subgroup analysis.

To date, the LCSG trial is the only published prospective randomized comparison of lobectomy and sublobar resection, including 267 patients with T1N0 (<3 cm; stage IA) lung cancers.[2] Findings of this study demonstrated an increase in local recurrence rates (17.2% vs. 6.4%) with sublobar resections and a trend toward worse OS. However, more contemporary studies have questioned these results. Several single institution series have consistently demonstrated lower morbidity and mortality rates and preserved pulmonary function for sublobar resections compared with lobectomy.[4–9]

In addition, several analyses of survival data from the SEER Program have been reported.[9–12] A large observational comparison from a clinical registry such as the NCDB or SEER, while subject to treatment selection bias, can supplement randomized trials with greater numbers, greater generalizability, and more contemporary data that can be regularly updated. Analysis of SEER data, by Wisnivesky et al.,[9] looked at 1165 patients with tumors less than or equal to 2 cm with propensity score adjustments and found equivalent OS and disease-free survival between lobectomy and sublobar resection. Similarly, Kates et al.[10] examined SEER data in patients with tumors less than or equal to 1 cm between 1988 and 2005, 688 with sublobar resection and 1402 with lobectomy. After propensity score matching, they also found no difference in OS or lung cancer-specific survival. However, Whitson et al.[12] examined SEER data in stage I patients with only squamous cell and adenocarcinomas of all sizes, undergoing lobectomy (13,892 patients) or segmentectomy (581 patients) between 1998 and 2007. They found significantly better OS after lobectomy, even after stratifying by tumor size.

The underlying reason for the conflicting results of our analysis and previous studies is difficult to determine. Our large sample size may allow for better identification of survival differences. Furthermore, our study used propensity matching to account for identified differences in patient and tumor characteristics. In addition, in our analysis, patients undergoing limited resection were significantly more likely to have a positive margin or inadequate lymphadenectomy, which could be contributing to worse OS. Finally, the large size and nationwide distribution of the NCDB reflects care given to nearly 70% of newly diagnosed cancer patients annually. As a result, this analysis may be more reflective of the general care of patients with early-stage NSCLC in the United States.

Furthermore, although several previous single institution series have suggested equivalent survival for sublobar resection for smaller tumors or with adequate lymphadenectomy, our results did not support this conclusion. Subgroup analysis in this study confirmed improved survival after lobectomy when compared with both sublobar approaches for tumors 1 to 2 cm. For tumors 1 cm or smaller, lobectomy was superior to wedge resection. Regardless, no significant interaction was identified between tumor size and extent of resection when evaluating the end point of OS. Similarly, survival after lobectomy was better than sublobar approaches regardless of the number of LN evaluated. In other words, patients treated with wedge resection and adequate mediastinal LN evaluation still fared worse than those who underwent lobectomy. Finally, as the majority of these single institution series were performed at academic facilities, we performed a subgroup analysis of OS stratified by treatment facility. With the exception of segmentectomy performed at comprehensive community cancer programs, survival after lobectomy remained superior regardless of academic or community treatment facility.

The major limitation of this analysis is its retrospective observational nature, which subjects it to possible unmeasured confounding. However, with the inclusion of 15 variables and nearly 2500 patients in each cohort, this study represents a well-balanced analysis of these three treatment methods. In addition, we are limited to patients treated in 2006 and earlier as long-term survival data is not available in the NCDB beyond that date. Given the wider adoption of positron emission tomography-computed tomography scanning and minimally invasive thoracoscopic techniques, results may be slightly different in a more contemporary cohort. Furthermore, data regarding ground glass opacities and subsolid nodules representing minimally invasive adenocarcinomas are unavailable in the NCDB. As a result, the distribution of these patients within the study cohort is unknown and could not be accounted for. It is possible that if there is a higher proportion of patients with ground glass opacities in one of the cohorts, this may have confounded the results.

Finally, no data are available on pulmonary function, preoperative functional status, or specific comorbidities in the NCDB other than the Charlson/Deyo comorbidity index. As a higher Charlson/Deyo comorbidity score cannot differentiate between the 10 included medical comoribidities, it is impossible to completely control for medical comorbidities/confounders. As a result, despite careful propensity matching, there is still the potential for selection bias between the cohorts as patients with worse pulmonary function testing or fraility are more likely to undergoing a wedge or segmental resection. Ultimately, a prospective, randomized study will be needed to determine the optimal surgical strategy. Based on these previous studies, the National Cancer Institute has sponsored Cancer and Leukemia Group B 140503, a phase III randomized trial comparing outcomes between lobectomy and sublobar resection for lung cancers smaller than 2 cm.

In summary, this analysis of the NCDB showed improved OS after lobectomy in comparison with both wedge resection and segmentectomy for patients with clinical T1A N0 NSCLC, regardless of treatment facility type, extent of resection, or tumor size (after wedge resection). Furthermore, patients undergoing wedge resection were more likely to have inadequate LN evaluation and to have positive margins. These results confirm that anatomical lobectomy should remain the standard of care treatment for stage IA NSCLC at this point. However, if margin status and LN evaluation are controlled, segmentectomy may be equivalent to lobectomy. Given the limitations of a retrospective database analysis, further prospective study is still needed to ultimately determine the optimal extent of surgery for early-stage lung cancer.

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