# The effect of extent of resection on outcomes in patients with limited stage small cell lung cancer



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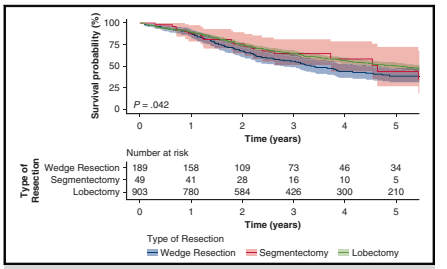
## ABSTRACT

**Background:** There is poor understanding of the comparative effectiveness of lobar and sublobar resections for limited-stage small cell lung cancer (SCLC). We analyzed the National Cancer Database to examine the outcomes of patients undergoing wedge resection (WR), segmentectomy (SR), and lobectomy (LB) for limited-stage SCLC.

**Methods:** Patients with cT1-2N0M0 SCLC (2004-2015) who underwent definitive surgery were identified and stratified by extent of resection: WR, SR, or LB. The primary outcome was overall survival (OS) and secondary outcomes were margin-positive resection (>R0) and pathologic nodal upstaging.

**Results:** A total 1948 patients met study criteria: 619 (32%) underwent WR, 96 (5%) SR, and 1233 (63%) LB. Patients receiving LB were more likely to be younger, have fewer comorbidities, and be privately insured. The unadjusted 5-year OS of WR, SR, and LB patients was 31% (95% confidence interval [CI], 27-35), 35% (95% CI, 25-49), and 45% (95% CI, 42-49), respectively. In a multivariable Cox model, WR was associated with worse OS (hazard ratio, 1.53; 95% CI, 1.31-1.79) and SR similar OS (hazard ratio, 1.20; 95% CI, 0.87-1.67) compared with LB. SR was associated with similar survival compared with LB in a propensity score–matched multivariable analysis as well. WR was also associated with greater odds of >R0 resection compared with LB.

**Conclusions:** In this study, patients with limited-stage SCLC undergoing WR experienced worse survival compared with those undergoing LB; survival was similar between segmentectomy and LB. (J Thorac Cardiovasc Surg 2021;161:1484-92)




**Lobectomy has better survival compared with wedge resection in early small cell lung cancer.**

**CENTRAL MESSAGE**

Segmental and lobar resection are associated with similar survival in patients with cT1-2N0M0 small cell lung cancer.

**PERSPECTIVE**

In this National Cancer Database study, patients undergoing wedge resection experienced worse survival compared with those receiving segmentectomy or lobectomy for limited stage small cell lung cancer.

See Commentaries on pages 1493, 1494, and 1495.

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The National Comprehensive Cancer Network guidelines recommend consideration of surgery for patients with limited-stage small cell lung cancer (SCLC).[1] Two prospective trials have examined the role of surgery in SCLC. The Medical Research Council trial[2] randomized 144 patients with resectable SCLC to surgery or definitive radiation and found that unadjusted mean survival was lower for patients in the surgery arm. Similarly, Lad and colleagues[3] randomized 146 patients with limited SCLC who demonstrated a response to initial chemotherapy to undergo surgery compared with no surgery and found similar median survival in the 2 groups. As a result, surgery has not been the mainstay treatment for even limited SCLC. However, these trials have several limitations. Both trials randomized few patients and analyzed patients in an intention-to-treat manner, and many patients assigned to surgery did not undergo resection. For instance, 52% of patients randomized to surgery in the Medical Research Council trial either received no surgery or a thoracotomy without resection.

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Scanning this QR code will take you to the table of contents to access supplementary information.

**Abbreviations and Acronyms**

CDCC = Charlson–Deyo Comorbidity Index
CI = confidence interval
HR = hazard ratio
LB = lobectomy
NCDB = National Cancer Database
OS = overall survival
SCLC = small cell lung cancer
SR = segmental resection
WR = wedge resection

Similarly, 17% of patients in the trial reported by Lad and colleagues did not undergo a resection. Both trials are also decades old. With the advent of platinum-based chemotherapy and improved staging and surgical techniques, the multimodal treatment of lung cancer has progressed significantly in the ensuing decades. Although contemporary observational studies have demonstrated that patients with limited-stage and even locally advanced SCLC undergoing surgery experience good outcomes compared with those undergoing chemoradiation, surgery remains underused.[4-13]

One of the primary concerns about surgery remains the perioperative morbidity and mortality associated with lobectomy (LB), which remains the standard of care in surgical treatment of lung cancer. Sublobar resection, including wedge resection (WR) and segmental resection (SR), has been described as an option for patients with poor pulmonary reserve or performance status in non–small cell lung cancer, with early perioperative data from the Cancer and Leukemia Group B/Alliance 14053 trial demonstrating similar perioperative mortality and morbidity in patients treated with lobar and sublobar resection.[14-16] However, there are no prospective data and few observational studies comparing lobar and sublobar resection in limited-stage SCLC.[17-20] The decision to offer surgery and the type of surgery to offer is further complicated by the timing of diagnosis of SCLC. SCLC is rarely diagnosed following a core needle biopsy, and histologic confirmation is often made during or after surgery, when a patient may have been committed to a particular initial treatment.

The aim of this study was to compare the outcomes of lobar and sublobar resection in patients undergoing definitive surgery for limited-stage SCLC. We hypothesized that LB would be associated with improved overall survival (OS) compared with WR and SR in this patient population.

## METHODS

### Data Source and Patient Selection

This study was deemed exempt by the Duke University Institutional Review Board. The National Cancer Database (NCDB) is a collaborative effort of the American Cancer Society and the American College of Surgeons. It contains data on approximately 80% of cancers diagnosed annually in the United States across 1500 centers.[21] Data are entered by certified, independent tumor registrars who use standardized guidelines. The NCDB was queried for patients with American Joint Commission on Cancer, 8th Edition, clinical stage T1-2N0M0 SCLC who underwent WR, SR, or LB between 2004 and 2015. Patients receiving a bilobectomy or bronchial sleeve resection were classified as LB. Patients who received nonsurgical treatment, other types of surgery including unknown description of surgery, who received neoadjuvant chemotherapy or radiation, or who had missing survival information were all excluded (Figure 1).

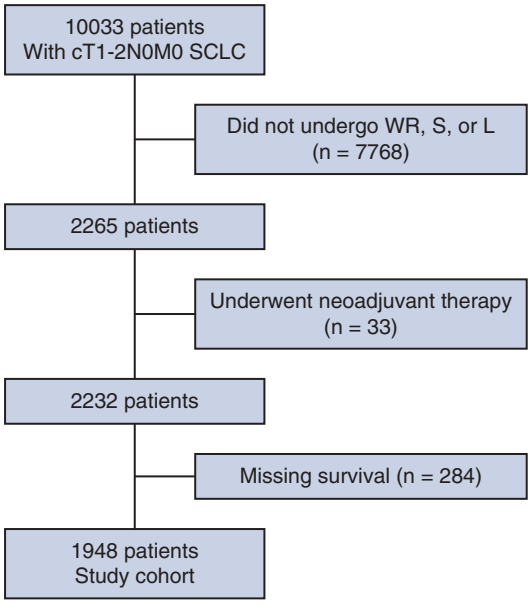


**FIGURE 1.** Patient selection scheme for the study. *SCLC*, Small cell lung cancer; *WR*, wedge resection; *S*, segmental resection; *L*, lobectomy.

### Study Design

Patients were stratified by type of resection: WR, SR, or LB. Background characteristics between the groups were compared using the Wilcoxon rank sum and Pearson $\chi^2$ tests for continuous and categorical measures, respectively. The primary outcome was OS, which was estimated using Kaplan–Meier and multivariable Cox proportional hazards methods. Variables included in the multivariable Cox model were selected a priori based on availability in the NCDB, previous literature demonstrating their association with survival, and from clinical experience: age, sex, race, year of diagnosis, Charlson–Deyo Comorbidity Index (CDCC) score, insurance status, treatment at an academic center, and tumor size. The proportional hazards assumption for the variables and overall model was checked with visual and quantitative representations of Schoenfeld residuals. In every model, the proportional hazards assumption was met; the *P* value of the Schoenfeld residual for the covariates and the overall model was <.05.

The secondary outcome measures were odds of a margin-positive resection and odds of pathologic nodal upstaging. These dichotomized outcomes were modeled with multivariable logistic regression using the same variables described previously. Only patients with nodes assessed in surgery were included in the logistic regression for pathologic nodal upstaging.

Several additional analyses were performed. (1) Because of the imbalances in preoperative characteristics between patients receiving SR and LB, a 1:1 propensity score-matched analysis was performed to compare these groups. A nearest-neighbor algorithm was used and a caliper width of 0.06.[22] The variables used for matching were determined a priori to

**TABLE 1. Background characteristics of patients**

| | Wedge resection (n = 619), n (%) | Segment resection (n = 96), n (%) | Lobectomy (n = 1233), n (%) | *P* value |
|---|---|---|---|---|
| Age, y, median (IQR) | 70 (64-76) | 70 (64-75) | 67 (61-73) | <.001 |
| Sex (female) | 339 (55) | 59 (62) | 681 (55) | .46 |
| Race | | | | .06 |
| White | 578 (94) | 85 (90) | 1119 (91) | |
| Black | 29 (5) | 8 (8) | 77 (6) | |
| Other | 5 (1) | 2 (2) | 30 (2) | |
| Year of diagnosis, median (IQR) | 2007 (2003-2010) | 2007 (2004-2009) | 2008 (2003-2010) | .22 |
| CDCC score | | | | .05 |
| 0 | 201 (43) | 26 (33) | 457 (47) | |
| 1 | 183 (39) | 37 (47) | 375 (39) | |
| 2+ | 87 (19) | 15 (19) | 139 (14) | |
| Insurance status | | | | .04 |
| Private | 152 (25) | 29 (31) | 383 (32) | |
| Government | 453 (74) | 66 (70) | 821 (67) | |
| None | 5 (1) | 0 (0) | 13 (1) | |
| Facility location | | | | .29 |
| Metro | 466 (79) | 76 (80) | 930 (79) | |
| Urban | 116 (20) | 15 (16) | 205 (18) | |
| Rural | 10 (2) | 4 (4) | 36 (3) | |
| Academic center | 194 (31) | 43 (45) | 418 (34) | .03 |
| Tumor size, mm, median (IQR) | 17 (12-23) | 19 (14-25) | 21 (15-30) | <.001 |
| Lymph nodes assessed in surgery | 268 (43) | 62 (65) | 1153 (94) | <.001 |
| Number of nodes examined, median (IQR) | 0 (0-3) | 2 (0-6) | 8 (4-14) | <.001 |
| Pathologic stage | | | | .001 |
| IA | 251 (78) | 45 (70) | 720 (65) | |
| IB | 18 (6) | 5 (8) | 124 (11) | |
| IIA | 5 (2) | 2 (3) | 54 (5) | |
| IIB | 24 (7) | 6 (9) | 131 (12) | |
| IIIA | 22 (7) | 6 (9) | 62 (6) | |
| IIIB | 0 (0) | 0 (0) | 0 (0) | |
| IIIC | 0 (0) | 0 (0) | 0 (0) | |
| IV | 1 (0) | 0 (0) | 10 (1) | |
| Pathologic N status | | | | <.001 |
| Unknown | 289 (47) | 29 (30) | 102 (8) | |
| N0 | 283 (46) | 56 (58) | 933 (76) | |
| N1 | 24 (4) | 7 (7) | 144 (12) | |
| N2 | 23 (4) | 4 (4) | 54 (4) | |
| N3 | 0 (0) | 0 (0) | 0 (0) | |
| Positive margins | 62 (11) | 8 (9) | 45 (4) | <.001 |
| Pathologic nodal upstaging | 403 (65) | 44 (46) | 291 (24) | <.001 |
| 30-d readmission | 19 (4) | 1 (1) | 35 (4) | .48 |
| Postoperative length of stay, d, median (IQR) | 4 (3-7) | 4 (3-7) | 6 (4-9) | <.001 |
| Postoperative 90-d mortality | 34 (5) | 1 (1) | 64 (5) | .07 |
| Adjuvant chemotherapy | 214 (35) | 26 (27) | 471 (38) | .05 |
| Adjuvant thoracic radiation | 178 (29) | 17 (18) | 281 (23) | .005 |
| Cranial radiation | 36 (6) | 3 (3) | 132 (11) | <.001 |

*IQR*, Interquartile range; *CDCC*, Charlson-Deyo Comorbidity Index.

be of prognostic significance: age, sex, race, CDCC score, insurance status, treatment at an academic center, and tumor size. Covariate balance was checked using standardized mean differences (Table E1 and Figure E1). Because only 70 events were observed in the propensity score–matched cohort, a limited multivariable Cox model was performed with variables chosen that most impacted the effect estimate of the type of surgery variable and most improved the precision of the confidence interval.[23] (2) Although only patients who received "definitive surgery" according to the NCDB were included in the study, we performed a subgroup analysis including only patients undergoing WR who underwent an intraoperative lymph node assessment as well, hypothesizing that these patients were treated with curative intent.[24] (3) There was substantial variation in pathologic nodal upstaging between the groups (Table 1). Because the NCDB does not contain information on how patients were clinically staged, including mediastinal nodal evaluation, we performed a subgroup analysis including only patients with proven, pathologic node-negative disease who had at least 1 node assessed in surgery. (4) The National Comprehensive Cancer Network guidelines recommend adjuvant chemotherapy with or without radiation for patients with clinically limited-stage SCLC who undergo resection. Because a minority of patients underwent guideline-concordant adjuvant chemotherapy and there were significant differences between the groups, we performed an analysis examining only patients who received a resection and adjuvant chemotherapy with or without radiation. Survival was computed from the initiation of adjuvant chemotherapy for this analysis. (5) Because WR was associated with significantly worse OS compared with LB, we wondered whether it would still be superior to definitive concurrent chemoradiation. To test this, we performed an analysis comparing patients who received WR without neoadjuvant therapy with those who received primary concurrent chemoradiation. Because we believed the burden of proof lay with surgery, we applied liberal inclusion criteria for surgery patients and restrictive inclusion criteria for chemoradiation patients. Patients were only included in the definitive chemoradiation group if they started chemotherapy and radiation within 30 days of each other, if they received at least 45.0 Gy of radiation altogether, and if they were not refused surgery after being deemed medically unfit. Patients receiving SR and LB were also included in this analysis for comparison. (6) Given the similar outcomes between patients who underwent SR and LB, we tested the question of whether there is a tumor size threshold at which LB is associated with improved survival compared with SR. We performed a multivariable Cox regression in patients who underwent either SR or LB using the same variables as reflected in Table 2 and included an interaction term between tumor size and type of surgery.

Missing data were handled with complete case analysis in regression. A comparison of baseline characteristics and outcomes between patients with complete data and missing covariate or survival data is presented in Table E2. All *P* values are 2-sided. All analyses were performed using R version 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

### Overall Survival

A total of 1948 patients met study criteria: 619 (32%) underwent WR, 96 (5%) SR, and 1233 (63%) LB. Background characteristics of study patients are summarized in Table 1. Patients who underwent LB were more likely to be younger, have fewer comorbidities, be privately insured, have a larger tumor, and a longer hospitalization after surgery compared with patients undergoing sublobar resection. A minority of patients in each group received adjuvant chemotherapy.

**TABLE 2. Multivariable Cox proportional hazards model for factors associated with survival, N = 1948**

| Variable | Hazard ratio (95% confidence interval) | *P* value |
|---|---|---|
| Age (per y) | 1.02 (1.01-1.03) | <.001 |
| Female sex (reference: male) | 0.84 (0.73-0.97) | .02 |
| Race (reference: white) | | |
| Black | 1.00 (0.73-1.35) | .98 |
| Year of diagnosis (per y) | 1.00 (0.97-1.04) | .94 |
| Charlson–Deyo Comorbidity index (reference: 0) | | |
| 1 | 1.00 (0.85-1.17) | .98 |
| 2+ | 1.34 (1.10-1.63) | .003 |
| Insurance status (reference: private) | | |
| Government | 1.19 (0.99-1.42) | .07 |
| None | 0.38 (0.12-1.19) | .10 |
| Academic center | 1.00 (0.86-1.17) | .97 |
| Tumor size (per 10 mm) | 1.16 (1.08-1.25) | <.001 |
| Type of surgery (reference: lobectomy) | | |
| Wedge resection | 1.53 (1.31-1.79) | <.001 |
| Segmentectomy | 1.20 (0.87-1.67) | .27 |

Unadjusted median survival for WR, SR, and LB patients was 28 months (95% confidence interval [CI], 26-34), 35 months (95% CI, 29-56), and 49 months (95% CI, 43-56), respectively. Five-year OS was 31% (95% CI, 27-35), 35% (95% CI, 25-49), and 45% (95% CI, 42-49) for WR, SR, and LB, respectively (Figure 2, *A*). In multivariable Cox regression, patients undergoing WR experienced worse survival compared with patients undergoing, whereas patients undergoing SR experienced similar survival compared with patients undergoing LB (Table 2).

A total of 74 pairs of patients receiving SR or LB were identified for the propensity score–matched analysis (Table E1). Patients undergoing SR and LB had an unadjusted 5-year OS of 32% (95% CI, 19-52) and 56% (95% CI, 44-71), respectively (Figure E2). In a multivariable regression, patients undergoing SR and LB had similar survival (Table 3).

### Secondary Outcomes

The incidence of positive margins in patients undergoing WR, SR, and LB was 11% (n = 62), 9% (n = 8), and 4% (n = 45), respectively (Table 1). In a multivariable logistic regression, WR was associated with a greater odds of margin-positive resection compared with LB (Table 4). SR was associated with similar odds of margin-positive resection compared with LB. In a multivariable logistic regression, both WR and SR were associated with similar nodal upstaging compared with LB (Table E3).

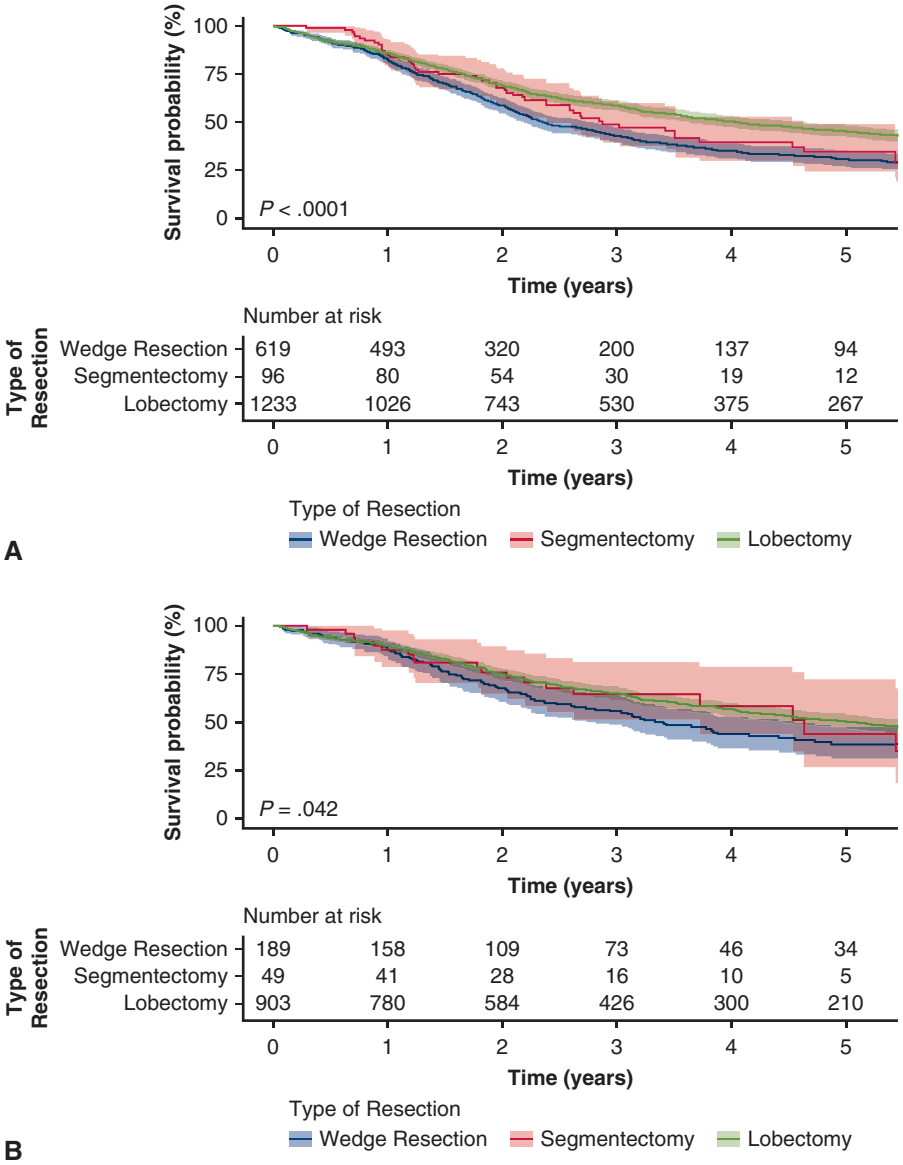


**FIGURE 2.** Kaplan–Meier survival curves for (A) patients with cT1-2N0M0 small cell lung cancer who underwent surgery, stratified by type of resection, and (B) a subgroup of patients with pathologic node-negative disease and at least 1 node assessed, stratified by type of resection. The *Y-axis* represents the probability of survival and the *X-axis* the time elapsed from diagnosis in years. The *shaded regions* demonstrate the bounds of the 95% confidence interval. The *P* value represents the result of the log-rank test. Numbers at risk are provided below each figure.

### Additional Analyses

In the first subgroup analysis, only patients undergoing WR who also received a lymph node assessment in surgery were included (n = 268; 43%). In a multivariable Cox regression, WR was again associated with worse OS compared with LB (adjusted hazard ratio [HR], 1.34; 95% CI, 1.09-1.65; $P = .005$). In the second subgroup analysis, only patients with proven, pathologic node-negative disease with at least 1 node assessed were included: 189 WR, 49 SR, and 903 LB. The 5-year unadjusted OS for patients undergoing WR, SR, and LB was 38% (95% CI, 31-48), 44% (95% CI, 27-72), and 50% (95% CI, 47-54), respectively (Figure 2, *B*). In multivariable analysis, WR was again associated with worse survival and SR similar survival compared with LB (Table 5).

In a third subgroup analysis including 481 patients who received adjuvant chemotherapy with or without radiation (108 WR, 16 SR, and 357 LB), WR was associated with worse survival (HR, 1.47; 95% CI, 1.05-2.07; $P = .02$)

**TABLE 3. Multivariable Cox proportional hazards model for factors associated with survival in propensity score–matched patients, N = 148**

| Variable | Hazard ratio (95% confidence interval) | *P* value |
|---|---|---|
| Age (per y) | 1.02 (0.99-1.06) | .19 |
| Year of diagnosis (per y) | 0.88 (0.79-0.98) | .02 |
| Charlson–Deyo Comorbidity index (reference: 0) | | |
| 1 | 1.01 (0.58-1.78) | .97 |
| 2+ | 1.97 (1.02-3.81) | .04 |
| Academic center | 0.91 (0.54-1.51) | .70 |
| Tumor size (per 10 mm) | 0.99 (0.97-1.02) | .57 |
| Type of surgery (reference: segmentectomy) | | |
| Lobectomy | 0.69 (0.42-1.14) | .14 |

and SR similar survival (HR, 0.61; 95% CI, 0.19-1.96; $P = .41$) compared with LB on multivariable analysis. In a fourth analysis comparing 1073 patients who underwent concurrent chemoradiation and those who underwent surgery, the unadjusted 5-year OS was 27% (95% CI, 24-30) for patients who underwent chemoradiation and 31% (95% CI, 27-35), 35% (95% CI, 25-49), and 45% (95% CI, 42-49) for patients undergoing WR, SR, and LB, respectively (Figure E3). WR was not associated with improved survival compared with chemoradiation (HR, 0.91; 95% CI, 0.78-1.06; $P = .22$) in a multivariable Cox model. SR was associated with similar survival compared with chemoradiation (HR, 0.73; 95% CI, 0.53-1.02; $P = .06$) and LB improved survival (HR, 0.63; 95% CI, 0.55-0.71; $P < .001$). In the last subgroup analysis, the interaction between tumor size and receipt of SR or LB was studied. An interaction term between tumor size and extent of resection was nonsignificant ($P = .48$) in a multivariable Cox model; this interaction is visualized in Figure E4.

**TABLE 4. Multivariable logistic regression model for factors associated with margin-positive resection, N = 1948**

| Variable | Odds ratio (95% confidence interval) | *P* value |
|---|---|---|
| Age (per y) | 1.00 (0.97-1.03) | .89 |
| Female sex (reference: male) | 1.12 (0.72-1.73) | .62 |
| Race (reference: white) | | |
| Black | 1.61 (0.71-3.69) | .26 |
| Year of diagnosis (per y) | 1.01 (0.92-1.10) | .86 |
| Charlson–Deyo Comorbidity index (reference: 0) | | |
| 1 | 0.90 (0.57-1.44) | .67 |
| 2+ | 0.79 (0.41-1.51) | .47 |
| Insurance status (reference: private) | | |
| Government | 0.89 (0.53-1.52) | .68 |
| Academic center | 0.91 (0.57-1.45) | .71 |
| Tumor size (per 10 mm) | 1.61 (1.31-1.97) | <.001 |
| Type of surgery (reference: lobectomy) | | |
| Wedge resection | 4.00 (2.49-6.41) | <.001 |
| Segmentectomy | 1.98 (0.74-5.30) | .17 |

**TABLE 5. Multivariable Cox proportional hazards model for factors associated with survival in subgroup of patients with pathologic node-negative disease, N = 1141**

| Variable | Hazard ratio (95% confidence interval) | *P* value |
|---|---|---|
| Age (per y) | 1.02 (1.01-1.04) | <.001 |
| Female sex (reference: male) | 0.89 (0.74-1.09) | .27 |
| Race (reference: white) | | |
| Black | 1.10 (0.74-1.64) | .62 |
| Year of diagnosis (per y) | 1.00 (0.96-1.05) | .96 |
| Charlson–Deyo Comorbidity index (reference: 0) | | |
| 1 | 0.99 (0.80-1.23) | .91 |
| 2+ | 1.46 (1.12-1.91) | .005 |
| Insurance status (reference: private) | | |
| Government | 1.17 (0.91-1.49) | .22 |
| None | 0.89 (0.28-2.87) | .85 |
| Academic center | 1.04 (0.85-1.28) | .68 |
| Tumor size (per 10 mm) | 1.02 (1.01-1.03) | .001 |
| Type of surgery (reference: lobectomy) | | |
| Wedge resection | 1.37 (1.07-1.75) | .01 |
| Segmentectomy | 0.94 (0.55-1.58) | .81 |

## DISCUSSION

In this NCDB analysis, we found that LB was associated with significantly improved OS compared with WR and similar survival compared with segmentectomy in patients with cT1-2N0M0 SCLC, including in patients with proven pathologic node-negative disease and those who received adjuvant chemotherapy. WR was associated with similar survival compared with definitive chemoradiation. Our study suggests that patients with early and limited-stage SCLC who can tolerate surgery should undergo anatomic resection.

The findings of our study largely corroborate existing literature. There are no prospective studies comparing the extent of resection in patients with SCLC. The existing observational studies uniformly

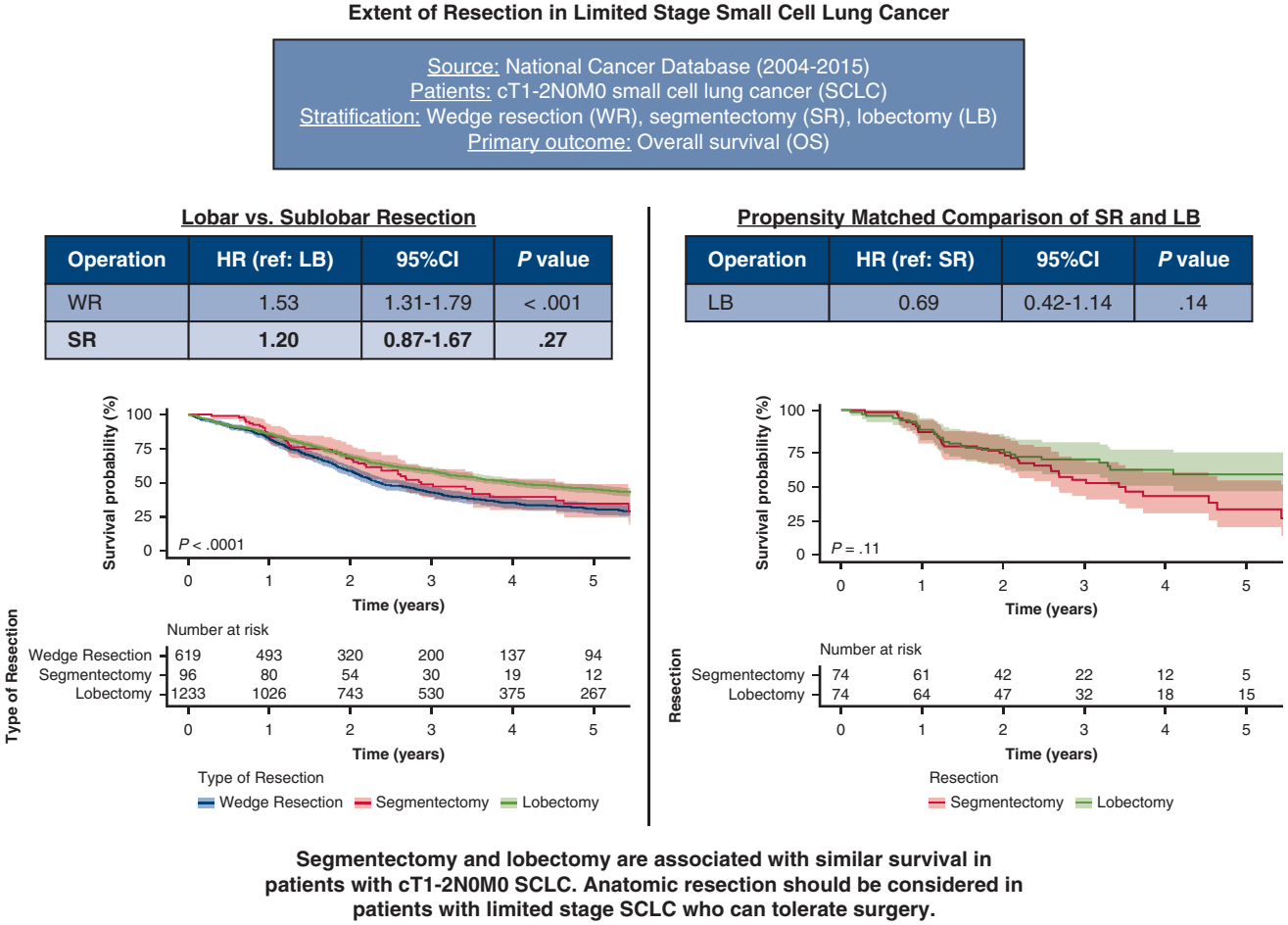


**FIGURE 3.** In this National Cancer Database study, patients receiving SR and LB experienced similar outcomes even after propensity score-matching. Patients receiving a WR had worse survival compared with those receiving lobectomy. Our study suggests that anatomic resection should be considered for patients with limited-stage SCLC. *HR*, Hazard ratio; *95% CI*, 95% confidence interval.

show that lobar resection is associated with improved survival compared with sublobar resection, although all these studies classify WR and SR together, in contrast with our study. Combs and colleagues[17] used the NCDB to examine the outcomes of surgery in patients with stage I-IIIA SCLC and found that sublobar resection was associated with worse adjusted OS compared with lobar resection (HR, 1.39; 95% CI, 1.12-1.81). However, this study examined WR and SR as a single category and included patients with a variety of stages. Three other studies used the Surveillance, Epidemiology and End Results registry to examine outcomes of surgery in SCLC. Weksler and colleagues[18] analyzed patients with early-stage SCLC and found that LB and pneumonectomy were associated with improved unadjusted survival compared with WR. They also found that WR was associated with improved unadjusted survival compared with no resection, although it is unclear what constituted nonsurgical treatment in the latter group. Gu and colleagues[19] studied 491 patients who underwent either sublobar or lobar resection for pT1N0M0 SCLC and found similar unadjusted overall and cancer-specific survival between the groups. In an analysis of 548 patients with T1-2N0M0 SCLC, Liu and coworkers[20] also found that LB was associated with improved survival compared with sublobar resection (HR, 0.54; 95% CI, 0.42-0.68); they also found that segmentectomy was associated with better survival than WR (HR, 0.47; 95% CI, 0.22-0.98).

In contrast with most of the existing literature, our study analyzed WR and SR as separate entities because

of the hypothesis that an anatomic resection may both offer a greater area of resection and offer a better probability of local control by removal of an area with common lymphatic drainage and vascular supply as the primary tumor.[16] Our finding that SR is associated with similar survival as LB suggests that patients who may tolerate an operation but not a LB may still benefit from a segmentectomy if the tumor is amenable to it. Further, with the propagation of minimally invasive techniques, the perioperative outcomes of segementectomy are excellent.[25] However, our finding that patients undergoing WR and definitive, concurrent chemoradiation experience similar survival suggests that a WR alone is not an acceptable surgical strategy compared with nonoperative management. We did find that SR was also associated with similar survival compared with chemoradiation, but this analysis was significantly limited by the small size of the SR cohort and consequent type II error.

Our findings are framed by important limitations. The most significant limitation is selection bias. We do not know why patients were assigned to a particular type of resection. Because the NCDB does not provide data about preoperative pulmonary function, frailty, or malnutrition, we cannot understand the reasons driving treatment assignment in this cohort. Although the NCDB reports the CDCC score for each patient that we used in our multivariable regression, this is a crude measure of overall health. We also do not know when the diagnosis of SCLC was made for patients in the NCDB; the decision to offer surgery and the choice of surgery are contingent on when the patient is known to have SCLC. Similarly, the NCDB does not provide information on how patients were clinically staged. We do not know, for example, how many patients received mediastinal nodal assessment. To mitigate confounding from staging, we performed a subgroup analysis only in patients with proven, pathologic node-negative disease and found that the study's overall findings held true. The NCDB also does not catalogue specific anatomic information about primary tumors, which would be important in distinguishing anatomic rather than patient fitness–related reasons for offering sublobar resection. There is also no information on the type of WR or SR performed (eg, single or composite segmentectomy). The description of postoperative outcomes of patients in this study was also limited by the lack of knowledge of specific complications. The NCDB also does not capture postoperative readmission to centers other than the one where patients were treated. Finally, although our study had a significant number of patients receiving wedge or lobar resection, we had a small number of patients who underwent segmentectomy. This likely affected the internal validity of the study and increased the risk of type II error. We attempted several additional analyses comparing patients undergoing SR and LB, including a propensity score–matched sensitivity analysis to assess the reproducibility of our primary analysis, but these supplemental analyses cannot overcome the intrinsic limitation of the small sample size of patients undergoing SR.

Nonetheless, in this analysis of the NCDB, we found that patients with limited-stage SCLC undergoing segmental and lobar resection experienced similar survival. However, patients who underwent WR had worse survival compared with those receiving LB and similar survival compared with those treated with definitive chemoradiation. LB was also associated with a lower odds of margin-positive resection compared with WR (Figure 3).

## Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

The American College of Surgeons is in a Business Associate Agreement that includes a data use agreement with each of its Commission on Cancer–accredited hospitals. The data used in the study are derived from a deidentified National Cancer Data Base file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology used or the conclusions drawn from these data by the investigators. We are grateful to Hanghang Wang, MD, PhD, for statistical review of this manuscript.

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**Key Words:** small cell lung cancer, sublobar resection, segmentectomy, lobectomy, early stage

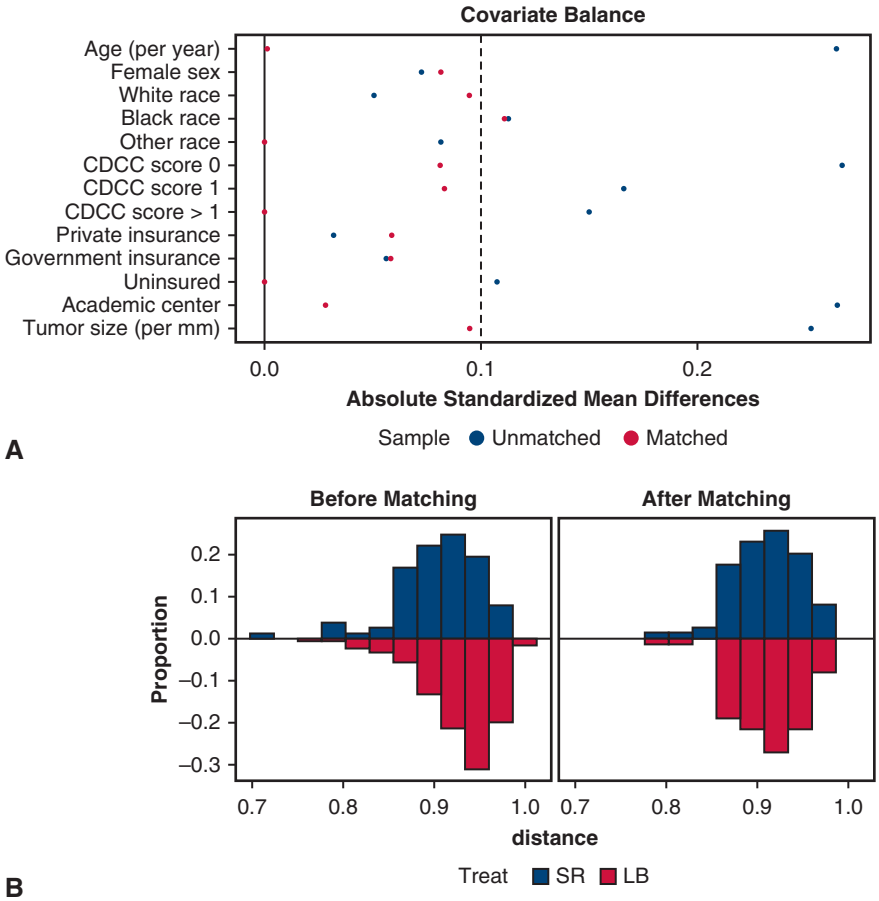


**FIGURE E1.** Balance diagnostics for propensity score-matched patients. A, Love plot demonstrating the spread of standardized mean differences in matched and unmatched patients and B, mirror histograms demonstrating the spread of propensity scores between the 2 treatment groups before and after matching. *CDCC*, Charlson–Deyo Comorbidity Index; *SR*, segmental resection; *LB*, lobectomy.

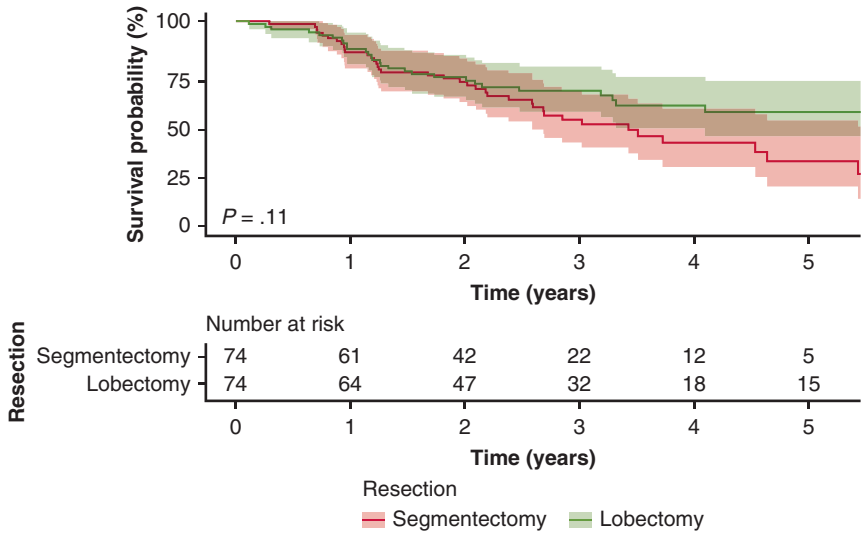


**FIGURE E2.** Kaplan–Meier survival curves for propensity score–matched patients with cT1-2N0M0 small cell lung cancer treated with segmentectomy or lobectomy. The *Y-axis* represents the probability of survival and the *X-axis* the time elapsed from diagnosis in years. The *shaded regions* demonstrate the bounds of the 95% confidence interval. The *P* value represents the result of the log-rank test. Numbers at risk are provided below each figure.

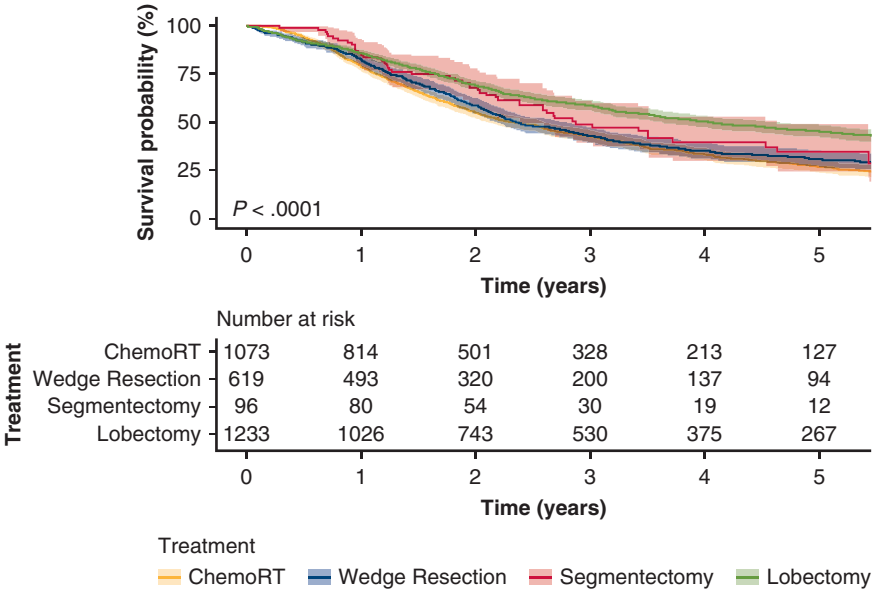


**FIGURE E3.** Kaplan–Meier survival curves for patients with cT1-2N0M0 small cell lung cancer treated with either surgery or definitive, concurrent chemoradiation. The *Y-axis* represents the probability of survival and the *X-axis* the time elapsed from diagnosis in years. The *shaded regions* demonstrate the bounds of the 95% confidence interval. The *P* value represents the result of the log-rank test. Numbers at risk are provided below each figure. *ChemoRT*, Chemoradiation.

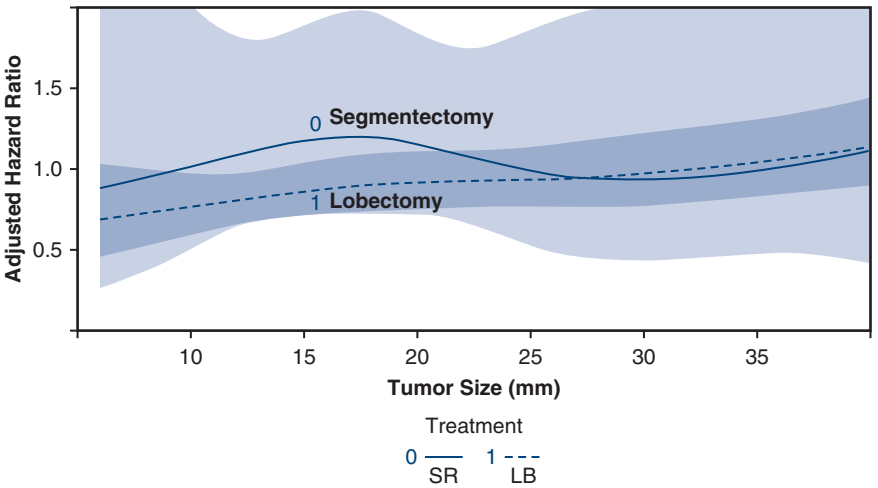


**FIGURE E4.** Graph of the interaction between tumor size and extent of resection in patients undergoing either SR or LB for cT1-2N0M0 small cell lung cancer. The *Y-axis* demonstrates the hazard ratio of a Cox model adjusted for age, sex, race, insurance status, year of diagnosis, Charlson score, treatment at an academic center, and tumor size. The *X-axis* shows tumor size as a continuous variable modeled using restricted cubic splines with 4 prespecified knots. The survival curves for patients undergoing segmentectomy (*bold line*) and lobectomy (*dashed line*) are shown. *Blue areas* represent the bounds of the 95% confidence interval. *SR*, Segmental resection; *LB*, lobectomy.

**TABLE E1. Background characteristics of propensity-matched patients**

| | Segment (n = 74), n (%) | Lobectomy (n = 74), n (%) | Standardized mean difference | *P* value |
|---|---|---|---|---|
| Age, y, median (IQR) | 70 (64-75) | 69 (65-73) | 0.002 | .78 |
| Sex (female) | 43 (58) | 50 (54) | 0.082 | .74 |
| Race | | | | .77 |
| White | 68 (92) | 70 (95) | | |
| Black | 5 (7) | 3 (4) | 0.11 | |
| Other | 1 (1) | 1 (1) | 0.00 | |
| Year of diagnosis, median (IQR) | 2008 (2005-2010) | 2009 (2006-2010) | | .38 |
| CDCC score | | | | .86 |
| 0 | 26 (35) | 23 (31) | | |
| 1 | 34 (46) | 37 (50) | 0.08 | |
| 2+ | 14 (19) | 14 (19) | 0.00 | |
| Insurance status | | | | .85 |
| Private | 21 (28) | 19 (26) | | |
| Government | 53 (72) | 55 (74) | 0.06 | |
| None | 0 (0) | 0 (0) | 0.00 | |
| Academic center | 33 (45) | 32 (43) | 0.03 | 1.00 |
| Tumor size, mm, median (IQR) | 19 (15-25) | 20 (14-30) | 0.09 | .68 |
| Lymph nodes assessed in surgery | 52 (70) | 69 (93) | | .001 |
| Pathologic N status | | | | .001 |
| Unknown | 19 (26) | 2 (3) | | |
| N0 | 46 (62) | 62 (84) | | |
| N1 | 6 (8) | 7 (10) | | |
| N2 | 3 (4) | 3 (4) | | |
| N3 | 0 (0) | 0 (0) | | |

*IQR*, Interquartile range; *CDCC*, Charlson–Deyo Comorbidity Index.

**TABLE E2. Background characteristics and postoperative outcomes of patients with missing survival or covariate data compared with complete cases**

| | Missing covariate data (n = 448), n (%) | Complete cases (n = 1500), n (%) | Missing survival (n = 284), n (%) | *P* value |
|---|---|---|---|---|
| Age, y, median (IQR) | 68 (61-74) | 68 (62-74) | 69 (62-75) | .67 |
| Sex (female) | 242 (54) | 837 (56) | 164 (58) | .61 |
| Race | | | | .83 |
| White | 404 (93) | 1378 (92) | 264 (93) | |
| Black | 22 (5) | 92 (6) | 15 (5) | |
| Other | 7 (2) | 30 (2) | 4 (1) | |
| Year of diagnosis, median (IQR) | 2000 (1999-2001) | 2009 (2006-2010) | 2012 (2012-2012) | <.001 |
| CDCC score | | | | .97 |
| 0 | 10 (50) | 674 (45) | 123 (43) | |
| 1 | 7 (35) | 588 (39) | 116 (41) | |
| 2+ | 3 (15) | 238 (16) | 45 (16) | |
| Insurance status | | | | .01 |
| Private | 145 (34) | 419 (28) | 81 (29) | |
| Government | 275 (65) | 1065 (71) | 194 (69) | |
| None | 2 (1) | 16 (1) | 7 (3) | |
| Facility location | | | | .54 |
| Metro | 340 (80) | 1132 (79) | 231 (83) | |
| Urban | 70 (17) | 266 (19) | 41 (15) | |
| Rural | 13 (3) | 37 (3) | 8 (3) | |
| Academic center | 145 (32) | 510 (34) | 100 (35) | .71 |
| Tumor size, mm, median (IQR) | 20 (15-29) | 20 (14-27) | 20 (15-29) | .005 |
| Surgery | | | | .14 |
| Wedge resection | 158 (35) | 461 (31) | 81 (29) | |
| Segmentectomy | 19 (4) | 77 (5) | 9 (3) | |
| Lobectomy | 271 (61) | 962 (64) | 194 (68) | |
| Lymph nodes assessed in surgery | 293 (65) | 1190 (79) | 242 (85) | <.001 |
| Number of nodes examined, median (IQR) | 3 (0-10) | 5 (1-11) | 7 (2-14) | <.001 |
| Pathologic stage | | | | .11 |
| IA | 183 (64) | 833 (69) | 158 (66) | |
| IB | 37 (13) | 110 (9) | 26 (11) | |
| IIA | 12 (4) | 49 (4) | 15 (6) | |
| IIB | 30 (11) | 131 (11) | 19 (8) | |
| IIIA | 20 (7) | 70 (6) | 21 (9) | |
| IIIB | 0 (0) | 0 (0) | 0 (0) | |
| IIIC | 0 (0) | 0 (0) | 0 (0) | |
| IV | 4 (1) | 7 (1) | 0 (0) | |
| Pathologic N status | | | | <.001 |
| Unknown | 150 (34) | 270 (18) | 33 (12) | |
| N0 | 245 (55) | 1027 (69) | 206 (73) | |
| N1 | 33 (7) | 142 (10) | 23 (8) | |
| N2 | 20 (5) | 61 (4) | 22 (8) | |
| N3 | 0 (0) | 0 (0) | 0 (0) | |
| Positive margins | 23 (6) | 92 (6) | 13 (5) | .56 |
| 30-d readmission | 1 (5) | 54 (4) | 13 (5) | .70 |
| Postoperative length of stay, d, median (IQR) | 5 (4-7) | 6 (4-8) | 5 (3-7) | .004 |
| Postoperative 90-d mortality | 21 (5) | 78 (5) | N/A | N/A |
| Adjuvant chemotherapy | 7 (2) | 704 (47) | 183 (64) | <.001 |

*(Continued)*

**TABLE E2. Continued**

| | Missing covariate data (n = 448), n (%) | Complete cases (n = 1500), n (%) | Missing survival (n = 284), n (%) | *P* value |
|---|---|---|---|---|
| Adjuvant thoracic radiation | 85 (19) | 391 (26) | 70 (25) | .009 |
| Cranial radiation | 8 (2) | 163 (11) | 38 (13) | <.001 |
| Time to last follow-up, median months (IQR) | 32 (17-80) | 27 (15-46) | N/A | N/A |

Patients with missing survival data were excluded from this study, whereas those with missing covariate data were excluded only from regression analyses. *IQR*, Interquartile range; *CDCC*, Charlson–Deyo Comorbidity Index; *N/A*, not available.



**TABLE E3. Multivariable logistic regression model for factors associated with pathologic nodal upstaging in patients with at least 1 node assessed in surgery**

| Variable | Odds ratio (95% confidence interval) | *P* value |
|---|---|---|
| Age (per y) | 1.00 (0.98-1.02) | .93 |
| Female sex (reference: male) | 0.81 (0.60-1.09) | .16 |
| Race (reference: white) | | |
| Black | 1.02 (0.55-1.88) | .95 |
| Year of diagnosis (per y) | 0.94 (0.88-1.00) | .04 |
| Charlson–Deyo Comorbidity Index (reference: 0) | | |
| 1 | 1.07 (0.77-1.47) | .69 |
| 2+ | 0.93 (0.59-1.48) | .76 |
| Insurance status (reference: private) | | |
| Government | 0.83 (0.58-1.19) | .32 |
| None | 0.41 (0.05-3.33) | .40 |
| Academic center | 1.27 (0.93-1.73) | .14 |
| Tumor size (per 10 mm) | 1.01 (1.00-1.03) | .05 |
| Type of surgery (reference: lobectomy) | | |
| Wedge resection | 1.23 (0.84-1.80) | .29 |
| Segmentectomy | 0.89 (0.42-1.88) | .76 |