Outcomes with segmentectomy versus lobectomy in patients with clinical T1cN0M0 non–small cell lung cancer

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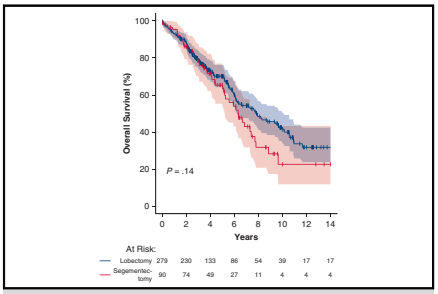
ABSTRACT

Objective: We hypothesize that segmentectomy is associated with similar recurrence-free and overall survival when compared with lobectomy in the setting of patients with clinical T1cNoMo non–small cell lung cancer (NSCLC; >2-3 cm), as defined by the American Joint Committee on Cancer 8th edition staging system.

Methods: We performed a single-institution retrospective study identifying patients undergoing segmentectomy (90) versus lobectomy (279) for T1c NSCLC from January 1, 2003, to December 31, 2016. Univariate, multivariable, and propensity score–weighted analyses were performed to analyze the following endpoints: freedom from recurrence, overall survival, and time to recurrence.

Results: Patients undergoing segmentectomy were older than patients undergoing lobectomy (71.5 vs 68.8, respectively, $P = .02$). There were no differences in incidence of major complications (12.4% vs 11.7%, $P = .85$), hospital length of stay (6.2 vs 7 days, $P = .19$), and mortality at 30 (1.1% vs 1.7%, $P = 1$) and 90 days (2.2% vs 2.3%, $P = 1$). In addition, there were no statistical differences in locoregional (12.2% vs 8.6%, $P = .408$), distant (11.1% vs 13.9%, $P = .716$), or overall recurrence (23.3% vs 22.5%, $P = 1$), as well as 5-year freedom from recurrence (68.6% vs 75.8%, $P = .5$) or 5-year survival (57.8% vs 61.0%, $P = .9$). Propensity score–matched analysis found no differences in overall survival (hazard ratio [HR], 1.034; $P = .764$), recurrence-free survival (HR, 1.168; $P = .1391$), or time to recurrence (HR, 1.053; $P = .7462$).

Conclusions: In the setting of clinical T1cNoMo NSCLC, anatomic segmentectomy was not associated with significant differences in recurrence-free or overall survival at 5 years. Further prospective randomized trials are needed to corroborate the expansion of the role of anatomic segmentectomy to all American Joint Committee on Cancer 8th Edition Stage 1A NSCLC. (J Thorac Cardiovasc Surg 2021;161:1639-48)



Segmentectomy yields similar outcomes compared with lobectomy in clinical T1cNo NSCLC.

CENTRAL MESSAGE

Segmentectomy is associated with similar recurrence-free and overall survival when compared with lobectomy in the setting of patients with AJCC 8th edition clinical T1cNoMo NSCLC (>2-3 cm).

PERSPECTIVE

Clinical T1cNoMo NSCLC is commonly encountered in patients undergoing consideration for anatomic lung resection. In this setting, segmentectomy may offer similar outcomes with minimal oncologic compromise when compared with lobectomy.

See Commentaries on pages 1649 and 1650.

There is considerable controversy regarding the extent of parenchymal resection required to minimize local recurrence while maximizing disease-free survival in the setting of stage I non–small cell lung cancer (NSCLC). Since its

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Abbreviations and Acronyms

CI = confidence interval
COPD = chronic obstructive pulmonary disease
CT = computed tomography
HR = hazard ratio
NSCLC = non–small cell lung cancer
OR = odds ratio
OS = overall survival
RFS = recurrence-free survival
TTR = time to recurrence

first intentional use for small peripheral lung cancers, described by Jensik and colleagues,[1] anatomic segmentectomy has been regarded as a compromised procedure, associated with increased locoregional recurrence risk.[2] Lobectomy remains the gold standard treatment for early-stage NSCLC in patients who can tolerate anatomic resection.[2-5]

Over the last decade, there has been increasing enthusiasm in many surgical groups for the use of anatomic segmentectomy in the setting of clinical stage I NSCLC.[6-8] Anatomic segmentectomy has been found to yield acceptable recurrence and survival rates when the tumor is small (ideally $\leq$2 cm), confined to a single segment, and node negative, if adequate surgical margins can be obtained.[8-11]

There are few data regarding the potential utility of anatomic segmentectomy for tumors larger than 2 cm. With the implementation of the 8th edition American Joint Committee on Cancer Lung Cancer Staging System, stage I tumors are now divided into T1a (<1 cm), T1b (1-2 cm), and T1c ($\geq$2 cm) lesions.[12] Under this new staging system, recently published research by Schuchert and colleagues suggest size to be major factor associated with recurrence following anatomic lung resection for clinical stage I NSCLC.[13] Because of this new distinction, we sought to compare clinical outcomes between anatomic segmentectomy and lobectomy for clinical stage Ic NSCLC using a propensity-matched competing risk model and multivariable parameter assessment.

METHODS

Patients

We performed a retrospective analysis of all patients who underwent anatomic segmentectomy or lobectomy for clinical-stage T1cN0M0 NSCLC at the University of Pittsburgh Medical Center between 2003 and 2016. Patients were staged according to the 8th edition of the American Joint Committee on Cancer staging system. Approval for this study was obtained from the institutional review board of the University of Pittsburgh, which waived the requirement for individual patient consent.

All patients underwent preoperative imaging (computed tomography [CT] scan and/or positron emission tomography/CT). Clinical stage was obtained with a combination of preoperative imaging and staging procedures. All patients with suspected nodal disease underwent preoperative nodal staging in the form of endobronchial ultrasound fine-needle aspiration or mediastinoscopy before resection. Specimens were analyzed intraoperatively with frozen section. Only patients with histology of adenocarcinoma, squamous cell, or large cell carcinoma were included in this study. Pathologic T stage was defined by dedicated thoracic pathologists by measuring the maximum diameter of the invasive component of the tumor. Lepidic portions of the tumor were not included in the final staging. Patients undergoing wedge resection, bi-lobectomy, concurrent lobectomy, and segmentectomy or pneumonectomy were excluded. In addition, patients who received neoadjuvant treatment, exhibited carcinoid or small cell carcinoma histology, had benign disease, synchronous tumors, positive margins, or inadequate preresection nodal staging were excluded. Figure E1 is a consort diagram summarizing the inclusion and exclusion criteria (Video 1).

Operative Technique

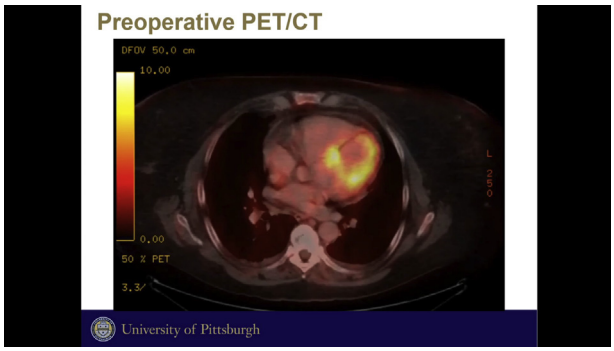
A total of 90 anatomic segmentectomies and 279 lobectomies for clinical T1cN0M0 NSCLC were performed. A video-assisted thoracoscopic surgical approach was performed in the majority of patients (71.0%), thoracotomy in 17.3% of patients, with the remaining 11.7% requiring conversion to open. Criteria favoring the use of segmentectomy included tumors confined to discrete anatomic segmental boundaries, the absence of central bronchial involvement, tumors located in the outer half of the lung parenchyma, and the absence of clinically positive hilar or mediastinal adenopathy.

Anatomic segmental resection was accomplished by the removal of 1 or more pulmonary segments with the goal of an R0 resection. This was accomplished by the individual isolation and division of targeted segmental bronchial and vascular structures. Parenchymal margins of resection incorporated the intersegmental plane and was sometimes extended to the adjacent segment of lung to ensure an adequate resection margin. Systematic hilar and mediastinal nodal sampling or dissection was performed. The distribution of segments and lobes performed is provided in Table E1.

Statistical Analysis

Primary endpoints included overall survival (OS), recurrence-free survival (RFS), and time to recurrence (TTR). OS was defined as the time from surgery to either death or last follow-up. RFS was defined as the time from surgery to recurrence, death, or last follow-up. Locoregional recurrence was defined as any recurrence in the ipsilateral lobar parenchyma, hilum, or mediastinum for patients who underwent anatomic segmentectomy and any hilar or mediastinal recurrence noted for patients who underwent lobectomy, without evidence of distance metastasis for either resection modality. Distant recurrence was defined as the presence of a recurrence in a different anatomic lobe of ipsilateral lung, contralateral mediastinum or lung, or any extra-thoracic metastatic disease. TTR was defined as the time from surgery to recurrence or last follow-up. All patients were clinically followed postoperatively with CT scans at 3- to 6-month intervals for the first 3 years, then yearly thereafter. Secondary endpoints studied were postoperative complications and death. Major complications included myocardial infarction, stroke, pulmonary embolism, pneumonia, respiratory failure, unplanned return to the operating room, and death. All complications were documented based on standard definitions established for the Society of Thoracic Surgeons General Thoracic Surgery Database.

The distributions of continuous variables (age, tumor size, lymph nodes harvested, operative time, estimated blood loss) were analyzed using Wilcoxon or *t* tests, as appropriate, whereas the Fisher exact test was used to compare frequencies of categorical measures (sex, histology, stage, incidence of any and major complications). The log-rank test was applied to product-limit (Kaplan–Meier) survival function estimates to compare lobectomy and segmentectomy cohorts without adjustment for covariates



VIDEO 1. Case presentation of a 64-year-old female patient with an incidental finding of a clinical T1cN0M0 non–small cell lung cancer measuring 2.3 × 2.9 cm in her right upper lobe. Given her compromised functional status and extensive comorbidities, the decision was made to perform an anatomic segmental resection. Video available at: https://www.jtcvs.org/article/S0022-5223(20)30706-6/fulltext.

or propensity score adjustment with respect to overall and RFS, as well as TTR. Multivariable analyses using proportional hazards (Cox) regression models were performed to compare lobectomy and segmentectomy cohorts with respect to overall and RFS as well as TTR, and the incidence of any and major complications. All statistical analyses were done using the R software package (v3.6.1; R Foundation for Statistical Computing, Vienna, Austria).

Propensity Score–Matched Sample Analysis

A propensity score–adjusted competing risk model was employed to assess the risks of death due to events related to the primary cancer and all other events. The propensity scores were generated by logistic regression. The first model of lobectomy versus segmentectomy used the following covariates: age, sex, history of chronic obstructive pulmonary disease (COPD), atrial fibrillation, asthma, coronary artery disease, chronic kidney disease, cerebral vascular accident/transient ischemic attacks, deep-vein thrombosis/pulmonary embolism, diabetes, hyperlipidemia, hypertension, gastroesophageal reflux disease, hypothyroidism, peripheral vascular disease, previous cancers, tumor size, and smoking history. The logistic regression model was then re-run with only the covariates that were significant in the first model at $P = .05$: age, history of COPD, coronary artery disease, and hypothyroidism. The second model was used to estimate the probability of being assigned to segmentectomy (the propensity score) for all 279 lobectomy and 90 segmentectomy patients. Ninety pairs of segmentectomy and lobectomy patients were selected by applying a 5-digit greedy matching algorithm. The cumulative incidence functions were calculated by the method of Fine and Gray, with confidence regions determined by non-parametric bootstrapping the propensity-score matched sample, with 90 patients undergoing segmentectomy and 90 patients undergoing lobectomy in each sample; the P values compare the differences between the lobectomy and segmentectomy functions for each cause of death.

RESULTS

Demographics

Table 1 depicts the demographic and clinical variables distribution between both groups. There was no difference in sex ($P = .81$), smoking status ($P = .68$), laterality ($P = .18$), lobar distribution ($P = .29$), histologic distribution ($P = .98$), surgical approach ($P = .57$), angiolymphatic invasion ($P = .07$), pathologic nodal upstaging ($P = .08$), or tumor size ($P = .07$). In total, there was no statistical difference in the number of patients who were pathologically upstaged in our cohort (37.8% vs 35.8%; $P = .80$). There was a larger percentage of patients in the segmentectomy group with pathologic T upstaging, but that was not found to be statistically significant (28.8% vs 18.9%; $P = .054$). Lastly, the margin/tumor size ratio was greater in the lobectomy group, but that was also not found to be statistically significant (0.89 vs 0.56, $P = .089$).

The segmentectomy group was older compared with the lobectomy group (71.5 vs 68.8; $P = .026$). There was a greater percentage of patients with a preoperative diagnosis of COPD in the segmentectomy group (45.55% vs 28.6%; $P = .004$). This was also reflected in lower preoperative predicted forced expiratory volume in 1 second (73.23% vs 83.83%; $P < .001$) and diffusing capacity of the lungs for carbon monoxide (71.71% vs 76.31%; $P = .028$). Pathologically, patients who underwent segmentectomy had a greater incidence of visceral–pleural invasion (16.6% vs 7.3%; $P = .013$), had closer margins (1.59 cm vs 2.37 cm; $P < .001$), and were associated with fewer lymph nodes harvested (9.55 vs 17.36; $P < .001$; Table 1). The segmentectomy group was found to have fewer N1 (4.7 vs 9.8, $P < .0001$) and N2 (4.5 vs 7.8, $P < .0001$) nodes harvested, compared with the lobectomy group.

Perioperative Outcomes

The median length of hospital stay was 5 days in the segmentectomy group compared with 6.0 in the lobectomy group ($P = .19$). There was a trend toward a decreased incidence of postoperative complications in the segmentectomy group (25.8% vs 37.3%; $P = .06$). Overall incidence of major complications was similar in both groups (12.4% vs 11.7%; $P = .85$; Table 2).

Thirty-day mortality was 1.1% in the segmentectomy group versus 1.7% in the lobectomy group ($P = 1$). Ninety-day mortality was 2.2% in the segmentectomy group compared with 2.1% in the lobectomy group ($P = 1$; Table 2).

Recurrence and Survival

At median follow-up of 4.9 years, Kaplan–Meier estimates of overall 5-year survival (57.8% vs 61.0%; $P = .6$) (Figure 1) and 5-year freedom from recurrence (68.6% vs 75.8%; $P = .5$) (Figure 2) similarly demonstrated no statistically significant differences between groups (Table 2). There was no difference in TTR (131.4 months vs 136.6 months, $P = .8$) (Figures 3 and 4). Among patients who received adjuvant therapy, some

TABLE 1. Patient demographic and clinical characteristics

Characteristic	Lobectomy (n = 279) No. of patients (%)	Segmentectomy (n = 90) No. of patients (%)	*P* value
Age, y, mean (SD)	68.8 (9.1)	71.5 (8.6)	.026
Sex			
Male	132 (47.3)	44 (48.8)	.809
Female	147 (52.6)	46 (51.1)	
Comorbidities			
Hypertension	156 (55.9)	51 (56.7)	1
Diabetes mellitus	40 (14.3)	19 (21.1)	.137
Chronic obstructive pulmonary disease	80 (28.6)	41 (45.5)	.004
Previous cancer	66 (23.7)	25 (27.8)	.482
Cerebral vascular accident	3 (1.1)	3 (3.3)	.153
Chronic kidney disease	4 (1.4)	2 (2.2)	.637
DVT/pulmonary embolism	7 (2.5)	2 (2.2)	1
Gastroesophageal reflux disease	36 (12.9)	12 (13.3)	1
Hypothyroidism	29 (10.4)	2 (2.2)	.015
Peripheral vascular disease	2 (0.7)	0 (0.0)	1
Coronary artery disease	61 (21.9)	14 (15.6)	.229
Asthma	3 (1.1)	2 (2.2)	.599
Hyperlipidemia	97 (34.8)	25 (27.8)	.247
Smoking status			.675
Ever	253 (91.3)	81 (90)	
Never	24 (8.7)	9 (10)	
FEV1, %, mean (SD)	83.84 (22.41)	73.23 (23.87)	<.001
DLCO, %, mean (SD)	76.31 (23.90)	71.71 (37.45)	.028
Histology			
Adenocarcinoma	178 (63.7)	60 (66.6)	.983
Squamous	83 (29.7)	25 (27.7)	
Adenosquamous	11 (3.9)	3 (3.3)	
Large cell carcinoma	7 (2.5)	2 (2.2)	
Laterality			.238
Right	169 (61.0)	47 (52.2)	
Left	109 (39.2)	43 (47.7)	
No. of missing PET scans	13 (4.7)	3 (3.3)	.77
No. undergoing neoadjuvant therapy	1 (0.4)	0 (0.0)	.99
No. undergoing adjuvant therapy	44 (15.8)	11 (12.2)	.50
Surgical approach			.57
VATS	194 (69.5)	68 (75.5)	
Open	50 (17.9)	14 (15.5)	
VATS converted to open	35 (12.5)	8 (8.8)	
Lymph nodes			
Mean no. of lymph nodes harvested (95% CI)	17.7 (16.2,19.1)	9.5 (7.8,11.2)	<.0001
No. of N1 lymph nodes	9.82 (6.84,8.85)	4.65 (3.58,5.71)	<.0001
No. of N2 lymph nodes	7.84 (0.021,0.14)	4.53 (3.34,5.71)	<.0001
Angiolymphatic invasion			.065
N	146 (45.7)	59 (65.5)	
Y	123 (54.2)	31 (34.4)	
Visceral pleural invasion			.013
N	251 (92.6)	75 (83.3)	
Y	20 (7.3)	15 (16.6)	

(Continued)

TABLE 1. Continued

Characteristic	Lobectomy (n = 279) No. of patients (%)	Segmentectomy (n = 90) No. of patients (%)	*P* value
Pathologic upstaging	99 (35.5)	34 (37.8)	.712
Pathologic T stage			.054
1c	226 (81)	64 (71.1)	
2a	53 (18.9)	26 (28.8)	
Pathologic N stage			.08
0	228 (81.7)	79 (87.7)	
1	36 (12.9)	4 (4.4)	
2	11 (3.9)	6 (6.6)	
X	4 (1.4)	1 (1.1)	
Mean surgical margin, cm	2.37	1.59	<.001
Mean margin:tumor size	0.89	0.56	.089
Follow-up time, y	5.0	4.7	.414

SD, Standard deviation; *DVT*, deep vein thrombosis; *FEV1*, forced expiratory volume in 1 second; *DLCO*, diffusing capacity of the lungs for carbon monoxide; *PET*, positron emission tomography; *VATS*, video-assisted thoracoscopic surgery; *CI*, confidence interval.

improvement in median survival was noted, but this was not found to be statistically significant (7.8 vs 5.5 years, $P = .08$).

Multivariable Analysis

On univariate analysis including all patients, distributions of age, COPD, hypothyroidism, and surgical margin were identified as differing between both cohorts. After we adjusted for age and surgical margin as statistically significant covariates, there were no differences in OS (hazard ratio [HR], 1.07; 95% confidence interval [CI], 0.74-1.52; $P = .73$), RFS (HR, 1.19; 95% CI, 0.85-1.66; $P = .32$), or TTR (HR, 1.24; 95% CI, 0.78-1.97; $P = .37$) between both cohorts.

Propensity Score–Matched Sample Analysis

The analysis of deviance of the first logistic regression model on all patients, used to develop the propensity score mode, is presented in Table E2. A second logistic regression model, using variables in the first model significant at $P < .05$, was used to calculate the propensity scores used for matching.

Based on the cohort of the 90 matched pairs, in concordance with the unweighted univariate and multivariable analysis, anatomic segmentectomy was not found to be an independent predictor of OS (HR, 1.23; 95% CI, 0.91-1.82; $P = .17$), RFS (HR, 1.23; 95% CI, 0.82-1.85; $P = .32$), TTR (odds ratio [OR], 0.80; 95% CI, 0.52-1.73; $P = .67$), incidence of major complications (OR, 0.80; 95% CI, 0.305-2.083; $P = .62$), and the incidence of any postoperative complication (OR, 0.52; 95% CI, 0.263-1.033; $P = .06$) (Table E3).

A total of 48 events occurred in the lobectomy group and 42 in the segmentectomy group. Eleven of these deaths were due to the primary cancer in the lobectomy group and 16 in the segmentectomy group. There were 31 and 32 deaths not related to the primary cancer in the lobectomy and segmentectomy groups, respectively. There was no difference in the cumulative incidence of either deaths related to the primary cancer ($P = .30$) (Figure 5) and deaths from all other causes ($P = .41$) (Figure 6).

DISCUSSION

With the advancement in clinical staging techniques and the introduction of CT screening programs, there has been a significant increase in the identification of clinically suspicious nodules suggestive of early-stage NSCLC.[14-20] As we await the final analysis of prospective randomized controlled studies from North America (CALGB 140503) and Japan (JCOG 0802/WJOG 4607L), the role of anatomic segmentectomy in the treatment of NSCLC remains incompletely defined. Recent large, propensity-matched studies suggest that anatomic segmentectomy can achieve similar oncologic outcomes compared with lobectomy in the setting of small, peripheral, clinically node negative NSCLC.[9,21] For larger tumors, lobectomy continues to be considered the standard of care for surgically resectable stage I disease.[2]

Tumor size has long been recognized as one of the primary prognostic factors following resection for stage I NSCLC.[13,21] Jensik and colleagues[1] suggested that anatomic segmentectomy is best reserved for T1 (<3 cm tumors). Larger tumors have an increased likelihood of extending centrally and encroaching on intersegmental planes, thus technically compromising the adequacy of resection margins in such cases.[22] Warren and Faber demonstrated increased locoregional recurrence risk and worse OS when comparing segmentectomy with

TABLE 2. Perioperative outcomes: segmentectomy versus lobectomy

Outcome	Lobectomy (n = 279)		Segmentectomy (n = 90)		*P* value
	Proportion	95% CI	Proportion	95% CI	
Median length of stay, d	6.0		5.0		.19
Any postoperative complication	0.373	0.316-0.432	0.258	0.171-0.362	.055
Major postoperative complication	0.117	0.081-0.161	0.124	0.063-0.210	.85
Mortality					
30 d	0.017	0.0058-0.0414	0.011	0.0003-0.0616	1
90 d	0.021	0.0080-0.0465	0.022	0.0027-0.0797	1
Site of recurrence					.051
None	0.774	0.671-0.787	0.767	0.569-0.784	
Locoregional	0.086	0.003-0.131	0.122	0.028-0.158	
Distant	0.139	0.122-0.221	0.111	0.091-0.265	
5-y freedom from recurrence	0.758	0.697-0.808	0.686	0.584-0.807	.5
5-y overall survival	0.610	0.537-0.681	0.578	0.448-0.701	.6
Time to recurrence, mo, median (95% CI)	136.6 (4.8, not reached)		131.4 (9.3, not yet reached)		.83

CI, Confidence interval.

lobectomy for tumors > 3 cm, although OS was similar for tumors < 3 cm.[23] Okada and associates further analyzed the impact of tumor size by stratifying patient groups into tumors ≤1 cm, 1-2 cm, >2-3 cm, and > 3 cm. Segmentectomy was associated with reduced lung cancer–specific survival at 5 years (81.3 vs 62.9%, $P = .049$) for tumors >3 cm when compared with lobectomy.[6]

Even within the T1 category, discrete differences in recurrence risk and survival are appreciated when comparing tumors ≤2 cm to those between 2 and 3 cm.[22,24,25] This observation has served as the basis for stratifying T1 tumors into 3 size descriptors (T1a-T1c) in the 8th edition of the lung cancer staging system. To date, the majority of studies evaluating the oncologic performance of segmentectomy has compared outcomes with lobectomy for tumors ≤2 cm. Smaller tumors are felt to be less prone to nodal and distant metastasis and are thus more likely to have equivalent outcomes when comparing segmentectomy to lobectomy.[26] Multiple studies over the last 20 years have corroborated this assertion, demonstrating equivalent recurrence and survival for tumors ≤2 cm.[6,11,20,21]

In a recent study analyzing the Surveillance, Epidemiology, and End Results database from 2002 to 2013 involving stage I NSCLC patients (using the 8th edition clinical staging for stage I NSCLC – T1a-c) undergoing lobectomy (n = 17,748) or anatomic segmentectomy (n = 1156), Qu and colleagues identified a modest improvement in survival with lobectomy when comparing outcomes in all patients.[27] However, when these investigators performed a propensity-matched analysis adjusting for potentially confounding covariates, no difference in OS (HR, 1.081; 0.937-1.248; $P = .286$) or lung cancer–specific survival (HR, 1.039; 0.861-1.253; $P = .692$) was noted between segmentectomy and lobectomy. When the outcome of these lobectomy and

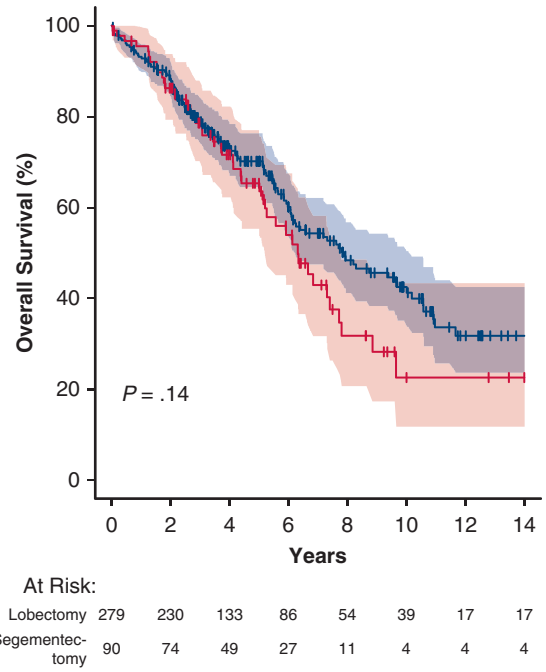


FIGURE 1. Kaplan–Meier curves depicting overall survival in an unmatched cohort of anatomic segmentectomy (*red line*, n = 90) versus lobectomy (*black line*, n = 279) for clinical T1cN0M0 non–small cell lung cancer. 95% confidence intervals are represented by the *shaded areas* (segmentectomy is shown in *red*, lobectomy in *gray*). The difference was not statistically significant in overall survival between both surgical groups ($P = .14$).

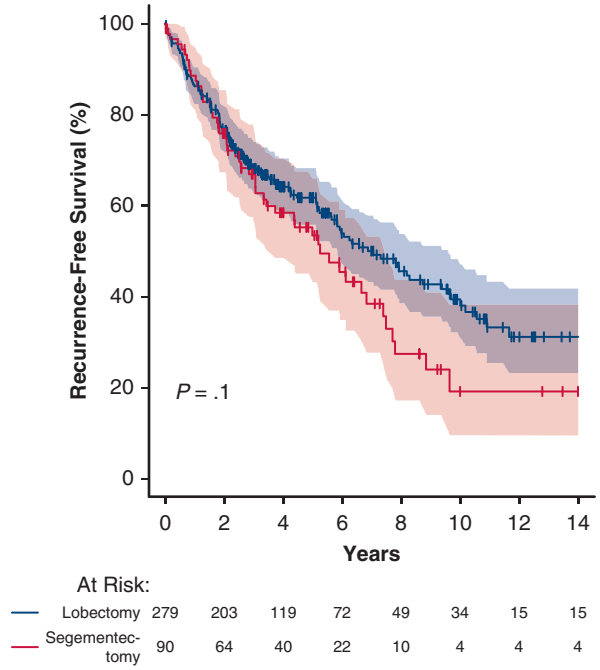


FIGURE 2. Kaplan–Meier curves depicting recurrence-free survival in an unmatched cohort of anatomic segmentectomy (*red line*, n = 90) versus lobectomy (*black line*, n = 279) for clinical T1cN0M0 non–small cell lung cancer. 95% confidence intervals are represented by the *shaded areas* (segmentectomy is shown in *red*, lobectomy in *gray*). The difference was not statistically significant in recurrence-free survival between both surgical groups ($P = .1$).

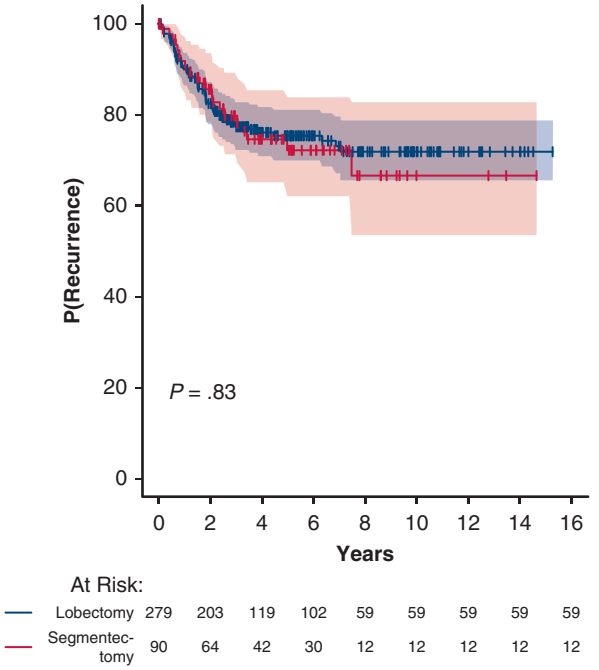


FIGURE 3. Kaplan–Meier curves depicting time to recurrence in an unmatched cohort of anatomic segmentectomy (*red line*, n = 90) versus lobectomy (*black line*, n = 279) for clinical T1cN0M0 non–small cell lung cancer. 95% confidence intervals are represented by the *shaded areas* (segmentectomy is shown in *red*, lobectomy in *gray*). The difference in time to recurrence was not statistically significant ($P = .83$).

segmentectomy patients was further evaluated using equivalent lymph nodes taken at surgery (>3 nodes evaluated—the limit of the database specificity), again, no difference in survival or recurrence pattern was noted.[26] The results of this large propensity score–matched analysis are in agreement with our previously published propensity-matched evaluation of segmentectomy versus lobectomy for stage I NSCLC, which similarly demonstrated no significant difference in recurrence or OS between groups.[9]

As surgical thoracic oncologists, we frequently encounter the clinical-stage 1c (21-30 mm diameter tumor, N0) patient, with impaired cardiopulmonary reserve and a marginal candidate for pulmonary lobectomy, whose tumor would fit anatomic criteria favorable for anatomic segmental resection. Oncologic outcomes have been a primary concern when comparing anatomic segmentectomy versus lobectomy for the surgical treatment of larger (>2 cm) tumors.[28] Several large series have been published including data on the 2- to 3-cm (T1c) subgroup.[9,24,25] In a retrospective comparison, Carr and associates[24] found that segmentectomy was associated with similar recurrence and cancer-specific survival compared with lobectomy for tumors (≥2-3 cm) using 7th Edition staging descriptors (T1b). Okada and associates found no significant difference in survival for tumors >2 to 3 cm when comparing lobectomy and segmentectomy (87.4 vs 84.6% at 5 years, respectively).[6] Similarly, in a comparison of propensity-matched cohorts, Landreneau and colleagues[9] observed no difference in TTR between groups for tumors up to 3 cm in size ($P = .395$).

In this current study, clinical T upstaging was observed in 21.4% of patients (79/369). T upstaging occurred in 28.8% of patients in the segmentectomy group and 18.9% in the lobectomy group ($P = .054$). Nodal upstaging was 15.4% (57/369) in the total cohort and 11.1% in the segmentectomy and 16.8% in the lobectomy group. This is similar to large series currently reported using the National Cancer Database. Bott and colleagues[22] published upstaging in 17.1% in a cohort of more than 50,000 patients with clinical-stage I NSCLC. The CALGB 9761 study also reported upstaging in 28.5% of their cohort in the context of only 12% of participants obtaining a positron emission tomography scan due to the timing of the study. These studies do not accurately reflect a cohort of patients with larger tumors, where a greater rate of upstaging is to be expected.

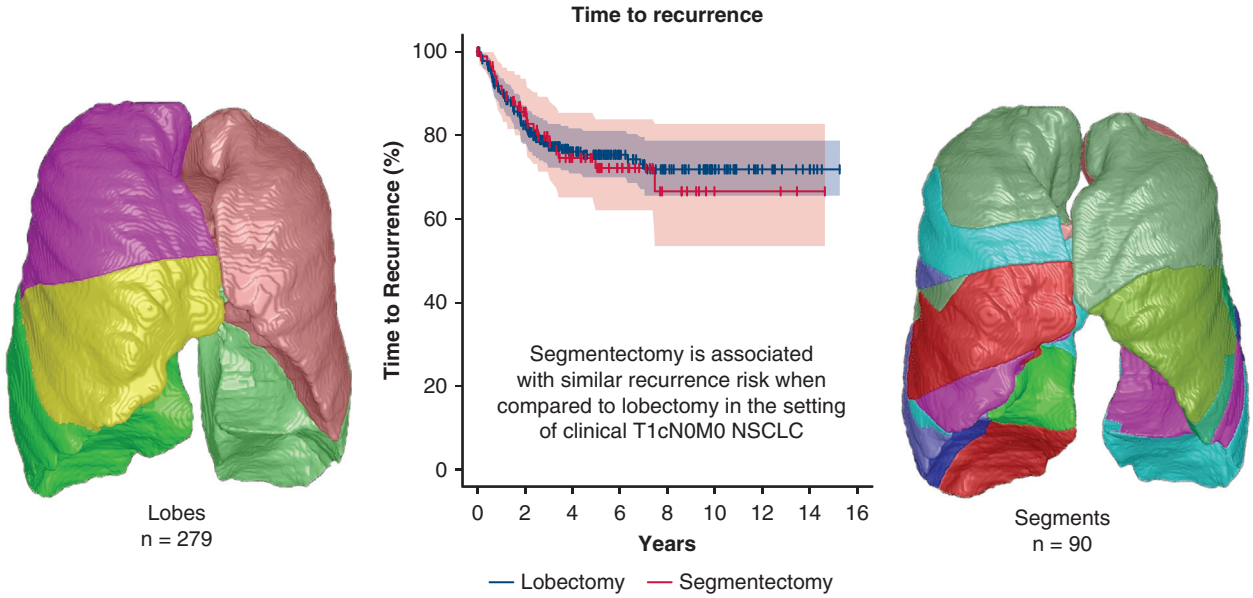


FIGURE 4. Cumulative incidence plot based on the 90 propensity-matched pairs (anatomic segmentectomy [*red*] vs lobectomy [*black*]) showing no difference in the incidence of deaths related to the primary non–small cell lung cancer ($P = .30$). 95% confidence intervals are represented by the *shaded areas* (segmentectomy is shown in *red*, lobectomy in *gray*). *NSCLC*, Non–small cell lung cancer.

Recurrence pattern is also of importance, given that the extent of surgical treatment will be more likely to influence the incidence of locoregional recurrence, more so than distant recurrence.[29] Tumor size of 2 cm or less along with obtaining a 2-cm margin, or margin to tumor size ratio of >1, has been shown to minimize recurrence risk.[6,8,11,14,24,25] Locoregional recurrence following anatomic segmentectomy in the current study was found to be 12.2%, compared with 8.6% ($P = .408$). Although these locoregional recurrence proportions are greater than previously published work with anatomic resection of tumors <2 cm,[8,11] we must take in consideration that these tumors are slightly larger and that local recurrence is increased with lobectomy also as tumor size increases.[25] Furthermore, there was a greater incidence of visceral pleural invasion in patients undergoing segmentectomy. While our study is unable to identify why this occurred in our cohort, we suspect that because surgeons are more inclined to perform a segmental resection in tumors that are more peripheral, these cases are intrinsically deal with tumors that are closer in proximity to the pleura.

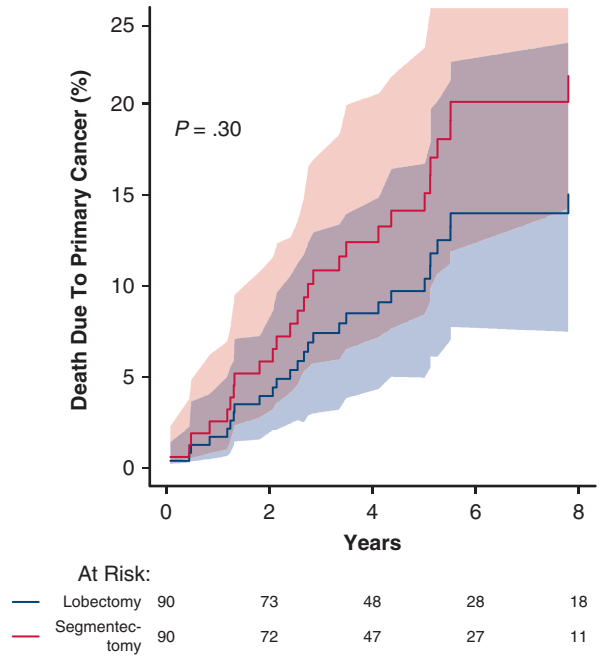


FIGURE 5. Cumulative incidence plot comparing 90 propensity-matched pairs (anatomic segmentectomy [*red*] vs lobectomy [*black*]) showing no difference in the incidence of all deaths not related to the primary non–small cell lung cancer ($P = .41$). 95% confidence intervals are represented by the *shaded areas* (segmentectomy is shown in *red*, lobectomy in *gray*).

When appropriately used and performed properly with respect to anatomic hilar dissection, lymph node assessment, and assurance of clear surgical margins, anatomic segmentectomy can achieve perioperative and oncologic outcomes similar to lobectomy for stage Ia-c NSCLC. In this study, patients undergoing anatomic segmentectomy were found to have significantly decreased pulmonary function tests when compared with the lobectomy group. Despite this difference, segmentectomy was found to have similar morbidity and mortality when compared to lobectomy in the setting of T1c NSCLC. Moreover, on propensity score analysis, anatomic segmentectomy was associated

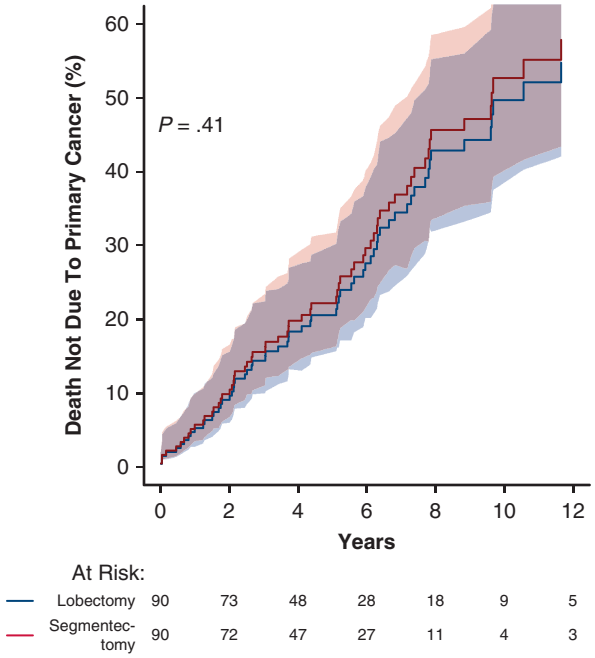


FIGURE 6. Kaplan–Meier curves depicting time to recurrence in an unmatched cohort of anatomic segmentectomy (*red line*, n = 90) versus lobectomy (*black line*, n = 279) for clinical T1cN0M0 non–small cell lung cancer. 95% confidence intervals are represented by the *shaded areas* (segmentectomy is shown in *red*, lobectomy in *gray*). The difference in time to recurrence was not statistically significant ($P = .83$).

with similar incidence of any and major postoperative complications. These results highlight that with the proper patient selection, patients may safely undergo anatomic segmentectomy with the additive benefit of a parenchymal preservation procedure if deemed necessary.[31] From a technical standpoint, anatomic segmentectomy for these larger 2- to 3-cm tumors is safe and feasible. There was an incidence of major complication of 11.7% in the lobectomy group and 12.4% in the segmentectomy group. Similarly, in a large robotic segmentectomy, Cerfolio and colleagues[26] reported a 2% major complication rate (2 pneumonias in first 100 patients). In the current literature, the rates reported by several prospective trials and large database analyses were between 35% and 38% for incidence of any complication with several of these major complications at ~10%.[27-29] In the segmentectomy cohort, there was an open rate of 15.5% with a conversion rate of 8.8% was noted. Similarly, in the lobectomy group, an open approach was used in 17.9% and 12.5% required conversion. However, when stratifying this by years, the majority of these occurred before 2009, with the overwhelming majority completed minimally invasively. This holds true in our lobectomy cohort as well, as we maintain our minimally invasive approach unless it compromises the patient's safety. Therefore, anatomic segmentectomy can be considered a valid surgical alternative to lobectomy in properly selected patients with clinical T1c NSCLC.

Although the retrospective nature of this study is a weakness, our attempts to control for important variables associated with management of stage I NSCLC through multivariable analysis as well as propensity matching of large comparable patient groups appear to aid in substantiating the clinical utility of anatomic segmentectomy for the larger-stage Ic NSCLC. In addition, a primary limitation of this study is sample size due to the relative rarity of clinical T1cN0M0 disease in the segmentectomy group. It is possible a larger cohort comparison may reveal statistically significant differences in several of our primary outcomes. We continue to await the long-term results of the large randomized trials of lobectomy and sublobar resection for stage I disease.

In conclusion, anatomic segmentectomy appears to be associated with similar recurrence risk in the treatment of 8th edition peripheral clinical T1cN0M0 NSCLC when compared with lobectomy. Furthermore, this approach may be associated with a reduced risk in overall perioperative complications. Prospective studies will be required to further validate these observations.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: non–small cell lung cancer, AJCC 8th edition stage T1cN0M0 NSCLC, anatomic segmentectomy, anatomic segmentectomy versus lobectomy, VATS surgery

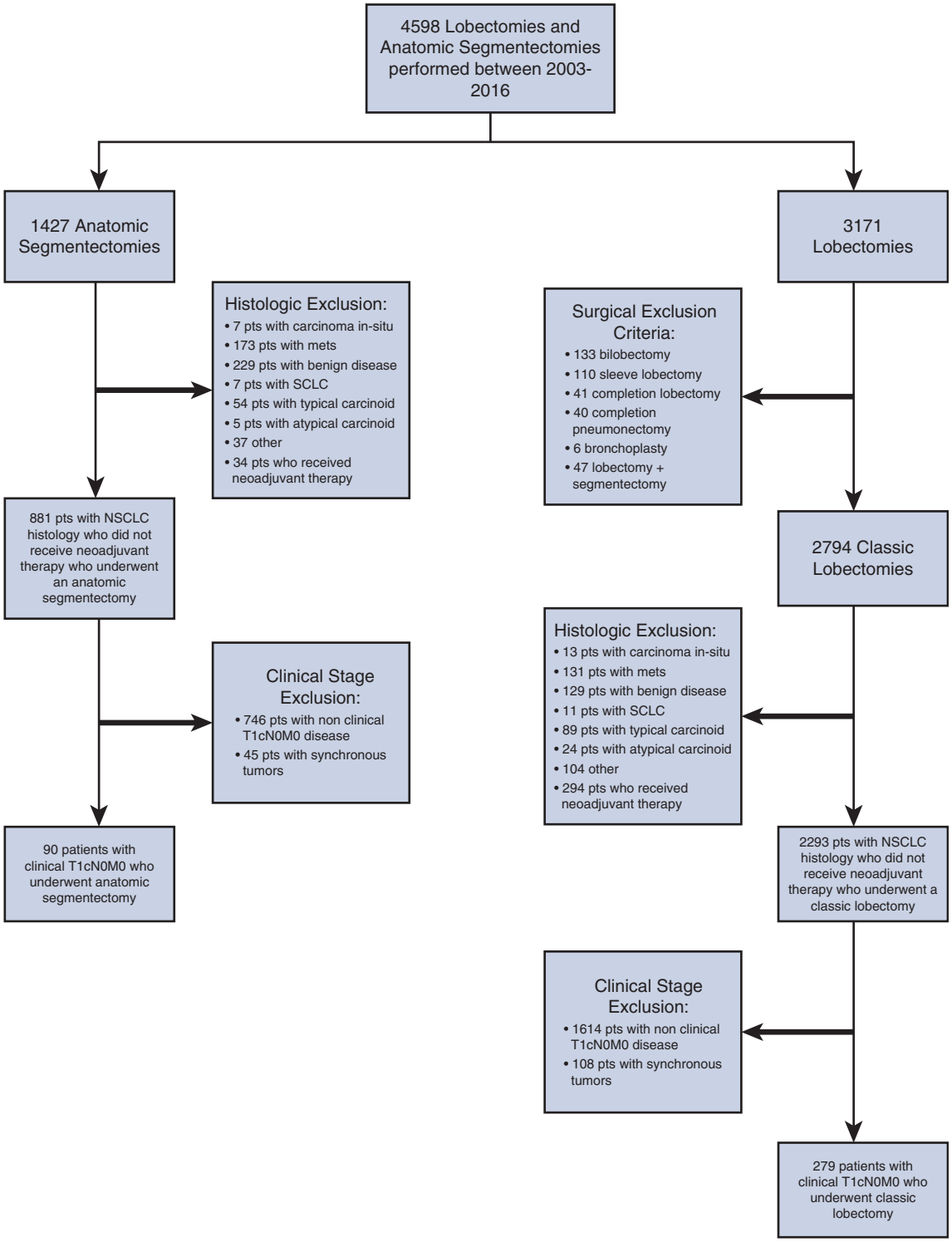

FIGURE E1. This CONSORT (Consolidated Standards Of Reporting Trials) diagram depicts the inclusion and exclusion criteria for this study. Exclusion criteria include those undergoing a greater-order resection (bilobectomy, sleeve/completion/bronchoplasty lobectomy, pneumonectomy), patients without non–small cell lung cancer, and patients with synchronous tumors. Included were 90 patients with clinical T1cN0M0 disease in the anatomic segmentectomy group and 279 patients in the lobectomy group. *NSCLC*, Non–small cell lung cancer; *SCLC*, small cell lung cancer.

TABLE E1. Distribution of anatomic segmentectomy and lobectomy procedures

Anatomic location	Lobectomy (n = 279) No. of patients (%)	Segmentectomy (n = 90) No. of patients (%)
Right upper lobe	98 (35.3)	23 (25.6)
Apical segment		11 (12.2)
Anterior segment		3 (3.3)
Posterior segment		7 (7.8)
Apicoposterior segment		2 (2.2)
Right middle lobe	12 (4.3)	2 (2.2)
Medial segment		1 (1.1)
Lateral segment		1 (1.1)
Right lower lobe	59 (21.2)	22 (24.4)
Superior segment		14 (15.6)
Basilar segment		8 (8.9)
Left upper lobe	69 (24.8)	24 (26.7)
Upper division segment		17 (18.9
Lingula segment		7 (7.8)
Left lower lobe	40 (14.4)	19 (21.1)
Superior segment		10 (11.1)
Basilar segment		9 (10)

TABLE E2. Analysis of deviance of logistic regression model used to select variables determining the propensity score

	Likelihood ratio χ^2	Df	*P* value
Age	7.6020	1	.006
Sex	0.3398	1	.560
Afib	0.0537	1	.817
Chronic obstructive pulmonary disease	8.3300	1	.004
Asthma	0.5907	1	.442
Coronary artery disease	6.1214	1	.013
Chronic kidney disease	0.6873	1	.407
Cerebral vascular accident	2.2476	1	.134
Transient ischemic attack	3.6277	1	.057
Deep vein thrombosis	0.1779	1	.673
Pulmonary embolism	1.7268	1	.189
Diabetes mellitus	3.7840	1	.052
Hyperlipidemia	0.5302	1	.467
Hypertension	0.2094	1	.647
Gastroesophageal reflux disease	0.0050	1	.943
Hypothyroidism	7.6888	1	.006
Peripheral vascular disease	0.3097	1	.578
Previous cancer	1.6845	1	.194
Tumor size	2.5167	1	.112
Smoking history	0.1033	1	.748

Afib, Atrial fibrillation.

TABLE E3. Propensity score–matched analysis

	Hazard ratio (confidence interval)	*P* value
Overall survival	1.23 (0.91-1.82)	.17
Recurrence-free survival	1.23 (0.82-1.85)	.32
Time to recurrence	0.95 (0.52-1.73)	.87
	Odds ratio (confidence interval)	
Incidence of any complication	0.524 (0.263-1.033)	.06
Incidence of major complication	0.804 (0.305-2.083)	.67