Node-Positive Segmentectomy for Non–Small-Cell Lung Cancer: Risk Factors and Outcomes

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Abstract

Segmentectomy for well-selected early stage non–small-cell lung carcinoma (NSCLC) has been shown to have similar survival compared to lobectomy. However, the outcomes of patients with node-positive disease is unknown. In this cohort of 4556 clinical stage I NSCLC patients with node-positive disease, segmentectomy was associated with similar overall survival compared to lobectomy.

Background: Segmentectomy for well-selected early stage non–small-cell lung carcinoma (NSCLC) has been shown to have similar oncologic outcomes and survival to lobectomy. However, these data are based on the presumption that the disease is node negative. Few data exist regarding the risk factors for and the outcomes of patients with disease treated with segmentectomy that is found to be node positive. We sought to determine the risk factors for and outcomes of clinical stage I NSCLC patients who are treated with segmentectomy but are determined to be node positive. **Patients and Methods:** We queried patients with clinical stage I NSCLC $\leq$ 3 cm within the National Cancer Data Base between 2004 and 2014 who were treated with segmentectomy or lobectomy and found to have positive nodes. Kaplan-Meier curves with log-rank tests were used to compare overall survival (OS) between segmentectomy and lobectomy. For comparison only, segmentectomy patients with pathologically node-negative disease were identified to determine predictors of node positivity after segmentectomy via multivariable logistic regression. **Results:** A total of 4556 patients with node-positive disease were identified, comprising 115 segmentectomy patients and 4441 lobectomy patients. Multivariable analysis identified increasing tumor size, squamous-cell histology, and increasing number lymph nodes sampled as significant predictors of node positivity after segmentectomy. There was no difference in OS between segmentectomy and lobectomy, with 3-year OS rates of 66.3% and 68.1%, respectively (P = .723). **Conclusion:** There are discrete risk factors for discovering positive nodes after segmentectomy. Segmentectomy is associated with similar OS compared to lobectomy for clinical stage I NSCLC found to be node positive.

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Introduction

The treatment strategies for early stage lung cancer have evolved dramatically over the past 2 decades. Specifically, sublobar resection, and in particular segmentectomy, have become more widely accepted as safe and oncologically sound operations for non–small-cell lung cancers (NSCLC) that are less than 3 cm in size.[1-4] However, essentially all the data supporting these conclusions require that mediastinal, hilar, and lobar lymph nodes are dissected at the time of operation and evaluated by frozen section.[5] Many practitioners recommend completion lobectomy at this time if the frozen analysis returns positive. However, intraoperative frozen analysis of lymph nodes is often imperfect as a result of sampling errors of collected lymph nodes and the lack of appropriately sampled mediastinal, hilar, lobar, and segmental lymph nodes during segmentectomy. Even in extremely well-selected populations, the rate of node positivity during segmentectomy in early stage NSCLC ranges between 1.5% and 6% in the world's most experienced centers.[6-8]

The proper management of patients with node-positive disease after segmentectomy remains unknown. Some have suggested that a radical segmentectomy where there has been extensive dissection of the lymph nodes may be sufficient local control, though there are few data on this subject.[6] Though it is clear that completion lobectomy after wedge resection of an early stage NSCLC is superior

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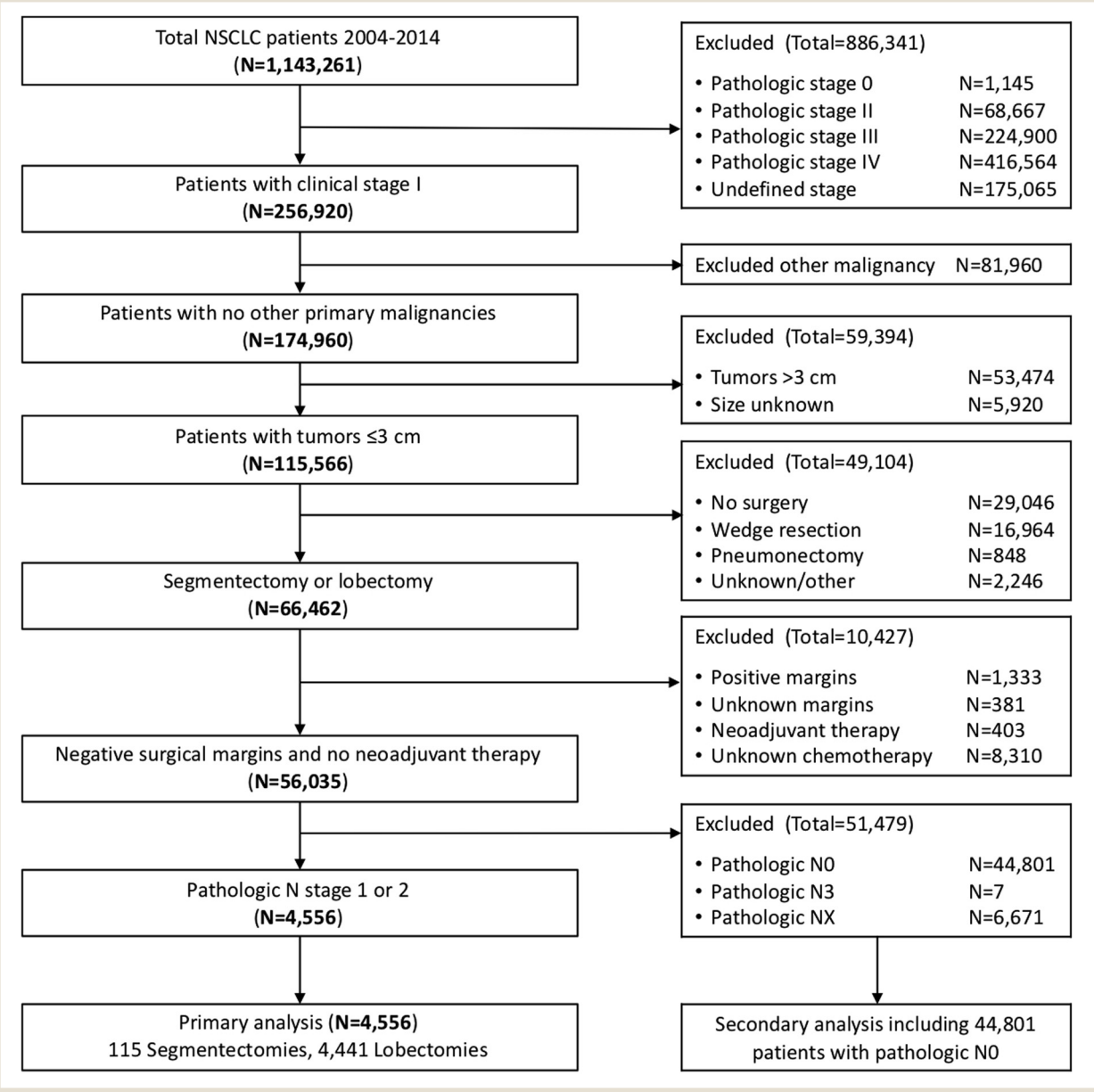
Figure 1 Inclusion Criteria



to wedge resection alone, it is unclear whether these data can be extrapolated to segmentectomies, as they are functionally and oncologically different operations.[9]

The aim of this study was to determine, using a large database, risk factors for node-positive segmentectomy and the survival outcomes for these patients compared to patients with node-positive disease treated with lobectomy.

Patients and Methods

Data Source, Patient Selection, and Variables Studied

The National Cancer Data Base (NCDB) is a nationwide facility-based data set that currently captures 70% of all newly diagnosed cancers in the United States reported annually from approximately 1500 hospitals with Commission on Cancer–accredited cancer programs.[10] The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology we used, or by the conclusions we drew. This project underwent institutional review board approval at the University of Pittsburgh (PRO18050224).

Patients diagnosed between 2004 and 2014 with American Joint Commission on Cancer (AJCC) 6th or 7th edition clinical stage I NSCLC $\leq$ 3 cm treated surgically with segmentectomy or lobectomy who postoperatively were found to have pathologic N stage 1 or 2 were selected for this study. Clinical stage was defined in the NCDB as the AJCC stage determined before treatment. The methods used to determine clinical stage are primarily pretreatment

Table 1 Cohort Characteristics

Characteristic	Segmentectomy	Lobectomy	*P*
Patients, n (%)	115 (2.5)	4441 (97.5)	
Age (y), median (IQR)	68 (62-75)	65 (58-72)	.009[a]
Year of Diagnosis			.421
2004	4 (3.5)	177 (4.0)	
2005	6 (5.2)	176 (4.0)	
2006	3 (2.6)	188 (4.2)	
2007	4 (3.5)	237 (5.3)	
2008	9 (7.8)	355 (8.0)	
2009	11 (9.6)	371 (8.4)	
2010	10 (8.7)	529 (11.9)	
2011	13 (11.3)	522 (11.8)	
2012	15 (13.0)	601 (13.5)	
2013	26 (22.6)	609 (13.7)	
2014	14 (12.2)	676 (15.2)	
Sex			.426
Male	46 (40.0)	1942 (43.7)	
Female	69 (60.0)	2499 (56.3)	
Race			.323
White	94 (81.7)	3778 (85.1)	
Nonwhite	21 (18.3)	663 (14.9)	
Median Income			.684
<$38,000	20 (17.4)	757 (17.1)	
$38,000 to $47,999	27 (23.5)	994 (22.4)	
$48,000 to $62,999	25 (21.7)	1214 (27.3)	
≥$63,000	42 (36.5)	1417 (31.9)	
Unknown	1 (0.87)	59 (1.3)	
Insurance			.313
Private	39 (33.9)	1730 (19.0)	
Medicare	68 (59.1)	2312 (52.0)	
None/other	8 (7.0)	399 (9.0)	
Comorbidity Index			.294
0	61 (56.0)	2324 (52.3)	
1	38 (33.0)	1564 (35.2)	
2	11 (9.6)	426 (9.6)	
≥3	5 (4.4)	127 (2.9)	
Facility Type			.107
Community	5 (4.4)	283 (6.4)	
Comprehensive	40 (34.8)	1977 (44.5)	
Academic	56 (48.7)	1658 (37.3)	
Integrated cancer network	12 (10.4)	479 (10.8)	
Unknown	2 (1.7)	44 (1.0)	
Tumor size (cm), median (IQR)	2.0 (1.5-2.5)	2.2 (1.7-2.5)	.033[a]
Histology			.429
Adenocarcinoma	41 (35.7)	1395 (31.4)	
Squamous-cell carcinoma	53 (46.1)	2319 (52.2)	
Other non–small cell	21 (18.2)	727 (16.4)	
Pathologic N Stage			.001[a]
pN1	56 (48.7)	2860 (64.4)	
pN2	59 (51.3)	1581 (35.6)	

Table 1 Continued

Characteristic	Segmentectomy	Lobectomy	*P*
Lymph nodes sampled, median (IQR)	7 (4-10)	9 (6-14)	<.001[a]
Chemotherapy			.178
No	33 (28.7)	1035 (23.3)	
Yes	82 (71.3)	3406 (76.7)	

Data are presented as n (%) unless otherwise indicated.
Abbreviation: IQR = interquartile range.
[a]Statistically significant.

imaging (computed tomography, positron emission tomography, magnetic resonance imaging, and endoscopic ultrasonography). Pathologic stage was defined in the NCDB as AJCC stage determined after resection from surgical specimen. Patients for whom there were no data on hospital category, chemotherapy, tumor location, or lymph node sampling and those with other malignancies, neoadjuvant therapy, and positive surgical margins were excluded from analysis. As part of a secondary comparison group, segmentectomy patients with pathologic N0 disease were selected. Inclusion criteria is further detailed in Figure 1.

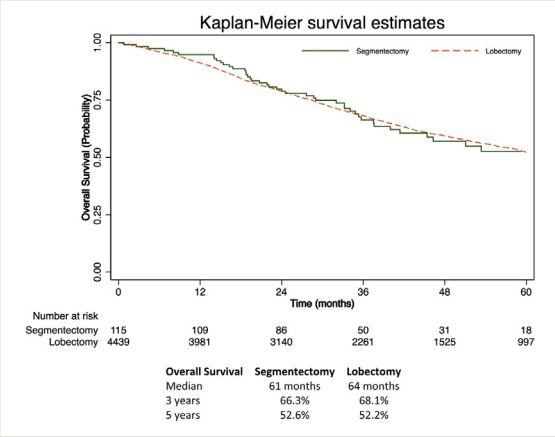
Surgical resection was stratified into 2 categories: segmentectomy and lobectomy. Patient factors studied were age, sex, race, zip code–based income, insurance status, and Charlson-Deyo comorbidity index. Facility characteristics included facility type. Tumor factors included tumor size, histology, and pathologic nodal staging. Treatment variables included lymph node sampling and chemotherapy; chemotherapy included, but did not differentiate, between single-agent and multiagent protocols.

Statistical Analysis

Chi-square and Wilcoxon rank-sum tests were used to compare patient, hospital, and clinical variables between segmentectomy and lobectomy, as indicated. Kaplan-Meier methods with log-rank tests were used to analyze overall survival (OS). Multivariable Cox regression analysis of OS was then performed, adjusting for potential confounding variables that were found to be significantly different between our comparison groups. A secondary analysis was performed using similar inclusion criteria as above but also including segmentectomy patients with pathologic N0 disease, followed by logistic regression modeling to identify factors associated with node positivity after segmentectomy. Stepwise regression was used in multivariable logistic regression modeling.

Statistical analyses were performed by Stata/SE 15.1 statistical software (StataCorp, College Station, TX). All tests were 2 sided, and $P < .05$ was considered statistically significant.

Figure 2 Kaplan-Meier Survival Curves for Segmentectomy Versus Lobectomy ($P = .723$)



Results

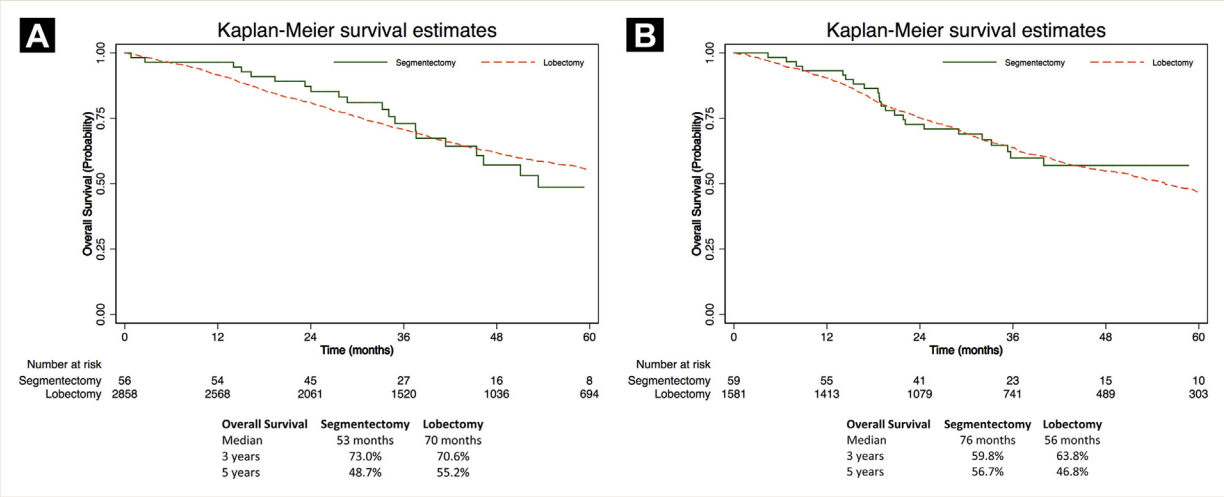
Segmentectomy Versus Lobectomy

We identified 4556 patients who met the primary inclusion criteria; 115 (2.5%) received segmentectomy and 4441 (97.5%) received lobectomy. Patients receiving segmentectomy had greater median age (68 vs. 65 years, $P = .009$) and had smaller median tumor size (2.0 vs. 2.2 cm, $P = .033$). The disease of 51.3% of the upstaged segmentectomy patients was upstaged to N2 disease, while the disease of only 35.6% of the upstaged lobectomy patients was upstaged to N2 disease. ($P = .001$). Segmentectomy patients also had fewer median lymph nodes sampled (7 vs. 9, $P < .001$) than those receiving lobectomy. There was no difference in rates of adjuvant chemotherapy (71.3% vs. 76.7%, $P = .178$). Table 1 lists the patient, facility, and tumor characteristics of the cohort.

Overall Survival Analysis

On Kaplan-Meier analysis, there was no difference in OS between node-positive segmentectomy patients and node-positive lobectomy patients, with the two groups having 3-year OS of 66.3% for segmentectomy compared to 68.1% for lobectomy ($P = .723$) (Figure 2). Five-year OS was 52.6% and 52.2% for segmentectomy and lobectomy, respectively. Subgroup analyses were separately performed for patients with pathologic N1 and N2 disease. There was no difference in OS between segmentectomy and lobectomy for patients that had pathologic N1 (Figure 3A, $P = .964$) or N2 (Figure 3B, $P = .449$) disease, although survival for N2-positive patients was worse than N1-positive patients regardless of resection type. Multivariable Cox regression analysis adjusting for age, tumor size, pathologic N stage, and lymph nodes resected demonstrated no significant difference in OS when comparing segmentectomy to lobectomy (hazard ratio = 0.91; 95% confidence interval, 0.67-1.23; $P = .562$).

Figure 3 Kaplan-Meier Survival Curves for Segmentectomy Versus Lobectomy in (A) pN1 Patients ($P = .964$) and (B) pN2 Patients ($P = .449$)



Identifying Predictors of Node-Positive Disease After Segmentectomy

A secondary analysis of patients with and without nodal disease was performed. Overall, there were 2370 segmentectomy patients (95.4%) with pathologic N0 disease and 115 (4.6%) with pathologic N1/N2 disease. For lobectomy, there were 49,357 patients (90.5%) with pathologic N0 disease and 4441 (9.5%) with pathologic N1/N2 disease. Thus, lobectomy was associated with higher rates of nodal upstaging (4.6% vs. 9.5%, $P < .001$).

Multivariable logistic regression analysis was performed to identify predictors of node-positive disease after segmentectomy. This analysis demonstrated that increasing tumor size, squamous-cell histology, and increasing number of lymph nodes sampled were significant predictors of node-positive disease after segmentectomy for clinical stage I NSCLC (Table 2).

Discussion

As segmentectomy continues to gain favor as a valid approach for early stage NSCLC, it is important that the limitations of this approach are understood. Current practice is that for well-selected patients with NSCLC, segmentectomy with intraoperative frozen analysis of mediastinal, hilar, lobar, and segmental lymph nodes is performed, followed by completion lobectomy if frozen analysis reveals node-positive disease. However, the risk factors for node-positive disease during segmentectomy are unclear. Here we have found that rate of positive nodal upstaging to be 4.6%. However, it is critical to remember that these are patients who left the operating room only receiving segmentectomy, and not those who were converted to completion lobectomy in the operating room. Nomori et al[6] found that in 275 segmentectomy patients their rate of intraoperative node-positive disease was 6% though only 2% left the operating room without completion lobectomy. In the ongoing CALGB 140503 trial comparing sublobar resection and lobectomy for early NSCLC, 6.4% of the NSCLC patients were not randomized because of the presence of nodal disease.[7] We determined that the risk factors for nodal positivity after segmentectomy were size, squamous-cell histology, and the number of lymph nodes sampled.

Many studies in node-negative tumors have suggested that the oncologic outcomes for well-selected patients between segmentectomy and lobectomy are equal.[2,11,12] However, few data exist for node-positive tumors. On unadjusted analysis, we found no difference in survival between upstaged node-positive segmentectomies and lobectomies. This finding was validated by multivariable analysis. The percentage of upstaged segmentectomy patients with disease upstaged to N2 was higher than that of lobectomy patients, as lobectomy patients had far more N1-level lymph nodes removed and were more likely to be N1 upstaged. Ultimately, it may be that the impact on survival of simply having node-positive disease is greater than the curative value of resecting the rest of the lobe, lymph nodes, and lymphatic tracts. This assertion is somewhat tangentially supported by the ACSOG Z0030 trial, which showed systematic lymph node sampling to be equivalent to lymph node dissection.[13] Also, the a priori bias of performing a segmentectomy would likely favor worse OS as a result of the segmentectomy patients. However, this was not the case, even though the segmentectomy patients were almost 3 years older on average than lobectomy patients, and even though there exists the potential for segmentectomy patients to have worse lung function than the lobectomy patients; this unfortunately is not captured by the NCDB.

However, the interpretation of these results should be taken with caution. We would not suggest on the basis of these data that segmentectomy should be the therapy of choice for all small tumors. Specifically, we looked at patients with disease that was upstaged rather than those known to have clinically node-positive disease up

Table 2 Multivariable Logistic Regression Identifying Predictors of Node Positivity (pN1/2) After Segmentectomy for All Clinical Stage I N0 Patients (N = 2485)

	Univariate		Multivariate	
Characteristic	**OR (95% CI)**	***P***	**OR (95% CI)**	***P***
Age	0.86 (0.71-1.04)	.106	—	—
Sex				
Male	1 (ref)		—	—
Female	0.91 (0.61-1.33)	.623	—	—
Race				
White	1 (ref)		—	—
Nonwhite	1.55 (0.95-2.52)	.080	—	—
Median Income				
<$38,000	1 (ref)		—	—
$38,000 to $47,999	1.16 (0.64-2.11)	.611	—	—
$48,000 to $62,999	0.83 (0.46-1.52)	.557	—	—
≥$63,000	0.85 (0.49-1.47)	.566	—	—
Insurance				
Private	1 (ref)		—	—
Medicare	0.71 (0.47-1.06)	.091	—	—
None/other	0.93 (0.43-2.04)	.864	—	—
Comorbidity Index				
0	1 (ref)		—	—
1	0.69 (0.46-1.05)	.084	—	—
2	0.53 (0.28-1.02)	.060	—	—
≥3	0.91 (0.36-2.31)	.840	—	—
Facility Type				
Community	1 (ref)		—	—
Comprehensive	0.81 (0.31-2.10)	.665	—	—
Academic	1.00 (0.39-2.56)	.995	—	—
Integrated cancer network	1.06 (0.36-3.10)	.911	—	—
Tumor size (cm)	1.89 (1.39-2.58)	<.001[a]	2.13 (1.53-2.95)	<.001[a]
Histology				
Adenocarcinoma	1 (ref)		1 (ref)	
Squamous-cell carcinoma	1.56 (1.01-2.41)	.047[a]	1.64 (1.05-2.54)	.029[a]
Other NSCLC	1.13 (0.63-2.02)	.668	1.22 (0.68-2.18)	.497
Lymph nodes sampled	1.04 (1.02-1.07)	.001[a]	1.04 (1.02-1.07)	<.001[a]

Abbreviations: CI = confidence interval; NSCLC = non–small-cell lung cancer; OR = odds ratio.
[a]Statistically significant.

front, which may represent a different, more aggressive tumor biology. It is likely that these patients did not have enlarged lymph nodes on preoperative computed tomography and were not positron emission tomography active, which introduces bias as to how they were treated. However, these data do suggest that if a well-selected patient treated with segmentectomy is found to be node positive, there may not be a compulsory reason to perform completion lobectomy. Especially in frail patients or those with limited cardiopulmonary reserve, completion lobectomy may expose the patient to unnecessary risk. Clearly chemotherapy is provided at a high rate to these patients, as demonstrated by such use in > 70% in this population. However, we did not evaluate the effectiveness of this subpopulation because of the heterogeneity of chemotherapeutic agents and the use the postoperative radiotherapy.

One final consideration from our results is that patients who received segmentectomy were less likely to be identified with node-positive disease (4.6%) compared to patients who received lobectomy (9.5%). Additionally, we found that node-positive segmentectomy patients had 2 fewer nodes removed on average compared to lobectomy, and the number of lymph nodes sampled was a significant predictor of upstaging for segmentectomy. Previous NCDB studies have demonstrated that rates of upstaging can be as high as 11% for patients with N0 disease undergoing lobectomy[14] and that extent of lymph node dissection independently predicts survival.[15] In early stage NSCLC patients, significant consideration should be given to performing adequate lymph node sampling during segmentectomy, with the knowledge that there is an intrinsic increase in lymph node collection with lobectomy.

This study has several limitations. It is retrospective, and as such is subject to all the biases intrinsic to this study type. Also, we were unable to identify patients who were found to be node positive by intraoperative frozen section analysis and converted to completion lobectomy. As a result of the way the data are available in the NCDB, these patients would be coded as receiving lobectomy. Additionally, the NCDB does not clarify how patients are determined to have nodal disease (by frozen or permanent section). Last, we do not have the ability to access the patient pulmonary function tests and other risk factors for mortality that could better help us analyze the data.

The ongoing randomized controlled study comparing sublobar resection to lobectomy for NSCLC < 2 cm may shed more light on this topic.[16] However, patients with pathologically positive lymph nodes at the time of operation are being excluded; thus, the information garnered on this topic will likely be generated by post hoc analysis. As our understanding of the biology of NSCLC improves, optimal therapies will need to be interrogated. Specifically, it is imperative that surgeons provide the optimal therapy while exposing the patient to minimal risk.

Clinical Practice Points

- The treatment strategies for early stage lung cancer have evolved dramatically over the past 2 decades. Specifically, sublobar resection, and in particular segmentectomy, have become more widely accepted as safe and oncologically sound operations for NSCLC that are < 2 to 3 cm and node negative.
- The risk factors and outcomes of patients with node-positive disease after segmentectomy remains unknown.
- Though completion lobectomy after wedge resection of an early stage NSCLC is superior to wedge resection alone, it is unclear whether these data can be extrapolated to segmentectomies, as they are functionally and oncologically different operations.
- The aim of this study was to compare the survival outcomes of segmentectomy and lobectomy for clinically early stage NSCLC found to be node positive.
- We queried the NCDB to identify all patients diagnosed between 2004 and 2014 with clinical stage I NSCLC ≤ 3 cm treated surgically with segmentectomy or lobectomy who postoperatively were found to have nodal disease; 4556 patients were included, with 115 patients treated with segmentectomy and 4441 treated with lobectomy.
- On Kaplan-Meier analysis, there was no difference in OS between the two groups, with 3-year survival of 66.3% for segmentectomy compared to 68.1% for lobectomy ($P = .723$).
- These data suggest, but do not prove, that if a well-selected patient treated with segmentectomy is found to be node positive, there may be no compulsory reason to perform completion lobectomy.

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Disclosure

The authors have stated that they have no conflict of interest.

References

1. Schuchert MJ, Abbas G, Awais O, et al. Anatomic segmentectomy for the solitary pulmonary nodule and early-stage lung cancer. *Ann Thorac Surg* 2012; 93:1780-5.
2. Landreneau RJ, Normolle DP, Christie NA, et al. Recurrence and survival outcomes after anatomic segmentectomy versus lobectomy for clinical stage I non−small-cell lung cancer: a propensity-matched analysis. *J Clin Oncol* 2014; 32: 2449-55.
3. Nomori H, Mori T, Ikeda K, Yoshimoto K, Iyama K, Suzuki M. Segmentectomy for selected cT1N0M0 non−small cell lung cancer: a prospective study at a single institute. *J Thorac Cardiovasc Surg* 2012; 144:87-93.
4. Tsutani Y, Miyata Y, Nakayama H, et al. Appropriate sublobar resection choice for ground glass opacity-dominant clinical stage IA lung adenocarcinoma: wedge resection or segmentectomy. *Chest* 2014; 145:66-71.
5. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non−small cell lung cancer. Lung Cancer Study Group. *Ann Thorac Surg* 1995; 60:615-22.
6. Nomori H, Mori T, Izumi Y, Kohno M, Yoshimoto K, Suzuki M. Is completion lobectomy merited for unanticipated nodal metastases after radical segmentectomy for cT1 N0 M0/pN1-2 non−small cell lung cancer? *J Thorac Cardiovasc Surg* 2012; 143:820-4.
7. Kohman LJ, Gu L, Altorki N, et al. Biopsy first: lessons learned from Cancer and Leukemia Group B (CALGB) 140503. *J Thorac Cardiovasc Surg* 2017; 153:1592-7.
8. Omasa M, Date H, Takamochi K, Suzuki K, Miyata Y, Okada M. Completion lobectomy after radical segmentectomy for pulmonary malignancies. *Asian Cardiovasc Thorac Ann* 2016; 24:450-4.
9. Wang Y, Wang R, Zheng D, et al. The indication of completion lobectomy for lung adenocarcinoma </= 3 cm after wedge resection during surgical operation. *J Cancer Res Clin Oncol* 2017; 143:2095-104.
10. Bilimoria KY, Stewart AK, Winchester DP, Ko CY. The National Cancer Data Base: a powerful initiative to improve cancer care in the United States. *Ann Surg Oncol* 2008; 15:683-90.
11. Schuchert MJ, Pettiford BL, Keeley S, et al. Anatomic segmentectomy in the treatment of stage I non−small cell lung cancer. *Ann Thorac Surg* 2007; 84:926-32.
12. Schuchert MJ, Kilic A, Pennathur A, et al. Oncologic outcomes after surgical resection of subcentimeter non−small cell lung cancer. *Ann Thorac Surg* 2011; 91:1681-7.
13. Darling GE, Allen MS, Decker PA, et al. Randomized trial of mediastinal lymph node sampling versus complete lymphadenectomy during pulmonary resection in the patient with N0 or N1 (less than hilar) non−small cell carcinoma: results of the American College of Surgery Oncology Group Z0030 Trial. *J Thorac Cardiovasc Surg* 2011; 141:662-70.
14. Gulack BC, Yang CF, Speicher PJ, et al. The impact of tumor size on the association of the extent of lymph node resection and survival in clinical stage I non−small cell lung cancer. *Lung Cancer* 2015; 90:554-60.
15. Samayoa AX, Pezzi TA, Pezzi CM, et al. Rationale for a minimum number of lymph nodes removed with non−small cell lung cancer resection: correlating the number of nodes removed with survival in 98,970 patients. *Ann Surg Oncol* 2016; 23:1005-11.
16. Altorki NK, Wang X, Wigle D, et al. Perioperative mortality and morbidity after sublobar versus lobar resection for early-stage non−small-cell lung cancer: post-hoc analysis of an international, randomised, phase 3 trial (CALGB/Alliance 140503). *Lancet Respir Med* 2018; 6:915-24.