Treatment of stage I non–small cell lung cancer: What’s trending?

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ABSTRACT

Objectives: Stage I non–small cell lung cancer traditionally is treated with lobectomy. Sublobar resection and stereotactic body radiation therapy provide alternative treatments for higher-risk groups. The purpose of this study was to determine the national treatment trends for stage I lung cancer.

Methods: The National Cancer Database was queried for patients with clinical stage I non–small cell lung cancer between 1998 and 2012. Patients were compared across treatment groups, and trends in treatment and disease were evaluated over the 15-year time period.

Results: The National Cancer Database contained 369,931 patients with clinical stage I non–small cell lung cancer. After removing patients who received chemotherapy as a first course of treatment and patients with pathologic stage IV, 357,490 patients were analyzed. The first recorded cases of stereotactic body radiation therapy are in 2003 and rapidly increased to 6.6% (2063) of all patients treated in 2012. The number of diagnoses of stage I non–small cell lung cancer steadily increased over the 15-year period, whereas the rate of lobectomy decreased from 55% in 1998 to 50% in 2012 ($P < .001$). Most of the decrease in lobectomy can be explained by the increase in the rate of sublobar resection from 12% to 17% ($P < .001$). The percentage of untreated patients remained stable at approximately 7% ($P = .283$).

Conclusions: Although the number of stage I non–small cell lung cancer cases continues to increase, lobectomy rates are decreasing while sublobar resection and stereotactic body radiation therapy rates are increasing. Although the increasing popularity of alternative therapies to lobectomy for treatment of stage I non–small cell lung cancer should allow more patients to undergo treatment, we did not observe this trend in the data. (*J Thorac Cardiovasc Surg* 2017;154:1080-7)

SBRT was introduced in 2003, and its use has been increasing exponentially.

Central Message

The rates of lobectomy and pneumonectomy for patients with stage I NSCLC have decreased, whereas SLR and SBRT have become more common.

Perspective

The results of this study demonstrate that the rate of surgery, particularly lobectomy, has decreased from 1998 to 2012, whereas the rates of SLR and stereotactic body radiation have increased and offset the decrease in lobectomy. Untreated patients encompass 7% of the cohort and have remained unchanged over the 15-year study period.

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The gold standard for treatment of stage I non–small cell lung cancer (NSCLC) is lobectomy and systematic mediastinal lymph node dissection (MLND).¹ Reported rates of survival after surgical resection for stage I NSCLC vary from 60% to 80% in the literature.¹⁻³ Unfortunately, up to 25% of these “resectable” patients are not offered

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Abbreviations and Acronyms

MLND	= mediastinal lymph node dissection
NCDB	= National Cancer Database
NSCLC	= non–small cell lung cancer
SBRT	= stereotactic body radiation therapy
SLR	= sublobar resection

lobectomy because of medical comorbidities, precluding safe resection.⁴ These high-risk patients subsequently may be offered a variety of other treatment options, including sublobar resection (SLR) (wedge resection or segmentectomy), radiofrequency ablation, or stereotactic body radiotherapy (SBRT). Not surprisingly, high-risk patients treated with these alternative therapies have lower 5-year survival reported in the literature.^{5,6} Of note, the definition of “medically inoperable” or “high-risk” patients is not well delineated.²

The purpose of this study was to describe national treatment and disease trends for clinical stage I NSCLC over the 15-year period from 1998 to 2012 using a large national cancer database. We hypothesized that the frequency of SBRT had increased over this time frame and that the percentage of patients receiving no treatment had decreased because of alternative therapies available for “higher-risk” patients.

MATERIALS AND METHODS

The National Cancer Database (NCDB) is a clinical oncology database from more than 1500 facilities accredited by the Commission On Cancer. It is estimated that 70% of all malignancies in the United States are captured by the NCDB. Deidentified data were obtained from the NCDB Participant User File for all patients with NSCLC between the years 1998 and 2012. Exemption was obtained from the University of Virginia Institutional Review Board because all of the data are deidentified and contain no protected health information.

Patients with reported clinical stage I NSCLC were eligible for inclusion in the current study. Patients were excluded if they did not have clinical stage I or they received chemotherapy as a first course of treatment. Patients were further excluded if they were coded as pathologic stage IV.

Patients with stage I NSCLC were further stratified on the basis of first treatment received: surgical or nonsurgical. Surgical treatment options were categorized as lobectomy, SLR (wedge resection or segmentectomy), or pneumonectomy. Nonsurgical treatments included stereotactic body radiation therapy (SBRT), conventional radiation, and no treatment. Patients were coded as having received SBRT if the treatment modality was indicated to be stereotactic radiosurgery, the regional radiation dose was between 3000 and 10,000 cGy, and the course of radiation ran at most 14 days. Patients were coded as having received conventional radiation if they were indicated to have received radiation with treatment modality other than stereotactic radiosurgery, they received a regional dose between 5000 and 10,000 cGy, and their course of treatment lasted 21 to 120 days. Patients with unknown treatment order, with missing data for whether or not treatment was given, or who received radiation or surgery (eg, local treatment) not conforming to the described categories were placed in an “unknown/other” category.

Variables that were abstracted for this study include age, race, sex, Charlson–Deyo Comorbidity Score (coded as 0, 1, or 2), insurance status

(Medicaid, Medicare, private, and unknown/uninsured), tumor histology (adenocarcinoma, large cell/other, and squamous cell cancers), and size in millimeters. Demographic and clinical information are shown for the overall cohort. In addition, we present time trends for treatment, tumor size, histology, regional nodes examined, and rates of pathologic upstaging.

Continuous variable comparisons were made using the Kruskal–Wallis test and are described as means or medians, as appropriate. Trends in continuous variables were assessed using weighted least squares. Categorical variables were analyzed using the chi-square test and the chi-square test for trend. Trends are illustrated using time series plots showing treatment rates by year. Analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC) and R 3.3.2 (R Core Team, Vienna, Austria).

RESULTS

Clinical Staging Information

Between 1998 and 2012, the NCDB captured 1,478,751 patients with a diagnosis of NSCLC. Some 25% of these patients (369,931) were diagnosed with clinical stage 1, and the remainder had stages 2 (5%), 3 (21%), 4 (34%), and missing (15%).

Of the 369,931 patients with clinical stage 1 NSCLC, we excluded 11,318 who received chemotherapy as a first treatment and 1123 who were ultimately pathologically upstaged to stage IV NSCLC, leaving 357,490 patients included in the analysis.

Patient Demographics and Treatment Modalities

Patient demographics overall and divided by first treatment are shown in Table 1. Patients had a median age of 70 years (interquartile range, 63–77), 48% were male, and 90% were white. Some 53% of patients had a Charlson score of 0, the median tumor size was 24 mm, 57% of patients were diagnosed with adenocarcinoma, and 67% of patients were insured by Medicare. Some 55% of patients received a lobectomy, 72% of patients received a surgical treatment, 6% received conventional radiation or SBRT, 7% of patients received no treatment at all, and 15% were placed in the unknown/other category. The majority of these patients (12%) were indicated to have received some form of treatment, mostly radiation, that did not conform to our definitions.

Men were more likely to receive pneumonectomy, whereas the surgery groups, particularly the lobectomy and pneumonectomy groups, tended to be younger. Treatment patterns did differ by race ($P < .001$), because whites were less likely than blacks to receive no treatment.

Patients with squamous cancers were more likely to receive pneumonectomies. In addition, the patients undergoing pneumonectomy had the largest tumors. Adenocarcinoma was relatively more likely to be treated with lobectomy or SLR, whereas squamous and large cell cancers had increased rates of patients treated with conventional radiation or SBRT and were relatively more likely to go untreated.

TABLE 1. Stage 1 patient demographics and disease characteristics overall and split by first treatment

	All patients	Lobectomy	SLR	Pneumonectomy
n	357,490	194,873 (54.5%)	55,769 (15.6%)	6664 (1.9%)
Male: n (%)	172,324 (48.2)	92,740 (47.6)	24,701 (44.3)	4343 (65.2)
Age: median (IQR)	70 (63-77)	69 (61-75)	71 (64-77)	65 (57-72)
Race—white: n (%)	318,919 (89.2)	174,384 (89.5)	50,480 (90.5)	6079 (91.2)
Black	28,405 (7.9)	14,429 (7.4)	3878 (7.0)	446 (6.7)
Asian/PI	5518 (1.5)	3542 (1.8)	686 (1.2)	75 (1.1)
Other	4648 (1.3)	2518 (1.3)	725 (1.3)	64 (1.0)
Insurance—Medicare: n (%)	230,289 (67.1)	116,518 (62.0)	37,444 (69.5)	3323 (52.7)
Private/other	100,981 (29.4)	64,645 (34.4)	14,660 (27.2)	2658 (42.1)
Medicaid	12,173 (3.5)	6654 (3.5)	1757 (3.3)	330 (5.2)
Uninsured/unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Charlson–Deyo comorbidity score=0: n (%)	138,776 (53.3)	74,213 (52.8)	20,936 (47.4)	2127 (52.6)
1	85,880 (33.0)	48,984 (34.8)	16,396 (37.1)	1438 (35.6)
2+	35,545 (13.7)	17,490 (12.4)	6881 (15.6)	477 (11.8)
Tumor size (mm): median (IQR)	24 (16-34)	25 (17-35)	18 (13-25)	35 (25-50)
Histology—adenocarcinoma: n (%)	204,395 (57.2)	124,769 (64.0)	35,218 (63.1)	2534 (38.0)
Squamous	113,572 (31.8)	55,633 (28.5)	15,488 (27.8)	3586 (53.8)
Large cell/other	39,523 (11.1)	14,471 (7.4)	5063 (9.1)	544 (8.2)

SLR, Sublobar resection; SBRT, stereotactic body radiation therapy; IQR, interquartile range; PI, Pacific Islander.

We further looked at why nonsurgical patients did not receive surgery. A reason is provided for approximately 25% of this cohort. Some 16% were contraindicated because of patient risk factors, 0.3% died before the operation could be performed, 2% had no specific reason, 4% refused, and 5% had surgery recommended, but it was unknown if it was performed. It is unclear why the remaining approximately 75% were not treated with surgery.

Trends in Stage I Diagnosis Rates

Diagnosis rates for stage 1 NSCLC were not constant over the study period. From 1998 to 2000, 26% of cases were clinical stage 1 each year. From 2001 to 2007, the rate was approximately 23%. In 2008, the rate increased to 26% and then to 28% by 2012.

Over the 15-year study period, there is a clear trend toward identifying smaller cancers. Mean tumor size decreased from 28.2 to 23.6 mm ($P < .001$), whereas the median, 25th, and 75th percentiles show similar decreases (Figure 1).

Histology trends are shown in Table 2. From 1998 to 2000, approximately 58% of stage 1 cancers were diagnosed as adenocarcinoma. This rate decreased to 55% between 2001 and 2005, and then increased to 60% by 2012. There is a dramatic shift starting at approximately 2001 from squamous diagnoses to large cell diagnoses.

Trends in Treatment

Table 3 shows trends in the rates of surgical treatment both by number of cases and percentage. Although the number of lobectomies increased by approximately 50%, the rate of lobectomies decreased from 55% to 50%

($P < .001$) of all patients with stage 1. The number of pneumonectomies decreased by approximately 50%, and the rate of pneumonectomies decreased from 3.4% to 1.1% of all patients ($P < .001$). These decreases were offset by a significant increase in the number and rate of SLRs (from 12% to 17%) and in radiation treatments. Significant use of radiation begins at approximately 2003, when 6% of patients were treated with conventional radiation. SBRT use also is first identified in 2003. As SBRT became more frequent (Figure 2), use of conventional radiation decreased, although by 2012 the 2 types of radiation combined were used for approximately 10% of patients.

Trends in Surgery

There is a strong trend toward examination of more regional lymph nodes (Table 4). The median lobectomy in patients was 5 nodes examined in 1998, compared with 8 in 2012. The other 2 surgical groups showed similar increases, although patients receiving SLRs had fewer nodes examined, with a median of 0 in 1998 increasing to a median of 2 in 2012. Patients undergoing pneumonectomy had a median of 8 lymph nodes examined in 1998, increasing to 11 in 2012. As might be expected, this additional focus on regional lymph nodes has led to dramatic increases in the rate of pathologic upstaging in the surgical population (Table 5). Although only 3% of patients undergoing lobectomy were upstaged to stage II or III in 1998, that number increased to 15% by 2012, with particularly large increases in 2003 and in 2010. The rate of upstaging in the other 2 surgical groups increased by a similar factor, and in 2012, 43% of pneumonectomy cases were upstaged (P values for the trends in all 3 groups $< .001$).

TABLE 1. Continued

Conventional radiation	SBRT	None	Unknown/other	P value
13,131 (3.7%)	7430 (2.1%)	26,498 (7.4%)	53,125 (14.9%)	
6657 (50.7)	3429 (46.2)	13,493 (50.9)	26,961 (50.8)	<.001
75 (68-81)	75 (69-81)	75 (67-81)	73 (66-80)	<.001
11,688 (89.0)	6714 (90.4)	22,577 (85.2)	46,997 (88.5)	<.001
1173 (8.9)	522 (7.0)	3126 (11.8)	4831 (9.1)	
128 (1.0)	63 (0.8)	390 (1.5)	634 (1.2)	
142 (1.1)	131 (1.8)	405 (1.5)	663 (1.2)	
10,310 (80.4)	5863 (80.2)	19,238 (76.7)	37,593 (74.8)	
2091 (16.3)	1245 (17.0)	4765 (19.0)	10,917 (21.7)	
427 (3.3)	198 (2.7)	1064 (4.2)	1743 (3.5)	
0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
7107 (57.2)	4457 (60.0)	11,123 (57.5)	18,813 (58.6)	<.001
3450 (27.8)	1901 (25.6)	5107 (26.4)	8604 (26.8)	
1862 (15.0)	1072 (14.4)	3101 (16.0)	4662 (14.5)	
27 (20-37)	21 (15-29)	27 (20-39)	27 (19,38)	<.001
4574 (34.8)	3445 (46.4)	11,456 (43.2)	22,399 (42.2)	<.001
5342 (40.7)	2505 (33.7)	9403 (35.5)	21,615 (40.7)	
3215 (24.5)	1480 (19.9)	5639 (21.3)	9111 (17.2)	

Approximately two thirds of the upstaged patients were upstaged to stage II, whereas the remaining patients were upstaged to stage III.

Trends in the National Cancer Database

The number of reporting facilities in the NCDB increased slowly from 1127 to 1998 to 1152 in 2003. Between 2003 and 2009, there was a faster rate of increase to 1286

facilities in 2009. From that point on, the number stayed relatively constant; there are 1279 facilities represented in our 2012 data set. Cases per facility increased at a relatively constant rate from 16.6 in 1998 to 24.4 in 2012.

DISCUSSION

In this study, we evaluated national trends for stage I NSCLC using a large, national database representing

FIGURE 1. Trends in tumor size. Mean, median, 25th percentile, and 75th percentile tumor sizes (millimeters) for patients with stage I by year of diagnosis.

more than 70% of lung cancer diagnoses in the United States. We demonstrate that the incidence of clinical stage I NSCLC represents 25% of newly diagnosed NSCLC, similar to rates quoted in the literature.⁷ Between 1998 and 2012, 13% of patients underwent SBRT, conventional radiation, or no treatment. El-Sherif and colleagues⁸ quote a rate of 20% unresectability, which is consistent with our results. We hypothesized that the rate of SBRT has been increasing over the last decade, which was supported by our findings. The overall rate of surgery for stage I NSCLC decreased slightly over the 15-year study period from 70% to 68% ($P < .001$), but this masks a significant shift from lobectomies to SLRs. The rate of lobectomy decreased from 55% to 50%, meaning that there has been a significant decrease in the proportion of patients receiving the gold standard management option.

The increasing rate of SLR as a treatment method may be explained by several studies demonstrating relative efficacy for 5-year survival when comparing lobectomy and SLR for peripheral stage I NSCLC. SLR confers the benefit of preserved pulmonary function in patients with intrinsic lung disease or low pulmonary reserve.^{2,8} Landreneau and colleagues⁹ demonstrated equivalent 5-year survival for patients undergoing video-assisted thoracoscopic surgery wedge resection when compared with patients undergoing lobectomy.⁹ More recently, a systematic review performed by De Zoysa and colleagues¹⁰ similarly demonstrated equivalent survival for patients undergoing limited resection versus lobectomy. El-Sherif and colleagues¹¹ showed similar results after adjusting for age and extent of node sampling. However, Landreneau and colleagues⁹ and De Zoysa and colleagues¹⁰ demonstrated increased locoregional recurrence with sublobar resection when compared with lobectomy. The increasing percentage of SLR and declining rate of lobectomy may be explained by an

increase of diagnoses in “high-risk patients,” which would help explain both the increase in SLR and the decrease in lobectomy. However, the NCDB does not collect detailed comorbidity information, such as pulmonary function or cardiac function, which makes it difficult to isolate and analyze the reasoning behind surgical procedure type.

The rate of untreated patients remained unchanged at 7%. Contrary to our hypothesis, our results suggest that the advent of SBRT may have raised the threshold for offering lobectomy rather than allowing more medically inoperable patients access to therapy with curative intent.

The results further demonstrate that once SBRT appeared as a viable treatment modality, an exponential increase in this treatment method is seen. This is not unexpected, because patients who were deemed medically inoperable previously had limited treatment options, including conventional radiation, with poor survival and high recurrence rates.¹² Since the advent of SBRT, medically inoperable or high-risk patients have seen improved survival; this may make it possible to treat more patients than was historically feasible. However, the only suggestion of this possibility in our results is the declining percentage of patients receiving standard treatments.

A propensity-matched study using the NCDB to compare long-term overall survival in patients with stage I NSCLC undergoing surgery or SBRT indicates that surgical patients have improved long-term survival (68.5% vs 46%).¹³ A pooled analysis of 2 open-label phase III trials attempted to help elucidate the answer to this important question. Unfortunately, both trials closed early because of slow accrual; however, the Stereotactic Ablative Radiotherapy in Stage I NSCLC Patients Who Can Undergo Lobectomy and the Trial of Either Surgery or Stereotactic Radiotherapy for Early Stage (IA) Lung Cancer studies evaluated patients with early-stage (T1-2a) neoplasms who were subsequently randomized in a 1:1 fashion to lobectomy or SBRT. A total of 58 patients were enrolled and randomized between the 2 studies, 27 to lobectomy and 31 to SBRT. The 3-year survival was 88% (95% confidence interval, 77-100) in the lobectomy group and 95% (95% confidence interval, 85-100) in the SBRT group ($P = .037$). In addition, there were no differences in 3-year local, regional, or distant control or in recurrence-free survival. However, the sample size in these 2 pooled analyses is small, so meaningful interpretation of the results is difficult.¹⁴ One current and one upcoming trial may help further compare outcomes in patients undergoing surgery versus SBRT for treatment of stage I NSCLC. The Sublobar Resection Versus Stereotactic Ablative Radiotherapy for lung cancer trial will randomize high-risk patients with tumors less than 4 cm to sublobar resection or SBRT to evaluate 3-year overall survival. The trial is currently recruiting participants.¹⁵ Likewise, the Veterans Administration Lung Cancer

TABLE 2. Histology by year along with chi-square test for trend

Year	Adenocarcinoma	Squamous	Large cell
1998	10,827 (57.9%)	7333 (39.2%)	548 (2.9%)
1999	10,768 (58.6%)	7085 (38.6%)	518 (2.8%)
2000	11,120 (59.7%)	6967 (37.4%)	551 (3.0%)
2001	11,102 (54.4%)	6809 (33.4%)	2483 (12.2%)
2002	11,526 (54.4%)	6877 (32.5%)	2775 (13.1%)
2003	11,587 (54.5%)	6754 (31.7%)	2937 (13.8%)
2004	11,333 (54.5%)	6501 (31.3%)	2943 (14.2%)
2005	12,599 (55.3%)	7028 (30.9%)	3136 (13.8%)
2006	13,096 (56.0%)	7137 (30.5%)	3155 (13.5%)
2007	14,073 (56.7%)	7562 (30.5%)	3178 (12.8%)
2008	15,810 (57.1%)	8507 (30.7%)	3353 (12.1%)
2009	17,033 (58.3%)	8900 (30.5%)	3269 (11.2%)
2010	16,910 (58.3%)	8479 (29.2%)	3610 (12.4%)
2011	17,928 (59.5%)	8670 (28.8%)	3547 (11.8%)
2012	18,683 (59.9%)	8963 (28.8%)	3520 (11.3%)
P value	<.001	<.001	<.001

TABLE 3. First treatment by year along with chi-square test for trend

Year	Lobectomy	SLR	Pneumonectomy	Radiation	SBRT	None	Unknown/other
1998	10,292 (55.0%)	2215 (11.8%)	640 (3.4%)	181 (1.0%)	0 (0.0%)	1282 (6.9%)	4098 (21.9%)
1999	10,401 (56.6%)	2034 (11.1%)	575 (3.1%)	141 (0.8%)	0 (0.0%)	1294 (7.0%)	3926 (21.4%)
2000	10,689 (57.4%)	2246 (12.1%)	496 (2.7%)	100 (0.5%)	0 (0.0%)	1224 (6.6%)	3883 (20.8%)
2001	11,241 (55.1%)	2383 (11.7%)	449 (2.2%)	95 (0.5%)	0 (0.0%)	1646 (8.1%)	4580 (22.5%)
2002	11,563 (54.6%)	2678 (12.6%)	462 (2.2%)	195 (0.9%)	0 (0.0%)	1721 (8.1%)	4559 (21.5%)
2003	12,202 (57.3%)	3382 (15.9%)	499 (2.3%)	1343 (6.3%)	16 (0.1%)	1798 (8.5%)	2038 (9.6%)
2004	12,140 (58.4%)	3254 (15.7%)	438 (2.1%)	1250 (6.0%)	39 (0.2%)	1696 (8.2%)	1960 (9.4%)
2005	13,280 (58.3%)	3761 (16.5%)	445 (2.0%)	1347 (5.9%)	101 (0.4%)	1664 (7.3%)	2165 (9.5%)
2006	13,418 (57.4%)	3965 (17.0%)	443 (1.9%)	1395 (6.0%)	224 (1.0%)	1618 (6.9%)	2325 (9.9%)
2007	13,852 (55.8%)	4317 (17.4%)	402 (1.6%)	1405 (5.7%)	472 (1.9%)	1685 (6.8%)	2680 (10.8%)
2008	14,925 (53.9%)	4794 (17.3%)	428 (1.5%)	1385 (5.0%)	658 (2.4%)	2070 (7.5%)	3410 (12.3%)
2009	15,303 (52.4%)	4914 (16.8%)	388 (1.3%)	1331 (4.6%)	1004 (3.4%)	2282 (7.8%)	3980 (13.6%)
2010	14,896 (51.4%)	5049 (17.4%)	328 (1.1%)	1105 (3.8%)	1235 (4.3%)	2171 (7.5%)	4215 (14.5%)
2011	15,236 (50.5%)	5361 (17.8%)	334 (1.1%)	955 (3.2%)	1618 (5.4%)	2125 (7.0%)	4516 (15.0%)
2012	15,435 (49.5%)	5416 (17.4%)	337 (1.1%)	903 (2.9%)	2063 (6.6%)	2222 (7.1%)	4790 (15.4%)
P value	<.001	<.001	<.001	<.001	<.001	.283	<.001

SLR, Sublobar resection; SBRT, stereotactic body radiation therapy.

Surgery or Stereotactic Radiotherapy trial has been approved and will begin enrollment soon.¹⁶

Tumor size over the study period has decreased significantly, from 2.8 to 2.4 cm. This is similar to findings from other studies, which have demonstrated a decrease in the tumor size detected because of increased use of computed tomography scans and lung cancer screening programs.¹⁷⁻¹⁹ The detection of smaller tumor sizes also may explain the increasing rates of SBRT and SLR. Tumors that would have previously been too large for these treatments are now amenable to less-invasive surgical or radiotherapy ablative procedures. The increased utility of computed tomography scans would presumably give rise to detection of NSCLC at an earlier stage; however, our results show an irregular pattern in the rate of stage I cancers. More

recent studies show that intentional limited resection for smaller tumors less than 2 cm may have comparable recurrence rates and survival to lobectomy.^{1,17,20} The Cancer and Leukemia Group B 140503 study is a randomized controlled trial that is nearing its accrual goal and will directly address this question.²¹

The Commission on Cancer recommends removal of at least 10 regional lymph nodes for stage I and II resected NSCLC.²² Our results demonstrate that by 2012, patients undergoing lobectomy had a median of 8 lymph nodes removed, less than the recommended number by the Commission on Cancer. As expected, patients undergoing any form of SLR have fewer nodes collected. Of note, patients undergoing lobectomy were twice as likely to be pathologically upstaged compared with patients undergoing SLR,

FIGURE 2. Trends in the treatment of stage I NSCLC. Annual number of stage I NSCLC cases, surgeries, and patients treated with SBRT from 1998 to 2012 (left), and the number of patients treated with SBRT with the axis rescaled to show the rapid rate of increase (right). SBRT, Stereotactic body radiation therapy.

TABLE 4. Number of regional nodes examined (median and interquartile range) by surgery type and year

Year	Lobectomy	Sublobar resection	Pneumonectomy
1998	5 (3-9)	0 (0-2)	8 (5-14)
1999	6 (3-10)	0 (0-3)	9 (5-15)
2000	6 (3-10)	0 (0-3)	8 (5-13)
2001	6 (3-10)	0 (0-3)	10 (6-14)
2002	6 (3-10)	0 (0-3)	9 (6-15)
2003	6 (3-10)	1 (0-3)	9 (5-15)
2004	6 (3-10)	1 (0-3)	10 (6-15)
2005	7 (4-11)	1 (0-4)	10 (6-15)
2006	7 (4-11)	1 (0-4)	10 (6-15)
2007	7 (4-11)	1 (0-4)	10 (6-15)
2008	7 (4-11)	1 (0-4)	12 (7-17)
2009	7 (4-12)	1 (0-4)	11 (7-17)
2010	7 (4-12)	1 (0-4)	12 (7-17)
2011	8 (4-12)	1 (0-4)	11 (6-17)
2012	8 (5-12)	2 (0-5)	11 (8-17)
P value	<.001	<.001	<.001

although this may be related to the lower lymph node sampling in SLR, leading to decreased identification of N1 or N2 disease. However, Darling and colleagues²³ randomized patients with known early-stage NSCLC to MLND or mediastinal lymph node sampling. They demonstrated no difference in long-term survival or local or regional recurrence in MLND versus rigorous sampling. The authors concluded that MLND should be performed because it does not increase morbidity and it provides the most accurate staging information for adjuvant therapy planning purposes.²³

TABLE 5. Pathologic upstaging by surgery type and year along with the overall percentage of patients upstaged to stage II and III by surgery type

Year	Lobectomy	Sublobar resection	Pneumonectomy
1998	3.0%	1.6%	11.1%
1999	3.4%	1.6%	13.2%
2000	3.4%	2.0%	14.0%
2001	3.6%	1.7%	16.2%
2002	4.0%	1.9%	13.5%
2003	6.1%	3.4%	19.6%
2004	5.6%	2.8%	17.7%
2005	5.0%	3.0%	18.9%
2006	5.5%	2.8%	16.2%
2007	6.3%	2.7%	22.6%
2008	10.9%	4.9%	32.8%
2009	11.3%	5.9%	33.3%
2010	15.1%	8.3%	45.6%
2011	14.8%	6.4%	46.6%
2012	15.4%	7.1%	43.0%
Pathologic stage II	5.3%	2.4%	14.9%
Pathologic stage III	2.7%	2.0%	7.4%

Study Limitations

First, although the NCDB does capture a large majority of cancer diagnoses in the United States, it does not capture all lung cancers. Although it is the largest and most generalizable database available, there may be some specific subgroups for which these results are not applicable, such as patients in rural communities who lack adequate access to healthcare or tertiary care facilities.

Second, the NCDB captures a wide breadth of information on 30 million patients. However, the comorbidity data are not accurate and are categorized into 3 subgroups of the Charlson–Deyo score. Of note, category 1 is defined as “no comorbid conditions recorded, or no comorbid conditions present.”²⁴ Cancer registrars are well trained in abstracting the demographic and cancer-related variables, but comorbidity assessment has not been a priority. Therefore, because we cannot adequately risk adjust for treatment bias, we have not compared survival or other outcome measures between treatment groups.

Finally, the increasing number of reporting facilities and difficult to document changes in referral patterns over the 15-year period may influence the underlying patient populations.

CONCLUSIONS

The rate of lobectomy for stage I NSCLC has declined between 1998 and 2012. Increasing use of SLR compensated for much of this decrease, although the reasons for the shifting treatment trends are unclear. Although the increasing popularity of alternatives to lobectomy for treatment of stage I NSCLC should allow more patients to undergo treatment, our results demonstrate that the percentage of untreated patients has remained stable at approximately 7% over the 15-year study period.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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