Title

Surgical Outcomes for Early Stage Non-small Cell Lung Cancer at Facilities With Stereotactic Body Radiation Therapy Programs

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BACKGROUND: Patients undergoing surgery for early stage non-small cell lung cancer (NSCLC) may be at high risk for postoperative mortality. Access to stereotactic body radiation therapy (SBRT) may facilitate more appropriate patient selection for surgery.

RESEARCH QUESTION: Is postoperative mortality associated with early stage NSCLC lower at facilities with higher use of SBRT?

STUDY DESIGN AND METHODS: Patients with early stage NSCLC reported to the National Cancer Database between 2004 and 2015 were included. Use of SBRT was defined by each facility's SBRT experience (in years) and SBRT to surgery volume ratios. Multivariate logistic regression was used to test for the associations between SBRT use and postoperative mortality.

RESULTS: The study cohort consisted of 202,542 patients who underwent surgical resection of cT1-T2N0M0 NSCLC tumors. The 90-day postoperative mortality rate declined during the study period from 4.6% to 2.6% ($P < .001$), the proportion of facilities that used SBRT increased from 4.6% to 77.5% ($P < .001$), and the proportion of patients treated with SBRT increased from 0.7% to 15.4% ($P < .001$). On multivariate analysis, lower 90-day postoperative mortality rates were observed at facilities with > 6 years of SBRT experience (OR, 0.84; 95% CI, 0.76-0.94; $P = .003$) and SBRT to surgery volume ratios of more than 17% (OR, 0.85; 95% CI, 0.79-0.92; $P < .001$). Ninety-day mortality also was associated with surgical volume, region, year, age, sex, and race, among other covariates. Interaction testing between these covariates showed negative results.

INTERPRETATION: Patients who underwent resection for early stage NSCLC at facilities with higher SBRT use showed lower rates of postoperative mortality. These findings suggest that the availability and use of SBRT may improve the selection of patients for surgery who are predicted to be at high risk of postoperative mortality.   CHEST 2022; 161(3):833-844

KEY WORDS: lung cancer; lung surgery; postoperative mortality; radiation therapy; SABR; SBRT; sterotactic body radiation therapy

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FOR EDITORIAL COMMENT, SEE PAGE 603

Take-home Points

Study Question: Is the availability and use of stereotactic body radiation therapy (SBRT) as an alternative to surgery for early stage non-small cell lung cancer (NSCLC) associated with lower rates of postoperative mortality rates for patients who are treated with surgery?

Results: In a retrospective analysis of > 200,000 patients undergoing surgical resection for early stage NSCLC, lower rates of 90-day postoperative mortality were observed at facilities with > 6 years of SBRT experience and SBRT to surgery volume ratios > 17%.

Interpretation: Patients with early stage NSCLC who are selected for surgery at institutions with greater use of SBRT show lower risks of postoperative mortality.

Surgical resection currently is the preferred upfront treatment for early stage non-small cell lung cancer (NSCLC).[1] It offers a safe and effective treatment option for appropriately selected patients and is associated with favorable long-term survival.[2,3] Surgical resection also is recommended often for patients at high risk of complications because of retrospective data that suggest longer-term survival when compared with alternative management options.[4] Yet, the potential benefits of surgical resection are undermined when a patient dies in the early postoperative period.

Fortunately, postoperative mortality rates for early stage NSCLC have declined steadily in recent decades because of advances in surgical technique and perioperative care. A recent publication from the Society of Thoracic Surgeons (STS) General Thoracic Database in 2020 reported a 30-day mortality of 1.3% for 38,461 patients who underwent lobectomy at one of 256 reporting sites between 2015 and 2017.[5] Mortality rates can vary according to institutional performance and in this contemporary STS publication ranged from 0.3% to 1.5%, depending on the star rating for the program. Postoperative mortality rates also can vary based on patient comorbidities, as demonstrated in a 2015 National Cancer Database (NCDB) study that reported a 30-day mortality rate of 2.6% to 4.4%, depending on the Charleson-Deyo comorbidity index.[6] Additional factors associated with postoperative mortality include surgery type and age, as published in a separate study of 74,739 patients reported to the NCDB between 2004 and 2013 that demonstrated unadjusted 90-day mortality rates of 1.8% to 7.8% and of 1.5% to 7.3% according to these factors, respectively.[7]

Stereotactic body radiation therapy (SBRT) is a method of delivering highly conformal and ablative doses of external beam radiotherapy that is associated with 5-year local control rates of > 90% that is a standard of care for patients with early stage node-negative NSCLC who are medically inoperable, at high risk of surgical complication, or decline surgery.[8-10] The intention of this study was to investigate the hypothesis that patients who are selected for surgery at facilities with higher use of SBRT demonstrate lower rates of postoperative mortality because of improved matching of patients to appropriate treatment.[7,11]

Study Design and Methods

The hypothesis that patients with early stage NSCLC show lower postoperative mortality rates if undergoing surgical resection at facilities with an active SBRT program was evaluated retrospectively using the NCDB, a national database. All protected patient information is deidentified before inclusion in the NCDB. As such, institutional review board approval was not required for this work.

Data Source

The NCDB is sponsored by the American College of Surgeons and the American Cancer Society.[12] It aggregates hospital registry data from > 1,500 Commission on Cancer-accredited facilities and represents > 70% of newly diagnosed cancer cases within the United States, containing a total of > 34 million patient records. The NCDB captures discrete information on patient characteristics, staging, treatment, and outcomes using standardized coding definitions.

Participants

The NCDB was queried for patients who had received a diagnosis of histologically proven clinical stage T1-T2 N0 M0 NSCLC between 2004 and 2015 to identify those treated with either surgery or radiation therapy. The NCDB Participant User File applies codes for radiation therapy method using unique identifiers that allow for

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patients treated with SBRT to be filtered. For the purposes of this analysis, patients coded as having the identifiers 11 (ie, lung subsite) for RAD_TREAT_VOLUME and 41 or 42 for RAD_REGIONAL_RX_MODALITY (eg, stereotactic radiotherapy) were considered as having received lung SBRT. Trends in treatment method and volume were generated from this cohort. The NCDB used the American Joint Committee on Cancer sixth edition to stage patients treated before 2010 and the seventh edition for those treated afterward. This complete cohort then was narrowed to include only patients treated with a sublobar resection, lobectomy, or pneumonectomy without prior exposure to chemotherapy or radiation therapy. To ensure that actuarial postoperative mortality could be calculated, patients without recorded vital status or surgery date also were excluded. The final analytic cohort consisted of patients with prognostic clinical stage T1-T2 N0 M0 who received definitive surgery as the initial treatment.[13]

Definition of Key Variables

Patients in the complete cohort treated with SBRT then were used to determine facility-level access to this method. Patient-level access to SBRT was defined for each surgical patient as follows: (1) SBRT experience, defined as the number of years a treating facility had been offering SBRT at the time of surgical resection (facilities with negative values had yet to offer SBRT), and (2) SBRT to surgery volume ratio, defined as the ratio of patients treated with SBRT to those treated with surgical resection at the treating facility during the year of surgical resection. Postoperative mortality rates were derived using vital status data and were censored by date of last follow-up. Binary survival outcomes for the 30-day and 90-day time points were tabulated using vital status at last recorded follow-up. Patients with last recorded vital status of alive before the 30-day or 90-day time point were censored from that respective analysis.

Statistical Analysis and Outcomes

Statistical analyses were performed using SAS version 9.4 software (SAS Institute, Inc.), and statistical significance was assessed with an α of 0.05.[14] Both independent variables, SBRT experience and SBRT to surgery volume ratio, were analyzed as quartiles. Covariates were selected a priori to evaluate for potential confounding and included facility-specific surgery volume, geographic region, year of diagnosis, age, sex, race, insurance status, facility type, Charlson-Deyo score, American Joint Committee on Cancer clinical T classification, histologic findings, anatomic location, surgery type, and a history of prior malignancy. Pearson χ^2 test and the analysis of variance were used to assess associations between exposures of interest and absolute mortality rates. Changes in annual 30-day and 90-day mortality rates were analyzed using the Cochran-Armitage trend test. Changes in the annual proportions of treatments and surgical techniques were estimated using the χ^2 test for trend in proportions.

Univariate and multivariate logistic regression analyses were performed for the association with 30-day or 90-day mortality by the exposure variables of SBRT experience and SBRT to surgery volume ratio, which were each recorded as continuous variables and were binned by quartiles. Multivariate logistic regression analyses with backward elimination were applied with a removal criterion of $P > 0.05$. The NCDB recorded data on the use of video-assisted thoracoscopic surgery from 2010 onward. The trend in video-assisted thoracoscopic surgery use was assessed, but this covariate was excluded from the postoperative mortality analysis given the absence of data from 2004 through 2009. Interaction testing was explored to assess whether a background covariate could be an effect modifier to the association between each SBRT use variable and clinical outcome, which further assures the nonconfoundedness of the associations of interest. Specifically, SBRT experience and SBRT to surgery volume ratio were assessed with respect to surgical volume and surgery type.

Results

The NCDB contains data from 1,535,577 patients with NSCLC who received a diagnosis from 2004 through 2015. During this period, the annual number of patients reported with early stage NSCLC more than tripled, from 13,214 to 40,188 (Fig 1). In total, 365,133 were found to have histologically proven clinical stage T1-T2 N0 M0 NSCLC. To define the study cohort, the following patients were excluded: 133,397 who had no documented surgery to the primary site, 2,508 who received prior chemotherapy or radiotherapy, and 26,686 without surgery date or postoperative vital status. This led to a final study cohort of 202,542 patients who underwent upfront surgical resection for clinically staged early stage NSCLC. Separately, a cohort of 49,212 patients with early stage NSCLC treated with SBRT was identified from the full cohort, and this group was used to determine facility-level SBRT use as described in the "Study Design and Methods" section.

Most patients in the study cohort demonstrated cT1N0 disease (69.4%), underwent lobectomy or bilobectomy (73.7%), and were White (88.8%), with a median age at diagnosis of 69 years (Table 1). Patients most commonly underwent surgical resection at a comprehensive community cancer program (42.7%) followed by an academic or research program (36.4%). The NCDB began coding for video-assisted thoracoscopic surgery in 2010, and a significant increase in the use of this procedure was observed since that time (26.8% in 2010 vs 49.8% in 2015; $P < .001$ for trend).

As demonstrated in Figure 2, the 30-day and 90-day postoperative mortality rates for patients treated with upfront surgical resection declined significantly from 2004 to 2015 (30 day, from 2.5% to 1.4% [$P < .001$ for trend]; 90 day, from 4.6% to 2.6% [$P < .001$ for trend]). During this period, the proportion of NCDB facilities offering SBRT increased from 4.6% to 77.5% and the proportion of patients treated with SBRT increased from 0.7% to 15.4% ($P < .001$ for trend for both). Increases in the use of SBRT and surgery were offset by significant decreases in the use of conventionally fractionated radiation therapy (from 21.6% to 12.1%; $P < .001$ for trend) and the proportion of patients without any recorded treatment (from 21.5% to 12.1%; $P < .001$ for trend). The median annualized SBRT experience increased from 0 to 7 years ($P < .001$), and the median

Figure 1 – **(A)** *Trends in treatment volumes for all patients diagnosed with early stage non-small cell lung cancer (NSCLC),* **(B)** *Trends in treatment modality for all patients diagnosed with early stage NSCLC. SBRT = stereotactic body radiation therapy.*
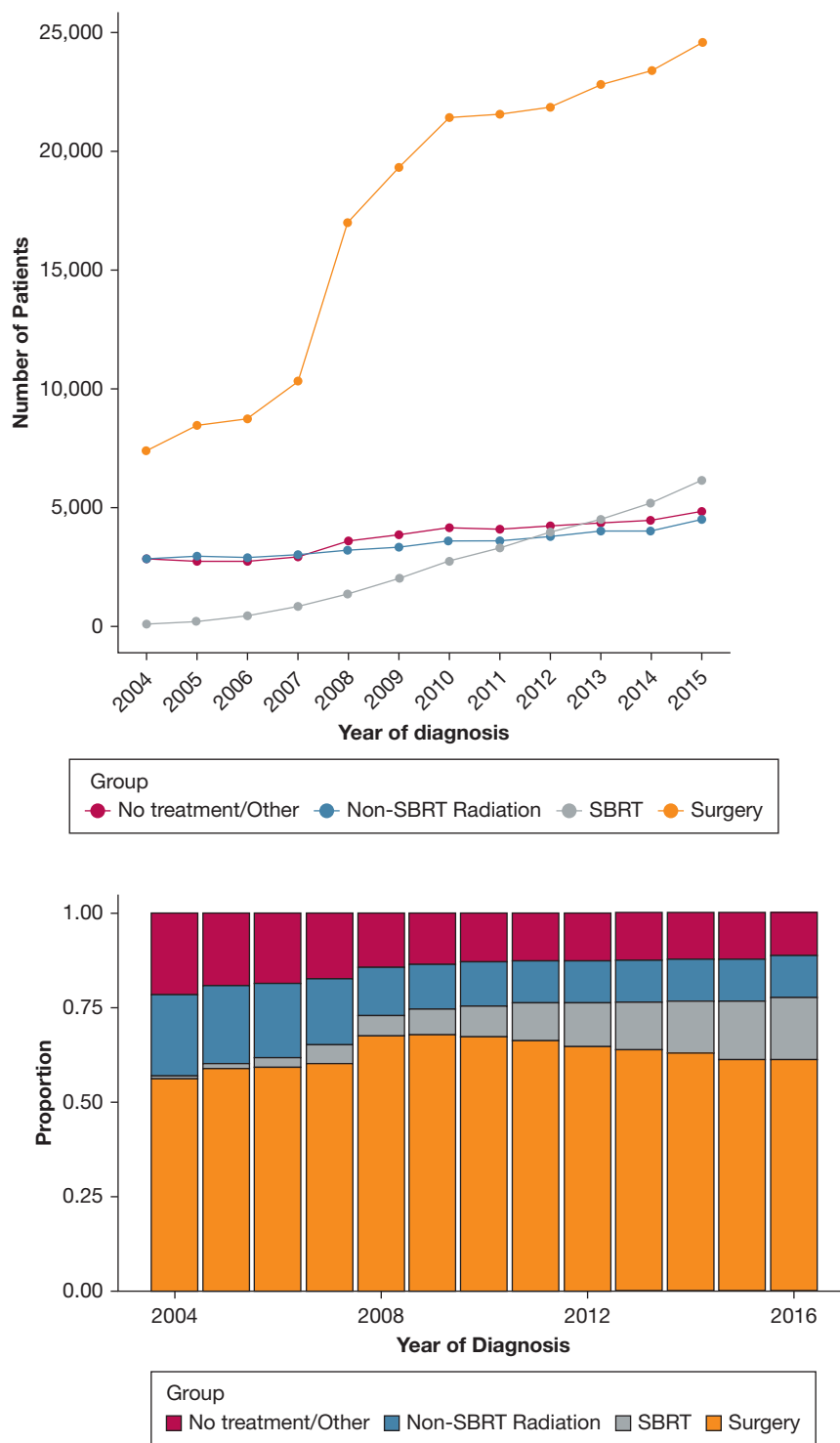
annualized SBRT to surgery volume ratio increased from 0 to 14.6% ($P < .001$).

Results of univariate and multivariate modeling demonstrated independent associations of SBRT experience with 30-day and 90-day mortality (Table 2). On multivariate analysis, associations of lower 30-day

postoperative mortality rates were observed for patients who underwent surgery at a facility with more than 3 years of SBRT experience (OR, 0.89; 95% CI, 0.81-0.98; $P = .021$) and lower 90-day postoperative mortality at facilities with more than 6 years of SBRT experience (OR, 0.84; 95% CI, 0.76-0.94; $P = .003$). Similarly, SBRT to surgery volume ratios of more than 4% and

Variable	Level	No. (%) (N = 202,542)
Facility type	Community cancer program	13,681 (6.8)
	Comprehensive community cancer program	85,875 (42.7)
	Academic or research program	73,141 (36.4)
	Integrated network cancer program	28,438 (14.1)
Sex	Male	92,928 (45.9)
	Female	109,614 (54.1)
Race	White	179,813 (88.8)
	Black	15,903 (7.9)
	Other	6,826 (3.4)
Charlson-Deyo score	0	101,313 (50.0)
	1	69,579 (34.4)
	≥ 2	31,650 (15.6)
Geographic region	Northeast	47,433 (23.6)
	South	75,178 (37.4)
	Midwest	53,076 (26.4)
	West	25,448 (12.7)
AJCC clinical T stage	cT1	140,728 (69.4)
	cT2 (nos)	61,814 (30.5)
Surgery type	Sublobar	48,502 (23.9)
	Lobectomy or bilobectomy	149,345 (73.7)
	Pneumonectomy	4,695 (2.3)
Histologic findings	Adenocarcinoma	102,352 (50.5)
	SCC	52,796 (26.1)
	Other	47,394 (23.4)
VATS (2010 onward)	Yes	53,428 (40.1)
	No	79,920 (59.9)
SBRT experience, y	≥ −12, ≤ 0	61,046 (31.1)
	> 0, ≤ 3	50,675 (25.9)
	> 3, ≤ 6	48,960 (25.0)
	> 6, ≤ 11	35,299 (18.0)
	Missing	6,562
Volume ratio, %	0	65,996 (33.7)

(Continued)

Variable	Level	No. (%) (N = 202,542)
	> 0, ≤ 0.043	32,005 (16.3)
	> 0.043, ≤ 0.167	49,940 (25.5)
	> 0.167, ≤ 14	48,039 (24.5)
	Missing	6,562
Surgery volume (no. of cases)	≥ 1, ≤ 26	51,218 (25.3)
	> 26, ≤ 48	51,402 (25.4)
	> 48, ≤ 85	49,907 (24.6)
	> 85, ≤ 523	50,015 (24.7)
Age at diagnosis, y	Median (range)	69.00 (18-90)

AJCC = American Joint Committee on Cancer; SBRT = stereotactic body radiation therapy; SCC = squamous cell carcinoma; VATS = video-assisted thoracoscopic surgery.

17% showed statistically significant associations with lower 30-day mortality (OR, 0.80; 95% CI, 0.73-0.88; $P < .001$) and 90-day mortality (OR, 0.85; 95% CI, 0.79-0.92; $P < .001$), respectively (Table 3). An independent association between surgical volume of > 85 cases per year and lower 30-day mortality rates (OR, 0.78; 95% CI, 0.69-0.88; $P < .001$) and 90-day mortality rates (OR, 0.82; 95% CI, 0.75-0.89; $P < .001$) also was observed.

Additional covariates that demonstrated independent associations with 30-day or 90-day mortality on multivariate analysis included: facility region, year of diagnosis (90-day mortality only), age, sex, race (90-day mortality only), insurance status, facility type, Charlson-Deyo score, clinical T classification, histologic findings, anatomic location, surgery type, and prior malignancy (90-day mortality only) for both SBRT experience and SBRT to surgery volume ratio models. Interaction testing between these independent covariates showed negative results, indicating that the association of SBRT experience and SBRT to surgery volume ratio were consistent across subgroups independent of year of treatment. The Spearman correlation coefficient relating SBRT experience and SBRT to surgery volume ratio across all patients was found to be 0.643.

Discussion

This analysis of a large observational database was conducted to investigate whether patients who underwent resection for early stage NSCLC showed lower rates of postoperative mortality if surgical

TABLE 2] Results of Univariate and Multivariate Modeling for SBRT Experience

Covariate	Value	30-D Mortality				90-D Mortality			
		univariate		multivariate		univariate		multivariate	
		OR (95% CI)	OR P Value	OR (95% CI)	OR P Value	OR (95% CI)	OR P Value	OR (95% CI)	OR P Value
SBRT experience (quartile), vs ≤ 0	> 0, ≤ 3	0.82 (0.76-0.89)	**< .001**	0.93 (0.85-1.01)	.082	0.82 (0.77-0.87)	**< .001**	0.95 (0.88-1.02)	.137
	> 3, ≤ 6	0.71 (0.65-0.78)	**< .001**	0.89 (0.81-0.98)	**.021**	0.76 (0.72-0.81)	**< .001**	1.00 (0.92-1.09)	.933
	> 6, ≤ 11	0.56 (0.50-0.62)	**< .001**	0.76 (0.67-0.85)	**< .001**	0.57 (0.52-0.61)	**< .001**	0.84 (0.76-0.94)	**.003**
Surgery volume (quartile), vs ≤ 26	> 26, ≤ 48	0.99 (0.91-1.08)	.831	1.05 (0.96-1.16)	.270	0.95 (0.89-1.01)	.104	0.99 (0.92-1.06)	.805
	> 48, ≤ 85	0.85 (0.78-0.93)	**< .001**	0.96 (0.86-1.06)	.381	0.86 (0.80-0.91)	**< .001**	0.93 (0.86-1.01)	.082
	> 85, ≤ 523	0.60 (0.55-0.66)	**< .001**	0.80 (0.71-0.90)	**< .001**	0.65 (0.61-0.70)	**< .001**	0.82 (0.75-0.89)	**< .001**
Facility region vs Northeast	South	1.75 (1.59-1.91)	**< .001**	1.55 (1.41-1.71)	**< .001**	1.69 (1.58-1.81)	**< .001**	1.51 (1.41-1.63)	**< .001**
	Midwest	1.54 (1.40-1.70)	**< .001**	1.36 (1.22-1.51)	**< .001**	1.49 (1.38-1.60)	**< .001**	1.32 (1.22-1.43)	**< .001**
	West	1.45 (1.29-1.64)	**< .001**	1.28 (1.13-1.46)	**< .001**	1.33 (1.22-1.45)	**< .001**	1.21 (1.10-1.33)	**< .001**
Year of diagnosis vs 2004	2005-2009		NS				NS		NS
	2010	0.82 (0.69-0.97)	**.025**			0.82 (0.72-0.93)	**.003**	0.95 (0.82-1.11)	.535
	2011	0.71 (0.59-0.85)	**< .001**			0.72 (0.63-0.83)	**< .001**	0.86 (0.73-1.00)	.056
	2012	0.72 (0.60-0.86)	**< .001**			0.77 (0.67-0.87)	**< .001**	0.91 (0.78-1.08)	.279
	2013	0.67 (0.56-0.80)	**< .001**			0.66 (0.58-0.75)	**< .001**	0.84 (0.71-0.99)	**.034**
	2014	0.60 (0.50-0.72)	**< .001**			0.60 (0.53-0.69)	**< .001**	0.79 (0.67-0.94)	**.007**
	2015	0.56 (0.47-0.68)	**< .001**			0.56 (0.49-0.64)	**< .001**	0.77 (0.65-0.92)	**.003**
Age at diagnosis (quartile) vs ≥ 18, ≤ 62	> 62, ≤ 69	1.60 (1.44-1.79)	**< .001**	1.39 (1.23-1.58)	**< .001**	1.63 (1.50-1.77)	**< .001**	1.38 (1.26-1.51)	**< .001**
	> 69, ≤ 75	2.28 (2.05-2.53)	**< .001**	1.94 (1.71-2.19)	**< .001**	2.36 (2.18-2.55)	**< .001**	1.90 (1.73-2.08)	**< .001**
	> 75, ≤ 90	3.57 (3.23-3.95)	**< .001**	3.12 (2.77-3.51)	**< .001**	3.60 (3.34-3.87)	**< .001**	2.92 (2.67-3.19)	**< .001**
Sex vs female	Male	2.01 (1.88-2.15)	**< .001**	1.64 (1.53-1.76)	**< .001**	2.00 (1.90-2.10)	**< .001**	1.63 (1.55-1.71)	**< .001**
Race vs White	Black	0.94 (0.83-1.06)	.279			0.85 (0.78-0.94)	**< .001**	0.99 (0.90-1.09)	.864
	Other	0.70 (0.57-0.86)	**< .001**			0.59 (0.50-0.70)	**< .001**	0.75 (0.63-0.89)	**.001**
Insurance status vs government	Not insured	0.80 (0.61-1.04)	.091	1.10 (0.81-1.48)	.553	0.65 (0.53-0.81)	**< .001**	0.94 (0.75-1.20)	.636
	Private insured	0.48 (0.45-0.53)	**< .001**	0.78 (0.71-0.86)	**< .001**	0.46 (0.43-0.49)	**< .001**	0.74 (0.69-0.80)	**< .001**
Facility type vs comprehensive community cancer program	Community cancer program	1.28 (1.15-1.43)	**< .001**	1.23 (1.07-1.40)	**.003**	1.25 (1.15-1.36)	**< .001**	1.18 (1.06-1.30)	**.002**

(Continued)

TABLE 2] *(Continued)*

Covariate	Value	30-D Mortality				90-D Mortality			
		univariate		multivariate		univariate		multivariate	
		OR (95% CI)	OR *P* Value	OR (95% CI)	OR *P* Value	OR (95% CI)	OR *P* Value	OR (95% CI)	OR *P* Value
	Academic or research program	0.68 (0.63-0.74)	**< .001**	0.92 (0.85-1.01)	.075	0.71 (0.67-0.75)	**< .001**	0.93 (0.87-1.00)	**.040**
	Network cancer program	0.81 (0.73-0.89)	**< .001**	0.91 (0.82-1.01)	.063	0.84 (0.78-0.90)	**< .001**	0.93 (0.86-1.00)	.061
Charlson-Deyo score vs 0	1	1.18 (1.10-1.27)	**< .001**	1.11 (1.03-1.20)	**.006**	1.19 (1.12-1.25)	**< .001**	1.11 (1.05-1.17)	**< .001**
	≥2	1.81 (1.67-1.97)	**< .001**	1.58 (1.46-1.73)	**< .001**	1.78 (1.67-1.89)	**< .001**	1.54 (1.44-1.64)	**< .001**
AJCC clinical T stage vs c1A	c1 (nos)	1.50 (1.36-1.65)	**< .001**	1.23 (1.10-1.36)	**< .001**	1.52 (1.41-1.63)	**< .001**	1.18 (1.07-1.30)	**< .001**
	c1B	1.35 (1.20-1.52)	**< .001**	1.15 (1.02-1.30)	**.021**	1.47 (1.35-1.61)	**< .001**	1.30 (1.19-1.42)	**< .001**
	c2 (nos)	2.20 (1.99-2.43)	**< .001**	1.41 (1.26-1.58)	**< .001**	2.46 (2.28-2.65)	**< .001**	1.57 (1.42-1.74)	**< .001**
	c2A	1.61 (1.43-1.81)	**< .001**	1.18 (1.04-1.34)	**.009**	1.87 (1.71-2.04)	**< .001**	1.44 (1.31-1.58)	**< .001**
	c2B	1.95 (1.63-2.33)	**< .001**	1.18 (0.98-1.43)	.087	2.26 (1.98-2.57)	**< .001**	1.47 (1.28-1.68)	**< .001**
Histologic findings vs adenocarcinoma	Other	0.97 (0.88-1.06)	.470	1.02 (0.93-1.12)	.657	1.03 (0.96-1.10)	.407	1.08 (1.01-1.15)	**.033**
	SCC	2.05 (1.92-2.20)	**< .001**	1.52 (1.41-1.64)	**< .001**	2.10 (1.99-2.21)	**< .001**	1.55 (1.47-1.64)	**< .001**
Anatomic location vs RML	RUL	1.54 (1.30-1.83)	**< .001**	1.51 (1.26-1.80)	**< .001**	1.47 (1.30-1.67)	**< .001**	1.41 (1.24-1.61)	**< .001**
	RLL	1.70 (1.43-2.02)	**< .001**	1.61 (1.34-1.93)	**< .001**	1.63 (1.44-1.85)	**< .001**	1.49 (1.31-1.70)	**< .001**
	LUL	1.44 (1.21-1.71)	**< .001**	1.32 (1.10-1.58)	**.003**	1.38 (1.22-1.56)	**< .001**	1.23 (1.08-1.40)	**.002**
	LLL	1.21 (1.01-1.46)	**.039**	1.09 (0.90-1.32)	.376	1.25 (1.09-1.42)	**.001**	1.09 (0.95-1.25)	.234
	Unknown/NOS	2.74 (2.22-3.38)	**< .001**	2.06 (1.64-2.57)	**< .001**	2.45 (2.10-2.87)	**< .001**	1.82 (1.54-2.16)	**< .001**
Surgery type vs bilobectomy or lobectomy	Sublobar	0.78 (0.72-0.85)	**< .001**	0.74 (0.68-0.81)	**< .001**	0.85 (0.81-0.91)	**< .001**	0.83 (0.78-0.88)	**< .001**
	Pneumonectomy	3.71 (3.29-4.18)	**< .001**	3.29 (2.87-3.76)	**< .001**	3.45 (3.13-3.79)	**< .001**	2.95 (2.65-3.28)	**< .001**
Sequence No. vs first	Prior malignancy	1.06 (0.99-1.14)	.074			1.11 (1.05-1.17)	**< .001**	1.10 (1.04-1.16)	**< .001**

Bold indicates statistically significant values. AJCC = American Joint Committee on Cancer; LLL = left lower lobe; LUL = left upper lobe; NOS = not otherwise specific; NS = not significant; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; SBRT = stereotactic body radiation therapy; SCC = squamous cell carcinoma.

TABLE 3] Results of Univariate and Multivariate Modeling for Volume Ratio

Covariate	Value	30-D Mortality				90-D Mortality			
		Univariate		Multivariate		Univariate		Multivariate	
		OR (95% CI)	OR P Value	OR (95% CI)	OR P Value	OR (95% CI)	OR P Value	OR (95% CI)	OR P Value
Volume ratio (quartile) vs 0	> 0, ≤ 0.043	0.73 (0.66-0.81)	**< .001**	0.94 (0.85-1.05)	.287	0.73 (0.68-0.78)	**< .001**	0.92 (0.85-1.00)	.057
	> 0.043, ≤ 0.167	0.71 (0.65-0.77)	**< .001**	0.88 (0.80-0.96)	**.005**	0.75 (0.70-0.79)	**< .001**	0.94 (0.87-1.01)	.078
	> 0.167, ≤ 14	0.66 (0.61-0.72)	**< .001**	0.80 (0.73-0.88)	**< .001**	0.68 (0.64-0.73)	**< .001**	0.85 (0.79-0.92)	**< .001**
Surgery volume (quartile) vs ≤ 26	> 26, ≤ 48	0.99 (0.91-1.08)	.831	1.05 (0.96-1.15)	.315	0.95 (0.89-1.01)	0.104	1.00 (0.93-1.07)	.937
	> 48, ≤ 85	0.85 (0.78-0.93)	**< .001**	0.94 (0.85-1.04)	.244	0.86 (0.80-0.91)	**< .001**	0.94 (0.87-1.02)	.119
	> 85, ≤ 523	0.60 (0.55-0.66)	**< .001**	0.78 (0.69-0.88)	**< .001**	0.65 (0.61-0.70)	**< .001**	0.82 (0.75-0.89)	**< .001**
Facility region vs Northeast	South	1.75 (1.59-1.91)	**< .001**	1.56 (1.41-1.72)	**< .001**	1.69 (1.58-1.81)	**< .001**	1.52 (1.41-1.63)	**< .001**
	Midwest	1.54 (1.40-1.70)	**< .001**	1.37 (1.23-1.52)	**< .001**	1.49 (1.38-1.60)	**< .001**	1.33 (1.23-1.44)	**< .001**
	West	1.45 (1.29-1.64)	**< .001**	1.29 (1.13-1.46)	**< .001**	1.33 (1.22-1.45)	**< .001**	1.21 (1.10-1.34)	**< .001**
Year of diagnosis vs 2004	2005-2009		NS				NS		NS
	2010	0.82 (0.69-0.97)	**.025**			0.82 (0.72-0.93)	**.003**	0.99 (0.85-1.15)	.860
	2011	0.71 (0.59-0.85)	**< .001**			0.72 (0.63-0.83)	**< .001**	0.88 (0.76-1.03)	.125
	2012	0.72 (0.60-0.86)	**< .001**			0.77 (0.67-0.87)	**< .001**	0.94 (0.81-1.10)	.460
	2013	0.67 (0.56-0.80)	**< .001**			0.66 (0.58-0.75)	**< .001**	0.85 (0.73-1.00)	.054
	2014	0.60 (0.50-0.72)	**< .001**			0.60 (0.53-0.69)	**< .001**	0.80 (0.68-0.94)	**.007**
	2015	0.56 (0.47-0.68)	**< .001**			0.56 (0.49-0.64)	**< .001**	0.77 (0.65-0.90)	**.002**
Age at diagnosis (quartile) vs ≥ 18, ≤ 62	> 62, ≤ 69	1.60 (1.44-1.79)	**< .001**	1.39 (1.23-1.58)	**< .001**	1.63 (1.50-1.77)	**< .001**	1.38 (1.26-1.51)	**< .001**
	> 69, ≤ 75	2.28 (2.05-2.53)	**< .001**	1.94 (1.71-2.19)	**< .001**	2.36 (2.18-2.55)	**< .001**	1.89 (1.73-2.08)	**< .001**
	> 75, ≤ 90	3.57 (3.23-3.95)	**< .001**	3.12 (2.77-3.51)	**< .001**	3.60 (3.34-3.87)	**< .001**	2.92 (2.67-3.19)	**< .001**
Male sex		2.01 (1.88-2.15)	**< .001**	1.64 (1.53-1.76)	**< .001**	2.00 (1.90-2.10)	**< .001**	1.63 (1.55-1.71)	**< .001**
Race vs White	Black	0.94 (0.83-1.06)	.279			0.85 (0.78-0.94)	**< .001**	0.99 (0.90-1.09)	.838
	Other	0.70 (0.57-0.86)	**< .001**			0.59 (0.50-0.70)	**< .001**	0.75 (0.63-0.89)	**< .001**
Insurance status vs government	Not insured	0.80 (0.61-1.04)	.091	1.09 (0.81-1.48)	.559	0.65 (0.53-0.81)	**< .001**	0.94 (0.74-1.19)	.625
	Private insured	0.48 (0.45-0.53)	**< .001**	0.78 (0.71-0.86)	**< .001**	0.46 (0.43-0.49)	**< .001**	0.74 (0.69-0.79)	**< .001**

(Continued)

TABLE 3] *(Continued)*

Covariate	Value	30-D Mortality				90-D Mortality			
		Univariate		Multivariate		Univariate		Multivariate	
		OR (95% CI)	OR *P* Value	OR (95% CI)	OR *P* Value	OR (95% CI)	OR *P* Value	OR (95% CI)	OR *P* Value
Facility type vs comprehensive community cancer program	Community cancer program	1.28 (1.15-1.43)	**<.001**	1.21 (1.06-1.38)	**.006**	1.25 (1.15-1.36)	**<.001**	1.16 (1.05-1.29)	**.004**
	Academic or research program	0.68 (0.63-0.74)	**<.001**	0.92 (0.85-1.01)	.079	0.71 (0.67-0.75)	**<.001**	0.93 (0.87-1.00)	**.043**
	Network cancer program	0.81 (0.73-0.89)	**<.001**	0.91 (0.82-1.01)	.083	0.84 (0.78-0.90)	**<.001**	0.93 (0.87-1.01)	.079
Charlson-Deyo score vs 0	1	1.18 (1.10-1.27)	**<.001**	1.11 (1.03-1.20)	**.005**	1.19 (1.12-1.25)	**<.001**	1.11 (1.05-1.17)	**<.001**
	≥ 2	1.81 (1.67-1.97)	**<.001**	1.59 (1.46-1.73)	**<.001**	1.78 (1.67-1.89)	**<.001**	1.54 (1.44-1.64)	**<.001**
AJCC Clinical T vs c1A	c1 (nos)	1.50 (1.36-1.65)	**<.001**	1.25 (1.13-1.38)	**<.001**	1.52 (1.41-1.63)	**<.001**	1.18 (1.07-1.30)	**<.001**
	c1B	1.35 (1.20-1.52)	**<.001**	1.16 (1.02-1.31)	**.019**	1.47 (1.35-1.61)	**<.001**	1.30 (1.19-1.42)	**<.001**
	c2 (nos)	2.20 (1.99-2.43)	**<.001**	1.44 (1.29-1.61)	**<.001**	2.46 (2.28-2.65)	**<.001**	1.57 (1.42-1.73)	**<.001**
	c2A	1.61 (1.43-1.81)	**<.001**	1.18 (1.04-1.34)	**.008**	1.87 (1.71-2.04)	**<.001**	1.44 (1.31-1.58)	**<.001**
	c2B	1.95 (1.63-2.33)	**<.001**	1.18 (0.98-1.43)	.082	2.26 (1.98-2.57)	**<.001**	1.47 (1.28-1.69)	**<.001**
Histologic findings vs adenocarcinoma	Other	0.97 (0.88-1.06)	.470	1.02 (0.93-1.12)	.710	1.03 (0.96-1.10)	0.407	1.08 (1.00-1.15)	**.037**
	SCC	2.05 (1.92-2.20)	**<.001**	1.52 (1.41-1.64)	**<.001**	2.10 (1.99-2.21)	**<.001**	1.55 (1.47-1.64)	**<.001**
Anatomic location vs RML	RUL	1.54 (1.30-1.83)	**<.001**	1.51 (1.26-1.80)	**<.001**	1.47 (1.30-1.67)	**<.001**	1.42 (1.24-1.61)	**<.001**
	RLL	1.70 (1.43-2.02)	**<.001**	1.61 (1.34-1.93)	**<.001**	1.63 (1.44-1.85)	**<.001**	1.49 (1.31-1.71)	**<.001**
	LUL	1.44 (1.21-1.71)	**<.001**	1.32 (1.10-1.58)	**.003**	1.38 (1.22-1.56)	**<.001**	1.23 (1.08-1.41)	**.002**
	LLL	1.21 (1.01-1.46)	**.039**	1.09 (0.90-1.32)	.368	1.25 (1.09-1.42)	**.001**	1.09 (0.95-1.25)	.230
	Unknown/NOS	2.74 (2.22-3.38)	**<.001**	2.06 (1.65-2.58)	**<.001**	2.45 (2.10-2.87)	**<.001**	1.83 (1.54-2.16)	**<.001**
Surgery type, vs bilobectomy or lobectomy	Sublobar	0.78 (0.72-0.85)	**<.001**	0.74 (0.68-0.81)	**<.001**	0.85 (0.81-0.91)	**<.001**	0.83 (0.78-0.88)	**<.001**
	Pneumonectomy	3.71 (3.29-4.18)	**<.001**	3.30 (2.88-3.77)	**<.001**	3.45 (3.13-3.79)	**<.001**	2.95 (2.65-3.28)	**<.001**
Sequence No. vs first	Prior malignancy	1.06 (0.99-1.14)	.074			1.11 (1.05-1.17)	**<.001**	1.10 (1.04-1.16)	**<.001**

Bold indicates statistically significant values. AJCC = American Joint Committee on Cancer; LLL = left lower lobe; LUL = left upper lobe; NOS = not otherwise specified; NS = not significant; RLL = right lower lobe; RML = right middle lobe; RUL = right upper lobe; SCC = squamous cell carcinoma.

resection was performed at a facility that also offered SBRT. The primary outcome measures were 30-day and 90-day mortality rates, with the latter being increasingly accepted as the principal measure of early postoperative outcomes.[15-18]

As hypothesized, patients showed lower postoperative mortality rates whenever undergoing surgical resection at a facility that also offered SBRT. Outcomes were improved further at facilities with a longer duration of SBRT experience and greater SBRT to surgery volume ratios. Lower rates of postoperative mortality also were associated with higher surgical volume, geographic region, year of diagnosis, age, sex, race, insurance status, facility type, Charlson-Deyo score, clinical T classification, histologic findings, anatomic location, surgery type, and prior malignancy. Interaction testing showed negative results between these covariates and SBRT experience or SBRT to surgery volume ratio, demonstrating that each of these factors was statistically unrelated to other measurable confounders. Kaplan-Meier analysis was excluded intentionally because the outcome of interest was a binary vital status value at two postoperative time points, rather than an overall survival duration. In addition, a logistic regression model was favored over a Cox proportional hazards model given the binary end point and short follow-

up, as opposed to a long-term, time-to-event analysis.[19] Furthermore, an OR is interpreted more intuitively in the setting of a binary end point.

The data from this investigation cannot confirm causative factors to explain higher observed surgical mortality rates at facilities that lack an SBRT program. However, it is plausible that facilities that perform both surgical resection and SBRT for early stage lung cancer provide a more comprehensive and multidisciplinary approach to care that facilitates a safer matching of patients to each of these treatments. Same-facility access to SBRT also may encourage increased consideration of this alternative because patients and providers may be reluctant to consider nonsurgical options that require referral to an unaffiliated institution. At the same time, clinicians at facilities without an SBRT program may be less aware of the merits of SBRT in select cases, including data from clinical trials that have reported 3-year survival rates of up to 95% after SBRT.[20-24] Thus, these results are particularly pertinent for clinicians in primary care, pulmonology, or general surgery who frequently steward patients who recently received a diagnosis of with lung cancer through their initial phases of care.
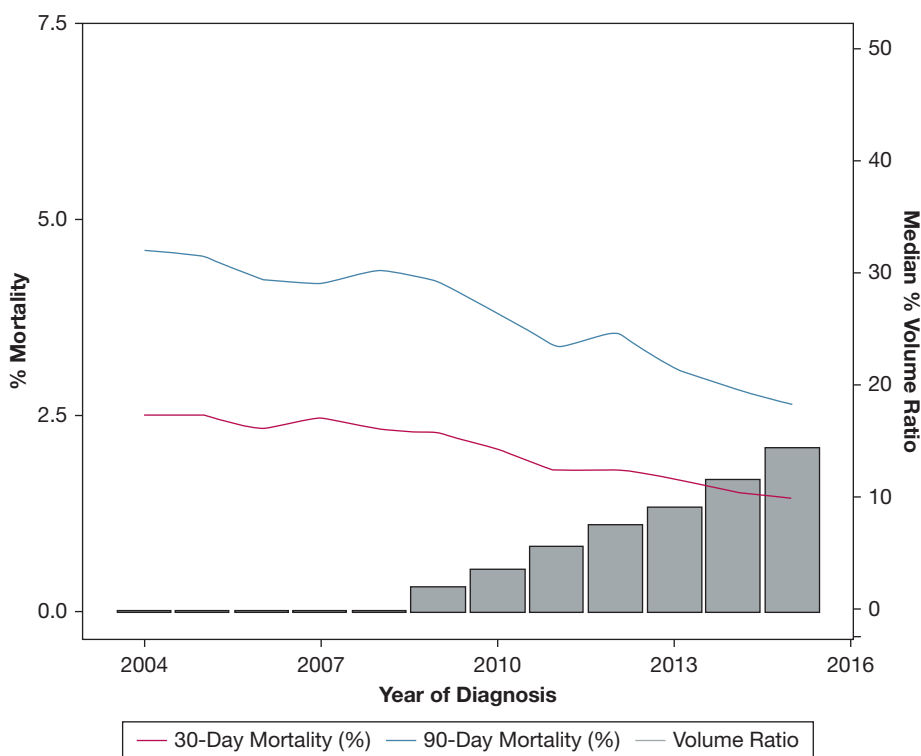

Figure 2 – *Trends in 30-day and 90-day postoperative mortality (lower and upper lines) and stereotactic body radiation therapy-to-surgery volume ratios (shaded bars).*

Although the findings of this study suggest that the availability and use of SBRT improves the selection of patients for surgery, it is understood that high-quality outcomes after surgery depend on multiple factors, including surgical volume, expertise, technique, and postoperative care, that are difficult to assess in retrospective databases. To address this issue, the STS has developed a publicly available resource that uses prospectively collected data to assign star ratings for thoracic surgery programs using a risk-adjusted outcome that considers patient-specific risk factors.[25] At this time, it is unclear whether the addition of same-facility availability and use ratios of SBRT may inform these STS models further.[26]

Study Limitations

As with any analysis of a large observational database, this study has limitations. The data in this report reflect the experience of medical facilities that are accredited by the American College of Surgeons Commission on Cancer that manages the NCDB and are subject to incomplete or inaccurate coding of patient data, including the radiotherapy method used. Trends in this report may not reflect those at non-NCDB reporting sites. Such trends include the observed declining rate of postoperative mortality, increasing use of SBRT, and observed associations of SBRT experience and SBRT to surgery volume ratios with lower postoperative mortality. A further limitation of this study is that the NCDB does not report pulmonary function testing results or individual patient age-adjusted mortality risks that are pertinent to stratifying surgical risk. As a result, this study cannot definitively confirm causation, that is, whether the lower mortality rates observed at facilities with experienced SBRT programs were the result of fewer high-risk patients not receiving surgery at these facilities or to the availability of an SBRT program acting as a surrogate for a more comprehensive lung cancer program that better matches patients to surgery or SBRT. Another limitation is the inability to adjust for the quality of preoperative staging, surgical technique, and perioperative care, which may have been associated with the availability and use of SBRT. Ultimately, comprehensive lung cancer programs offer multiple advantages beyond increased use of SBRT that can influence surgical mortality.

Interpretation

Postoperative mortality rates for early stage NSCLC reported to the NCDB declined steadily between 2004 and 2015, while use of SBRT increased. Lower postoperative mortality rates were observed among patients who underwent surgery at facilities with more years of SBRT experience and higher SBRT to surgery volume ratios. Lower rates of postoperative mortality were observed only above certain levels of SBRT experience and SBRT to surgery volume ratio, suggesting that the consideration of SBRT as an alternative to surgery by patients and surgeons may not occur immediately on the introduction of a lung SBRT program. The observation of higher postoperative mortality rates at facilities without an SBRT program merits further investigation.

Acknowledgments

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