A Comparative Analysis of Long-Term Survival of Robotic Versus Thoracoscopic Lobectomy

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Background. **Minimally invasive lobectomy can be performed robotically or thoracoscopically. Short-term outcomes between the 2 approaches are reported to be similar; however, the comparative oncological effectiveness is not known. We sought to compare long-term survival after robotic and thoracoscopic lobectomy.**

Methods. **We performed a propensity-matched analysis of SEER (Surveillance, Epidemiology and End Results)-Medicare patients with non-small cell lung cancer from 2008 to 2013 who underwent minimally invasive lobectomy using either a thoracoscopic (n = 3881) or a robotic-assisted (n = 426) approach. Patients in the 2 groups were propensity matched 1:1 based on demographics, comorbidities, treatment, and tumor characteristics. We compared the overall survival (OS) and cancer-specific mortality (CSM) between the 2 groups.**

Results. **Within the matched cohort (n = 409 per group), the median age at surgery was 73 (range, 65-91) years, with a median follow-up of 35 months postsurgery. There was no difference in OS or CSM between the thoracoscopic and robotic-assisted groups (OS: 71.4% vs 73.1% at 3 years, overall $P = .366$; CSM: 16.6% vs 14.9% at 3 years, overall $P = .639$).**

Conclusions. **Our propensity-matched analysis demonstrates that patients undergoing robotic-assisted lobectomy have similar OS and CSM compared with those patients undergoing thoracoscopic lobectomy. Oncologic outcomes are similar between the 2 minimally invasive approaches. These results demonstrate that further investigation is needed in the form of a randomized control trial, its variations, or additional large-scale registry analyses to verify these results.**

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Lung cancer is a leading cause of cancer death worldwide.[1] Surgical resection of early-stage disease affords the best chance of cure. The standard approach to lobectomy has been through a thoracotomy. Minimally invasive approaches such as thoracoscopic lobectomy have been performed for more than 20 years and have gained popularity in multiple centers as the approach of choice for the resection of lung cancer. However, its adoption has been slow despite its reported advantages of fewer complications, faster functional recovery, and equivalent oncologic outcomes.[2-7] To date, no large-scale randomized control trial (RCT) has been done to evaluate equivalence.

Robotic-assisted lobectomy has been introduced over the last decade as an alternative approach to thoracoscopic lobectomy. Proponents of the robotic approach argue that it is easier to adopt than thoracoscopic methods and allows for improved lymph node yields with a potential for improved overall survival (OS).[8-13] Again, no large-scale RCT has been done to evaluate superiority or equivalence. The SEER (Surveillance, Epidemiology and End Results)-Medicare program links data from 17 cancer registries to Medicare data to create a nationally representative large longitudinal cohort.[14] SEER-Medicare data were analyzed to compare the oncologic effectiveness of robotic-assisted vs thoracoscopic lobectomy.

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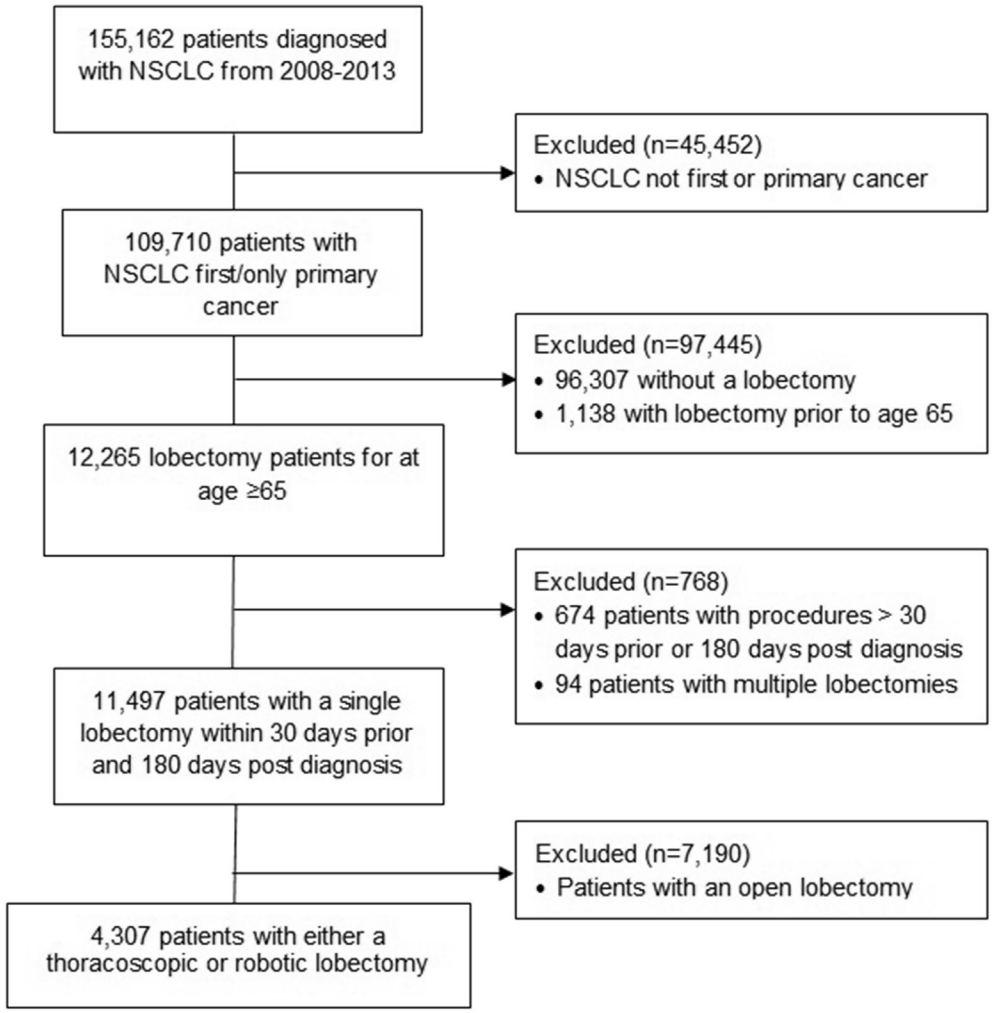

Figure 1. CONSORT diagram. (NSCLC, non-small cell lung cancer.)

Patients and Methods

Data Source

The SEER-Medicare dataset includes patient demographics, cancer diagnosis and treatment-related information, and cause of death linked to Medicare data. The Medicare linkage provides Medicare hospital, outpatient, physician, home health, and hospice claims. Medicare insures approximately 97% of people 65 years of age and older in the United States, allowing approximately 93% of that population in the SEER registry to be linked to the Medicare enrollment file.[14,15] The current release contains patients diagnosed through 2013 linked to Medicare claims through 2014, with enrollment and survival data through 2015. The study was approved by the Saint Barnabas Medical Center Institutional Review Board (Protocol No. 17-67).

Study Cohort

Medicare patients greater than or equal to 65 years of age who underwent a single lobectomy in the time period from 1 month before to 6 months after diagnosis of a first primary non-small cell lung cancer from 2008 to 2013 were eligible for inclusion in this study. These years were chosen as the code for thoracoscopic lobectomy (International Classification of Diseases-Ninth Revision-Clinical Modification code 32.41) became available in 2007, and the code for robotic assistance (International Classification of Diseases-Ninth Revision-Clinical Modification code 17.4) was available beginning in 2009. Patients with prior primary cancer diagnoses were excluded (Figure 1).

Outcomes

OS was defined as time from surgery until death or loss to follow-up (December 31, 2015). SEER provides information about disease-specific cause of death, allowing us to determine cancer-specific mortality (CSM). The primary outcome measure examined was to compare OS and CMS between robotic-assisted and thoracoscopic lobectomy. Immediate postoperative outcomes were secondary measures and assessed as previously described.[3,4,9]

Variables

We categorized patients by disease, site, demographic, and surgery-specific variables provided in the SEER

Table 1. Patients' Baseline Characteristics for Thoracoscopic and Robotic-Assisted Lobectomy in the Propensity-Matched Cohort

Variable	Surgery Type		Standardized Difference (*P*)
	Thoracoscopic (n = 409)	Robotic (n = 409)	
Age, y[a]	74 (65-88)	73 (65-91)	.048
Age group			.128
65-69 y	102 (24.9)	111 (27.1)	
70-74 y	124 (30.3)	131 (32.0)	
75-79 y	107 (26.2)	85 (20.8)	
80+ y	76 (18.6)	82 (20.0)	
Sex[a]			.059
Female	233 (57.0)	221 (54.0)	
Male	176 (43.0)	188 (46.0)	
Race[a]			.057
White	355 (86.8)	347 (84.8)	
Black	22 (5.4)	26 (6.4)	
Other	32 (7.8)	36 (8.8)	
Married			.037
No	157 (39.9)	165 (41.8)	
Yes	236 (60.1)	230 (58.2)	
2010 ACS median income quartile (thousands)[a]			.033
12.5-45.5	119 (29.1)	118 (28.9)	
45.5-63.2	88 (21.5)	91 (22.2)	
63.2-85.4	103 (25.2)	98 (24.0)	
85.4-250	99 (24.2)	102 (24.9)	
Location[a]			.047
Metropolitan	361 (88.3)	367 (89.7)	
Nonmetropolitan	48 (11.7)	42 (10.3)	
Diabetes[a]			.024
No	323 (79.0)	319 (78.0)	
Yes	86 (21.0)	90 (22.0)	
Hypertension[a]			.050
No	162 (39.6)	152 (37.2)	
Yes	247 (60.4)	257 (62.8)	
Coronary artery disease[a]			.065
No	299 (73.1)	287 (70.2)	
Yes	110 (26.9)	122 (29.8)	
Congestive heart failure[a]			.065
No	390 (95.4)	384 (93.9)	
Yes	19 (4.6)	25 (6.1)	
Chronic pulmonary disease[a]			.020
No	195 (47.7)	191 (46.7)	
Yes	214 (52.3)	218 (53.3)	
Peripheral vascular disease			.081
No	362 (88.5)	372 (91.0)	
Yes	47 (11.5)	37 (9.0)	
Year of surgery[a]			.121
2008	<11	<11	
2009	<11	12 (2.9)	
2010	21 (5.1)	25 (6.1)	
2011	88 (21.5)	80 (19.6)	
2012	>136 (33.3)	>143 (>35.0)	
2013	129 (31.5)	122 (29.8)	
2014	13 (3.2)	16 (3.9)	
Stage[a]			.087
1	273 (66.7)	281 (68.7)	
2	42 (10.3)	45 (11.0)	
3	77 (18.8)	64 (15.6)	
4	17 (4.2)	19 (4.6)	
Histology[a]			.074
Adenocarcinoma	219 (53.5)	211 (51.6)	
Adenosquamous	12 (2.9)	13 (3.2)	
Bronchioloalveolar carcinoma	17 (4.2)	14 (3.4)	
Squamous	147 (35.9)	159 (38.9)	
Other	14 (3.4)	12 (2.9)	
Site[a]			.057
Lower	>147 (>35.9)	>150 (>36.7)	
Middle	27 (6.6)	23 (5.6)	
Upper	224 (54.8)	225 (55.0)	
Other	<11	<11	
Tumor size, mm[a]	25 (3-86)	25 (5-150)	.112
Tumor size group[a]			.154
1-20 mm	139 (34.0)	147 (35.9)	
21-30 mm	124 (30.3)	102 (24.9)	
31-40 mm	69 (16.9)	72 (17.6)	
41-50 mm	41 (10.0)	38 (9.3)	
51+ mm	36 (8.8)	50 (12.2)	
Hospital procedure volume[a]			.026
1-4	20 (4.9)	20 (4.9)	
5-19	117 (28.6)	119 (29.1)	
20-39	178 (43.5)	173 (42.3)	
40+	94 (23.0)	97 (23.7)	
Neoadjuvant therapy[a]			.119
Chemotherapy	<11	15 (3.7)	
Radiation	<11	<11	
Chemoradiation	<11	<11	
None	>376 (>91.9)	>372 (>91.0)	
Adjuvant therapy[a]			.083
Chemotherapy	60 (14.7)	60 (14.7)	
Radiation	13 (3.2)	<11	
Chemoradiation	<11	15 (3.7)	
None	>325 (79.5)	>323 (79.0)	

[a]Used for propensity matching.

Values are median (range) or n (%).

registry, including pathological stage (Derived AJCC Stage Group, 6th edition), histology (adenocarcinoma, adenosquamous, squamous, bronchioloalveolar carcinoma, other), side, site (lower, middle, upper lobe), tumor size and number of nodes examined, age on surgery date, year of procedure, sex, race (black, white, other), marital status at diagnosis, metropolitan area (rural, urban), zip code per-capita income, and hospital procedure volume based on the number of procedure in the cohort. Within the full cohort, in cases in which the number of nodes examined was unknown or unstated but documented as being done (n = 400, 9.3%), the median number of nodes observed in the full cohort (9) was imputed. Additionally, we identified patients with a diagnosis of diabetes, hypertension, congestive heart failure, coronary artery disease, peripheral vascular disease, and chronic pulmonary disease during the surgical hospitalization as done previously (Supplemental Table 1).[3,9] Data from inpatient (MEDPAR [Medicare Provider Analysis and Review]), outpatient, and carrier claims (National Claims History) files were used to identify neoadjuvant and adjuvant therapy, defined as treatment with chemotherapy, radiation, or a combination of the 2 within 180 days prelobectomy or postlobectomy, respectively (Supplemental Table 1). The first day of the month was used to define the date of diagnosis, given that only the month and year are provided, and patients with an unknown month or year of diagnosis were excluded. Cell counts of 1 to 10 were coarsened in the data summaries in accordance with the SEER-Medicare data use agreement.

Statistical Analysis

Propensity score matching was used to match patients in the thoracoscopic and robotic surgery groups using a logistic regression approach, with nearest-neighbor matching, and a caliper of 0.2 standard deviations. Variables included in the propensity model were age at surgery, sex, race, site, stage, histology, tumor size, surgery year, location, hospital volume, median income, diabetes, hypertension, congestive heart failure, coronary artery disease, chronic pulmonary disease, and neoadjuvant and adjuvant therapy. Patient and treatment characteristics were assessed across groups using the standardized difference. OS was estimated using the Kaplan-Meier method, with differences in groups assessed with a log-rank test. CSM was estimated using the cumulative incidence method, with non–cancer-related mortality considered a competing risk, and differences assessed between groups using Gray's test. All analyses were carried out using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patients

A total of 4307 patients undergoing lobectomy were identified (thoracoscopy: n = 3881; robotic-assisted: n = 426). Patient demographics, comorbidities, and tumor characteristics are listed in Table 1 for the matched cohort

Table 2. In-Hospital Outcomes Comparison for Thoracoscopic vs Robotic-Assisted Lobectomy in the Propensity-Matched Cohort

Variable	Surgery Type		Standardized Difference (*P*)
	Thoracoscopic (n = 409)	Robotic (n = 409)	
Nodes	9 (0-87)	9 (0-57)	.005
Nodes quartile			.111
0-5	111 (27.1)	93 (22.7)	
5-9	134 (32.8)	149 (36.4)	
9-14	65 (15.9)	69 (16.9)	
14-90	99 (24.2)	98 (24.0)	
Arrhythmia			.064
No	311 (76.0)	322 (78.7)	
Yes	98 (24.0)	87 (21.3)	
Pneumonia			.072
No	381 (93.2)	388 (94.9)	
Yes	28 (6.8)	21 (5.1)	
Atelectasis			<.001
No	363 (88.8)	363 (88.8)	
Yes	46 (11.2)	46 (11.2)	
Ventilation			.109
No	382 (93.4)	392 (95.8)	
Yes	27 (6.6)	17 (4.2)	
Sepsis			.098
No	>398 (>97.3)	>398 (>97.3)	
Yes	<11	<11	
Stroke			.043
No	395 (96.6)	398 (97.3)	
Yes	14 (3.4)	11 (2.7)	
Myocardial infarction			.059
No	>398 (>97.3)	>398 (>97.3)	
Yes	<11	<11	
Puncture			.041
No	>398 (>97.3)	>398 (>97.3)	
Yes	<11	<11	
Pneumothorax			.123
No	363 (88.8)	346 (84.6)	
Yes	46 (11.2)	63 (15.4)	
Pulmonary edema			.070
No	>398 (>97.3)	409 (100.0)	
Yes	<11	0	
Renal failure			.114
No	374 (91.4)	386 (94.4)	
Yes	35 (8.6)	23 (5.6)	
Bleeding			.041
No	>398 (>97.3)	>398 (>97.3)	
Yes	<11	<11	
Length of stay, d	5 (1-49)	5 (1-45)	.022
In-hospital mortality			.100
No	>398 (>97.3)	>398 (>97.3)	
Yes	<11	<11	

Values are median (range) or n (%).

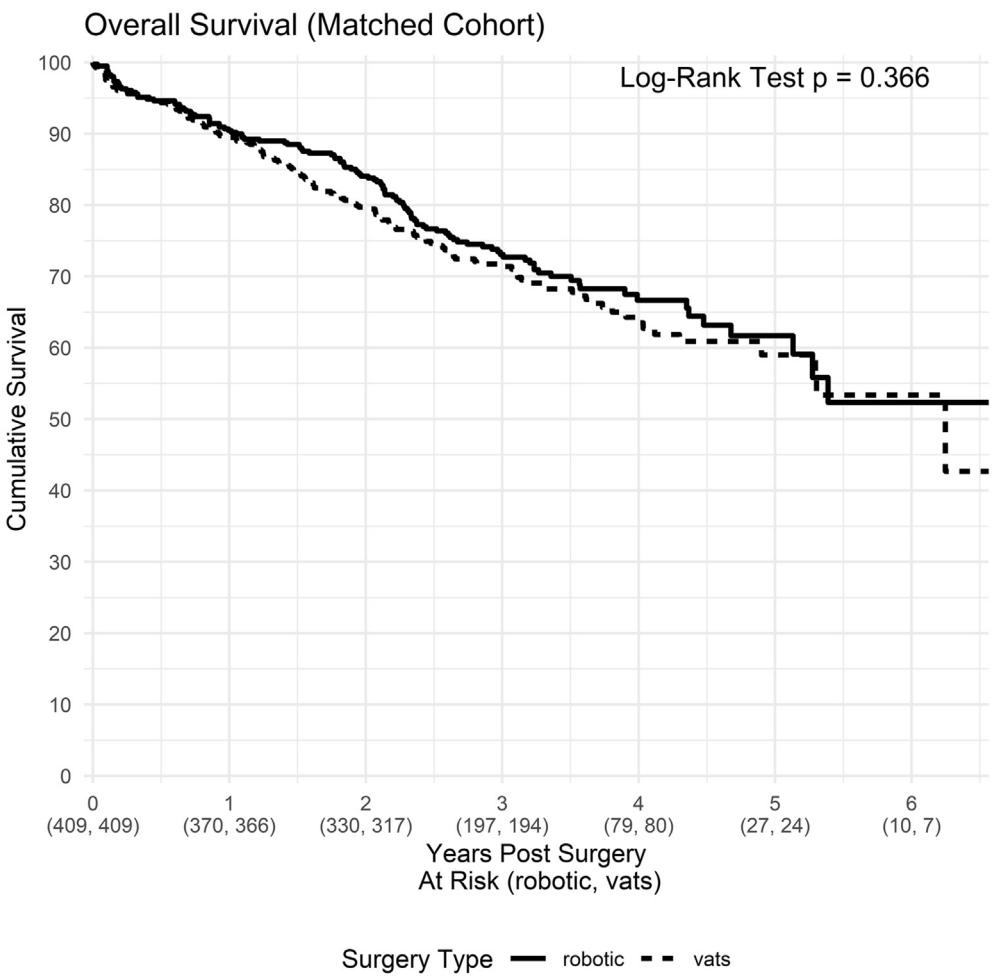

Figure 2. Overall survival in the propensity-matched cohort. (VATS, video-assisted thoracoscopic surgery.)

and in Supplemental Table 2 for the full cohort. Patients undergoing thoracoscopic and robotic-assisted lobectomy were similar in age, sex, median income, and the site of surgery. Patients undergoing thoracoscopic lobectomy were less likely to have coronary artery disease and more likely to have peripheral vascular disease. Histologic characteristics of the tumors were similar between the 2 groups, with the majority of patients having adenocarcinoma or subtypes of adenocarcinoma (Supplemental Table 2). However, patients undergoing thoracoscopic lobectomy had more adenocarcinomas resected and less squamous carcinoma compared with those patients undergoing robotic-assisted lobectomy (Supplemental Table 2). Within the thoracoscopic group, 3.8% of patients received neoadjuvant therapy and 18.6% received adjuvant therapy, while in the robotic group, 5.4% received neoadjuvant therapy and 20% received adjuvant therapy. Chemotherapy was the primary neoadjuvant and adjuvant therapy given.

The matched cohort consisted of 409 patients in each treatment category, and balance was achieved based on available variables (C-index = 0.58) (Table 1).

Morbidity and Mortality

In the matched and unmatched cohorts, thoracoscopic and robotic-assisted lobectomy patients had similar rates of postoperative complications as well as in-hospital mortality (Table 2 and Supplemental Table 3).

OS and CSM

The median follow-up for all patients in the full and matched cohorts was 39 and 35 months, respectively. In our unmatched and matched analysis, there was no difference in OS and CSM between the thoracoscopic and robotic approaches (matched cohort [Figure 2]: 3-year OS, 71% vs 73%; $P = .366$; matched cohort [Figure 3]: 3-year CSM, 17% vs 15%; $P = .639$; full cohort [Supplemental Figure 1]: 3-year OS, 72% vs 71%; $P = .924$; full cohort [Supplemental Figure 2]: 3-year CSM, 18% vs 16%; $P = .141$).

Comment

Our propensity-matched analysis of long-term OS and CSM after lobectomy suggests that there are no

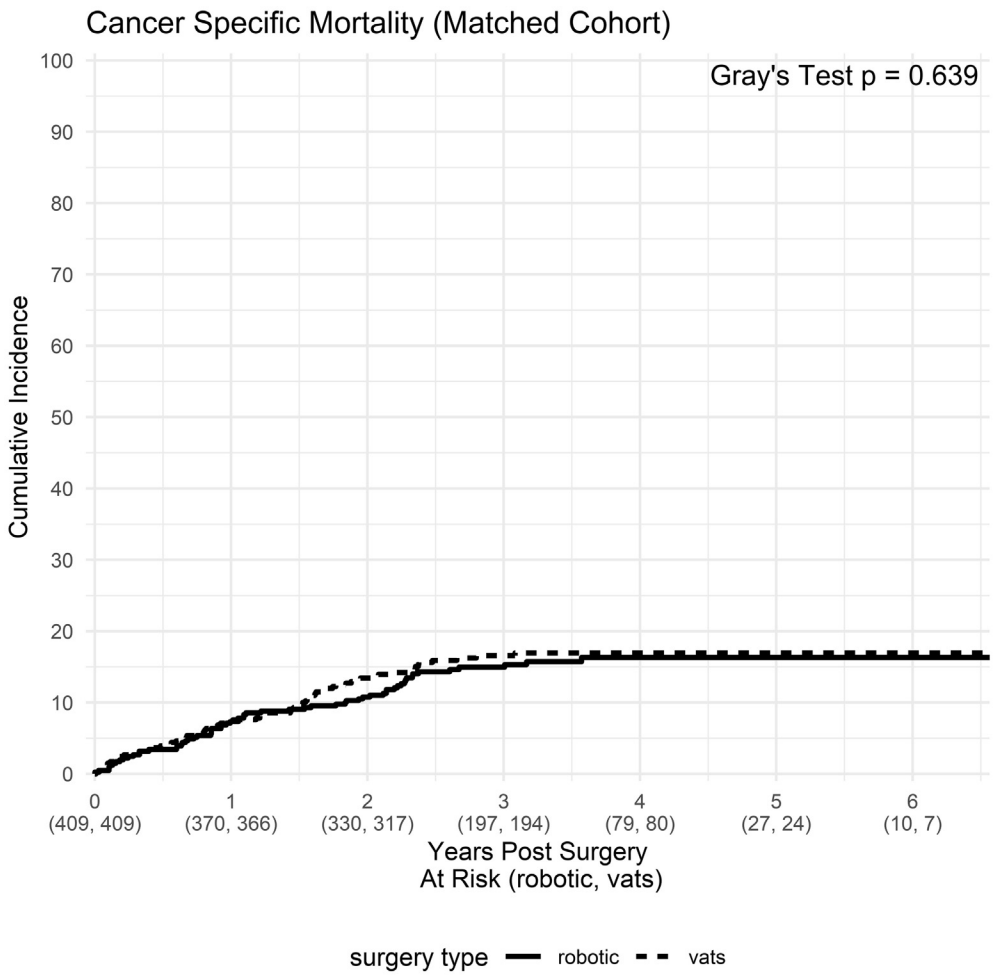

Figure 3. Cancer-specific mortality in the propensity-matched cohort. (VATS, video-assisted thoracoscopic surgery.)

differences in long-term outcomes in patients undergoing robotic-assisted or thoracoscopic lobectomy. These minimally invasive lobectomy approaches also have similar in-hospital outcomes with the exception of mortality, which was higher in the thoracoscopic group.

Our results differ from those published from multi-institutional case series, while supporting other single-institution case series (Table 3).[11,16] The improved OS seen in the multiinstitutional series could be because of unknown confounding that is specifically minimized in a RCT. Our study as well is not immune to unknown confounding. As it is a population-based analysis of registry and administrative data, implicit biases in the selection of patients can exist that cannot be balanced by propensity matching. Moreover, our results represent a national sample and not the results of a select group of robotic surgeons whose results may not be reproducible in the community.

Our results support other population-based analyses comparing long-term survival after thoracoscopic and thoracotomy lobectomy approaches. These studies demonstrate the noninferiority of thoracoscopic lobectomy for long-term survival when compared with lobectomy by thoracotomy.[3] Proponents of various approaches argue that some approaches allow for better lymph node harvesting, a "no touch" technique with limited manipulation of the tumor, or decreased cytokine production leading to improved long-term survival.[6,8,10,11,17,18] In our view, as long as the surgical approach adheres to the principles of oncologic surgery with attention to an R0 resection and adequate lymph node dissection, the outcome should not vary by approach whether thoracotomy, mulitportal or uniportal thoracoscopic, or robotic-assisted.

Detractors of minimally invasive lobectomy or solely robotic surgery may argue that these results suggest that because approach does not matter, why offer robotic-assisted lobectomy at all? Clearly, there may be associated costs for the robotic platform as well as an inherent learning curve in using new technology. As the utilization of minimally invasive lobectomy is low, any technique that is reproducible and safely adopted by surgeons should be encouraged as long as the long-term oncologic efficacy is the same, cost and learning curve considerations aside. Promising growth has been appreciated in robotic lobectomy with recent analysis of the Florida State Inpatient Database showing an increase in use of robotic lobectomy from less than 1.0% in 2008 to 25% in 2014.[19]

Table 3. Recent Population-Based Analysis Comparing Robotic-Assisted, Video-Assisted, and Open Lobectomy for Treatment of Non-Small Cell Lung Cancer

Author	Source	Sample Size	Population	Lobectomy Comparator	Years	Conclusion
Paul et al[3]	SEER-Medicare	2390	Stage I-IIIa	VATS, open	2007-2009	No difference in OS, CSS, and DFS
Lee et al[21]	Single-institution prospective database	416	Stage I-IIIa	VATS, open	1990-2011	No difference in OS or DFS
Higuchi et al[22]	Single-institution prospective database	160	Stage IA	VATS, open	2002-2012	No difference in DFS or OS
Yang et al[16]	Single-institution prospective database	470	Stage I	RATS, VATS, open	2002-2012	No difference in OS or DFS
Li et al[23]	Single-institution prospective database	121	Stage IIb-IIIa	RATS, VATS	2014-2017	No difference in 3-y DFS and 3-y OS
Kneuertz et al[24]	STS-GTS	514	Stage I-IIIa	RATS, VATS, open	2012-2017	No difference in OS or RFS between RATS, VATS, and open

CSS, cancer-specific survival; DFS, disease-free survival; OS, overall survival; RATS, robotic-assisted thoracic surgery; RFS, recurrence-free survival; SEER, Surveillance, Epidemiology, and End Results; STS-GTS, Society of Thoracic Surgeons General Thoracic Surgery; VATS, video-assisted thoracic surgery.

From a technological perspective, it would be hard for adopters of minimally invasive lobectomy or the patient (as a consumer) to want to switch back to open techniques. As technology progresses, minimally invasive techniques may offer new modalities such as intraoperative imaging techniques to identify vessels and tissues planes or automate some of the surgical process. It is rare that technology ever moves into the background, except in the setting of nostalgia.

Our analysis suggests that a large-scale RCT may provide additional insight in answering the question of whether oncologic outcomes are the same for the 2 approaches. However, it is unclear that a large-scale trial can be completed with the inherent biases of both patients and surgeons for or against new technology. The VIOLET (VIdeo Assisted Thoracoscopic Lobectomy Versus Conventional Open LobEcTomy for Lung Cancer) multicenter randomized controlled trial, whose results were recently presented comparing open and thoracoscopic techniques, is admirable in that it was completed.[20] However, it is almost too late, as new technologies such as robotics, stereotactic body radiation therapy, and other ablative technologies seek to replace thoracoscopic lobectomy. RCTs are difficult to accomplish in this space because of inherent biases from large-volume hospitals and surgeons who may favor one approach over another, or because marketing and financial pressures may make the completion of a trial impossible. Other innovative approaches to compare surgical techniques in real time may be required, such as through national registries or RCTs using clustering of surgical techniques.

We recognize that there are several limitations to our analysis. Foremost, this is not an RCT, and there are inherent selection biases, which can be adjusted for but never completely eliminated. We attempted to account for apparent biases in our propensity matching. However, we cannot account for differences between the 2 groups that are not known, such as surgeon experience and surgical technique. An intention-to-treat analysis cannot also be performed, as conversion rates to thoracotomy are not known. SEER-Medicare does not capture clinical staging data. Therefore, we are unable to evaluate pathologic upstaging data. In addition, SEER-Medicare does not provide disease recurrence. Last, the overall quality of postoperative care and surveillance cannot be extrapolated from SEER-Medicare data.

In conclusion, our population-based analysis of SEER-Medicare data, with its inherent limitations, suggests that patients undergoing robotic-assisted lobectomy have similar long-term survival outcomes compared with those patients undergoing thoracoscopic lobectomy. Further investigation in the form of an RCT, its variations, if possible, or additional large-scale registry analyses is warranted for evaluation of this technology.

This study used the linked SEER-Medicare database. The interpretation and reporting of these data are the sole responsibility of the authors. The authors acknowledge the efforts of the National Cancer Institute; the Office of Research, Development and Information, CMS; Information Management Services (IMS), Inc.; and the Surveillance, Epidemiology, and End Results (SEER) Program tumor registries in the creation of the SEER-Medicare database.

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