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Evolution in the Surgical Care of Non-Small Cell Lung Cancer (NSCLC) Patients in the Mid-South Quality of Surgical Resection (MS-QSR) Cohort

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Abstract

Objective—Surgery is the most important curative treatment modality for patients with early stage non-small cell lung cancer (NSCLC). We examined the pattern of surgical resection for NSCLC in a high incidence and mortality region of the US over a 10-year period (2004–2013) in the context of a regional surgical quality improvement initiative.

Methods—We abstracted patient-level data on all resections at 11 hospitals in 4 contiguous Dartmouth Hospital Referral Regions in North Mississippi, East Arkansas and West Tennessee. Surgical quality measures focused on intraoperative practice, with emphasis on pathologic nodal staging. We used descriptive statistics and trend analyses to assess changes in practice over time. To measure the impact of an ongoing regional quality improvement intervention with a lymph node specimen collection kit, we used period effect analysis to compare trends between the pre- and post-intervention periods.

Results—Of 2,566 patients, 18% had no preoperative biopsy, only 15% had a preoperative invasive staging test, and 11% underwent mediastinoscopy. The rate of resections with no mediastinal lymph nodes examined decreased from 48% to 32% ($p < 0.0001$) while the rate of

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resections examining 3 or more mediastinal stations increased from 5% to 49% ($p<0.0001$). There was a significant period effect in the increase in the number of N1, mediastinal and total lymph nodes examined (all $p<0.0001$).

Conclusion—A quality improvement intervention including a lymph node specimen collection kit shows early signs of having a significant positive impact on pathologic nodal examination in this population-based cohort. However, gaps in surgical quality remain.

INTRODUCTION

The predicted aggregate 5-year survival of the 230,000 individuals diagnosed annually with lung cancer in the US is approximately 18%.¹ Most of these 5-year survivors are patients with early stage non-small cell lung cancer (NSCLC) who had curative-intent surgical resection.² However, fewer than 50% of patients who have surgery for lung cancer survive 5 years.^{3, 4} Gaps in the quality of resection and pathologic nodal staging are associated with lower-than-expected long term survival rates in populations.^{5–8}

In the surgical resection population, the pathologic nodal stage is a major determinant of prognosis.⁹ Variation in the quality of pathologic nodal staging drives long-term survival disparities.^{5–8,10,11} Theoretically, improving access to high-quality surgical care for early-stage NSCLC is a major opportunity to improve population-level lung cancer survival. Such efforts must focus on improving surgical and pathologic processes critical for thorough and accurate pathologic nodal staging in order to provide the intrinsic benefit of oncologically sound resection, ensure identification of residually high-risk patients who may benefit from existing adjuvant therapy and, importantly, correctly categorize patients enrolled into clinical trials of novel adjuvant treatments.

The Mid-South region of the US, which includes North Mississippi, East Arkansas and West Tennessee, has some of the highest lung cancer incidence and mortality rates in the US. Major problems of healthcare access, quality, and outcome disparities exist in this region.^{12–14} Using a comparative observational population-based cohort study design, we examined the pattern of surgical resection for NSCLC in a heterogeneous group of institutions in this region to test the early, population-level impact of specific regional quality improvement efforts.

METHODS

Patient cohort

The study was approved, with a waiver of informed consent, by the Institutional Review Boards at all participating institutions. We retrospectively studied all patients receiving primary lung cancer surgery from January 1, 2009, to December 31, 2013, at 11 hospitals from 4 pre-specified, geographically contiguous Dartmouth Referral Regions in East Arkansas, North Mississippi and West Tennessee. Six of the 11 institutions had participated in a previous, more limited retrospective review of lung cancer resections from January 1, 2004 to December 31, 2008 (Appendix 1).¹⁴ Institutions within these Hospital Referral Regions were eligible to participate in this Mid-South Quality of Surgical Resection (MS-QSR) database if they averaged 5 or more curative-intent resections per year. The degree of

detail about preoperative tests and disease characteristics in the earlier database was more limited, but operative, post-operative, and pathology details were consistent across all 10 years. The MS-QSR database is now prospectively updated, but the current analysis is based on retrospectively collected data up to the point of prospective collection.

Patients at each institution were identified and screened for eligibility by cross-referencing three separate lists provided by each institution's Health Information Management (using ICD-9 procedure codes 32.20 – 32.90 [wedge to pneumonectomy, plus "other excision"]), Tumor Registry, and Pathology Departments (using self-selected search algorithms). Resections for benign lung disease, small cell lung cancer, and non-lung primary cancers were excluded. Only the first resection was included for analysis for patients receiving multiple lung resections. At the time of data censoring, the MS-QSR database contained records of 2,566 eligible patients (Appendix 2). Except where noted, analysis was limited to variables available over the full 10 years.

Data abstraction

Trained, dedicated research staff reviewed all available inpatient and outpatient clinical records, starting with the final post-resection pathology report and working back to the initial radiology report that showed an abnormal lung lesion, to abstract all relevant data from operation reports, admission notes, discharge summaries, nurses' notes, progress notes, pre-surgical physiologic clearance tests, clinic notes, radiologic studies, invasive diagnostic and staging tests, and their associated pathology reports. The number of lymph nodes examined was strictly abstracted from the pathology reports. Whole lymph nodes were counted individually, all reference to lymph node fragments or non-quantitative descriptions such as 'multiple' were counted as a single lymph node to avoid over-counting bias.

Definition of quality measures for surgical care

We grouped surgical quality care measures into three categories: preoperative, intraoperative, and postoperative. We measured the pattern of use of certain preoperative diagnostic and staging tests as a surrogate for the quality of pre-surgical care. Diagnostic tests were defined as any attempted pre-resection biopsy to confirm a suspected lung cancer. Staging tests were classified as either non-invasive or invasive. Non-invasive staging tests included PET/CT scans and non-thoracic radiographic scans performed after lesion identification, but before surgical resection. Invasive staging tests were defined as any attempted biopsy of an anatomic site other than the site of the primary lung lesion. These included mediastinoscopy and bronchoscopic lymph node biopsies.

Intraoperative measures of surgical quality included the rates of pneumonectomy, margin-positivity, and use of minimally-invasive surgical techniques. Intraoperative lymph node examination quality was defined by two broad parameters: median lymph node counts and rates of lymph node examination. Median lymph counts included lymph nodes sampled from station 10 (hilar), stations 11–14 (intrapulmonary), all N1, all mediastinal, and all lymph node stations. Lymph node examination rates included resections with zero lymph nodes (pNX rate), resections with no mediastinal lymph nodes, resections with sampling of hilar, and subcarinal (station 7) lymph nodes, and resections with 3 or more mediastinal

stations (a quality standard recommended by the National Comprehensive Cancer Network).¹⁵ Intraoperative lymph node counts were restricted to the surgical resection only, and do not include lymph node sampling done pre-operatively with invasive staging biopsies.

Postoperative quality measures were 30- and 60-day readmission rates, mortality rates at 30-, 60-, and 90-days, and 1-year overall survival rates.

Quality improvement initiatives

From 2008 to 2010, our research group analyzed the pattern of surgical resection in Metropolitan Memphis Hospitals from 2004 to 2007 and shared summary details on the prevalence and survival implications of the pathologic nodal staging quality gap with administrators, surgeons and pathologists at participating hospitals.^{7,8,12,14} In 2009, we began a coordinated program to improve mediastinal lymph node examination. This initiative had two parallel tracks: a regional educational effort to inform clinicians about the quality gap in surgical lymph node examination (problem definition)^{14, 16} and the introduction, in 2010, of a lymph node specimen collection kit for use in the operating room (solution implementation).^{12,17,18} Details on the characteristics of this kit have been provided previously (Appendix 3).^{17,18} The ongoing educational effort includes multiple individual and group meetings with hospital administrators, surgeons, pathologists and cardiovascular surgery operating room staff across the region. In 2010, we began pilot studies with the lymph node specimen collection kit at 2 institutions. This has since expanded to a regional intervention project using a multiple baseline, staggered implementation strategy.¹⁹ Using a conservative approach, we chose 2010, the year the kit was introduced, as the fulcrum date between the pre- and post-implementation periods.

By comparing the difference between trends in the pre-intervention (2004 – 2009) and post-intervention (2010 – 2013) periods, we sought early signals of the impact of this quality improvement program on process measures of the quality of lung cancer surgical practice at the broad population level.

Statistical methodology

We used descriptive statistics to summarize patients' socio-demographic, clinical and management characteristics, including procedures performed pre-, intra- and post-operatively. All trend plots are unadjusted; T-test was used for comparing continuous variables, and chi-squared test for categorical variables.

To test linear trends and period effects of surgical quality indicators, we employed linear regression models for continuous outcomes, and logistic regression for binary outcomes including pneumonectomy, resection margin, and open thoracotomy over time. We used Poisson regression to assess the trend of the total number of lymph nodes, mediastinal lymph nodes, and intrapulmonary lymph nodes examined over time. Period effects were assessed by including the period indicator, 2010 (when the lymph node collection kit was introduced), in the various models. The difference in trends between the pre-intervention and post-intervention periods was assessed with the interaction between time and period in the same models. If the difference was statistically significant, this constituted a period effect. If

the difference was not statistically significant, then the interaction term was dropped from the model. Multi-variable analyses were also performed, adjusting for stage, margin status, age, sex, race, insurance, histology, number of comorbidities, institution, and use of the lymph node kit (not included in the period effect model), and are reported where notably different from univariate analyses. We explicitly included the surgical kit use indicator in the various models to assess the impact of surgical kit use on the quality indicators related to lymph nodes. Finally, we performed a sensitivity analysis restricted to the 6 institutions (representing 79% of the cohort) with data available over the full timespan of the study.

In this way, we used a trend analysis to illustrate significant changes in practice over the full 10-year timespan, and the period effect analysis to examine for significant change in trends between the pre-intervention and post-intervention periods that were associated with our quality improvement initiatives. All statistical analyses were performed using SAS 9.4. (2013, SAS Institute Inc., Cary, NC). All tests were two-sided, and $p < 0.05$ was considered statistically significant. We made no adjustments for multiple testing.

RESULTS

Overall cohort characteristics

For this analysis, the MS-QSR cohort includes 2,566 patients with NSCLC, of which 1,215 (47%) were female and 1,351 (53%) male. The majority of patients were Caucasian (78%), 21% were African-American and 1% were of another race. The median age of the cohort was 67 years, 49% had Medicare as their primary insurance, 35% had primary commercial insurance, 12% had Medicaid and 4% were uninsured.

Fifty-two percent of patients had adenocarcinoma, 35% had squamous cell carcinoma and 13% had other histologic variants. In this surgical resection population, 84% had either pT1 or pT2 tumors. Nodal metastasis was noted in the final pathology result in 21% of cases: 13% were pN1 and 8% were pN2. The majority of patients (83%) were Stage IA – IIB; 15% were Stage IIIA – IV; 17 patients (1%) were pathologic Stage 0; and the records were insufficient to report pathologic stage for 15 patients (Table 1).

Pattern of pre-operative care

Because of missing data in the earlier (2004–2008) dataset, the pre-operative quality of care analysis over the full 10 years was limited to use of PET/CT scan and mediastinoscopy as staging tests. Over that timespan, 1,631 patients (64%) had a pre-operative PET/CT, but only 283 (11%) had a pre-operative mediastinoscopy. Pre-operative chemotherapy and/or radiation therapy was used in 136 patients (5%).

Pattern of operative care

Seventy-three percent of patients underwent lobectomy, 13% had sublobar resections and 14% received bi-lobectomy or pneumonectomy. Seventy-seven percent of resections were completed as open thoracotomy, 14% were video-assisted thoracoscopic resections and 9% were robotically-assisted. Final resection margins were positive in 6% of cases (Table 2a).

Overall quality of pathologic nodal staging

Nine percent of resections had no lymph nodes (pNX), 16% had no N1 lymph nodes, and 31% had no mediastinal lymph nodes. The median number of lymph nodes examined per resection was 6, with an interquartile range (IQR) of 3–10. The median (IQR) number of mediastinal lymph nodes, and mediastinal lymph node stations were 2 (0–5), and 1 (0–2), respectively. The median number of N1 lymph nodes was 3 (1–6), which consisted of a median of 2 (0–5) intrapulmonary lymph nodes (stations 11–14), and 1 (0–2) hilar lymph node (Table 2b).

Post-operative events—The 30-day and 60-day readmission rates for the 2009–2013 era were 7% and 13%, respectively. Postoperative mortality rates were 4% at 30-, 7% at 60-, and 8% at 90-days. 1-year overall survival was 83% (95% confidence interval: 81–84%). One-year survival was 90% for Stage IA patients; 82% for Stage IB; 81% for Stage IIA; 74% for Stage IIB; 73% for Stage IIIA; 72% for Stage IIIB; and 68% for Stage IV. Median (IQR) follow up for the cohort was 2.9 years (1.5,5.4) (Table 2a).

Overall trend analysis

There was a significant overall trend ($p<0.0001$) in the use of PET/CT as a non-invasive staging test, increasing from an average usage rate of 36% from 2004–2008, to 80% from 2009–2013. The use of pre-operative mediastinoscopy was stable over the 10-year period. The pneumonectomy rate decreased from a high of 14% in 2005 down to 5% in 2013 (unadjusted $p=0.0007$; adjusted $p=0.22$). The use of open thoracotomy decreased significantly ($p<0.0001$) from a high of 95% in 2005 to a low of 66% in 2013, as the rates of minimally-invasive resection techniques increased ($p=0.73$) (Figure 1).

The evolution of major adverse post-operative outcomes varied. In-hospital mortality decreased over time ($p=0.0940$; adjusted $p=0.0332$) but 30-, 60-, and 90-day mortality rates were not significantly different. A similar pattern of fluctuation with no significant trend was observed with the rate of resections with positive margins.

Period effect analysis

Having looked at significant trends over the full 10-year span, we next looked at differences between trends in the periods before (2004–2009) and after (2010–2013) the implementation of our quality improvement initiatives (period effect analysis), in order to test the impact of our quality improvement efforts. The pNX rate showed no significant overall ($p=0.24$) or period effect ($p=0.072$; adjusted $p=0.31$) trend (Figure 2a). However, there was a significant period effect for total lymph node count, as the median number of lymph nodes examined increased from 5 in the pre-intervention period (2004–2009) to 8 in the post-intervention period (2010–2013) ($p<0.0001$) (Figure 2b).

We observed a period effect increase in station 10 sampling, with a median of 0 lymph nodes in the pre-intervention era and a median of 1 in the post-intervention era ($p<0.0001$). There was also an increase in the total number of N1 (stations 10–14) lymph nodes examined, and the rate of resections with examination of station 10 (both $p<0.0001$) (Figures 3a, b).

Similarly, a period effect increase ($p<0.0001$) was observed with the median number of mediastinal lymph nodes examined. However, although we observed a significant overall decrease in resections without mediastinal lymph nodes examined ($p<0.0001$; adjusted $p=0.0021$) and increase in resections with 3 or more mediastinal lymph node stations examined ($p<0.0001$), no significant period effect was observed for either of these quality measures (Figures 4a, b, c). Despite these changes in the pattern of lymph node examination, pathologic stage distribution remained stable over time.

Subset analysis of an early intervention-adopting institution

In order to isolate the effect of our primary quality improvement intervention – a lymph node specimen collection kit – we also performed a descriptive sub-analysis of the most recent 5 years (2009–2013) of surgical practice at an early adopting institution. At this institution, use of the surgical lymph node specimen collection kit rose from 0% in 2010, to 4% in 2011, 57% in 2012, and 62% in 2013.

During this period, 488 resections were performed without, and 159 resections were performed with, the lymph node collection kit at this institution. Resections performed without the kit had a pNX rate of 9%, whereas those performed with the kit had a pNX rate of 0% ($p<0.0001$). The rate of resections with no mediastinal lymph node examination dropped from 30% with non-kit cases to 0% for kit cases ($p<0.0001$). With use of the kit, the rate of resections without examination of stations 10 and 7 dropped from 44% to 4% and from 64% to 3%, respectively. Use of the kit was associated with an increase in the median N1 nodal count from 4 to 6 ($p<0.0001$; adjusted $p=0.0213$), N2 nodal count from 2 to 8 ($p<0.0001$), and total nodal count from 7 to 15 ($p<0.0001$) (Table 3).

DISCUSSION

The pattern of surgical resection for NSCLC in this population-based cohort showed trends towards higher quality. Most measures of the quality of lymph node examination, except for the pNX rate, showed significant improvement in the whole cohort, with a period effect correlated to the timing of our quality improvement initiative. The pNX rate in this community-based series compares favorably to analyses of large US databases, from which the detrimental prognostic implications of this major quality of care deficit have been demonstrated.⁸ From the early results in the early-adopting institution, we expect that the pNX rate will diminish with wider adoption of the specimen collection kit.

Missing data, such as the absence of early-era data for 5 institutions, absence of data on performance status and recurrence-free survival, limit this retrospective study. The study design precludes rigorous control for unrelated secular changes and a causal analysis. The evolution towards higher quality surgical practice is probably attributable to multiple factors. Quantifying local practice patterns and providing direct feedback on the quality gap probably had a beneficial effect, exemplified by the declining rate of resections without mediastinal nodal examination. There may also have been a Hawthorne effect from awareness of the effort to monitor surgical quality. This effect cannot be separated from the effect of our direct stakeholder education campaign. We also observed statistically significant trends in practice within the pre-intervention period that suggests movement,

which accelerated in the post-intervention period, had begun before formal introduction of our intervention.

The 5 institutions contributing data for only 2009–2013 were also not yet directly involved in our quality improvement work. They represent a smaller percentage of cases (21% of total cohort) than the other 6 institutions. A sensitivity analysis performed with only the 6 institutions present over the full timespan of this study showed results consistent with the results of the analysis of the whole cohort.

Both the period effect analysis and the early results from an institution with early adoption of the surgical kit intervention highlight the potential significance of a solution specifically designed to eliminate the pathologic nodal staging quality gap. Simply educating surgeons and their operating room teams about the quality gap may be insufficient to sustain practice improvement. In our pilot studies, we showed how post-intervention surgical practice falls back to pre-intervention levels when the kit is not used.¹⁸ The problem of suboptimal nodal staging is multifaceted and extends beyond the operation and the surgical team, to include aspects of specimen labeling and transfer, and the pathology gross examination.^{12,17,18} Heightened awareness is insufficient to eliminate the problem. Simple, practical, logically designed and carefully tested corrective interventions are needed.

More broadly, we see secular changes in lung cancer surgical practice. The use of pneumonectomy is decreasing across the region, minimally-invasive resection techniques are supplanting open thoracotomy, and adjusted in-hospital mortality has improved. However, other measures of short-term post-operative mortality have not changed; the rate of margin-positive resections remains at 6%, slightly higher than the National Cancer Database average of 4.6%.⁵ The 30-day mortality rate in this cohort, although slightly higher than recent reports from analysis of the Society of Thoracic Surgeons General Thoracic Surgery database (STS-GTS), is competitive with other reports.^{20,21} Unlike the STS-GTS, and reports from Japan, the MS-QSR cohort is population-based, relatively unselected (all data from all institutions with 5 or more resections within pre-specified Dartmouth Hospital Referral Regions are included), rigorously audited, and not based on self-reporting.^{20,22,23}

Other problems remain. The ultimate goal of eliminating the nodal staging quality gap is to change the distribution of pathologic nodal stage, by correctly identifying previously understaged patients who may be offered beneficial adjuvant therapy, or enrollment into clinical trials of novel therapies. Unrelated changes in preoperative evaluation, such as greater use of PET/CT scanning in the more recent era, may have blunted the expected migration to higher pathologic nodal stage. Despite this bias to the null, we see early signals of potential stage-migration. Our staggered implementation design, which allows each institution to be used in the future as its own control while adjusting for secular changes in the aggregate population, will enable rigorous future analyses of pathologic nodal stage distribution and survival, which are not yet possible at this early phase.

The infrequent use of invasive pre-operative nodal staging procedures is probably worthy of specific intervention, given the likely additional impact on patient selection, use of neo-adjuvant therapeutic modalities, and long-term survival.^{24,25} Such intervention studies will

potentially confound the analysis of stage migration, as more patients with mediastinal nodal metastasis are triaged away from primary surgical resection.

The ongoing surgical specimen collection kit deployment only addresses two of the three points of origin of the nodal staging quality gap: improved surgical hilar and mediastinal lymph node harvest, and communication between the operating room and pathology teams including the secure transfer of resected nodal specimens. It does not address the problem of incomplete intrapulmonary lymph node retrieval which is usually the responsibility of the specimen gross dissector in the pathology laboratory.^{26,27} We are currently testing a novel gross dissection method to address this problem.²⁸

The nodal staging quality gap is widest in community-level institutions, where 80% of NSCLC patients receive their care in the US. Although slightly narrower, the quality gap also exists in academic centers.²⁹ Therefore, large pragmatic dissemination and implementation studies are needed to evaluate the impact on care provided to a diversity of patients, by different types of surgery and pathology teams, in different types of institutions. The ultimate aim must be to understand the best approaches to raise the overall standards of surgical care for patients with early stage NSCLC in the places where they choose to seek care, with the goal of improving population-level lung cancer survival.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Dr. Osarogiagbon has a patent application for the surgical specimen collection kit under review.

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Glossary of Abbreviations

NSCLC	Non-small cell lung cancer
MS-QSR	Mid-South Quality of Surgical Resection
PET/CT	Positron-emission tomography/computerized axial tomography
IQR	Interquartile range
STS-GTS	Society of Thoracic Surgeons General Thoracic Surgery database

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Perspective

Over 80% of lung cancer patients receive their care at community-level hospitals. Pathologic nodal stage is the key prognostic factor for survival of lung cancer patients. In a high lung cancer incidence and mortality region of the US, a quality improvement initiative in community hospitals shows significant trends in improving the quality of pathologic nodal staging.

Central Message

A regional quality improvement project has a positive impact on the quality of lung cancer resections as measured by pathologic nodal assessment at community-level hospitals.

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Figure 1. significant decrease in use of open thoracotomy ($p<0.0001$) mirrored in rise of minimally-invasive surgical techniques.

Figure 2.

- a) no significant trend ($p=0.24$) or period effect ($p=0.072$; adjusted $p=0.99$) in rate of resections without lymph node examination;
- b) significant period effect increase in median total number of lymph nodes per resection ($p<0.0001$).

Figure 3.

- a) significant period effect increase in number of station 10 ($p < 0.0001$) and total N1 lymph nodes ($p < 0.0001$);
- b) significant period effect increase in rate of station 10 examination ($p < 0.0001$)

Figure 4.

- a) period effect increase in median total number of mediastinal lymph nodes examined ($p < 0.0001$; adjusted $p = 0.87$);
- b) significant overall decrease in rate of resections with no mediastinal lymph nodes examined ($p < 0.0001$), period effect ($p = 0.93$; adjusted $p = 0.88$);
- c) significant overall increase in rate of resections with 3 or more mediastinal lymph node stations examined ($p < 0.0001$), period effect ($p = 0.6$; adjusted $p = 0.16$).

Table 1**Patient Demographic and Clinical Characteristics**

Demographic Characteristics	All Stages (n = 2,566)			Stage IA – IIB (n = 2,143)			Early Era (2004–2009) (n = 1,296)			Late Era (2010–2013) (n=1,270)		
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	Median	IQR	Median
Age	67	(61,74)	68	(61,74)	67	(61,74)	68	(61,74)	68	(61,74)		
	No.	%	No.	%	No.	%	No.	%	No.	%		
Age Group												
<65	950	37	766	36	484	37	466	37	466	37		
65–74	1049	41	880	41	512	40	537	42	537	42		
75–84	534	21	471	22	282	22	252	20	252	20		
>85	33	1	26	11.22	18	1	15	1	15	1		
Sex												
Male	1351	53	1125	52	685	53	666	52	666	52		
Female	1215	47	1018	48	611	47	604	48	604	48		
Race												
White	2013	78	1693	79	999	77	1014	80	1014	80		
Black	532	21	431	20	291	22	241	19	241	19		
Other	21	1	19	1	6	1	15	1	15	1		
Insurance												
Medicare	1257	49	1081	50	673	52	584	46	584	46		
Medicaid	313	12	256	12	152	12	161	13	161	13		
Commercial	901	35	738	34	427	33	474	37	474	37		
None	95	4	68	3	44	3	51	4	51	4		
Histology												
Adenocarcinoma	1348	52	1108	52	664	51	684	54	684	54		
Squamous	889	35	772	36	461	36	428	34	428	34		
Adenosquamous	72	3	61	3	45	3	27	2	27	2		
Large Cell	115	4	91	4	63	5	52	4	52	4		

Demographic Characteristics	All Stages (n = 2,566)			Stage IA – IIB (n = 2,143)			Early Era (2004–2009) (n = 1,296)			Late Era (2010–2013) (n = 1,270)		
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	Median	IQR	Median
Others	142	6	111	5	63	5	79	5	63	5	79	6
Histologic Grade												
Well differentiated	271	11	249	12	117	9	154	9	117	9	154	12
Moderately differentiated	1076	42	922	43	556	43	520	43	556	43	520	41
Poorly differentiated	774	30	627	29	392	30	382	30	392	30	382	30
Undifferentiated	55	2	42	2	24	2	31	2	24	2	31	2
Not Reported	390	15	303	14	207	16	183	14	207	16	183	14
	Median	Std. Dev.			Median	Std. Dev.	Median	Std. Dev.	Median	Std. Dev.	Median	Std. Dev.
Tumor Size (in cm)	2.50	4.68			2.5	5.98	2.6	5.98	2.5	5.98	2.6	5.98
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Pathologic T classification												
T1	1172	46	1097	51	614	47	558	44	614	47	558	44
T2	987	38	864	40	502	39	485	38	502	39	485	38
T3	266	10	177	8	88	7	178	14	88	7	178	14
T4	101	4	--	--	72	6	29	2	72	6	29	2
Others	40	2	5	0	20	1	20	2	20	1	20	2
Pathologic N classification												
N0	1785	70	1671	78	902	70	883	70	902	70	883	70
N1	333	13	256	12	171	13	162	13	171	13	162	13
N2	212	8	--	--	95	7	117	9	95	7	117	9
NX	236	9	216	10	128	10	108	8	128	10	108	8
Pathologic M classification												
M0	2051	80	1727	81	804	62	1247	98	804	62	1247	98
M1	49	2	--	--	27	2	22	1	27	2	22	1
MX	466	18	416	19	465	36	1	1	465	36	1	1

Demographic Characteristics	All Stages (n = 2,566)		Stage IA – IIB (n = 2,143)		Early Era (2004–2009) (n = 1,296)		Late Era (2010–2013) (n = 1,270)	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Pathologic stage								
IA	1011	39	1011	47	522	40	489	38
IB	629	24	629	29	335	26	294	23
IIA	232	9	232	11	92	7	140	11
IIB	271	11	271	13	136	10	135	10
IIIA	284	11	--	--	112	9	172	13
IIIB	57	2	--	--	54	4	3	1
IV	50	2	--	--	28	2	22	2
0	17	1	--	--	4	1	13	1
Not Reported	15	1	--	--	13	1	2	1

Table 2**a - Surgical Characteristics**

Surgical Characteristics	All Stages (N=2566)		Stage IA – IIB (N=2143)		Early Era (2004–2009) (N=1296)		Late Era (2010–2013) (N=1270)	
	No.	%	No.	%	No.	%	No.	%
Extent of Resection								
Pneumonectomy	209	8	141	7	121	9	88	7
Bilobectomy	159	6	127	6	84	6	75	6
Lobectomy	1880	73	1608	75	936	72	944	74
Segmentectomy	76	3	66	3	34	3	42	3
Wedge	242	10	201	9	121	9	121	10
Surgical Technique								
Open	1976	77	1619	76	1049	81	927	73
RATS	238	9	209	10	50	4	188	15
VATS	352	14	315	15	197	15	155	12
Gross Margins								
Positive	147	6	92	4	80	6	67	5
Negative	2326	91	1984	93	1173	91	1153	91
Not reported	93	3	67	3	43	3	50	4
30 Day Readmission* (2009–2013)								
No	1505	94	1267	94	N/A		1190	94
Yes	110	7	83	6	N/A		80	6
60 Day Readmission*(2009–2013)								
No	1404	87	1188	88	N/A		1118	88
Yes	211	13	162	12	N/A		152	12
Mortality (number of deaths, %)								
In-hospital mortality	118	5	98	5	69	5	49	4
30-day mortality	114	4	93	4	62	5	52	4
60-day mortality	172	7	136	6	99	8	73	6
90-day mortality	218	8	167	8	120	9	98	8
1 year survival (number initially at								

a - Surgical Characteristics

	All Stages (N=2566)	Stage IA – IIB (N=2143)	Early Era (2004–2009) (N=1296)	Late Era (2010–2013) (N=1270)
risk, %)				
All Stages	2118	83		
Stage IA	1011	90		
Stage IB	629	82		
Stage IIA	232	81		
Stage IIB	271	74		
Stage IIIA	284	73		
Stage IIIB	57	72		
Stage IV	50	68		

b – Surgical Lymph Node Examination

	All Stages (N=2566)	Stage IA – IIB (N=2143)	Early Era (2004–2009) (N=1296)	Late Era (2010–2013) (N=1270)
Surgical Lymph Node (LN)				
Examination	No.	%	No.	%
pNx				
No	2330	91	1927	90
Yes	236	9	216	10
Any LNs with metastatic disease?				
No	2017	79	1883	88
Yes	549	21	260	12
Any N1 LNs examined?				
No	399	16	351	16
Yes	2167	84	1792	84
Any N1 LNs with metastasis?				
No	2110	72	1883	88
Yes	456	18	260	12
Any mediastinal LN examination?				
No	794	31	700	33

b – Surgical Lymph Node Examination

	All Stages (N=2566)	Stage IA – IIB (N=2143)	Early Era (2004–2009) (N=1296)	Late Era (2010–2013) (N=1270)
Yes	1772	1443	807	965
No	794	721	489	305
Any N2 LN with metastasis?				
Yes	2354	2143	1201	1153
No	212	0	95	117
Station 10 examination?				
Yes	1262	1069	741	521
No	1304	1074	555	749
No. of mediastinal LN stations sampled				
0	794	721	489	305
1–2	1170	954	661	509
≥3	602	468	146	456
LN counts	Median	Median	Median	Median
Total LNs	6 (3,10)	6 (3,10)	5 (2,8)	8 (4,12)
Total N2 LNs	2 (0,5)	2 (0,4)	1 (0,3)	3 (1,6)
Total mediastinal stations sampled	1 (0,2)	1 (0,2)	1 (0,2)	2 (1,3)
Total N1 LNs	3 (1,6)	3 (1,6)	3 (1,5)	4 (2,7)
Total station 10 LNs	1 (0,2)	1 (0,2)	0 (0,1)	1 (0,2)
Total intrapulmonary LNs (stations 11–14)	2 (0,5)	2 (0,5)	2 (0,4)	2 (0,5)
Total LN count by extent of resection	Median			
Pneumonectomy	6 (7,17)			
Lobectomy/Bilobectomy	10 (3,11)			
Segmentectomy	3 (1,7)			
Wedge	0 (0,2)			
Mediastinal LN count by extent of resection	Median			
Pneumonectomy	3 (1,6)			
Lobectomy/Bilobectomy	2 (0,5)			
Segmentectomy	2 (0,4,5)			

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b – Surgical Lymph Node Examination

	All Stages (N=2566)	Stage IA – IIB (N=2143)	Early Era (2004–2009) (N=1296)	Late Era (2010–2013) (N=1270)
Wedge	0	(0.2)		

Table 3

Effect of Kit in an Early Adopting Institution

	NON-KIT CASES n=488	KIT CASES n=159	p-value	Adjusted p-value
pNx Rate	9%	0%	<.0001	<0.0001 *
pN0	69%	75%	0.1381	0.0081
pN1	13%	14%	0.6646	0.73
pN2	9%	11%	0.5843	0.97
Rate of non-examination of mediastinal lymph nodes	30%	0%	<.0001	<0.0001 *
Rate of non-examination of station 10	44%	4%	<.0001	<0.0001
Rate of non-examination of station 7	64%	3%	<.0001	<0.0001
N1 lymph node count: median (IQR)	4 (1–7)	6 (3–11)	<.0001	0.0213
N2 lymph node count: median (IQR)	2 (0–5)	8 (5–12)	<.0001	<0.0001
Total lymph node count: median (IQR)	7 (3–11)	15 (10–23)	<.0001	<0.0001

* model only controlled for stage due to zero cell frequency