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Thoroughness of Mediastinal Staging in Stage IIIA Non-Small Cell Lung Cancer

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Abstract

Introduction—Guidelines recommend that patients with clinical stage IIIA non-small cell lung cancer (NSCLC) undergo histologic confirmation of pathologic lymph nodes. Studies have suggested that invasive mediastinal staging is underutilized, though practice patterns have not been rigorously evaluated.

Methods—We used the Surveillance, Epidemiology, and End Results-Medicare database to identify patients with stage IIIA NSCLC diagnosed from 1998 through 2005. Invasive staging and use of positron emission tomography (PET) scanning were assessed using Medicare claims. Multivariable logistic regression was used to identify patient characteristics associated with use of invasive staging.

Results—Of 7583 stage IIIA NSCLC patients, 1678 (22%) underwent invasive staging. Patients who received curative intent cancer treatment were more likely to undergo invasive staging than patients who did not receive cancer specific therapy (30% vs. 9.8%, adjusted odds ratio [OR} 3.31, 95% CI 2.78–3.95). The oldest patients (age 85–94) were less likely to receive invasive staging than the youngest ((age 67–69) (27.6 % vs. 11.9%, OR 0.46, 95% CI 0.34–0.61)). Sex, marital status, income and race were not associated with the use of the invasive staging. The use of invasive staging was stable throughout the study period, despite an increase in the use of PET scanning from less than 10% of patients prior to 2000 to almost 70% in 2005.

Conclusion—Nearly 80% of Medicare beneficiaries with stage IIIA NSCLC do not receive guideline adherent mediastinal staging; this failure cannot be entirely explained by patient factors or a reliance on PET imaging. Incentives to encourage use of invasive staging may improve care.

Keywords

Non-small cell lung cancer; mediastinal staging; mediastinoscopy

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Introduction

Accurate staging of lung cancer is essential to the determination of appropriate treatment. Stage IIIA non-small cell lung cancer (NSCLC) is most commonly defined by cancer spread to ispsilateral mediastinal (N2) lymph nodes. Prior studies have indicated that CT and PET scanning lack sufficient sensitivity or specificity to serve as the sole staging modality.[1–10] A 1997 statement from the ATS/ERS statement noted that invasive staging of enlarged lymph nodes is mandatory.[11] The American Thoracic Society (ATS), European Respiratory Society (ERS), and American College of Chest Physicians (ACCP), have for many years endorsed invasive sampling of mediastinal lymph nodes suspected of containing malignant cells.[1,11–13] Therefore, patients should not be given the diagnosis of clinical stage IIIA NSCLC based on PET scan findings without tissue confirmation.

Prior work has suggested that use of mediastinal staging is far lower than recommended by guidelines[14–16]. One analysis of trends in staging of Medicare patients diagnosed with NSCLC between 1998 and 2002 found that 65% of Stage IIIA patients were staged with CT scan only, 30% with CT in addition to either PET or invasive biopsy, and 5% with CT, PET and invasive biopsy[17]. This analysis also found a positive association between use of additional staging modalities and survival.

We examined the actual practice for mediastinal staging of Medicare patients with stage IIIA NSCLC to explore the reasons for its underutilization. The advantages of studying the Medicare population include ethnic, socioeconomic and geographic diversity as well as a stable single payer insurance coverage for the entire period of study. We identified which staging modalities were most frequently used during the years 1998–2005 and examined patient factors associated with the use of invasive staging.

Methods

Data Source and Study Sample

This study was deemed exempt by the Yale Human Investigations Committee. Data were obtained from the SEER-Medicare linked database, which contains tumor registry data linked to Medicare claims for patients representing 26% of the US population.[18,19] Prior to 2000, only 11 of the current 16 registries participated in the SEER program; this subset of registries, which represented 14% of the population, is referred to in this study as the pre-expansion registries.

We selected subjects ages 67–94 who were diagnosed with Stage IIIA NSCLC between 1998 and 2005. Patients were identified as IIIA using the American Joint Committee on Cancer (AJCC) stage variable prior to 2004 or collaborative stage variable after 2004 provided by SEER. The collaborative stage variable uses all data available from both clinical staging techniques and surgical resection if performed. Exclusion criteria included the following: unknown month of diagnosis, diagnosis reported on death certificate or autopsy, prior lung cancer diagnosis, or any other cancer diagnosis in the 6 months before and after the stage IIIA NSCLC diagnosis. In order to ensure that we had complete data for the sample, patients had to have been continuously enrolled in fee-for-service Medicare Parts A and B beginning 24 months prior to diagnosis through the earliest of the following events: initiation of treatment, death, or 6 months after diagnosis.

We also analyzed a subgroup of Stage IIIA patients treated with both chemotherapy and radiation but not surgery within six months of diagnosis. This analysis allowed us to confirm our findings in a group of patients healthy enough for aggressive treatment and without the impact of unsuspected N2 disease found incidentally at the time of surgical resection.

Treatment Groups

Treatment was assessed using Medicare claims in the 6 months after diagnosis (Appendix 1). We divided patients into 3 groups: Patients who did not receive chemotherapy, surgery or radiation were classified as best supportive care. Patients who received chemotherapy or radiation alone were classified as cancer specific therapy. Patients who received combination chemotherapy and radiation therapy or any therapy that involved surgical resection were classified as curative intent therapy.

Outcome

The primary outcome was receipt of invasive mediastinal staging. We used the inpatient, outpatient, and physician Medicare claims to search for Current Procedural Terminology (CPT) codes for PET scan, mediastinoscopy, mediastinotomy, TBNA, EUS, or VATS biopsies (Appendix 1). For the majority of the study period, EBUS-TBNA and conventional TBNA were billed using the same CPT code, so we could not separate these two procedures. For analytic purposes, we combined mediastinoscopy and mediastinotomy into one group. We searched for mediastinal staging procedures performed 6 months before diagnosis through the initiation of treatment or for 6 months after diagnosis in the case of patients who were not treated with any cancer specific therapy.

As a secondary outcome, we calculated the 3-year survival of the subset of stage IIIA NSCLC patients who were diagnosed in 1998–2004 and received both chemotherapy and radiation within six months of diagnosis, but did not undergo surgery.

Co-variates

The following variables were selected a priori as factors that might influence whether a patient received invasive staging: age, sex, race, comorbidities, marital status, income, health care system access, treatment group as defined above, SEER registry, and year of diagnosis. Age was categorized as 67–69, 70–74, 75–79, 80–84, ≥85; race as white, black, or other; and marital status as married, unmarried, or unknown. Income was defined as the median household income at the zip code level, categorized into quintiles. We created a dichotomous variable indicating whether a claim had been submitted for influenza vaccination in the 18 months prior to the diagnosis, which has been used previously as marker for healthcare system access[20].

Comorbidity was assessed by searching all Medicare claims in the 2 years prior to diagnosis. We used the comorbid conditions recommended by Elixhauser et al[21] that we had previously determined were significantly associated with survival (Appendix 2). Only codes that appeared on at least 1 inpatient claim or 2 or more outpatient/physician claims occurring more than 30 days apart were used. We created a sum score of the number of comorbidities each patient had and then stratified patients into 3 groups: 0, 1–2, or ≥3 comorbidities.

Statistical analysis

We determined the percent of patients receiving each type of invasive staging procedure for each year during the study period (1998–2005). Bivariate and multivariate logistic regression was used to identify patient factors associated with receipt of invasive staging. For the secondary analysis, we conducted a logistic regression analysis using 3-year survival as the outcome. SAS statistical software, version 9.2 (SAS Institute Inc., Cary, North Carolina), was used for all analysis

Results

Our sample consisted of 7,583 patients (Table 1). Of the 7,583 patients, 1678 (22%) underwent at least one invasive staging procedure. Of these, 88% received a single invasive staging procedure such as mediastinoscopy alone, while 12% received 2 or more invasive staging procedure such as TBNA followed by mediastinoscopy.

As shown in Figure 1, mediastinoscopy (or mediastinotomy) was the most commonly used invasive procedure (76% of invasively staged patients) followed by TBNA with or without ultrasound guidance (26% of invasively staged patients). VATS and EUS were rarely used.

The use of invasive staging did not change significantly during the study period. However, the use of PET scanning increased from 2.4% in 1998 to 68.4% in 2005 (Figure 2).

In the unadjusted analysis, older age, black race, higher comorbidity, or being unmarried significantly decreased the likelihood of receiving invasive staging (Table 2). Patients who received aggressive cancer treatment were significantly more likely to have received invasive staging. However, even among these patients, only a minority (30%) underwent invasive staging. Furthermore, even in the “high likelihood” subgroups (no comorbidities, white, married) less than 30% underwent invasive staging.

After adjusting for all significant variables, only age, comorbidity, receipt of influenza vaccination, and treatment type remained independently associated with use of invasive staging. Patients with ≥3 comorbidities were less likely to have received invasive staging compared to patients without any comorbidity (OR 0.81; 95% CI 0.69–0.95), while patients who had greater healthcare access, as measured by receipt of influenza vaccination, were more likely to have received invasive staging compared to patients who did not receive the vaccine (OR 1.23; 95% CI 1.09–1.39). However, in all subgroups, the use of invasive staging was the exception rather than the rule.

There was significant geographic variation in the use of invasive staging between SEER regions (Tables 2, 3).

Receipt of cancer specific therapy and curative intent therapy were associated with use of invasive staging. However, even in the subset of patients who received combined radiation therapy and chemotherapy, only 30% underwent invasive staging. Only age, SEER region, and receipt of influenza vaccination were significant covariates (Table 3).

In patients treated with both chemotherapy and radiation but not surgical resection, 3-year survival was 21%. In multivariate analysis of this group, invasive staging was associated with improved 3-year survival (adjusted HR 1.61, 95% CI 1.21–2.12). Other factors associated positively with survival included younger age and fewer comorbidities (Table 4).

Discussion

We found an underutilization of histologic confirmation in clinical staging during the years 1998–2005. This practice was inconsistent with evidence based guidelines. The failure of physicians to follow clinical practice guidelines is well documented across different specialties. A review by Cabana et al. described reasons that guidelines are not followed which are discussed below.[22]

Physicians might be unaware of evidence supporting recommendations for invasive staging in IIIA lung cancer patients. The extensive evidence base supporting the guidelines and the

lack of an obvious change following publication of the American College of Chest Physician guidelines in 2003 suggest that this is not the case.

Clinicians might disagree with guidelines even at a population level. This seems unlikely given the lack of debate in the literature regarding the value of staging IIIA NSCLC. However, diagnostic and therapeutic nihilism related to the perception that little can be done for patients with lung cancer may be pertinent[23,24].

Clinicians might agree with guidelines on a population level but feel they were not relevant to an individual patient. For example, a physician might believe that the positive predictive value of CT and PET in an individual patient is sufficiently reliable to obviate the need for histologic confirmation while acknowledging that this position is not supported by evidence. Many clinicians may not feel confident in their ability to perform invasive staging techniques specified by guidelines. This may subconsciously increase the likelihood of a physician recommending guideline discordant care for a particular patient.

Limited access to invasive staging procedures may discourage adherence to guidelines. Only approximately 12% of pulmonologists perform TBNA[25–27] and less than 10% of lung cancer surgery is performed by dedicated thoracic surgeons[28]. General surgeons or cardiac surgeons performing thoracic surgery are less likely to truly be comfortable with mediastinoscopy. However, shifting all NSCLC care to specialized expertise is anything but simple. Even if all NSCLC cancer treatment was centralized at large centers, it is not clear if there are sufficient physicians trained to meet the needs of this large group of patients. Moreover, in the United States, such centralization would require a major cultural shift and many elderly patients would likely be unwilling to travel for this care.

The data suggests that some physicians routinely performed invasive staging and did so throughout the study period; while another larger group, routinely did not. Simply publishing guidelines and evidence supporting them is not sufficient to change practice. The rate of invasive staging is likely to reflect the availability of physicians with the skills and training to routinely perform invasive mediastinal staging. To actually improve patient care, leaders need to ensure that physicians have the resources needed to provide the recommended care and that incentives are aligned to encourage best practices.

Training physicians who currently care for lung cancer patients in invasive staging techniques and providing institutional resources for them may be the key to achieving guideline adherent care. For example, both practicing pulmonologists and practicing surgeons have successfully adopted EBUS-TBNA.[29] However, the process of becoming an expert in a new procedure is arduous and the profession’s experience with the introduction of laparoscopy taught us to be cautious.[30] Medical simulation is expensive but can reduce the learning curve for a new procedure and has been used in thoracic surgery.[31] Even after use of simulation training, many physicians still want mentoring during their initial procedures. Unfortunately, there are many regulatory barriers to obtaining this mentoring including lack of reciprocity for licensing and credentialing. Addressing the need for effective continuing medical education should be a priority for medical leaders who desire to increase the rate of invasive staging of NSCLC.

Physicians and institutions also need incentives to pursue the difficult and expensive process of safely introducing invasive staging into their lung cancer practices. One policy based approach that may be effective is using the rate of invasive staging as quality indicator for the care of lung cancer patients. The recent past has shown us examples of how selection of quality indicators can dramatically impact practice in areas such as management of myocardial infarction.

The rate of use of invasive staging was not impacted by the increased use of PET. This shows that at least in stage IIIA patients PET was not replacing invasive staging, because this would have led to a decrease in invasive staging. Moreover, identification of PET avid lymph nodes did not prompt invasive staging for confirmation as recommended by guidelines since an increase in invasive would have accompanied this later scenario. This again suggests that guidelines alone are insufficient to change practice.

Our analysis is consistent with and expands on previous work.[17] By separating patients invasively staged from those staged with a combination of CT scan and PET, we can appreciate how actual practice is differing from guidelines and expert opinion. We noted even higher rates of utilization of PET scanning than reported by Farjah et al[17]. This may be due to our inclusion of additional CPT codes for PET scanning not utilized in their study as well as our extended study period. Additionally, we did not observe the decline in utilization of invasive staging procedures that they reported. This is likely related to our inclusion of TBNA as an invasive staging procedure and our focus on patients with stage IIIA NSCLC who may be more likely to receive invasive staging than patients with either earlier or more advanced stages.

Our study has several limitations. First, data are only available on patients diagnosed through 2005. The impact of the dissemination of technologies such as EBUS and EUS over the last 5 years cannot be assessed. Second, we specifically evaluated an older Medicare population, and the results may not be generalizable to younger patients with other insurance. However, while age and insurance status are known to impact cancer therapies, most lung cancer patients are older than 65 years of age. Third, the use of SEER regions to examine geographic variability does not reflect geographic distribution of healthcare resources. However, our point in including this variation is only to provide additional evidence that variability in the use of staging techniques is due to factors other than patient characteristics. Further, due to the fact that patients may have diagnostic and treatment procedures at multiple institutions, assigning the responsibility for their care to single institution for research purposes is difficult. Therefore, we do not have data on the providers that treated any particular patient. Fourth, the SEER-Medicare database does not allow the determination of the results of an individual staging procedure in any given patient. Additionally, we are subject to the limitations of using an administrative database. For example, if a TBNA were to be performed but not billed, we would classify the patient incorrectly as not having had a TBNA. However, since this billing database is how providers are reimbursed, we are likely to capture the majority of procedures. The presence of patients in whom the absence of invasive staging would be considered medically acceptable is a potential confounder in our study.

Some patients may have been classified as IIIA in the SEER database but were only found postoperatively to have N2 involvment (“incidental N2”). However, one can argue these patient should have had invasive staging to prevent this situation, and studies indicate the rate of incidental N2 should be small. Another group for whom invasive staging can be questioned is those with mediastinal infiltration of tumor to the extent that individual nodes can no longer be discerned. However, in clinical practice this group would clearly be a minority of patients with stage IIIA disease. Finally, comorbidities may preclude considering curative intent treatment. Data from this study suggest that over 36% had no co-mordbidities.

In the end, the lack of invasive staging cannot be explained away as having been appropriate due to tumor extent or comorbidities. Even in the most favorable subgroups and youngest patients without comorbidities the rate of invasive staging was remarkably low (<30%). Furthermore, our analyses excluding surgical patients (and thus any incidental N2 patients)

did not affect the results. Although the exact rate of invasive staging that should be performed cannot be determined, there is little doubt it should be substantially higher than <25%.

Conclusion

The majority of patients with stage IIIA NSCLC did not receive invasive mediastinal staging as recommended by guidelines and associated with improved survival. This was evident for patients of all races and socioeconomic strata. Patient related factors such as age and comorbidity do not fully explain this practice variation. This combined with the observed geographic variation in rates of invasive staging suggest that provider, not patient, factors are responsible. Incentives to encourage use of invasive staging may be useful in improving quality of care.

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Appendix 1

Codes for identification of Staging techniques and treatments

CPT Codes for Invasive Staging Techniques	Endobronchial ultrasound	31620
	Bronchoscopy with TBNA	31629 (additional lobes 31633)
	Thoracoscopy of mediastinal space without bx	32605
	VATS mediastinal biopsy	32606
	Mediastinotomy	39000 or 39010
	Mediastinoscopy	39400
	Esophageal ultrasound	43231, 43242, 43259, 76975
	Esophageal ultrasound guided aspiration	43232
Codes for Surgical Resection	Carinal reconstruction	
	Open pneumonectomy	32440
	Removal of lung, total pneumonectomy; with resection of segment of trachea followed by broncho-tracheal anastomosis (sleeve pneumonectomy)	32442
	Removal of lung, total pneumonectomy; extrapleural	32445
	Open lobectomy	32480
	Open Bilobectomy	32482
	Open segmentectomy	32484
	Open sleeve lobectomy	32486
	Open completion pneumonectomy	32488
	Open apical resection	32503
	Resection of lung; with resection of chest wall	32520
	Resection of lung; with reconstruction of chest wall, without prosthesis	32522
	Resection of lung; with major reconstruction of chest wall, with prosthesis	32525
	VATS segmentectomy/lobectomy	32663
Codes for Radiation Treatment	Brachytherapy	77750–77799, 0182T
	Any External Beam (3-D Conformal)	77402–416
	Any IMRT	(77301 and 77427), 77418, 0073T, G0174
	Stereotactic Surgery (“Radiosurgery/cyberknife”)	G0173, G0242, G0243, G0251, G0338, G0339, G0340, 0082T-0083T
	Any Proton Beam	77520–77525
	Any IGRT	77421
Codes for Chemotherapy Treatment (any chemo drug)	HCPCS Codes for Chemotherapy	96400–96549, Q0083–Q0085, J9000–J9999, G0355–62
	ICD9 Code for Chemotherapy	V58.1
PET Scan Codes	G Codes	G0211, G0212, G0125, G0126, G0210, G0212, G0234

	CPT Codes	78811, 78812, 78813, 78815, 78816

Appendix 2

Comorbid Conditions

Comorbid condition	**N**	**%**
Chronic Pulmonary Disease	2401	31.66
Diabetes Uncomplicated	1284	16.93
Cardiac Arrhythmia	1257	16.58
Peripheral Vascular Disorders	1027	13.54
Congestive Heart Failure	978	12.9
Solid Tumor without Metastasis	827	10.91
Fluid and Electrolyte Disorders	592	7.81
Valvular Disease	503	6.63
Depression	433	5.71
Diabetes Complicated	329	4.34
Deficiency Anemia	294	3.88
Rheumatoid Arthritis/collagen disease	241	3.18
Other Neurological Disorders	224	2.95
Renal Failure	202	2.66
Weight Loss	161	2.12
Pulmonary Circulation Disorders	146	1.93
Alcohol Abuse	105	1.38
Coagulopathy	101	1.33
Liver Disease	72	0.95
Metastatic Cancer	72	0.95
Psychoses	71	0.94
Paralysis	68	0.9
Lymphoma	60	0.79
Drug Abuse	33	0.44
AIDS/HIV	*	*

* Suppressed due to small cell size

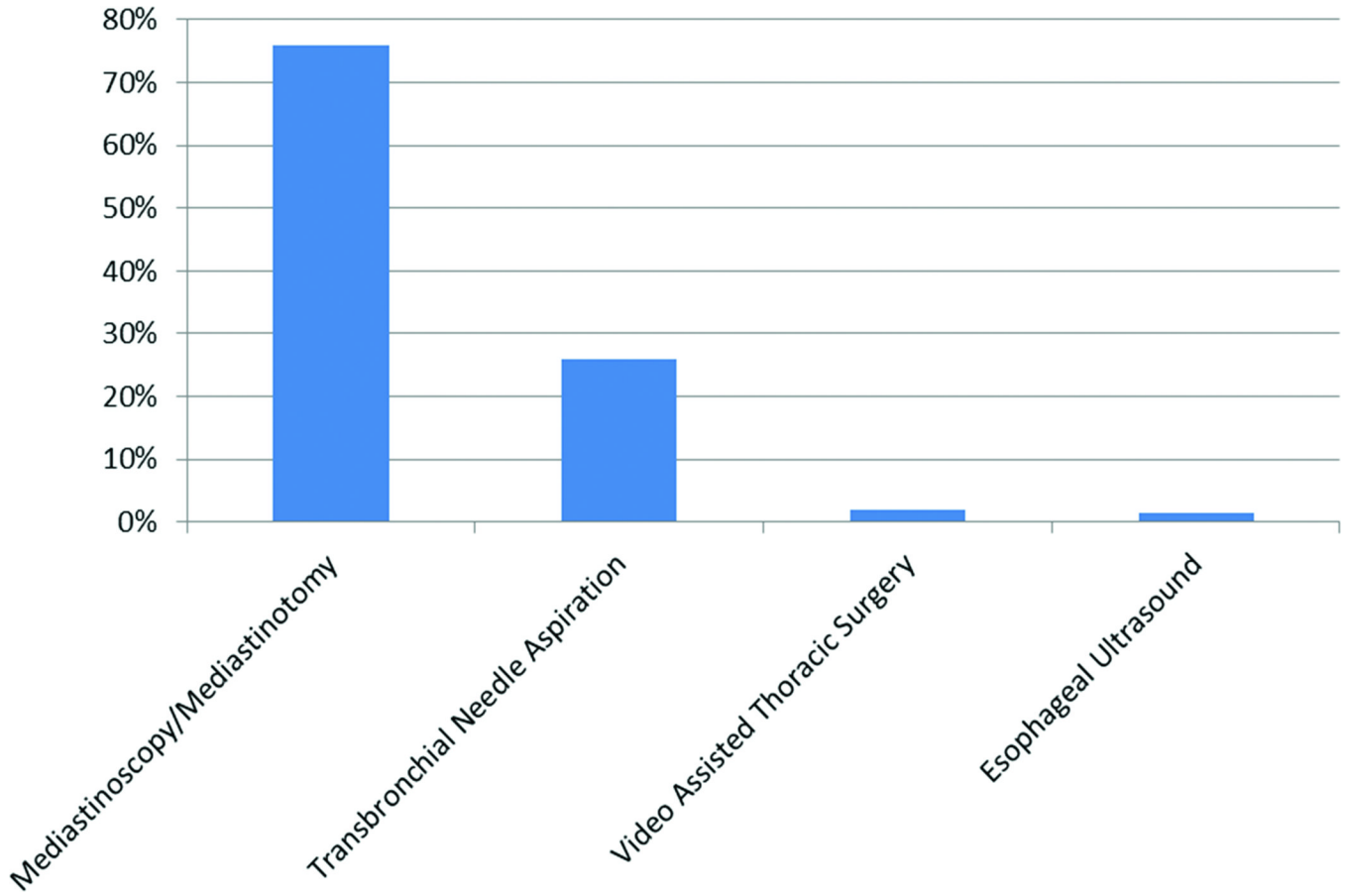

Figure 1.
Invasive Staging Techniques
1678 patients underwent invasive staging. Mediastinoscopy/Mediastinotomy was used in 1270 patients (76%), Transbronchial Needle Aspiration in 451 (26%), Video Assisted Thoracic Surgery in 35 (2%) and Esophageal Ultrasound in 28 (1.6%). Since 12.5% of invasively staged patients underwent more than one procedure, the numbers sum to > 100%.

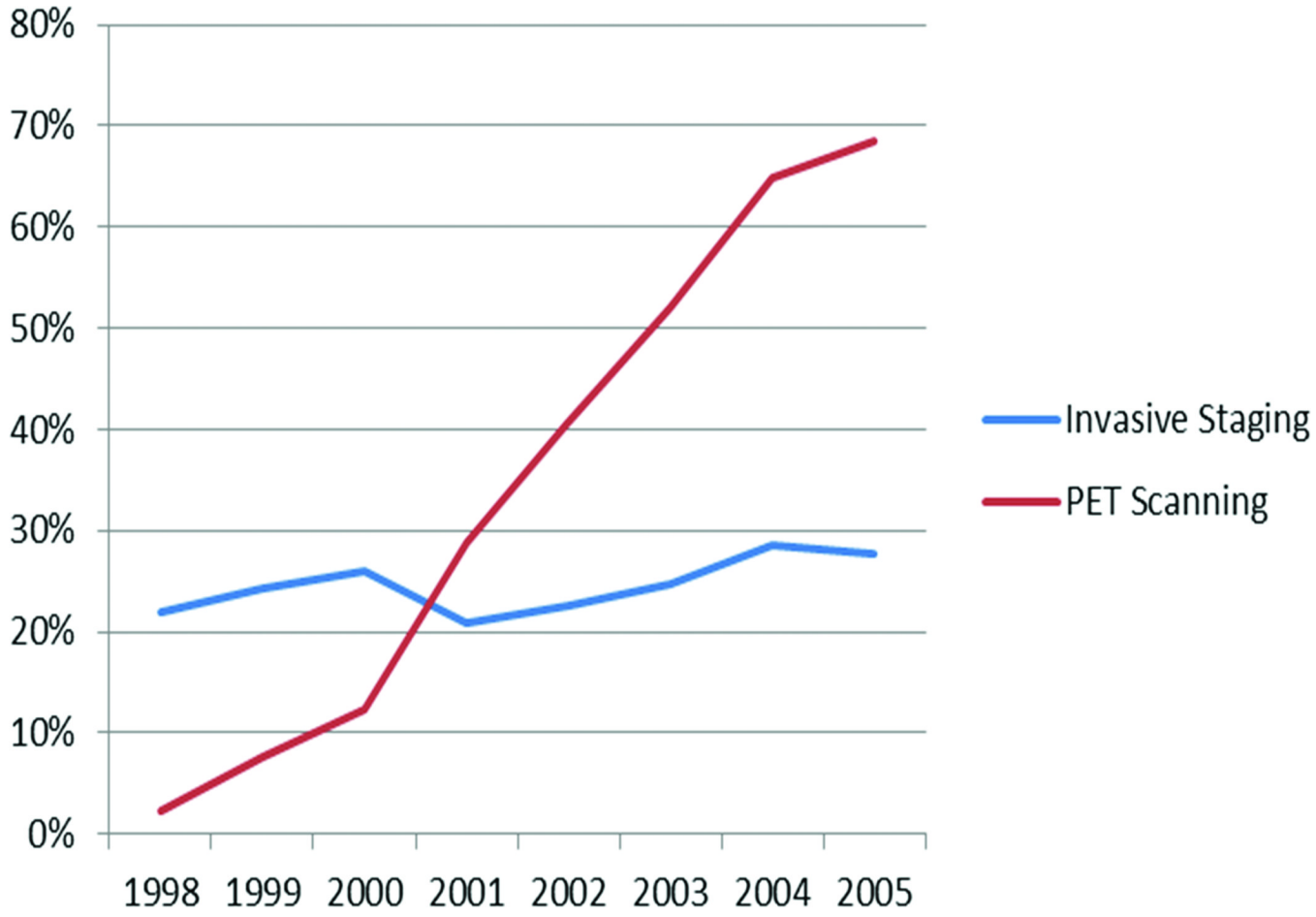

Figure 2.
Use of PET scanning and invasive staging, 1998–2005 in pre-expansion registries

Table 1

Baseline Characteristics of Cohort and Use of Invasive Staging Techniques in Stage IIIA NSCLC N=7583

Age	
67–69	1118 (15%)
70–74	2305 (30%)
75–79	2197 (29%)
80–84	1331 (18%)
85–94	632 (8%)
Sex	
Male	4308 (57%)
Female	3275 (43%)
Race	
White	6653 (88%)
Black	635 (8%)
Other	295 (4%)
Marital Status	
Married	3972 (52%)
Unmarried	3349 (44%)
Unknown	262 (4%)
Income	
1st quintile	1449 (19%)
2nd quintile	1451 (19%)
3rd quintile	1446 (19%)
4th quintile	1450 (19%)
5th quintile	1447 (19%)
Unknown	340 (4%)
Influenza Vaccination	
Influenza Vaccination in last 18 months	4013 (53%)
No Influenza Vaccination	3570 (47%)
Treatment Group*	
Best supportive care	1834 (24%)
Cancer specific therapy	2051 (27%)
Curative intent therapy	3698 (49%)
Invasive Staging	
Any Invasive Staging Technique	1678 (22%)
No Invasive Staging	5905 (78%)

*Patients classified as best supportive care did not receive any cancer specific therapy (chemotherapy, radiation, or surgery). Patients who received chemotherapy or radiation alone were classified as cancer specific therapy. Patients who received combination chemotherapy and radiation therapy or any therapy that involved surgical resection were classified as curative intent therapy.

Table 2

Unadjusted and adjusted odds ratios for receipt of invasive staging

			Unadjusted		Adjusted	
	N	**% staged**	**OR**	**95% CI**	**OR**	**95% CI**
Age group						
67–69	1118	27.6	1.00	--	1.00	--
70–74	2305	25.4	0.90	0.76–1.05	0.92	0.78–1.09
75–79	2197	22.4	0.76	0.64–0.90	0.81	0.68–0.96
80–84	1331	16.3	0.51	0.42–0.62	0.57	0.46–0.70
85–94	632	11.9	0.35	0.27–0.47	0.46	0.34–0.61
Sex						
Male	4308	22.1	1.00	--	n/a	n/a
Female	3275	22.2	1.01	0.91–1.13	n/a	n/a
Race						
White	6653	22.5	1.00	--	1.00	--
Black	635	17.3	0.72	0.58–0.89	0.88	0.69–1.12
Other	295	24.4	1.11	0.85–1.46	1.33	0.97–1.83
Comorbidities						
0	2747	24.1	1.00	--	1.00	--
1–2	3169	22.6	0.92	0.82–1.04	0.93	0.82–1.05
≥3	1667	18.1	0.70	0.60–0.81	0.81	0.69–0.95
Marital Status						
Married	3972	24.3	1.00	--	1.00	--
Unmarried	3349	19.7	0.82	0.72–0.92	0.93	0.83–1.05
Unknown	262	19.9	0.78	0.55–1.10	1.01	0.73–1.40
Income						
1st quintile	1449	17.7	1.00	--	1.00	--
2nd quintile	1451	21.4	1.26	1.05–1.52	1.07	0.87–1.30
3rd quintile	1446	22.4	1.34	1.12–1.61	0.99	0.81–1.22
4th quintile	1450	24.3	1.49	1.24–1.78	1.09	0.88–1.34

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			Unadjusted		Adjusted	
	N	% staged	OR	95% CI	OR	95% CI
5th quintile	1447	24.9	1.54	1.28–1.84	1.12	0.90–1.39
Unknown	340	22.1	1.31	0.98–1.75	1.13	0.83–1.54
Flu shot in prior 18 months						
No	3570	19.7	1.00	--	1.00	--
Yes	4013	24.3	1.31	1.17–1.46	1.23	1.09–1.39
Year of diagnosis						
1998	502	22.7	1.00	--	n/a	n/a
1999	461	24.3	1.09	0.81–1.47	n/a	n/a
2000	1033	22.6	0.99	0.77–1.28	n/a	n/a
2001	983	19.8	0.84	0.65–1.09	n/a	n/a
2002	1038	18.8	0.79	0.61–1.02	n/a	n/a
2003	1130	21.2	0.92	0.71–1.18	n/a	n/a
2004	1247	23.7	1.06	0.83–1.36	n/a	n/a
2005	1189	24.6	1.11	0.87–1.43	n/a	n/a
Treatment type						
Best supportive care	1834	9.8	1.00	--	1.00	--
Cancer specific therapy	2051	19.1	2.18	1.80–2.63	2.18	1.80–2.66
Curative intent therapy	3698	30.0	3.96	3.34–4.69	3.31	2.78–3.95
SEER region						
San Francisco	253	13.8	1.00	--	1.00	--
Connecticut	558	26.5	2.25	1.50–3.37	2.07	1.36–3.14
Detroit	866	25.5	2.13	1.45–3.15	2.04	1.36–3.06
Hawaii	131	13.7	0.99	0.54–1.83	0.68	0.35–1.30
Iowa	602	24.6	2.03	1.36–3.04	1.87	1.21–2.88
New Mexico	140	17.1	1.29	0.73–2.27	1.29	0.71–2.34
Seattle	486	32.5	3.00	2.00–4.50	3.05	1.99–4.66
Utah	94	22.3	1.79	0.98–3.27	1.69	0.91–3.17
Atlanta	258	21.3	1.69	1.06–2.69	1.55	0.96–2.50

			Unadjusted		Adjusted	
	N	% staged	OR	95% CI	OR	95% CI
San Jose	153	20.3	1.58	0.93–2.69	1.33	0.77–2.30
Los Angeles	496	30.0	2.68	1.78–4.01	2.48	1.63–3.78
Rural Georgia	**	**	0.86	0.29–2.59	0.91	0.29–2.80
Greater California	1181	20.1	1.56	1.07–2.30	1.51	1.01–2.26
Kentucky	840	15.5	1.14	0.76–1.71	1.05	0.69–1.63
Louisiana	562	15.1	1.11	0.73–1.70	1.14	0.72–1.79
New Jersey	930	23.0	1.86	1.26–2.75	1.70	1.13–2.54

Best supportive care = not treated with surgery, chemo or radiation, Cancer specific therapy = treated with chemotherapy or radiation alone, Curative intent therapy = treated with combination chemotherapy and radiation or any combination that included surgical resection. N=number of patients, %staged=percent of patients who underwent invasive clinical staging, Adjusted OR = adjusted odds ratio adjusted for age, race, SEER region, comorbidities, income and access to health care services as measured by receipt of influenza vaccination

** Suppressed to protect confidentiality due to cell size

Table 3

Multivariable Analysis to predict use of invasive staging among subset of Stage IIIA patients Treated with Combined Chemotherapy and Radiation

Variable	Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Age				
Age 67–69	Ref	n/a	Ref	n/a
Age 70–74	0.85	0.66–1.12	0.80	0.61–1.04
Age 75–79	0.63	0.47–0.83	0.58	0.43–0.77
Age 80–84	0.47	0.33–0.67	0.27	027–0.57
Over Age 85	0.41	0.21–0.80	0.36	0.18–0.71
Gender				
Male	Ref	n/a	n/a	n/a
Female	1.18	0.97–1.43	Not significant	Not significant
Race				
White	Ref	n/a		
Black	0.72	0.49–1.06	Not significant	Not significant
Other	1.68	1.02–2.78	Not significant	Not significant
Comorbidities				
0	Ref	n/a	n/a	n/a
1–2	1.00	0.81–1.24	Not significant	Not significant
≥3	0.80	0.60–1.06	Not significant	Not significant
Marital Status				
Married	Ref	n/a	n/a	n/a
Unmarried	0.98	0.80–1.20	Not significant	Not significant
Unknown	1.13	0.65–1.95	Not significant	Not significant
Income				
1st quintile	Ref	n/a	n/a	n/a
2nd quintile	1.37	1.00–1.89	1.30	0.92–1.84
3rd quintile	1.32	0.96–1.83	1.06	0.74–1.52
4th quintile	1.45	1.05–2.00	1.11	076–1.61
5th quintile	1.58	1.14–2.18	1.28	0.86–1.88

Variable	Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
Unknown	1.14	0.67–1.94	0.86	0.49–1.52
Influenza Vaccination				
Negative Vaccination	Ref	n/a	n/a	n/a
Positive Vaccination	1.28	1.05–1.56	1.31	1.06–1.61
Year of Diagnosis				
1998	Ref	n/a	n/a	n/a
1999	1.03	0.58–1.84	Not significant	Not significant
2000	1.04	0.64–1.70	Not significant	Not significant
2001	0.62	0.37–1.05	Not significant	Not significant
2002	0.67	0.40–1.10	Not significant	Not significant
2003	0.75	0.46–1.22	Not significant	Not significant
2004	1.07	0.67–1.70	Not significant	Not significant
2005	0.97	0.61–1.55	Not significant	Not significant
SEER Registry				
San Francisco	Ref	n/a		
Connecticut	3.72	1.46–9.34	4.57	1.74–12.01
Detroit	4.18	1.71–10.20	5.46	2.15–13.86
Hawaii	1.19	0.31–4.65	0.64	0.15–2.68
Iowa	3.71	1.49–9.24	4.33	1.65–11.38
New Mexico	2.63	0.88–7.88	3.31	1.05–10.40
Seattle	5.53	2.21–13.84	6.52	2.51–16.92
Utah	2.87	0.80–10.26	3.07	0.83–11.44
Atlanta	3.18	1.20–8.49	4.19	1.52–11.58
San Jose	2.24	0.74–6.80	2.51	0.81–7.80
Los Angeles	5.47	2.13–14.06	6.82	2.57–18.10
Rural Georgia	1.02	0.11–9.84	1.71	0.17–16.94
Greater California	2.26	0.93–5.51	2.71	1.07–6.86
Kentucky	2.03	0.81–5.06	2.43	0.93–6.38
Louisiana	2.14	0.84–5.42	2.78	1.04–7.43

Variable	Odds Ratio	95% CI	Adjusted Odds Ratio	95% CI
New Jersey	2.90	1.18–7.09	3.58	1.42–9.06

Table 4

Results of Multivariable Analysis to predict 3-year survival for Patients Treated with Chemotherapy and Radiation*

Variable	Odds Ratio	95% CI	Adjusted Odd Ratio	95% CI
Age				
Age 67–69	Ref	n/a	n/a	n/a
Age 70–74	0.60	0.42–0.85	0.61	0.43–0.90
Age 75–79	0.70	0.49–0.99	0.75	0.52–1.08
Age 80–84	0.47	0.30–0.75	0.533	0.33–0.86
Age >85	0.22	0.07–0.73	0.26	0.08–0.86
Gender				
Male	Ref	n/a	n/a	n/a
Female	1.57	1.21–2.03	1.52	1.17–1.99
Race				
White	Ref	n/a	n/a	n/a
Black	0.98	0.60–1.6	1.18	0.70–2.0
Other	0.93	0.43–2.00	0.85	0.39–1.85
Comorbidities				
0	Ref	n/a	n/a	n/a
1–2	0.96	0.73–1.27	1.02	0.77–1.35
≥3	0.43	0.27–0.68	0.49	0.31–0.78
Marital Status				
Married	Ref	n/a	n/a	n/a
Unmarried	0.86	0.65–1.3	Not significant	Not significant
Unknown	0.75	0.33–1.68	Not significant	Not significant
Income				
1st quintile	Ref	n/a	n/a	n/a
2nd quintile	1.21	0.72–1.74	1.11	0.71–1.75
3rd quintile	1.20	0.78–1.86	1.21	0.76–1.91
4th quintile	1.54	1.01–2.35	1.51	0.97–2.37

Variable	Odds Ratio	95% CI	Adjusted Odd Ratio	95% CI
5th quintile	1.42	0.92–2.18	1.41	0.89–2.34
Unknown	0.78	0.33–1.82	0.83	0.35–1.97
Influenza Vaccination				
Negative Vaccination	Ref	n/a	n/a	n/a
Positive Vaccination	1.21	0.86–1.46	Not significant	Not significant
Year of Diagnosis				
1998	Ref	n/a	n/a	n/a
1999	1.31	0.6–2.85	Not significant	Not significant
2000	1.01	0.51–2.01	Not significant	Not significant
2001	1.53	0.58–2.30	Not significant	Not significant
2002	1.59	0.82–3.08	Not significant	Not significant
2003	1.49	0.78–2.87	Not significant	Not significant
2004	1.81	0.96–3.41	Not significant	Not significant
SEER Region				
San Francisco	Ref	n/a	n/a	n/a
Connecticut	2.26	0.72–7.08	Not significant	Not significant
Detroit	2.55	0.86–7.55	Not significant	Not significant
Hawaii	2.00	0.45–9.00	Not significant	Not significant
Iowa	2.11	0.69–6.43	Not significant	Not significant
New Mexico	0.85	0.18–4.11	Not significant	Not significant
Seattle	2.06	0.66–6.38	Not significant	Not significant
Utah	2.27	0.50–10.29	Not significant	Not significant
Atlanta	1.47	0.43–5.04	Not significant	Not significant
San Jose	1.76	0.45–6.84	Not significant	Not significant
Los Angeles	2.33	0.73–7.49	Not significant	Not significant
Rural Georgia	1.70	0.16–18.44	Not significant	Not significant
Greater California	1.52	0.51–4.54	Not significant	Not significant
Kentucky	1.45	0.47–4.43	Not significant	Not significant
Louisiana	1.13	0.35–3.63	Not significant	Not significant

Variable	Odds Ratio	95% CI	Adjusted Odd Ratio	95% CI
New Jersey	1.38	0.45–4.18	Not significant	Not significant