Variability in the Treatment of Elderly Patients with Stage IIIA (N2) Non–Small-Cell Lung Cancer

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Introduction: We evaluated treatment patterns of elderly patients with stage IIIA (N2) non–small-cell lung cancer (NSCLC).

Methods: The use of surgery, chemotherapy, and radiation for patients with stage IIIA (T1-T3N2M0) NSCLC in the Surveillance, Epidemiology, and End Results–Medicare database from 2004 to 2007 was analyzed. Treatment variability was assessed using a multivariable logistic regression model that included treatment, patient, tumor, and census track variables. Overall survival was analyzed using the Kaplan–Meier approach and Cox proportional hazard models.

Results: The most common treatments for 2958 patients with stage IIIA (N2) NSCLC were radiation with chemotherapy (n = 1065, 36%), no treatment (n = 534, 18%), and radiation alone (n = 383, 13%). Surgery was performed in 709 patients (24%): 235 patients (8%) had surgery alone, 40 patients (1%) had surgery with radiation, 222 patients had surgery with chemotherapy (8%), and 212 patients (7%) had surgery, chemotherapy, and radiation. Younger age ($p < 0.0001$), lower T-status ($p < 0.0001$), female sex ($p = 0.04$), and living in a census track with a higher median income ($p = 0.03$) predicted surgery use. Older age ($p < 0.0001$) was the only factor that predicted that patients did not get any therapy. The 3-year overall survival was 21.8 ± 1.5% for all patients, 42.1 ± 3.8% for patients that had surgery, and 15.4 ± 1.5% for patients that did not have surgery. Increasing age, higher T-stage and Charlson Comorbidity Index, and not having surgery, radiation, or chemotherapy were all risk factors for worse survival (all p values < 0.001).

Conclusions: Treatment of elderly patients with stage IIIA (N2) NSCLC is highly variable and varies not only with specific patient and tumor characteristics but also with regional income level.

Key Words: Non–small cell, Stage IIIA, Surgery, Elderly.

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Stage IIIA non–small-cell lung cancer (NSCLC) encompasses a heterogeneous group of patients, including T4N0, T3-4N1, and T1-3N2.[1] Patients in the subset due to N2 lymph node metastases represent approximately 10% of all patients diagnosed with NSCLC.[2] Multimodality therapy with some combination of surgical resection, chemotherapy, and radiation therapy is the preferred approach for patients with stage IIIA (N2) NSCLC, but the optimal management strategy has not been definitively established by randomized controlled data.[3–7] In particular, the benefit of surgery when radiation and chemotherapy have been used is unclear.[8–10] Induction chemotherapy and radiation therapy followed by surgical resection for patients with stage IIIA disease is feasible but may only provide survival benefit to selected patients.[11]

Treatment guidelines reflect the lack of available definitive evidence for this stage of NSCLC. Guidelines such as those from the National Comprehensive Cancer Network (NCCN) recognize the need for local therapy in addition to systemic therapy but do not explicitly specify the role of surgery versus radiation therapy.[12] NCCN treatment recommendations for patients pathologically confirmed to have N2 lymph node involvement but not distant metastatic disease include both definitive concurrent chemoradiation and induction chemotherapy followed by surgery if repeat staging does not demonstrate disease progression. The NCCN also recommends consideration of radiation therapy either before or after surgery and additional chemotherapy after surgery. Considering the lack of clear data and guidelines that allow several options for treatment, the combination and timing of treatment modalities may have significant variability in clinical practice. Treatment may also vary according to specific patient characteristics, considering that disparities in overall lung cancer treatment and prognosis are known to exist for race, socioeconomic status, educational status, and geographical location.[13–26] This study was designed to examine patterns of care for elderly patients with stage IIIA (N2) NSCLC in a national database and test the hypothesis that nonclinical characteristics play an important role in whether surgery is performed for patients. We focused on examining characteristics and outcomes associated with surgery to attempt to understand how patients are selected for surgery in this setting, as randomized trials have failed to definitively show a survival advantage to performing surgical resection in patients that are treated with chemotherapy and radiation.[10,11]

PATIENTS AND METHODS

This study was performed with approval by the Duke University Institutional Review Board. A retrospective cohort study of patients diagnosed with NSCLC was conducted

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using the Survival, Epidemiology, and End Results (SEER)–Medicare database, which brings together Medicare administrative claims data with detailed clinical tumor registry data in a representative sample covering approximately 14% of the U.S. population across a wide geographic variation.[27] The SEER-Medicare database was initially queried to identify patients with lung cancer from the years 2004 to 2007. The analysis was limited to the years 2004–2007 to allow appropriate identification of the patients of interest (T1-3N2M0), because earlier data in the database provided overall stage but did not provide detailed tumor, node, and metastasis status to allow identification of patients who were stage IIIA due to N2 lymph node status. In SEER, the reported stage is the pathologic stage for patients who did not receive any pre resection treatment. The reported stage is the clinical stage for patients who do not undergo resection or who receive any neo-adjuvant treatment before resection.

From the entire lung cancer cohort, patients aged 65 years or older and definitively identified as having a NSCLC histologic type were selected. Patients younger than 65 years were excluded because these patients in the Medicare data consist of individuals who are disabled or have end-stage renal disease. Only patients who had both continuous Part A and Part B Medicare coverage with no health maintenance organization enrollment at all between 1 year before and 6 months after diagnosis, or until the month of death for patients who died within 6 months of diagnosis, were included in the analysis, to minimize the chance that our analysis could fail to capture treatment because of non-Medicare coverage. This requirement that patients had continuous Medicare coverage for 1 year before diagnosis effectively meant that only patients aged 66 years or older at the time of diagnosis were included in the analysis. In addition, we excluded patients who did not have a lung cancer diagnosis code in their Medicare claims within 2 months before and 3 months after the date of their lung cancer diagnosis in SEER, because of concerns that treatment information derived from the Medicare records was potentially inaccurate due to the discrepancy between the lung cancer identified in SEER but seemingly not confirmed in Medicare. For each patient, the Charlson Comorbidity Index was measured at the date of diagnosis using Medicare records during a year before the date of diagnosis according to specifications previously described.[28,29] Patients were identified as having received surgery, radiation, and chemotherapy if there was at least one indicator of treatment within 6 months of diagnosis in the Medicare Provider Analysis and Review, Outpatient Claims, Durable Medical Equipment and Carrier Claims Medicare files using Health Care Common Procedure Coding System codes, International Classification of Diseases, Ninth Revision (ICD-9) diagnosis and procedure codes, Current Procedural Terminology codes, Revenue Center Codes, and Diagnostic-Related Group Codes as previously described (Supplemental Tables 1–3, Supplemental Digital Content 1, http://links.lww.com/JTO/A407).[30–33] The date of onset of chemotherapy was identified using methods originally developed for date of disease onset.[34]

Method of mediastinal staging was assessed as follows. We used the inpatient, outpatient, and physician Medicare claims to search for Current Procedural Terminology or Health Care Common Procedure Coding System codes for computed tomography scan, positron emission tomography (PET) scan, mediastinoscopy, mediastinotomy, endobronchial ultrasound, endoscopic ultrasound, or video-assisted thoracoscopic surgery biopsies (Supplemental Table 4, Supplemental Digital Content 1, http://links.lww.com/JTO/A407). Patients were considered to have invasive mediastinal staging if they had mediastinoscopy, mediastinotomy, endobronchial ultrasound, endoscopic ultrasound, or a video-assisted thoracoscopic biopsy. We searched for mediastinal staging procedures performed 3 months before diagnosis through the initiation of treatment or for 3 months after diagnosis in the case of patients who were not treated with any cancer-specific therapy.

Both univariate- and multivariable-adjusted logistic regression analyses were performed relating surgery use to the following patient characteristics: age, T-stage, sex, race (black versus others), comorbidities, and the following information from the patient's census tract based on the 2000 census bureau survey: median income, percentage of blacks, percentage of persons 25 years or older with at least 4 years of college education, and percentage of residents living below the poverty level. Similar logistic regression analysis relating the use of any therapy with the same variables was also performed. Survival analyses were performed both with the Kaplan–Meier method comparing survival curves with the log-rank test and with the multivariate-adjusted Cox proportional hazard model that included age, T-stage, the Charlson comorbidity index, and treatment with surgery, chemotherapy, and radiation. A similar survival analysis was repeated on a subset of patients that included only those patients who received some local therapy in the form of either surgery or radiation.

Unpaired Student's *t* tests were used to compare continuous data, and χ^2 for categoric variables. A two-tailed *p* value of less than 0.05 was considered significant. Data are presented as counts (%), mean (SD), OR, or hazard ratios (HR) (95% confidence intervals) where appropriate. The SAS 9.2 statistical package (SAS Institute, Cary, NC) was used for statistical analyses.

RESULTS

Initially, 136,699 individuals with lung cancer from 2004 to 2007 were identified in the database, of whom 82,062 were 65 years or older with non–small-cell histology. Of 6350 patients aged 65 years or older and stage IIIA (N2) NSCLC, 2958 patients who met all inclusion criteria were identified. The details of treatment are listed in Table 1. Treatment was quite variable, and there was not a single dominant treatment regimen. The most common treatments were radiation with chemotherapy (n = 1065, 36%), no treatment (n = 534, 18%), and radiation alone (n = 383, 13%). Overall, treatment included surgery, radiation, and chemotherapy in 212 patients (7%), two of these modalities in some combination in 1327 patients (45%), and only one of these modalities in 885 patients (30%).

Most patients received some form of local therapy with either surgery or radiation, although 801 patients (27%) did not receive local treatment, with 267 patients (9%) being

TABLE 1. Treatments Used for 2958 Patients with Stage IIIA (N2) in the Surveillance, Epidemiology, and End Results –Medicare Database from 2004 to 2007

Treatment	*n*
Trimodal therapy	
Surgery, radiation, and chemotherapy	212 (7%)
Radiation before surgery	68 (2%)
Chemotherapy before surgery	64 (2%)
Chemotherapy after surgery	4 (0.1%)
Radiation after surgery	144 (5%)
Chemotherapy before surgery	11 (0.4%)
Chemotherapy after surgery	133 (5%)
Bimodal therapy	
Radiation and chemotherapy	1065 (36%)
Surgery and radiation	40 (1%)
Radiation before surgery	4 (0.1%)
Radiation after surgery	36 (1%)
Surgery and chemotherapy	222 (8%)
Chemotherapy before surgery	47 (2%)
Chemotherapy after surgery	175 (6%)
Unimodal therapy	
Radiation alone	383 (13%)
Surgery alone	235 (8%)
Chemotherapy alone	267 (9%)
No therapy	534 (18%)

treated with chemotherapy alone. Chemotherapy was the often used modality (*n* = 1766, 60%). Radiation was used in most of the patients (*n* = 1700, 57%). In the patients that received radiation, no other therapy was used in 23% of patients (*n* = 383), whereas 63% of patients (*n* = 1065) received radiation with only chemotherapy and 2% of patients (*n* = 40) received radiation with only surgery, but only 12% of patients (*n* = 212) had all three treatment modalities.

Only a minority of patients had surgery (*n* = 709, 24%). Of the 709 patients for whom surgery was performed, 235 patients (33%) had surgery alone, 40 patients (6%) had surgery with radiation only, 222 patients (31%) had surgery with chemotherapy only, and 212 patients (30%) had all three treatments. Of the 252 patients (8%) who received both surgery and radiation, 72 patients (28%) received preoperative radiation, and 180 patients (72%) had postoperative radiation. Of the 434 patients who received both surgery and chemotherapy, most of the patients (*n* = 322, 74%) were given chemotherapy after surgery. The extent of surgery is listed in Table 2, along with the timing of other therapies for each specific surgical approach. Most patients who had surgery had a lobar resection (*n* = 563, 79%), whereas a minority had either a sublobar resection (n=50, 7%) or a pneumonectomy (*n* = 63, 9%).

The uses of PET scans and invasive staging modalities are summarized in Table 3. Overall, a PET scan was used for staging in 1615 patients (55%). Invasive mediastinal staging was done in 506 patients (17%). Patients who had surgery were more likely to have had invasive mediastinal staging compared with patients who did not have surgery. Compared with patients who received any therapy, patients who did not receive any therapy were less likely to have been staged with either a PET scan or with invasive mediastinal staging.

The characteristics of the patients who had and who did not have surgery are listed in Table 4. The factors that predicted the use of surgery in multivariate-adjusted analysis were younger age ($p < 0.0001$), lower T-stage ($p < 0.0001$), female sex ($p = 0.04$), and living in a census track with a higher median income ($p = 0.03$) (Table 5). The characteristics of the patients who had or did not have any therapy are also

TABLE 2. Extent of Surgery, along with Timing Related to Other Therapy, for 709 Patients with Stage IIIA (N2) in the Surveillance, Epidemiology, and End Results –Medicare Database Who Had Surgery

	Lobar Resection (*n* = 563)	Sublobar Resection (*n* = 50)	Pneumonectomy (*n* = 63)	Local Treatment (*n* = 32)	Unknown Extent of Surgery (*n* = 1)
Surgery alone	178 (32%)	23 (46%)	24 (38%)	10 (31%)	0
Surgery, chemotherapy, and radiation	167 (30%)	15 (30%)	19 (31%)	11 (34%)	0
Radiation presurgery	55 (10%)	2 (4%)	8 (13%)	3 (9%)	0
Chemotherapy presurgery	54 (10%)	2 (4%)	7 (11%)	1 (3%)	0
Chemotherapy postsurgery	1 (0.2%)	0	1 (2%)	2 (6%)	0
Radiation postsurgery	112 (20%)	13 (26%)	11 (18%)	8 (25%)	0
Chemotherapy presurgery	9 (2%)	1 (2%)	1 (2%)	0	0
Chemotherapy postsurgery	103 (18%)	12 (24%)	10 (16%)	8 (25%)	0
Surgery and chemotherapy	191 (34%)	7 (14%)	17 (27%)	7 (22%)	0
Chemotherapy presurgery	39 (7%)	1 (2%)	6 (10%)	1 (3%)	0
Chemotherapy postsurgery	152 (27%)	6 (12%)	11 (17%)	6 (19%)	0
Surgery and radiation	27 (5%)	5 (10%)	3 (5%)	4 (12%)	1 (100%)
Radiation presurgery	4 (1%)	0	0	0	0
Radiation postsurgery	23 (4%)	5 (10%)	3 (5%)	4 (12%)	1 (100%)

TABLE 3. Staging Modalities Used for 2958 Patients with Stage IIIA (N2) in the Surveillance, Epidemiology, and End Results–Medicare Database from 2004 to 2007

Variable	All Patients (*n* = 2958)	Surgery (*n* = 709)	No Surgery (*n* = 2249)	*p* Value	Any Therapy (*n* = 2424)	No Therapy (*n* = 534)	*p* Value
Positron emission tomography scan	1615 (55%)	403 (57%)	1212 (54%)	0.7	1456 (60%)	159 (30%)	<0.0001
Invasive staging	506 (17%)	201 (28%)	305 (14%)	<0.0001	468 (19%)	38 (7%)	<0.0001

TABLE 4. Specific Characteristics of 2958 Patients with Stage IIIA (N2) in the Survival, Epidemiology, and End Results–Medicare Database from 2004 to 2007, Stratified by Both Whether Surgery Was Used or Not and Whether Any Therapy Was Used or Not

Variable	Surgery (*n* = 709)	No Surgery (*n* = 2249)	*p* Value	Any Therapy (*n* = 2424)	No Therapy (*n* = 534)	*p* Value
Age, yr			<0.0001			<0.0001
66–69	187 (26%)	421 (19%)		525 (22%)	83 (16%)	
70–74	224 (32%)	613 (27%)		703 (29%)	134 (25%)	
75–79	185 (26%)	576 (26%)		638 (26%)	123 (23%)	
80–84	92 (13%)	428 (19%)		398 (16%)	122 (23%)	
85+	21 (3%)	211 (9%)		160 (7%)	72 (13%)	
T-stage T1			<0.0001			0.02
T2	203 (29%)	524 (23%)		620 (26%)	107 (20%)	
T3	453 (64%)	1367 (61%)		1476 (61%)	344 (64%)	
T3	53 (7%)	358 (16%)		328 (14%)	83 (16%)	
Chemotherapy			0.35			<0.0001
Yes	434 (61%)	1332 (59%)		1766 (73%)	0 (0%)	
No	275 (39%)	917 (41%)		658 (27%)	534 (100%)	
Radiation therapy			<0.0001			<0.0001
Yes	252 (35%)	1448 (64%)		1700 (70%)	0 (0%)	
No	457 (65%)	801 (36%)		724 (30%)	534 (100%)	
Sex			0.02			0.8
Male	355 (50%)	1241 (55%)		1305 (54%)	291 (54%)	
Female	354 (50%)	1008 (45%)		1119 (46%)	243 (46%)	
Race			0.001			0.5
Black	37 (5%)	205 (9%)		202 (8%)	40 (7%)	
Nonblack	672 (95%)	2044 (91%)		2222 (92%)	494 (93%)	
Charlson comorbidity index			0.06			0.4
0	199 (28%)	562 (25%)		632 (26%)	129 (24%)	
1	176 (25%)	485 (22%)		553 (23%)	108 (20%)	
2	125 (18%)	436 (19%)		457 (19%)	104 (19%)	
3	80 (11%)	309 (14%)		309 (13%)	80 (15%)	
4+	129 (18%)	457 (20%)		473 (20%)	113 (21%)	
Census tract median income	53,501±24,954	47,759±21,422	<0.0001	49,719±22,968	46,491±19,726	0.003
Census tract % of black	7.4±15.9	10.7±21.1	<0.0001	9.6±19.6	11.2±21.8	0.11
Census tract % of people with 4 years of college education	28.0±18.0	24.4±16.4	<0.0001	25.7±17.0	23.7±16.0	0.02
Census tract % of people living below the poverty line	9.9±8.6	11.8±9.9	<0.0001	11.1±9.5	12.5±10	0.004

Continuous data are presented as mean ± SD.

listed in Table 4. The only factor that predicted that patients did not receive any therapy in multivariate-adjusted analysis was older age ($p < 0.0001$) (Table 5).

The overall 3-year survival of all patients was 21.8 ± 1.5% (Fig. 1A). Patients who had surgery had an overall 3-year survival of 42.1 ± 3.8%, whereas the overall 3-year

TABLE 5. Multivariable Models of Both the Use of Surgery and the Use of No Therapy for 2958 Patients with Stage IIIA (N2) in the Survival, Epidemiology, and End Results–Medicare Database from 2004 to 2007

	Outcome = Surgery Used			Outcome = No Therapy Used		
Predictor	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Age, yr			<0.0001			<0.0001
70–74 vs. 66–69	0.82	0.65–1.04		1.2	0.88–1.62	
75–79 vs. 66–69	0.67	0.52–0.86		1.21	0.89–1.65	
80–84 vs. 66–69	0.45	0.33–0.60		1.93	1.40–2.65	
85+ vs. 66–69	0.24	0.15–0.39		2.67	1.82–3.92	
T-stage			<0.0001			0.07
T2 vs. T1	0.91	0.74–1.12		1.28	1.00–1.64	
T3 vs. T1	0.42	0.30–0.59		1.42	1.02–1.98	
Census tract % of people with 4 years of college education	1	1.00–1.01	0.45	1	0.99–1.01	0.6
Census tract % of black	1	0.99–1.00	0.27	1	1.00–1.01	0.2
Charlson Comorbidity Index			0.24			0.44
1 vs. 0	1.07	0.84–1.37		0.94	0.70–1.26	
2 vs. 0	0.83	0.63–1.09		1.03	0.76–1.39	
3 vs. 0	0.82	0.60–1.12		1.21	0.88–1.68	
4+ vs. 0	0.86	0.66–1.12		1.19	0.89–1.60	
Census Tract Median Income	1	1.00–1.00	0.03	1	1.00–1.00	0.5
Race (black vs. nonblack)	0.7	0.45–1.10	0.12	0.68	0.43–1.09	0.11
Sex (male vs. female)	0.83	0.70–0.99	0.04	1.04	0.86–1.27	0.7
Census tract % of people living below the poverty line	1	0.98–1.01	0.8	1.01	0.99–1.02	0.32

CI, confidence interval.

survival of patients who did not have surgery was 15.4 ± 1.5% (Fig. 1B). In the multivariate-adjusted Cox proportional hazard regression model, factors that predicted worse survival were not having surgery, not having radiation therapy, not getting chemotherapy, increasing age, higher T-stage, and a Charlson comorbidity index of two or greater (Table 6).

When only patients who received local therapy with either surgery or radiation were included in the survival analysis, the overall 3-year survival was 25.6 ± 1.9% (Fig. 1C). As above, patients who had surgery with or without radiation had an overall 3-year survival of 42.1 ± 3.8%. The overall 3-year survival of patients who only had radiation was 17.5 ± 2.0% (Fig. 1D). After multivariable adjustment, the risk factors that predicted worse survival were not having surgery, not getting chemotherapy, increasing age, higher T-stage, and Charlson comorbidity index of two or greater (Table 7). In this subset of patients, a tumor T-stage of T3 was the strongest predictor of worse survival (hazard ratios, 1.90; $p < 0.0001$).

DISCUSSION

In this study, we demonstrated that the treatment of elderly patients with stage IIIA (N2) NSCLC in the SEER-Medicare database is highly variable. Radiation is used in most of the patients (57%), and the most common treatments are radiation with chemotherapy (36%), no treatment (18%), and radiation alone (13%). Surgical resection is used as part of the treatment regimen in only 24% of elderly patients. The use of surgery is dependent on patient-specific factors, such as age, tumor T-status, and comorbidities, but also socioeconomic factors such as the median income of the census tract where patients live.

Stage IIIA (N2) accounts for a minority but still significant number of patients with lung cancer, considering that lung cancer is the most common cause of cancer-related mortality in the United States with over 222,000 new cases and over 157,000 deaths in 2010.[1,2,35,36] The reported 5-year survival rates for stage IIIA (N2) vary from 15% to 42%.[2,4,7,9,37] Providing treatment that optimizes the chance for cure and minimizes morbidity is critical, and multimodality therapy with some combination of surgical resection, chemotherapy, and radiation therapy is generally considered the preferred approach.[3] Both induction and adjuvant chemotherapy improve survival compared with surgical resection for patients with clinical stage IIIA based on suspected N2 nodal involvement.[4–7,38,39] However, the role of adding induction radiation therapy to chemotherapy, and even the role of surgery when radiation and chemotherapy have been used is unclear.[8–10,40] Adding induction radiation therapy to induction chemotherapy has not been shown to give a survival benefit compared with induction chemotherapy alone in randomized controlled trials, phase II studies, or retrospective reviews.[35,41–45] Induction chemotherapy and radiation therapy (45 Gy) followed by surgical resection for patients with stage IIIA disease has been demonstrated to be feasible, but did not improve survival compared with chemotherapy and radiation (61 Gy) without surgical resection in a randomized phase III

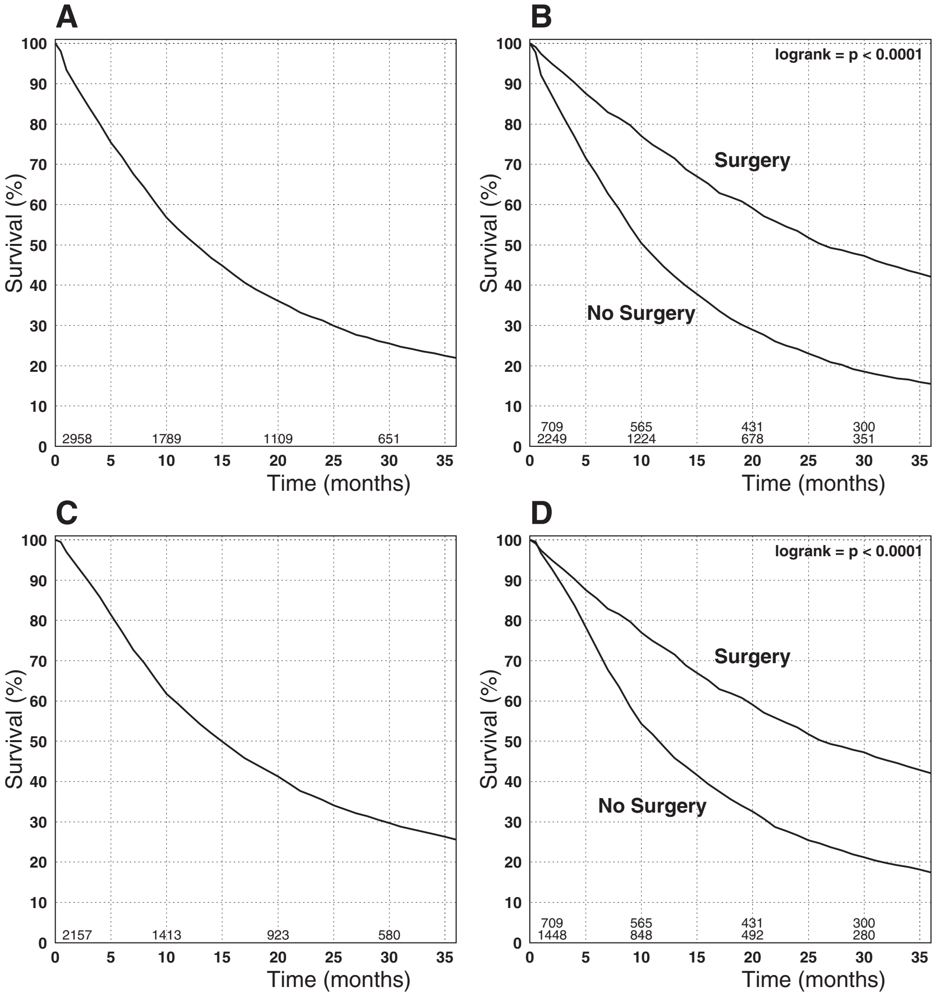

FIGURE 1. (*A*) Survival curve for all patients. (*B*) Survival curve for all patients stratified by surgery versus no surgery. (*C*) Survival curve for all patients who received either surgery or radiation. (*D*) Survival curve for all patients who received either surgery or radiation stratified by surgery vs. no surgery.

TABLE 6. Multivariable Model of Survival for 2958 Patients with Stage IIIA (N2) in the Survival, Epidemiology, and End Results–Medicare Database from 2004 to 2007

Predictor	Hazard Ratio	*p*
Surgery (no surgery vs. surgery)	2.19	<0.0001
Radiation (no vs. yes)	1.17	0.0009
Chemotherapy (no vs. yes)	1.45	<0.0001
Age, yr		
70–74 vs. 66–69	1.17	0.01
75–79 vs. 66–69	1.3	<0.0001
80–84 vs. 66–69	1.39	<0.0001
85+ vs. 66–69	1.4	0.0002
T-stage		
T2 vs. T1	1.49	<0.0001
T3 vs. T1	2.1	<0.0001
Charlson Comorbidity Index		
1 vs. 0	1.08	0.2
2 vs. 0	1.2	0.005
3 vs. 0	1.25	0.002
4+ vs. 0	1.36	<0.0001

TABLE 7. Multivariable Model of Survival for 2157 Patients Treated with Either Surgery or Radiation for Stage IIIA (N2) in the Survival, Epidemiology, and End Results–Medicare Database from 2004 to 2007

Predictor	Hazard Ratio	*p*
Surgery (no surgery vs. surgery)	1.79	<0.0001
Radiation (no vs. yes)	0.85	0.13
Chemotherapy (no vs. yes)	1.43	<0.0001
Age, yr		
70–74 vs. 66–69	1.15	0.06
75–79 vs. 66–69	1.2	0.01
80–84 vs. 66–69	1.32	0.001
85+ vs. 66–69	1.26	0.04
T-stage		
T2 vs. T1	1.44	<0.0001
T3 vs. T1	1.9	<0.0001
Charlson Comorbidity Index		
1 vs. 0	1.09	0.26
2 vs. 0	1.18	0.03
3 vs. 0	1.2	0.04
4+ vs. 0	1.37	<0.0001

study.[11] However, exploratory analysis in this randomized phase III study did suggest that surgical resection might convey some survival benefit over chemotherapy and radiation therapy alone in patients whose surgical resection consisted of lobectomy.[11] In addition, subgroup analysis of the patients that underwent surgical resection demonstrated that patients who had pathological evidence of clearance of disease from their mediastinal lymph nodes after chemotherapy and radiation therapy had improved survival over patients who had persistent nodal disease despite chemotherapy and radiation therapy.

Given the lack of clear evidence to guide treatment, and that many studies have demonstrated potential benefit for several strategies, the results of this study demonstrating variability in the treatment of stage IIIA (N2) patients in a large national cohort are not necessarily unexpected. A significant number of patients (18%) did not receive any treatment at all, with patient age apparently being the most important factor in the treatment decision-making process in this setting. The use of surgery in only 24% of patients is not surprising, given the available evidence on the benefits of surgical resection. However, this study does show that certain variables are associated with the use of surgery. The most powerful predictors for the use of surgery are patient and tumor specific, such as age and T-stage, and are likely at least in part predictors of patients who may not be medically or technically resectable. These findings suggest that the treatment used for many patients is appropriately chosen based on individual patient factors. However, nonmedical patient characteristics, notably related to the income level of the census tract where patients live, were also significant predictors for the use of surgery, although the association of this factor with surgery was much weaker than that of the important identified clinical factors. Interestingly, black race was important in predicting the use of surgery in univariate analysis but not multivariate analysis when other factors were considered.

These results are consistent with other studies that have demonstrated disparities in the incidence, treatment, and survival of lung cancer. Blacks have a higher incidence of lung cancer, undergo surgery less often, and have worse survival for resectable lung cancers compared with white patients.[13–19] However, stage-specific survival does not differ between blacks and whites if treatment strategy, comorbidities, patient functional status, and other potential confounding factors are considered.[46,47] Socioeconomic status, educational status, and geography also contribute importantly to both the incidence of and the outcomes associated with lung cancer.[13,20–26] Blacks and patients with low socioeconomic status are most likely to present with advanced disease at the time of diagnosis of lung cancer and are less likely to receive what would be considered the evidence-based standard therapy for all stages of lung cancer.[14,48,49] Therefore, the observed disparities can most likely be explained by differences in the way lung cancer patients present, are diagnosed, and ultimately treated. Considering that the results of the current study show that the treatment regimen used for stage IIIA (N2) NSCLC is dependent on the socioeconomic status of the census tract where patients live, part of the treatment variability could be because of differences in the ways patients in lower socioeconomic regions have access to, are offered, or choose therapy.

Although this study suggested a survival benefit to the use of surgery for stage IIIA (N2) NSCLC, the results cannot be construed as being definitive evidence of the advantage of surgery over other treatment regimens that do not include surgery. Even when patients are limited to the subset of stage IIIA because of N2 involvement, there is still potentially significant heterogeneity in the extent of nodal involvement. Mediastinal nodal involvement can vary from microscopic disease recognized on pathologic examination after resection or unexpectedly at the time of resection, to nonbulky single station or multistation mediastinal lymph node metastases recognized and proven before any treatment, or bulky multistation N2 disease.[3] These pathologic details are not available in the SEER-Medicare database, and the improved outcomes seen with surgery could possibly be due to the preferential use of surgery with more limited nodal involvement. In addition, SEER-Medicare does not contain information on other important clinical variables, including a patient's overall functional status, pulmonary function data, and smoking status. Surgery may have been preferentially selected for patients with better functional status, better pulmonary function, and less significant current and past smoking use, which are all factors that can impact both treatment selection and outcomes such as survival.

This study does have other limitations, including its retrospective nature and reliance on an administrative database in which some data may be missing. The data only include patients aged 65 years or older, and these results may not be generalizable to younger patients with lung cancer. Also, including a comorbidity index is helpful in limiting the impact of selection bias based on comorbid conditions, but the comorbidity index does not guarantee that the acuity and severity of comorbid conditions are well balanced between the different groups evaluated. Also, all patients in this study had insurance coverage through Medicare, and therefore the results are not necessarily generalizable to a population of patients that include uninsured or underinsured patients. Finally, given that SEER did not record details on N status until 2004 and includes follow-up only until 2007, the overall follow-up period for the patients in the study is relatively short. However, use of the population-based SEER-Medicare database has the significant advantage of allowing evaluation of a large number of patients with an uncommon disease stage. The expense and complexity of enrolling patients and performing a study that involves both a relatively uncommon disease stage and potentially a major surgical procedure make it unlikely that a prospective study could ever accumulate anywhere near the number of patients that are available for analysis in this database.

In conclusion, stage IIIA (N2) NSCLC represents a heterogeneous group of patients for which the optimal treatment is not well established. Treatment of elderly patients with this stage of disease is highly variable in the United States and varies with age, T-stage, and socioeconomic factors of the area where patients live. Before initiating treatment, multidisciplinary evaluation of all patients with this stage of lung cancer with appropriate consideration of all potential treatment options may limit variability in care such that only patient and tumor-specific factors drive the choice of therapy, which may optimize outcomes while avoiding treatment-related morbidity.

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