Pulmonologist Involvement, Stage-Specific Treatment, and Survival in Adults with Non–Small Cell Lung Cancer and Chronic Obstructive Pulmonary Disease

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Abstract

Rationale: Up to 80% of patients with lung cancer have comorbid chronic obstructive pulmonary disease (COPD). Many of them are poor candidates for stage-specific lung cancer treatment due to diminished lung function and poor functional status, and many forego treatment. The negative effect of COPD may be moderated by pulmonologist-guided management.

Objectives: This study examined the association between pulmonologist management and the probability of receiving the recommended stage-specific treatment modality and overall survival among patients with non-small cell lung cancer (NSCLC) with preexisting COPD.

Methods: Early- and advanced-stage NSCLC cases diagnosed between 2002 and 2005 with a prior COPD diagnosis (3–24 months before NSCLC diagnosis) were identified in Surveillance, Epidemiology, and End Results tumor registry data linked to Medicare claims. Study outcomes included receipt of recommended stage-specific treatment (surgical resection for early-stage NSCLC and chemotherapy for advanced-stage NSCLC [advNSCLC]) and overall survival. Pulmonologist management was considered present if one or more Evaluation and Management visit claims with pulmonologist specialty were observed within 6 months after NSCLC diagnosis. Stage-specific multivariate logistic regression tested association between pulmonologist management and treatment received. Cox proportional hazard models examined the independent association between pulmonologist care and mortality. Two-stage residual inclusion instrumental variable (2SRI-IV) analyses tested and adjusted for potential confounding based on unobserved factors or measurement error.

Measurements and Main Results: The cohorts included 5,488 patients with early-stage NSCLC and 6,426 patients with advNSCLC disease with preexisting COPD. Pulmonologist management was recorded for 54.9% of patients with early stage NSCLC and 35.7% of patients with advNSCLC. Of those patients with pulmonologist involvement, 58.5% of patients with early NSCLC received surgical resection, and 43.6% of patients with advNSCLC received chemotherapy. Pulmonologist management post NSCLC diagnosis was associated with increased surgical resection rates (odds ratio, 1.26; 95% confidence interval, 1.11–1.45) for early NSCLC and increased chemotherapy rates (odds ratio, 1.88; 95% confidence interval, 1.67–2.10) for advNSCLC. Pulmonologist management was also associated with reduced mortality risk for patients with early-stage NSCLC but not AdvNSCLC.

Conclusions: Pulmonologist management had a positive association with rates of stage-specific treatment in both groups and overall survival in early-stage NSCLC. These results provide preliminary support for the recently published guidelines emphasizing the role of pulmonologists in lung cancer management.

Keywords: non–small cell lung carcinoma; pulmonology medicine; chronic obstructive pulmonary disease; survival

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Chronic obstructive pulmonary disease (COPD) and lung cancer cause significant morbidity and mortality. Between 50 and 80% of patients with lung cancer have COPD, and recent estimates of lung cancer risk in COPD have been as high as 167 per 10,000 person-years, substantially higher than the overall risk of 6.1 per 10,000 person-years (1, 2). Non–small cell lung cancer (NSCLC) is the most common form of lung cancer, accounting for 85% of all cases, and more than two-thirds of NSCLC cases are diagnosed in persons aged 65 years or older (3). Recommended treatment modalities for NSCLC include surgical resection, systemic agents such as chemotherapy, and radiation, with regimens that vary by stage, histology, tumor location, and patient performance status (PS). Surgical resection has been the standard of care for early-stage NSCLC, with estimated 5-year survival rates of 60 to 80% for resected stage I and 30 to 50% for resected stage II NSCLC, respectively (4).

However, there is an increasing proportion of patients with newly diagnosed disease who do not receive surgical treatment (5, 6). Poor lung function and overall poor PS may delay or prevent many patients with COPD from having potentially curative resection (7). Without therapy, survival is relatively brief, with 2-year survival for untreated clinical stage I or II (early stage) NSCLC of approximately 20% (8, 9). Nonsurgical therapies such as stereotactic body radiotherapy and radiofrequency ablation are therapeutic options in patients with early-stage lung cancer who are medically unfit for resection. They appear to extend survival compared with historical controls of untreated early-stage lung cancer, but data on the benefit compared with surgical resection are limited (10–16). Hence, it is important to increase the proportion of patients with early-stage NSCLC disease who are medically eligible for surgery. In medically fit patients with advanced NSCLC (advNSCLC), especially those who do not harbor actionable target mutations, systemic chemotherapy remains the standard of care. Compared with best supportive care, chemotherapy (platinum-doublets) prolongs survival without substantially impairing quality of life (17). Patients with poor overall PS, including those with poor lung function associated with COPD, generally receive single-agent therapy or may forgo treatment entirely, with rapid progression to death (18).

Population-based studies using data from the 1990s revealed that between 22 and 31% of elderly patients with advNSCLC received chemotherapy during the course of their disease. More recent estimates reveal that an increasing but still small proportion receive therapy (19). Improving fitness for patients who desire therapy and who may benefit from therapy is an important goal.

Proper medical management of COPD before and after lung cancer diagnosis may ameliorate some of the negative effects of COPD on lung cancer treatment and outcomes. Optimizing medical management and/or pulmonary rehabilitation may improve lung function sufficiently for the patient to undergo surgery and even to withstand side effects of aggressive chemotherapy regimens. Researchers have begun to examine ways in which medical management of patients with lung cancer with COPD, such as using pulmonary rehabilitation and implementing nutritional support before lung cancer surgery, may affect outcomes (20, 21). A recent joint statement by the American Thoracic Society and the European Respiratory Society (ATS/ERS) noted that pulmonologists are key members of multidisciplinary teams responsible for care of patients with lung cancer (22). Pulmonologists may be involved from initial diagnosis and staging through treatment, restaging, support, and often palliative care. Diagnosis and management of lung cancer require the competent use of endoscopic procedures to acquire specimens that can stage and guide targeted therapy while minimizing respiratory side effects and complications (22). Most studies focus on this role but not on the role of the pulmonologist beyond this initial phase.

In this study, we use a retrospective, observational design applied to large-scale registry, enrollment, and claims data for Medicare beneficiaries, to examine whether pulmonologist involvement in COPD management increases the receipt of lung cancer surgery or chemotherapy in early-stage NSCLC and advNSCLC, respectively, and improves survival. Some of the results of this study have been previously reported in conference abstracts (23, 24).

Methods

Data Source and Cohort Selection

Patients were identified from the National Cancer Institute's Surveillance, Epidemiology, and End Results database (SEER), which collects data from state and regional registries covering 28% of the U.S. population. For Medicare beneficiaries, SEER data are matched to Medicare enrollment and claims files. This aggregated dataset contains information on cancer stage, histology, diagnosis date, initial treatment, and demographics; claims can be used to describe service level information for inpatient and outpatient care (25).

The sample included incident NSCLC cases, aged 66 years or older, diagnosed from 2002 to 2005, with a corresponding COPD diagnosis. We selected only patients with a COPD diagnosis 3 to 24 months before the lung cancer diagnosis to avoid concurrent diagnoses. The COPD diagnosis was established by presence of one inpatient claim with a relevant International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code (490, 491, 491.0–2, 491.20–22, 491.8–9, 492, and 496) in any position. These codes were selected based on codes for COPD used by the Centers for Medicare and Medicaid Services Chronic Condition Warehouse (26). In the absence of an inpatient claim, patients were qualified by the occurrence of two or more outpatient claims with ICD-9-CM codes for COPD within a 12-month period, but with a gap of at least 29 days between two claims. The date of the first COPD qualifying claim was the index date, which was compared with the NSCLC diagnosis date. Patients were excluded if they had more than one NSCLC primary, had incomplete information concerning dates of NSCLC diagnosis or death, survived fewer than 30 days post NSCLC diagnosis, or had any period without Medicare Parts A and B or with Medicare Advantage enrollment during the 24 months before or any time after diagnosis. The 30-day mortality exclusion was adopted because these patients were likely too sick to receive recommended therapy and unable to experience measurable benefit from pulmonologist intervention. The latter exclusion was necessary to ensure completeness of Medicare claims records.

Table 1. Characteristics, pulmonologist management, and lung resection among Medicare beneficiaries with chronic obstructive pulmonary disease diagnosed with early-stage non-small cell lung cancer

	Overall (*N* = 5,488)		No Pulmonologist Management (*N* = 2,476)		Pulmonologist Management (*N* = 3,012)		*P* Value
	N	%	N	%	N	%	
Prior period of COPD diagnosis, mo							0.109
3–6	506	9.2	243	9.8	263	8.7	
7–12	734	13.4	330	13.3	404	13.4	
13–18	976	17.8	465	18.8	511	17.0	
19–24	3,272	59.6	1,438	58.1	1,834	60.9	
Tumor characteristics							
Histology							0.208
Adenocarcinoma	2,113	38.5	927	37.4	1,186	39.4	
Squamous cell	2,020	36.8	913	36.9	1,107	36.8	
Other, NOS	1,355	24.7	636	25.7	719	23.9	
Tumor behavior/grade							0.011
Well/moderately differentiated	1,835	33.4	806	32.6	1,029	34.2	
Poorly/undifferentiated	2,006	36.6	876	35.4	1,130	37.5	
Grade unknown	1,647	30.0	794	32.1	853	28.3	
Basic demographics and health status							
Age at diagnosis, yr							<0.001
66–69	806	14.7	372	15.0	434	14.4	
70–74	1,584	28.9	694	28.0	890	29.5	
75–79	1,659	30.2	698	28.2	961	31.9	
80–84	1,039	18.9	491	19.8	548	18.2	
85+	400	7.3	221	8.9	179	5.9	
Sex							0.819
Female	2,576	46.9	1,158	46.8	1,418	47.1	
Male	2,912	53.1	1,318	53.2	1,594	52.9	
Race							0.003
White	4,888	89.1	2,173	87.8	2,715	90.1	
Black	363	6.6	195	7.9	168	5.6	
Other/unknown	237	4.3	108	4.4	129	4.3	
Marital status							<0.001
Single (never married)	379	6.9	210	8.5	169	5.6	
Currently married	2,868	52.3	1,182	47.7	1,686	56.0	
Previously married (includes separated, divorced, and widowed)	2,241	40.8	1,084	43.8	1,157	38.4	
Residence							<0.001
Metro (includes big metro and metro)	4,477	81.6	1,922	77.6	2,555	84.8	
Urban (includes urban and less urban)	875	15.9	484	19.5	391	13.0	
Rural	136	2.5	70	2.8	66	2.2	
Median household income, per census tract	$42,430		$41,272.5		$44,016		<0.001
>25% Persons with ⩾4 yr college, per census tract	1,952	35.6	799	32.3	1,153	38.3	<0.001
Prior year Medicaid/MSP	1,034	18.8	555	22.4	479	15.9	<0.001
Charlson Comorbidity Index							<0.001
0	407	7.4	227	9.2	180	6.0	
1	2,459	44.8	1,033	41.7	1,426	47.3	
2	1,379	25.1	605	24.4	774	25.7	
⩾3	1,243	22.7	611	24.7	632	21.0	
Poor disability status	574	10.5	347	16.7	227	7.5	<0.001
Year of diagnosis							0.041
2002	1,272	23.2	616	24.9	656	21.8	
2003	1,328	24.2	599	24.2	729	24.2	
2004	1,341	24.4	591	23.9	750	24.9	
2005	1,547	28.2	670	27.1	877	29.1	
Pulmonologist visit							
Within 6 mo post NSCLC diagnosis	3,012	54.9					
Before NSCLC diagnosis	2,588	47.2					
Surgical resection	3,005	54.8	1,244	50.2	1,761	58.5	<0.001

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; MSP = Medicare Savings Program; NOS = not otherwise specified; NSCLC = non-small cell lung cancer; SEER = Surveillance, Epidemiology, and End Results.
Data from SEER–Medicare cases of NSCLC, 2002–2005 (37).

The cohort was stratified by stage at NSCLC diagnosis using the American Joint Commission on Cancer, version 6. For purposes of analysis, we grouped stages I and II (early-stage NSCLC) and assigned patients with stage IV and stage IIIb with pleural effusion to the advNSCLC group, consistent with version 7. We did not study stage IIIa and IIIb without effusion, as there is substantial variability in recommended treatments depending on the tumor size and position, as well as variability in how multimodality therapy is administered.

Measurement of Outcomes

We examined receipt of stage-specific treatment modality and all-cause mortality. For early-stage NSCLC, we measured receipt of surgical lung resection in the period 3 months before through 5 months after the lung cancer diagnosis month, as indicated in the SEER registry data (codes 10–70, 90) and/or the presence of claims with relevant ICD-9 procedure codes (32.29–32.99,18) or Common Procedure Terminology codes (32440–32525, 32657, or 32663). For advNSCLC, we identified chemotherapy initiated within 90 days of diagnosis, captured in claims with Healthcare Common Procedures Coding System or National Drug Code numbers for specific chemotherapy agents. Patients with advNSCLC but who were reported to have a surgical lung resection were excluded. Survival time was measured from the first day of the month during which the cancer was diagnosed until the date of death or censoring at December 31, 2007, the end of the data available to the study team.

Measurement of Pulmonologist Management

Pulmonologist involvement in patient care was identified if there was at least one physician claim for an Evaluation and Management visit, with pulmonologist reported as the physician specialty (Health Care Financing Administration specialty code 30) any time during the 6 months post NSCLC diagnosis. We included only claims for care delivered in a physician office, hospital outpatient (excluding emergency department), or nursing home setting. Visits with diagnostic bronchoscopy procedures were excluded. For purposes of sensitivity analysis we measured pulmonologist visits during the 24 months before NSCLC diagnosis.

Patient Characteristics

Multivariate analyses adjusted for tumor characteristics (histology and grade), sociodemographics, baseline health status, and year of diagnosis. Sociodemographic characteristics included age, race, sex, marital status, and concurrent enrollment in Medicaid in the year before diagnosis. We also included census tract level measures of urbanicity of residence, median household income, and an indicator that more than 25% of adults reported at least 4 years of college. Health status was measured using the Charlson Comorbidity Index, a summary score derived from 19 conditions measured 12 months before cancer diagnosis and weighted to reflect expected contribution to noncancer mortality (27, 28). We also included a measure of predicted poor disability status (DS), a claims-based proxy for poor performance status (29). We attempted to measure current or history of tobacco use and receipt of smoking cessation–related services, but reported rates were very low and lacked face validity, so we did not include them in our analysis.

Statistical Methods

Bivariate analyses described treatment receipt by NSCLC stage and pulmonologist management. We estimated multivariable logistic regression models to examine the association between pulmonologist management and receipt of the designated stage-specific treatment modalities, stratified by NSCLC stage. Kaplan-Meier statistics and Cox proportional hazard models examined the association between pulmonologist management and overall survival, with stratification by NSCLC stage. Both types of models controlled for the sociodemographic characteristics, health status, time since COPD diagnosis, and tumor histology and grade.

Estimates of pulmonologist involvement in lung cancer care may be subject to indication bias. Patients referred to a pulmonologist may have worse lung function, and this may bias the effect of the pulmonologist downward. Alternatively, patients may be referred to a pulmonologist if they are healthier and there is an expectation of treatment, which would overstate the effect of the pulmonologist. In addition, our pulmonologist visit measure (at least one visit within 6 mo of diagnosis) was subject to potential reverse causality, as patients who lived longer would have a longer period during which a pulmonologist visit could be observed. We used two-stage residual inclusion (2SRI) instrumental variable analysis to test for possible bias in our estimates. The instrument we used was a county-level measure of pulmonologist visit rates for all patients with lung cancer, linked back to each observation in the cohort, while excluding information from that observation from both the numerator and denominator of the calculated rate. This instrument was a highly significant first-stage predictor of the individual patient visiting a pulmonologist. The second-stage treatment and survival models included both the indicator for pulmonologist visit and a residual calculated for each patient based on estimates from the first-stage model, with bootstrapped standard errors. Inclusion of this residual controls for the effects of unobservable factors on the outcomes. The significance and direction of the estimated coefficient on the residual is a test for confounding; when there is no evidence of confounding, we revert to the base (non-2SRI) model because the coefficients are estimated more precisely. Additional detail concerning the 2SRI method is provided in the online supplement.

All statistical analyses were conducted with STATA/MP version 12. This research was approved by the University of Maryland Institutional Review Board.

Results

The study cohorts consisted of 5,488 patients with early-stage NSCLC (Table 1) and 6,426 patients with advNSCLC (Table 2) with COPD. Both cohorts were overwhelmingly white (89.1% early-stage NSCLC, 86.6% advNSCLC), aged 75 years or older (56.4% early-stage NSCLC, 60.2% advNSCLC), and 60% of both groups had been diagnosed with COPD more than 18 months before their lung cancer diagnosis. More than half (54.9%) of patients with early-stage NSCLC had pulmonologist involvement in their care after diagnosis, but the practice was less common (35.7%) among those with advNSCLC. Patients with NSCLC with pulmonologist management were generally healthier (fewer comorbidities and less likely to have poor DS) and had higher socioeconomic status than those without pulmonologist

Table 2. Characteristics, pulmonologist management, and receipt of chemotherapy for Medicare beneficiaries with chronic obstructive pulmonary disease diagnosed with advanced non-small cell lung cancer

	Overall (*N* = 6,246)		No Pulmonologist Management (*N* = 4,129)		Pulmonologist Management (*N* = 2,297)		*P* Value
	N	%	N	%	N	%	
Prior period of COPD diagnosis, mo							0.040
3–6	576	9.0	340	8.2	236	10.3	
7–12	917	14.3	597	14.5	320	13.9	
13–18	1,082	16.8	712	17.2	370	16.1	
19–24	3,851	59.9	2,480	60.1	1,371	59.7	
Tumor characteristics							
Histology							0.144
Adenocarcinoma	2,118	33.0	1,358	32.9	760	33.1	
Squamous cell	1,432	22.3	892	21.6	540	23.5	
Other, NOS	2,876	44.8	1,879	45.5	997	43.4	
Tumor behavior/grade							<0.001
Well/moderately differentiated	699	10.9	430	10.4	269	11.7	
Poorly/undifferentiated	1,682	26.2	1,011	24.5	671	29.2	
Grade unknown	4,045	63.0	2,688	65.1	1,357	59.1	
Basic demographics and health status							
Age at diagnosis, yr							0.018
66–69	874	13.6	561	13.6	313	13.6	
70–74	1,688	26.3	1,077	26.1	611	26.6	
75–79	1,844	28.7	1,153	27.9	691	30.1	
80–84	1,321	20.6	850	20.6	471	20.5	
85+	699	10.9	488	11.8	211	9.2	
Sex							0.004
Female	2,872	44.7	1,900	46.0	972	42.3	
Male	3,554	55.3	2,229	54.0	1,325	57.7	
Race							<0.001
White	5,562	86.6	3,521	85.3	2,041	88.9	
Black	537	8.4	382	9.3	155	6.7	
Other/unknown	327	5.1	226	5.5	101	4.4	
Marital status							<0.001
Single (never married)	524	8.2	377	9.1	147	6.4	
Currently married	3,088	48.1	1,876	45.4	1,212	52.8	
Previously married (includes separated, divorced, and widowed)	2,814	43.8	1,876	45.4	938	40.8	
Residence							<0.001
Metro (includes big metro and metro)	5,278	82.1	3,330	80.6	1,948	84.8	
Urban (includes urban and less urban)	1,000	15.6	697	16.9	303	13.2	
Rural	148	2.3	102	2.5	46	2.0	
Median household income, per census tract	$41,751		$41,054.5		$44,279		<0.001
>25% Persons with ⩾4 yr of college, per census tract	2,138	33.3	1,303	31.6	835	36.4	<0.001
Prior year Medicaid/MSP	1,436	22.4	1,032	25.0	404	17.6	<0.001
Charlson Comorbidity Index							<0.001
0	547	8.5	390	9.4	157	6.8	
1	2,722	42.4	1,649	39.9	1,073	46.7	
2	1,570	24.4	1,006	24.4	564	24.6	
⩾3	1,587	24.7	1,084	26.3	503	21.9	
Poor disability status	1,008	15.7	777	18.8	231	10.1	<0.001
Year of diagnosis							0.368
2002	1,473	22.9	972	23.5	501	21.8	
2003	1,576	24.5	1,017	24.6	559	24.3	
2004	1,673	26.0	1,058	25.6	615	26.8	
2005	1,704	26.5	1,082	26.2	622	27.1	
Pulmonologist visit							
Within 6 mo post NSCLC diagnosis	2,297	35.7					
Before NSCLC diagnosis	2,177	33.9					
Chemotherapy	2,121	33.0	1,119	27.1	1,002	43.6	<0.001

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; MSP = Medicare Savings Program; NOS = not otherwise specified; NSCLC = non-small cell lung cancer; SEER = Surveillance, Epidemiology, and End Results.
Data from SEER–Medicare cases 2002–2005, claims from 2000–2007 (37).

involvement. More than half (54.8%) of the patients with early-stage NSCLC also received a surgical resection. Surgery rates were lower (50.2%) for those without pulmonologist visits compared with 58.5% among those with pulmonologist involvement ($P < 0.001$). One-third of patients with advNSCLC received chemotherapy, with rates ranging from 27.1% among those with no pulmonologist visits to 43.6% among those with pulmonologist visits after lung cancer diagnosis ($P < 0.001$).

Multivariable analyses confirmed that pulmonologist involvement post-NSCLC diagnosis was associated with an increase in surgical resection in early-stage NSCLC (odds ratio [OR], 1.26; 95% confidence interval [CI], 1.11–1.45; $P < 0.001$) and increased chemotherapy rates in advNSCLC (OR, 1.88; 95% CI, 1.67–2.10; $P < 0.001$) (Table 3; full models are reported in Tables E2–E5 in the online supplement). The estimated residuals in the 2SRI models were not significant (OR, 0.91; 95% CI, 0.73–1.14 and OR, 1.14; 95% CI, 0.85–1.52 for early NSCLC and advNSCLC, respectively). Other factors associated with reduced likelihood of surgery in patients with early-stage NSCLC were longer duration of COPD, nonadenocarcinoma histology, poorly differentiated or undifferentiated, or grade unknown, age 80 years or older, black race, poor DS, and prior year Medicaid enrollment. Factors associated with lower likelihood of receiving chemotherapy for patients with advNSCLC at diagnosis were nonadenocarcinoma histology, unknown grade, increasing age, greater comorbidity burden, and poor DS. Being currently married was associated with a higher probability of receiving treatment, as was residence in a census tract with higher incomes and later diagnosis years (2003 and 2005 relative to 2002).

Pulmonologist involvement post NSCLC diagnosis was also associated with reduced mortality risk. Kaplan-Meier curves present unadjusted comparisons of survival by pulmonologist management, stratified by NSCLC stage (Figures 1A and 1B). Adjusted results indicate that among early-stage NSCLC, pulmonologist management was associated with a 20% reduction in mortality risk (hazard ratio [HR], 0.80; 95% CI, 0.75–0.85; $P < 0.001$) (Table 3). This effect remains after controlling for residual confounding in the 2SRI model. Findings were qualitatively similar for advNSCLC, where we observed a lower risk of death with pulmonologist management in our base model (HR, 0.66; 95% CI, 0.63–0.70; $P < 0.001$) (Table 3). However, the significance of the residual in the 2SRI model (HR, 0.87; 95% CI, 0.76–0.99; $P < 0.05$) indicates bias in the base model estimates. Furthermore, the 2SRI estimates suggest that the effect of pulmonologist visits is fairly small (HR, 0.89; 95% CI, 0.68–1.17; $P = 0.41$) and did not achieve significance. Estimates associated with other characteristics are presented in the full models in the online supplement.

In sensitivity analyses (Table 4) where we substituted a measure for pulmonologist visit pre-NSCLC, we found effects similar to the main results for treatment and survival in early-stage NSCLC. The magnitude of treatment effect in advNSCLC was smaller than the main effect (OR, 1.24; 95% CI, 1.10–1.39; $P < 0.001$), and the survival effect was similar in magnitude to the 2SRI estimate but highly significant. When we limited to a subgroup with minimum 6 months' survival, we observed small but significant benefits associated with pulmonologist involvement in care.

Table 3. Estimated effects of pulmonologist visit on non-small cell lung cancer treatment and outcomes

	OR or HR Associated with Pulmonologist Visit	95% CI
Treatment, early-stage NSCLC (*N = 5,488*)		
Single-stage logistic regression	1.26	1.11–1.45*
2SRI estimate	1.52	0.96–2.40
Residual	0.91	0.73–1.14
Survival, early-stage NSCLC		
Single-stage Cox PH regression	0.80	0.75–0.85*
2SRI estimate	0.79	0.63–0.99†
Residual	1.00	0.90–1.12
Treatment, advanced-stage NSCLC (*N = 6,426*)		
Single stage logistic regression	1.88	1.67–2.10*
2SRI estimate	1.44	0.78–2.66
Residual	1.14	0.85–1.52
Survival, advanced-stage NSCLC		
Single-stage Cox PH regression	0.66	0.63–0.70*
2SRI estimate	0.89	0.68–1.17
Residual	0.87	0.76–0.99†

Definition of abbreviations: 2SRI = two-stage residual inclusion; CI = confidence interval; HR = hazard ratio; NSCLC = non-small cell lung cancer; OR = odds ratio; PH = proportional hazard; SEER = Surveillance, Epidemiology, and End Results.
Adjusted for duration of chronic obstructive pulmonary disease diagnosis, tumor characteristics, basic demographics, and health status. Data from SEER–Medicare NSCLC cases diagnosed between 2002–2005 (37).
*Estimated OR or HR significant at $P < 0.001$.
†Estimated OR or HR significant at $P < 0.05$.

Discussion

Comorbid COPD is associated with lower NSCLC treatment rates through its effect on diminished lung function. Although new therapeutic options have been developed for NSCLC, and survival has improved over the past 2 decades (30), additional improvements may be possible if a greater proportion of patients are eligible for and can tolerate effective therapies. The results of this study demonstrate a positive association between pulmonologist management and improved care for patients with lung cancer with comorbid COPD. We examined early-stage NSCLC, where surgical resection is recommended for fit patients, and advNSCLC, where chemotherapy delays progression, palliates symptoms, and improves survival. In this analysis, pulmonologist involvement after a lung cancer diagnosis was associated with increased treatment rates in both stages

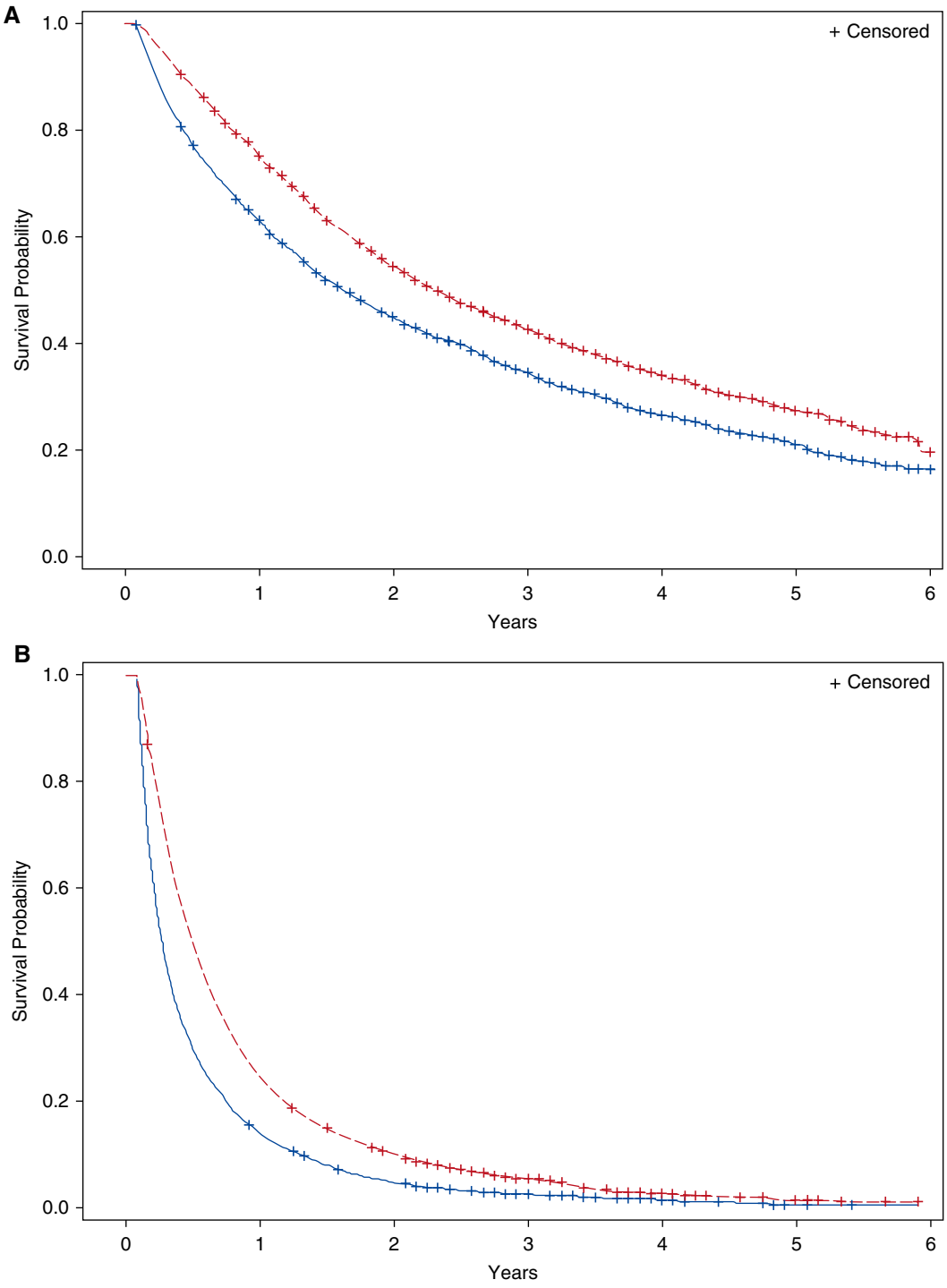

Figure 1. (*A*) Kaplan-Meier curve comparing overall survival among patients with early-stage non-small cell lung cancer (NSCLC) with comorbid chronic obstructive pulmonary disease (COPD). *Red line* = with pulmonologist involvement; *blue line* = without pulmonologist involvement. Overall survival higher in patients with pulmonologist involvement ($P < 0.001$). (*B*) Kaplan-Meier curve for overall survival among patients with advanced-stage NSCLC with comorbid COPD. *Red line* = with pulmonologist involvement; *blue line* = without pulmonologist involvement. Overall survival higher in patients with pulmonologist involvement ($P < 0.001$).

and increased survival in patients with early-stage disease. Our study provides empirical support for the recent joint statement by the ATS/ERS concerning the role of pulmonologists in diagnosis and management of lung cancer (22).

Our study scope did not include examination of the ways in which pulmonologist management improves

Table 4. Sensitivity analyses using alternative measures of pulmonologist management

Pulmonologist Visit Pre-NSCLC Diagnosis	OR or HR	95% CI	*P* Value
Treatment			
Early-stage NSCLC (*N = 5,488*)	1.25	1.09–1.43	*
Advanced-stage NSCLC (*N = 6,426*)	1.24	1.10–1.39	*
Survival			
Early-stage NSCLC (*N = 5,488*)	0.86	0.80–0.92	*
Advanced stage NSCLC (*N = 6,426*)	0.85	0.81–0.90	*
Limit to 6-mo survivors	HR		
Survival			
Early-stage NSCLC (*N = 4,594*)	0.92	0.85–0.99	†
Advanced-stage NSCLC (*N = 2,409*)	0.91	0.84–1.00	†

Definition of abbreviations: CI = confidence interval; HR = hazard ratio; NSCLC = non-small cell lung cancer; OR = odds ratio; SEER = Surveillance, Epidemiology, and End Results.
Adjusted for duration of chronic obstructive pulmonary disease diagnosis, tumor characteristics, basic demographics, and health status. Data from SEER-Medicare NSCLC cases diagnosed between 2002–2005 (37).
*Estimated OR or HR significant at $P < 0.001$.
†Estimated OR or HR significant at $P < 0.05$.

treatment rates, but we hypothesize a variety of mechanisms. For patients with early-stage NSCLC, pulmonologists may play an important role in identification and referral of patients likely to benefit from nonsurgical therapeutic options, assessing preoperative risks and optimizing care before surgical resection, including referral to pulmonary rehabilitation shown to decrease postoperative complication rates (21). In the postsurgical period, pulmonologists may further improve symptom management and decrease respiratory complications, thereby preventing functional status decline. For patients with advanced-stage disease, pulmonologists may improve symptom management and facilitate earlier engagement with palliative care, associated with improved survival (32).

Although we can describe the potential mechanisms for increased treatment and improved outcomes, there is not yet strong evidence for specific differences in COPD or lung cancer treatment and outcomes associated with management by pulmonologists compared with other providers. Several studies compared COPD management by pulmonologists and primary care providers, finding that pulmonologists are more likely to adhere to medication management guidelines, although neither group referred many patients for pulmonary rehabilitation (33–35). Only one prior study addressed the broader role that a pulmonologist may play in improving management of patients with lung cancer with comorbid COPD. Using the Scottish Cancer registry, Ferguson and colleagues found that involvement of a respiratory physician in initial patient management increased the probability that patients with lung cancer received active treatment with surgery, radiotherapy, or chemotherapy (31). In addition, survival rates were higher in patients who saw a pulmonologist, with estimates of 24.4 versus 11.1% for 1-year and 8.1 versus 3.7% for 3-year survival. The results of our study confirm the findings from the Ferguson study in a large U.S. Medicare-enrolled population.

Study Limitations

This study is subject to a variety of limitations associated with the use of administrative claims data and the observational study design. Although the cohort of patients with NSCLC and related data on stage and histology were captured from cancer registry data, identification of persons with comorbid COPD was based on ICD-9-CM diagnostic codes, which are subject to coding error and do not provide information on COPD severity. Furthermore, clinical parameters to assess severity, such as pulmonary function tests, were not available. Pulmonologist involvement was measured based on the presence of claims for Evaluation and Management services. Although we were able to quantify the number of such visits, our main measure did not capture temporal relationships between visits and NSCLC therapy. In our study we used the instrumental variable analysis to test for indication bias. Despite having strong instruments needed to use this method, we acknowledge that failure to find evidence of bias does not prove lack of residual bias in our estimates. High area-level rates of pulmonologist management may be associated with generally good access to care and, in particular, with market penetration by academic medical centers, which may be more likely to include pulmonologists in multidisciplinary treatment teams. These factors may also be associated with increased lung cancer treatment and improved outcomes, which would undermine the validity of our instrument. Unfortunately, we were not able to explicitly test for these patterns in the available data.

Despite our concerns, we note that our sensitivity analyses using pulmonologist management pre-NSCLC diagnosis showed similar effects on treatment and survival. Pulmonologist involvement pre-NSCLC diagnosis may have improved COPD management generally; hence, our analyses would pick up that effect. The prediagnosis measure does not capture potential benefits associated with pulmonologist involvement in guiding therapy choices or in managing side effects of therapy. Finally, the observation period for the study did not permit us to study the effects of newer targeted therapies, referral to pulmonary rehabilitation, or the role of newer surgical and nonsurgical methods. We expect that the potential role of the pulmonologist in helping to select treatment options has increased, suggesting that our findings from earlier data represent a lower bound estimate. Prescription medications were not covered by Medicare during this period; thus, we were not able to assess the effect of pulmonologist intervention on drug regimens used to manage COPD and related symptoms or their effect on cancer treatment or survival. Finally, our results are based on analysis of adults older than age 65 years; treatment patterns and the role of pulmonologists may vary for younger adults with cancer.

Despite these limitations, the results from this study indicate a positive association between the pulmonologist management of the patient with lung cancer with COPD across multiple dimensions,

with a significant positive benefit with respect to overall survival in early-stage cases. This provides empirical support to the recent ATS/ERS guidelines. Before recommending specific changes in practice, we believe that this issue warrants much further study. To better assess the pulmonologist role, an updated observational study with more detailed analysis of COPD management and alternative NSCLC treatments used would be informative. Medicare has covered prescription medications since 2006, and the associated claims are available to researchers as part of SEER–Medicare. Alternatively, interventional trials that add routine pulmonologist assessment and management to lung cancer therapeutic teams can provide valuable evidence for specific impacts. The Patient Protection and Affordable Care Act is expected to result in changes in oncology practice and reimbursements, which may be directly tied to measures such as use of lowest-cost therapies, patient satisfaction, rates of hospitalizations, and end-of life counseling (36). Additional evidence on the role played by pulmonologists in lung cancer care can provide important guidance to policy makers, permitting them to assess adequacy of coverage for specific services provided as part of an enhanced care model. Based on the results of this study, which is in line with the recent ATS/ERS guidelines, we expect that pulmonologists will be found to play a crucial role in managing comorbidities, symptoms, and palliative care, which we hope will lead to decreased hospitalizations and morbidity from therapies. ■

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