ORIGINAL ARTICLE

Timely Curative Treatment and Overall Mortality Among Veterans With Stage I NSCLC

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ABSTRACT

Introduction: Early stage lung cancer (LC) outcomes depend on the receipt of timely therapy. We aimed to determine the proportions of Veterans with stage I NSCLC in the age group eligible for LC screening (LCS) receiving timely curative treatment (≤12 wk after diagnosis), the factors associated with timely treatment and modality, and the factors associated with overall mortality.

Methods: Retrospective cohort study in Veterans aged 55 to 80 years when diagnosed with stage I NSCLC during 2011 to 2015. We used multivariate logistic regression models to determine factors associated with receiving timely therapy and receiving surgery versus stereotactic body radiation therapy (SBRT). We used multivariate Cox proportional hazards regression analysis to determine factors associated with overall mortality.

Results: We identified 4796 Veterans with stage I NSCLC; the cohort was predominantly older, White males, current or former smokers, and living in urban areas. Overall, 84% underwent surgery and 16% underwent SBRT. The median time to treatment was 63 days (61 d for surgery; 71 d for SBRT), with 30% treated more than 12 weeks. Unmarried Veterans with higher social deprivation index were less likely to receive timely therapy. Black race, female sex, and never smoking were associated with lower overall mortality. Older Veterans receiving treatment >12 wk, with higher comorbidity index, and squamous cell carcinoma had higher overall mortality.

Conclusions: A total of 30% of the Veterans with stage I NSCLC in the age group eligible for LCS received curative treatment more than 12 weeks after diagnosis, which was associated with higher overall mortality. Delays in LC treatment could decrease the mortality benefits of LCS among the Veterans.

Keywords: Veterans; Early-stage lung cancer; Non–small cell lung cancer; Lung cancer screening

Introduction

Lung cancer (LC) is the second most frequently diagnosed cancer and the leading cause of cancer death in the United States.[1] The 5-year relative survival of Americans diagnosed with LC is only 22.9% because many cancers are diagnosed at an advanced stage when survival is 7%.[1] Nevertheless, when patients with LC are diagnosed at an early stage and receive curative treatment with surgery or radiation, the median 5-year

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survival is up to 80% to 90%.[2] Screening high-risk patients with low-dose computed tomography (CT) reduces LC mortality by increasing detection of patients with early stage LC and being able to offer them treatment (surgery or radiation) when the chance of cure is greater.[3,4]

Veterans have higher rates of tobacco use than the general population,[5–7] and LC represents 20% of all cancers diagnosed in the Veteran Health Administration (VHA).[8] Similar to the general population, most Veterans with LC are diagnosed with advanced stage, with only 20% having early stage disease at diagnosis.[8,9] The VHA implemented a national LC screening program in 2017. Screening could detect more Veterans with early stage LC who could then receive curative therapy at specialized centers. Nevertheless, the success of a screening program depends on patients with early stage LC receiving timely curative treatment.[10–14]

We reviewed VHA national data to identify Veterans, aged 55 to 80 years, with stage I NSCLC, who received curative treatment, either surgery or radiation. These ages aligned with the 2014 U.S. Preventive Services Task Force (USPSTF) eligibility criteria for LC screening.[15] We evaluated the patient and clinical factors associated with modality of curative treatment, receipt of timely treatment ($\leq$12 wk), and the impact of time to treatment on overall mortality. VHA is an appropriate setting for evaluating early stage NSCLC treatment and mortality outcomes because it provides full access to care for all enrolled Veterans and captures comprehensive national demographic and clinical data in a common electronic health record.

Materials and Methods

Design

This is a retrospective cohort study.

Data Settings and Sources

The VHA is the largest integrated health care system in the United States, providing care to more than 9 million enrolled Veterans. It has 1298 health care facilities, including 171 VA medical centers. According to the 2016 VHA Cancer Care Survey Report, approximately 61% of VA medical centers offer on-site thoracic surgery, whereas only 28% of VA medical centers provide on-site radiation therapy.

We extracted data from the national VHA Corporate Data Warehouse (CDW) and VA Central Cancer Registry (VACCR) to identify Veterans between the ages of 55 and 80 years newly diagnosed with stage I NSCLC in fiscal years 2011 to 2015. We had follow-up data to 2019. The start date was chosen to coincide with the publication of the National Lung Screening Trial (NLST), which revealed that screening persons with histories of heavy tobacco use with low-dose CT decreased LC mortality by detecting more patients with early stage LC and offering them curative treatment.[4] The age range was based on the 2014 LC screening recommendations issued by the USPSTF.[15] CDW data elements extracted from VHA's integrated electronic health record and administrative files included patient demographics and residence, inpatient and outpatient visits, laboratory results, pharmacy records, and vital signs. The CDW oncology module contains elements from the VACCR, including diagnosis date, cancer histology, diagnostic stage, treatment, time between diagnosis and treatment, cause of death, date of death, and tobacco use. Additional information on patient geography and primary site of care was obtained from the VHA Planning Systems Support Group–geocoded veteran enrollment files and the Primary Care Management Module, respectively.

The study design was reviewed and approved by IRB committee. Informed consent by patients was waived. The study used a national database registry, de-identified individuals.

Subjects

We initially identified 7826 Veterans who were diagnosed with having stage I NSCLC in a VHA facility within the 50 American states. Patients were excluded if their age range was not between 55 and 80 years, had another recent diagnosis of other metastatic cancer before the LC diagnosis, had an unconfirmed diagnosis, or had missing address information. We also excluded patients with no documented treatment within 1 year of diagnosis. The final cohort included 4796 VHA patients with stage I NSCLC (Fig. 1). For the analyses of "time to treatment," we excluded 934 patients whose records indicated that the diagnosis date was the same as the date of receiving curative therapy (surgery).

Baseline Measures

Patient Characteristics. These included demographics, socioeconomic status, tobacco use, alcohol use, family history of cancer, comorbid conditions, and VHA health care utilization. Marital status was categorized as married, single/widowed/divorced, or unknown. Race and ethnicity were categorized as non-Hispanic White, Black, other, and unknown. Tobacco use was categorized as current or quit within 1 year, former (quit >1 y ago), former (quit date unknown), never used, and unknown. Chronic lung disease was identified using International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis codes (ICD-9, CM 490–492.8, 493.00–493.92, 494–494.1, 495.0–505.x, 506.4) from inpatient and outpatient encounters during the

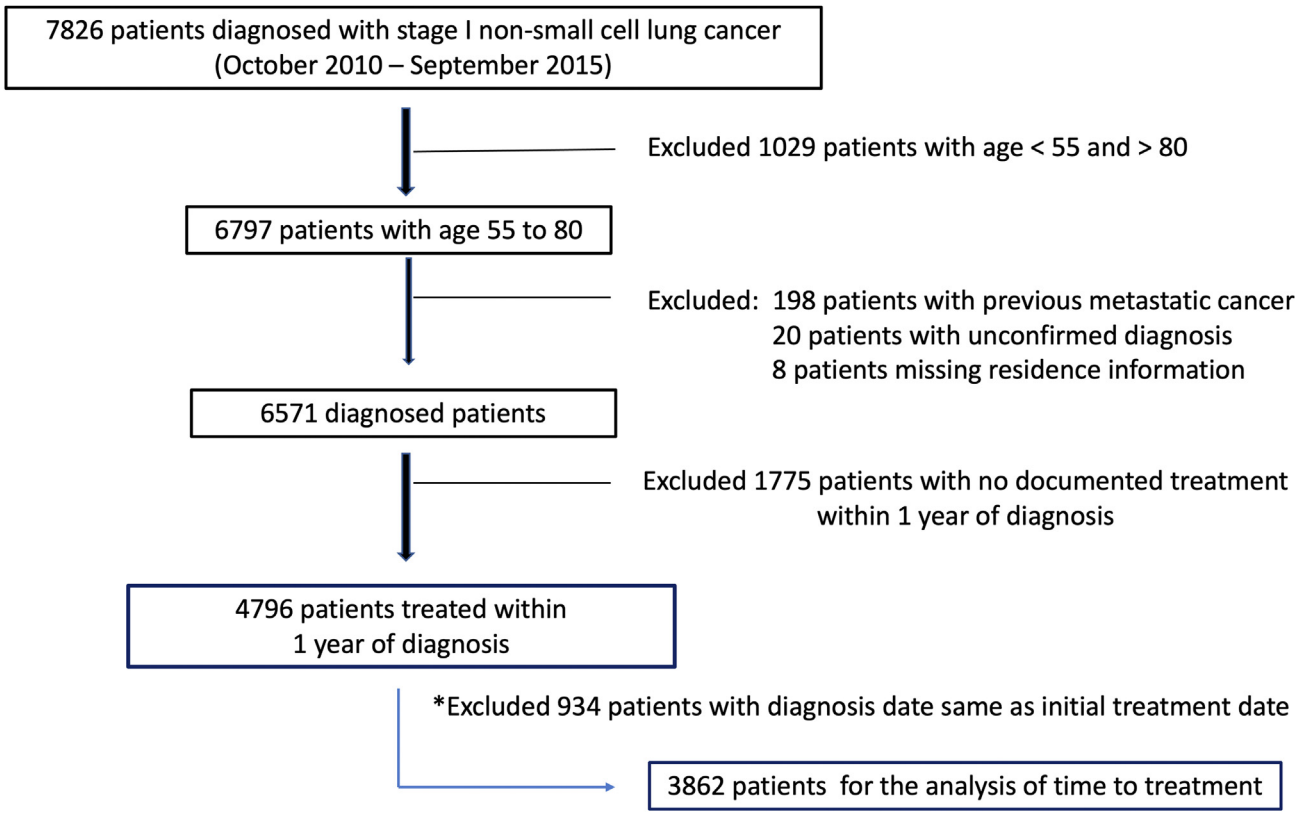

Figure 1. Cohort selection.

12 months before LC diagnosis.[16] We calculated the Charlson comorbidity index score using diagnoses from the 12 months before LC diagnosis.[17] We used the Social Deprivation Index to describe potential impacts of neighborhood social disadvantage on diagnosis.[18] Social Deprivation Index is a composite measure of area-level deprivation on the basis of seven demographic characteristics (income, education, employment, housing, household characteristics, transportation, and demographics). Higher scores indicate higher disadvantage. We also identified patients with a VA primary care visit within 12 months before the diagnosis of LC and those with VHA hospitalizations. Finally, we identified the patient's assigned VHA primary site of care from the Primary Care Management Module.

Geocoding. We defined residence using rural-urban commuting area codes, which classify U.S. census tracts using 33 separate categories to represent population density, urbanization, and daily commuting.[19] These 33 categories were condensed and grouped into four subcategories—urban, large rural, small rural, and isolated rural—according to a recommended algorithm.[20] Region of the country was defined using U.S. census regions (Northeast, South, West, and Midwest).

Tumor Characteristics

Early Stage NSCLC. We defined early stage NSCLC as stage I for having the highest survival rate after curative therapy. Veterans with stage I were identified according to the eighth edition of the TNM classification for LC by the International Association for the Study of Lung Cancer.[2]

Histology. Tumor histology was described as adenocarcinoma, squamous cell carcinoma (SCC), or other. We excluded Veterans with SCLC because they are seldom diagnosed at an early stage and their management differs from NSCLC.

Time of Diagnosis. We used the date of clinical diagnosis reported in the VACCR. This date is usually determined by the medical practitioner on the basis of clinical, radiological, or pathologic evaluation.

Curative Treatment. Defined as surgical resection of the tumor by thoracotomy or video-assisted thoracoscopic surgery, including lobectomy, sublobar resection (wedge or segmentectomy), and pneumonectomy, or radiation therapy by stereotactic body radiation therapy (SBRT). We looked only at SBRT because conventional radiotherapy is seldomly used for the treatment of early stage LC owing to its poor results with an overall

survival at 5 years between 0% and 40% and up to 70% of failure to local tumor control.[21] We defined timely curative treatment as receipt of surgery or SBRT less than or equal to 12 weeks after diagnosis.[13]

Mortality. We assessed overall mortality to the end of 2019. The maximum follow-up period was 5 years, and the median follow-up was 49.6 months (interquartile range: 32.5–59.8 mo). We used overall mortality instead of LC mortality to avoid bias in attributing cause of death. We also wanted to be consistent with other VHA studies addressing overall survival in NSCLC.[13]

Statistical Analysis

We used multivariate logistic regression models to determine factors associated with receiving timely curative therapy and to determine factors associated with timely receipt of surgery versus SBRT. The models included the subcategories of large rural, small rural, and isolated rural areas using urban as the reference category. The models were also adjusted for patient sociodemographic and clinical characteristics and region of the country. We included random facility intercepts to control for facility-level variation in treatment patterns, where facility was defined as the patient's assigned facility. We used multivariate Cox proportional hazards regression analysis to determine factors associated with overall mortality. Model variables included patient demographics and clinical characteristics and time of first curative therapy less than or equal to 6 weeks,[22] more than 6 to 12 weeks, or more than 12 weeks after diagnosis. Models were fitted using SAS Enterprise Guide version 7.4. Copyright 2014 by SAS Institute Inc., Cary, NC. The Institutional Review Board at the Iowa City VA approved this study.

Results

Between October 1, 2010, and September 30, 2015, we identified 4796 Veterans with stage I NSCLC (Fig. 1). The most common histology was adenocarcinoma (57%) followed by SCC (35%). Table 1 illustrates the baseline characteristics of the patients with stage I NSCLC who had documented receipt of curative treatment within 1 year of diagnosis. Notably, 84% of the patients received curative surgery and 16% underwent SBRT. Most stage I NSCLC cases were diagnosed in older, White, male Veterans with a current or former tobacco use, living in urban areas (79%), or in the Southern (42%) or Midwest (28%) regions of the country. Approximately half of the patients had chronic lung disease, the average Charlson comorbidity index score was 1.93, and 97% had had a VA primary care visit within the 12 months before diagnosis.

To evaluate time from diagnosis to curative treatment, we excluded 934 Veterans whose date of diagnosis was the same as the date of receiving curative surgery, leaving us with 3862 patients for further analysis. The overall median time between diagnosis and curative treatment was 63 days; 61 and 71 days for those who underwent surgery and SBRT, respectively. Overall, 70% of the patients received timely curative therapy after diagnosis ($\leq$12 wk) (Table 2).

The multivariable odds for receiving timely curative therapy (surgery or SBRT) less than or equal to 12 weeks after diagnosis and for receiving timely SBRT versus surgery are presented in Table 3. Veterans who were unmarried (versus married) and those with higher Social Deprivation Index scores (more disadvantaged) were less likely to receive timely curative therapy. Veterans diagnosed in 2015 (versus 2011) and with unknown smoking history (versus current smokers) were more likely to receive timely curative therapy. Veterans with age more than 60 years versus 55 to 60 years, history of lung disease versus none, higher Charlson comorbidity index scores (per unit increase in score), SCC or other histology versus adenocarcinoma, diagnosed in 2014 and 2015 versus 2011, living in small rural areas versus urban, having a previous VHA hospitalization in the past 12 months, and being unmarried (versus married) were more likely to receive SBRT versus surgery. Living in the northeast region of the country (versus the south), having a previous visit to VHA primary care in the past 12 months, rurality, and having never used tobacco were associated with lower likelihood of receiving SBRT versus surgery.

The multivariate Cox proportional hazards regression analysis to determine factors associated with overall mortality is presented in Table 4. We found important associations between time from diagnosis to curative treatment and overall mortality. Those receiving therapy less than or equal to 6 weeks versus more than 12 weeks (hazard ratio = 0.65, 95% confidence interval: 0.58–0.75, $p < 0.001$) and more than 6 to 12 weeks versus more than 12 weeks (hazard ratio = 0.72, 95% confidence interval: 0.65–0.81, $p < 0.001$) had lower overall mortality. We found no significant mortality difference between receiving therapy less than or equal to 6 weeks versus more than 6 to 12 weeks. Females versus male, Black race versus White, and never smokers versus current smokers were also associated with lower overall mortality. Age 75 to 80 years versus less than 60 years, higher Charlson index scores (per unit increase in score), and SCC were associated with worse overall mortality.

Discussion

We evaluated a cohort of Veterans, aged 55 to 80 years diagnosed with having stage I NSCLC between October 1, 2010, and September 30, 2015, who

Table 1. Patient Characteristics by Receipt of Curative Treatment Within 1 Year of Diagnosis, Stage I (IA, IB, INOS) NSCLC Diagnosed 2011 to 2015

	Curative Treatment Received ≤1 y of Diagnosis		
Variables	All Patients	Surgery[a]	SBRT Alone
Total patients	4796	4029 (84)	767 (16)
Patient characteristics			
Age			
55-59	460 (9.59)	421 (10.45)	39 (5.08)
60-64	1197 (24.96)	1023 (25.39)	174 (22.69)
65-69	1567 (32.67)	1353 (33.58)	214 (27.90)
70-74	883 (18.41)	710 (17.62)	173 (22.56)
75-80	689 (14.37)	522 (12.96)	167 (21.77)
Sex			
Female	161 (3.36)	142 (3.52)	19 (2.48)
Male	4635 (96.64)	3887 (96.48)	748 (97.52)
Race			
White	4057 (84.59)	3401 (84.41)	656 (85.53)
Black	646 (13.47)	545 (13.53)	101 (13.17)
Other	53 (1.11)	46 (1.14)	7 (0.91)
Unknown	40 (0.83)	37 (0.92)	3 (0.39)
Marital status			
Married	2321 (48.39)	1979 (49.12)	342 (44.59)
Single/widowed/divorced	2475 (51.61)	2050 (50.88)	425 (55.41)
Region			
Northeast	608 (12.68)	547 (13.58)	61 (7.95)
South	2019 (42.10)	1649 (40.93)	370 (48.24)
Midwest	1349 (28.13)	1126 (27.95)	223 (29.07)
West	820 (17)	707 (17.55)	113 (14.73)
Rurality (RUCA)			
Urban	3777 (78.75)	3190 (79.18)	587 (76.53)
Large rural	548 (11.43)	196 (4.86)	95 (12.39)
Small rural	244 (5.09)	453 (11.24)	48 (6.26)
Isolated	227 (4.73)	190 (4.72)	37 (4.82)
Any previous VA primary care visit (past 12 mo)	4643 (96.81)	3910 (97.05)	733 (95.57)
Any previous VA inpatient admission (past 12 mo)	1082 (22.56)	858 (21.30)	224 (29.20)
Tobacco history			
Current/quit ≤1 y	2529 (52.73)	2115 (52.49)	414 (53.98)
Former: quit >1 y	1216 (25.35)	989 (24.55)	227 (29.60)
Former: quit date unknown	515 (10.74)	446 (11.07)	69 (9)
Never used	131 (2.73)	125 (3.10)	6 (0.78)
Unknown	405 (8.44)	354 (8.79)	51 (6.65)
Chronic lung disease	2581 (53.82)	2021 (50.16)	560 (73.01)
Charlson index (mean)	1.93	1.83	2.44
Social Deprivation Index (mean)	0.64	0.61	0.83
Stage			
IA	3594 (74.94)	2995 (74.34)	599 (78.10)
IB	1093 (22.79)	943 (23.41)	150 (19.56)
INOS	109 (2.27)	91 (2.26)	18 (2.35)
Histology			
Adenocarcinoma	2741 (57.15)	2389 (59.30)	352 (45.89)
Squamous cell	1664 (34.70)	1354 (33.61)	310 (40.42)
Other	391 (8.15)	209 (7.0)	105 (13.69)
Fiscal year of diagnosis			
2011	921 (19.20)	801 (19.88)	120 (15.65)
2012	918 (19.14)	797 (19.78)	121 (15.78)
2013	942 (19.64)	804 (19.96)	138 (17.99)
2014	966 (20.14)	790 (19.61)	176 (22.95)
2015	1049 (21.87)	837 (20.77)	212 (27.64)

Note: INOS: stage I, no specified as IA or IB. All values are n (%) unless otherwise specified.

[a]Includes four patients who received surgery and radiation.

RUCA, rural-urban commuting area; SBRT, stereotactic body radiation therapy; VA, Veterans.

Table 2. Treatment Modality and Time to Initial Treatment (N = 3862 Patients)

Curative Treatment	All	Surgery	SBRT Alone
Modality of curative treatment received within 1 y	3862	3100 (80.27%)	762 (19.73%)
Median time to treatment (d)	63 (41-93)	61 (39-89)	71 (50-104)
≤6 wk	1045 (27%)	915 (30%)	130 (17%)
>6-12 wk	1673 (43%)	1339 (43%)	334 (44%)
>12-52 wk	1144 (30%)	846 (27%)	298 (39%)

Note: Excludes 934 patients with initial treatment date on same date as diagnosis.
SBRT, stereotactic body radiation therapy.

underwent curative treatment (surgery or SBRT) within the first year of diagnosis. Overall, 84% underwent surgery and 16% received SBRT. The median time between diagnosis and treatment was 63 days, and 70% received curative therapy within 12 weeks. Time between diagnosis and receiving curative treatment was associated with overall mortality. Veterans undergoing therapy within 12 weeks had better overall mortality than those receiving therapy after 12 weeks.

Our findings are similar to another VHA study where Veterans of all ages with stage I NSCLC receiving surgical resection more than 12 weeks after diagnosis had a higher likelihood of cancer recurrence and worse overall survival.[13] Although there is still no consensus on the ideal time from diagnosis to curative treatment for early stage NSCLC, waiting times from diagnosis to surgery longer than 6, 8, and 12 weeks have been associated with upstaging, recurrence, and worse survival among patients with NSCLC.[10–14,23,24] The wide range of threshold time to surgery associated with worse LC outcomes may be related to the variability in the definitions used for time of diagnosis.[13,25]

We recognize that our cohort of Veterans with early stage NSCLC likely differs from the VHA cohort that would be detected by LC screening programs. We could not quantify tobacco use or assess surgical candidacy as recommended by LC screening guidelines.[26] In addition, LC in our cohort was most likely discovered incidentally (because LC screening programs were not yet established). Nevertheless, our study highlights the need to further assess the mortality impact of implementing LC screening programs in the VHA. The success of a LC screening program depends on detecting patients with early stage LC and offering them timely curative treatment. The reported national average time between radiographic diagnosis and surgical resection in Veterans with stage I NSCLC is between 71 and 91 days,[13,27] much longer than that of the general population (38–46 d)[10,12,28] and the time recommended by national guidelines.[29] The time delays in curative treatment among Veterans with early stage LC could potentially decrease the benefit of LC screening on LC mortality. The reasons for the time delays in receiving curative LC treatment in the VHA are unclear and deserve further investigation.

In general, the median time between diagnosis and LC treatment is influenced by several factors including the stage of the disease (higher stages being treated sooner), the patient's functional status and comorbidities, presence of symptoms, inpatient versus outpatient diagnosis, and the modality of treatment (surgery usually associated with longer waiting times).[27,30] It also depends on the definitions used for time of diagnosis (clinical, radiological, preoperative, or intraoperative histology, or some combination).[13,25] In our study, only higher social deprivation index score and marital status other than married were associated with lower likelihood of receipt of timely curative therapy. In general, married patients have better cancer outcomes than unmarried patients, and in LC, this association seems to be mediated by higher chances of undergoing surgical resection or receiving chemotherapy.[31,32] To the best of our knowledge, this is the first study to describe an association between marital status and timely curative therapy for early stage NSCLC.

In the general population, social deprivation has been associated with worse cancer outcomes, mostly explained by inequity in access to health care for screening and treatment.[33] VHA is a national integrated health care system. By promoting equal and improved health care access (e.g., transportation and extended clinic hours), the VHA attenuates some of the health outcome disparities observed in the general population. In our study, even though higher social deprivation was associated with lower likelihood of receiving timely curative therapy, it was not independently associated with worse overall mortality. Being diagnosed in 2015 as compared with 2011 was associated with higher likelihood of receiving timely curative treatment, probably because professional guidelines have advocated more recently for timely LC therapy, especially in early stage NSCLC.[34]

We found the time to curative therapy for those receiving SBRT to be longer than for those receiving surgery, probably because SBRT is offered only in very few VHA hospitals. Delays arise because most Veterans are referred to tertiary radiation centers outside the VHA (approximately 95% of the radiation treatments occur at

Table 3. Relative Odds of Receiving Early Curative Treatment (≤12 wk After Diagnosis) and SBRT in Patients With Stage I (IA, IB, INOS) NSCLC on the Basis of Multivariable Models (N = 3862)

Patient Characteristics	Curative Treatment (Surgery, SBRT, or Both) ≤ 12 Wks Versus >12 and <52 Wks OR (95% CI; *p* Value)	SBRT Alone Versus Surgery OR (95% CI; *p* Value)
Age group (reference: <60)		
60-64	0.99 (0.75-1.31; $p = 0.97$)	2.16 (1.42-3.28; $p < 0.001$)
65-69	1.03 (0.78-1.35; $p = 0.85$)	1.90 (1.25-2.89; $p = 0.002$)
70-74	0.83 (0.61-1.11; $p = 0.24$)	2.76 (1.79-4.26; $p < 0.001$)
75-80	0.73 (0.54-1; $p = 0.05$)	4.38 (2.80-6.84; $p < 0.001$)
Female sex (reference: male)	1.36 (0.88-2.11; $p = 0.16$)	1.74 (0.22-13.65; $p = 0.60$)
Race (reference: white)		
Black	0.83 (0.65-1.03; $p = 0.09$)	1.04 (0.77-1.41; $p = 0.78$)
Other	0.74 (0.38-1.45; $p = 0.38$)	0.70 (0.28-1.78; $p = 0.46$)
Unknown	0.53 (0.26-1.10; $p = 0.09$)	0.42 (0.11-1.64; $p = 0.21$)
Marital status (reference: married)		
Single/widowed/divorced	0.78 (0.67-0.90; $p = 0.001$)	1.38 (1.14-1.67; $p < 0.001$)
SDI	0.96 (0.94-0.99; $p = 0.003$)	1.03 (0.99-1.06; $p = 0.09$)
Region		
Northeast	0.89 (0.58-1.37; $p = 0.61$)	0.42 (0.21-0.85; $p = 0.01$)
Midwest	0.90 (0.64-1.27; $p = 0.56$)	0.76 (0.46-1.24; $p = 0.27$)
West	1.05 (0.69-1.57; $p = 0.82$)	0.76 (0.41-1.43; $p = 0.39$)
South	Reference	
Rural category (reference: urban)		
Isolated rural	0.93 (0.65-1.33; $p = 0.69$)	1.11 (0.71-1.72; $p = 0.65$)
Small rural	1.07 (0.76-1.51; $p = 0.68$)	1.51 (1.01-2.25; $p = 0.04$)
Large rural	0.97 (0.76-1.23; $p = 0.79$)	1.32 (0.98-1.77; $p = 0.06$)
Any previous VA primary care (reference: none)	1.15 (0.78-1.70; $p = 0.48$)	0.39 (0.24-0.64; $p < 0.001$)
Any previous VA inpatient admission past 12 mo (reference: none)	0.95 (0.79-1.14; $p = 0.57$)	1.33 (1.06-1.66; $p = 0.01$)
Tobacco history (reference: current/quit within 1 y)		
Never used	1.40 (0.88-2.24; $p = 0.15$)	0.26 (0.11-0.64; $p = 0.003$)
Former: quit >1 y	1.18 (0.98-1.42; $p = 0.07$)	1.12 (0.9-1.40; $p = 0.31$)
Former: quit date unknown	1.17 (0.90-1.54; $p = 0.24$)	0.91 (0.64-1.29; $p = 0.60$)
Unknown	1.52 (1.09-2.12; $p = 0.012$)	1.05 (0.67-1.63; $p = 0.83$)
Chronic lung disease (reference: none)	1.18 (1-1.39; $p = 0.05$)	2.57 (2.07-3.18; $p < 0.001$)
Charlson index	0.98 (0.92-1.04; $p = 0.57$)	1.28 (1.19-1.38; $p < 0.001$)
Cancer histology (reference = adenocarcinoma)		
Squamous cell	1.02 (0.87-1.20; $p = 0.78$)	1.31 (1.07-1.60; $p = 0.007$)
Other	0.91 (0.70-1.20; $p = 0.52$)	2.80 (2.05-3.82; $p < 0.001$)
Fiscal year of diagnosis (reference: 2011)		
2012	0.95 (0.74-1.21; $p = 0.67$)	1.01 (0.72-1.40; $p = 0.96$)
2013	1.05 (0.82-1.33; $p = 0.70$)	1.14 (0.82-1.58; $p = 0.44$)
2014	0.99 (0.77-1.27; $p = 0.96$)	1.72 (1.25-2.36; $p < 0.001$)
2015	1.35 (1.05-1.73; $p = 0.02$)	1.96 (1.43-2.68; $p < 0.001$)

Note: Excludes 934 patients with initial treatment date on same date as diagnosis.
CI, confidence interval; INOS, stage I no specified A or B; SBRT, stereotactic body radiation therapy; SDI, social deprivation index; VA, Veterans.

non-VA facilities). In addition, patients often undergo extensive preoperative testing before they are excluded as surgical candidates. Veterans undergoing SBRT were older (≥75 y) and had a higher prevalence of chronic lung disease than those undergoing surgery (73% versus 50%).

The surgical resection rate in this cohort was slightly lower than that reported in stage I NSCLC from LC screening trial participants such as NLST (approximately 90%).[35] There are several explanations for these findings. First, surgery is the standard therapy for stage I NSCLC, with SBRT usually being reserved for patients ineligible for operation owing to advanced age and comorbidities. This is supported by our findings: older Veterans with chronic lung disease, higher Charlson comorbidity index, and recent hospitalizations were more likely to receive SBRT instead of surgery. Because our

Table 4. Risk-Adjusted Overall Mortality of Patients With Stage IA, IB, INOS NSCLC Treated Within 1 Year of Diagnosis (N = 3862) on the Basis of Multivariable Cox Regression

	Univariable Relative Odds	Multivariable Relative Odds
Patient Characteristics	Hazard Ratio (95% CI)	Hazard Ratio (95% CI)
Surgery or SBRT (reference = ≥12 wks to 1 y)		
≤6 wks	0.59 (0.52-0.68; $p < 0.001$)	0.65 (0.57-0.74; $p < 0.001$)
6-12 wks	0.67 (0.60-0.75; $p < 0.001$)	0.72 (0.65-0.81; $p < 0.001$)
Age group (reference: <60 y)		
60-64	0.96 (0.81-1.13; $p = 0.62$)	0.89 (0.74-1.08; $p = 0.23$)
65-69	1.07 (0.92-1.26; $p = 0.39$)	0.92 (0.76-1.11; $p = 0.37$)
70-74	1.20 (1.01-1.42; $p = 0.033$)	1.04 (0.85-1.27; $p = 0.70$)
75-80	1.52 (1.29-1.80; $p < 0.001$)	1.39 (1.14-1.71; $p = 0.001$)
Female sex (reference: male)	0.52 (0.40-0.69; $p < 0.001$)	0.70 (0.50-0.98; $p = 0.037$)
Race (reference: white)		
Black	0.82 (0.72-0.93; $p = 0.003$)	0.78 (0.66-0.91; $p = 0.002$)
Other	0.92 (0.63-1.35; $p = 0.66$)	1.00 (0.64-1.58; $p = 0.99$)
Unknown	0.74 (0.46-1.19; $p = 0.21$)	0.83 (0.48-1.44; $p = 0.61$)
Marital status (reference: married)		
Single/widowed/divorced	1.15 (1.06-1.25; $p < 0.001$)	1.10 (1-1.22; $p = 0.05$)
Social deprivation	1.02 (1.01-1.03; $p = 0.007$)	1.11 (1.00-1.22; $p = 0.045$)
Region (reference: south)		
Northeast	0.81 (0.70-0.93; $p = 0.003$)	0.85 (0.71-1.01; $p = 0.07$)
Midwest	0.74 (0.66-0.82; $p < 0.001$)	0.87 (0.76-0.99; $p = 0.037$)
West	0.95 (0.84-1.07; $p = 0.37$)	1.05 (0.90-1.22; $p = 0.55$)
Rural category (reference: urban)		
Isolated rural	1.02 (0.84-1.24; $p = 0.84$)	NS
Small rural	0.96 (0.79-1.16; $p = 0.66$)	NS
Large rural	1.09 (0.96-1.24; $p = 0.17$)	NS
Any previous VA primary care (reference: none)	0.77 (0.63-0.93; $p = 0.008$)	0.85 (0.65-1.10; $p = 0.21$)
Any previous VA inpatient admission past 12 mo (reference: none)	1.49 (1.36-1.63; $p < 0.001$)	1.10 (0.97-1.23; $p = 0.13$)
Tobacco history (reference: current/quit within 1 y)		
Never used	0.54 (0.39-0.73; $p < 0.001$)	0.56 (0.38-0.81; $p = 0.002$)
Former: quit >1 y	0.83 (0.75-0.92; $p < 0.001$)	0.90 (0.80-1.02; $p = 0.10$)
Former: quit date unknown	0.99 (0.87-1.13; $p = 0.99$)	0.93 (0.79-1.10; $p = 0.40$)
Unknown	0.92 (0.78-1.08; $p = 0.33$)	0.98 (0.81-1.19; $p = 0.85$)
Chronic lung disease (reference: none)	1.38 (1.27-1.50; $p < 0.001$)	NS
Charlson index	1.22 (1.19-1.25; $p < 0.001$)	1.20 (1.16-1.24; $p < 0.001$)
Histology (reference = adenocarcinoma)		
Squamous cell	1.31 (1.20-1.43; $p < 0.001$)	1.11 (1.00-1.22; $p = 0.04$)
Other	1.36 (1.18-1.57; $p < 0.001$)	Included in reference
Fiscal year of diagnosis (reference: 2011)		
2012	1.02 (0.90-1.16; $p = 0.77$)	NS
2013	1.02 (0.90-1.16; $p = 0.72$)	NS
2014	0.92 (0.81-1.05; $p = 0.22$)	NS
2015	0.89 (0.78-1.03; $p = 0.11$)	NS

Note: Excludes 934 patients with initial treatment date on same date as diagnosis.
CI, confidence interval; NS, not statistically significant; SBRT, stereotactic body radiation therapy; VA, Veterans.

inclusion criterion was based only on age, and we were not able to confirm eligibility for screening, our cohort of Veterans would be expected to include a higher rate of nonsurgical candidate patients. Second, the higher rates of tobacco use among Veterans compared with the general population[5–7,36] may also result in higher prevalence of tobacco-related comorbidities, which may decrease the rate of surgical candidacy. As exemplified in our cohort, 54% of Veterans with stage I NSCLC had chronic lung disease. Finally, sociodemographic factors, such as marital status, may have also influenced a lower rate of surgical resection in our cohort. Unmarried patients with LC seem to be less likely to undergo surgical resection than their married counterparts,[31,32] an

observation that correlates with our findings. Veterans have higher rates of divorce and relationship separation than the general population.[37] Although 16% of Veterans with stage I NSCLC in our cohort received SBRT, it is still unclear whether this therapeutic modality would offer similar LC outcomes when compared with surgery.[38]

In the general U.S. population, Blacks have worse LC outcomes than Whites,[39,40] which is attributed to Blacks having higher LC stage at diagnosis, poorer overall health, higher rates of tobacco use, lower socioeconomic status, and limited access to health care.[41–44] According to SEER data from 2004 to 2013, Black patients with early stage NSCLC in the United States were less likely to receive curative surgery and had higher standardized LC case-fatality rates compared with Whites.[44] Nevertheless, the difference in LC outcomes between Blacks and Whites disappear and may even reverse when adjusting for access to health care.[44–47] A large VHA study reported lower overall mortality among Black Veterans with NSCLC compared with their White counterparts, despite Black Veterans having higher stage at diagnosis and being less likely to receive stage-specific guideline-concordant care.[46] Another national VHA study revealed that Black Veterans with early stage NSCLC were less likely to receive curative surgery compared with Whites; however, there was no racial difference in overall and LC survival.[47] We observed no racial differences in the time of receipt or modality of curative therapy. Black Veterans with stage I NSCLC, however, had lower overall adjusted mortality risk compared with Whites. These findings may suggest that similar access to health care among Veterans would mitigate the racial disparities observed in LC outcomes in the general population. Fully addressing the racial differences in overall mortality is beyond the scope of this article. Nevertheless, we observed that Black Veterans were younger and less likely to have chronic lung disease than White Veterans.

Female Veterans with stage IA NSCLC had a lower adjusted risk for overall mortality than their male counterparts. Similar findings have been described in the general population. Lower tobacco smoking rates, differences in tumor histology and driving mutation profile, and estrogen exposure may account for some of these sex differences in LC outcomes.[48]

We did not observe a relationship between rurality and either receiving timely curative therapy or overall mortality. We previously reported that among Veterans with NSCLC, living in rural areas was not associated with higher stage at diagnosis when compared with those living in urban areas.[9] These findings together suggest that contrary to what is described in the general U.S. population,[49] rurality may not be associated with poor LC outcomes in the VHA, probably because Veterans with LC have similar access to health care and can receive cancer care in specialized VA centers. Similarly, in the general U.S. population, when rural residents receive cancer care at urban institutions, the LC outcomes disparities with urban residents dissipate.[50]

The VHA leadership issued LC screening guidelines in 2017; however, the national screening rates among Veterans have remained low, varying from less than 0.5% to up to 10%.[51] Our Veteran cohort included a period before the VHA implementation of LCS; however, we did notice an increase in the percentage of stage IA LC diagnosis over time (17.4% in 2011 to 21.4% in 2015), likely related to the incorporation of LCS by physicians into their practice after the publication of the NLST in 2011. Nevertheless, for LCS programs to affect LC mortality among Veterans, VHA would need to create and implement a national plan to improve its adoption and adherence, standardize radiology report templates for low-dose CT, and create efficient diagnostic and therapeutic pathways for the detected early stage LC to minimize delays in the timeliness of care of patients with LC. Although LCS is being implemented throughout VHA, we are not aware of any national plans addressing timeliness of diagnosis and care of patients with LC.

There are some limitations in our study. We excluded 934 subjects in our time-to-treatment analyses because the dates of diagnosis and treatment were identical. We could have created a selection bias by excluding these patients, although in further analysis, we did not find any significant clinical or demographic differences between the groups. We also recognized that coding for a variable such as "time of diagnosis to treatment" in national databases can be based on inconsistent clinical and pathologic diagnostic criteria.[13] These errors can create misclassification bias. Other authors have tried to avoid this bias by using the last CT chest done before curative therapy as the time of diagnosis.[13,52] Nevertheless, this strategy would be susceptible to bias too, especially in patients with high rate of comorbidities requiring more extensive preoperative workup. Finally, the results of this VHA study may not be applicable to the general U.S. population.

In conclusion, among Veterans with stage I NSCLC within the age group eligible for LC screening, 70% received curative therapy within 12 weeks of diagnosis with a median time of 61 days. Delays in receiving curative therapy more than 12 weeks were associated with higher overall mortality. LC screening in the VHA will increase the number of early stage NSCLC and may stress the VHA ability to provide timely treatment.

CRediT Authorship Contribution Statement

Rolando Sanchez: Study design, Interpretation of the data, Writing the manuscript.

Richard Hoffman: Funding, Study design, Interpretation of the data, Critical revision of the manuscript.

Mary S. Vaughan Sarrazin: Production and interpretation of the data, Critical revision of the manuscript.

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Appendix
RUCA Definitions:

1 Metropolitan area core: primary flow within an urbanized area (UA)
  1.0 No additional code
  1.1 Secondary flow 30% to 50% to a larger UA
2 Metropolitan area high commuting: primary flow 30% or more to a UA
  2.0 No additional code
  2.1 Secondary flow 30% to 50% to a larger UA
3 Metropolitan area low commuting: primary flow 10% to 30% to a UA
  3.0 No additional code
4 Micropolitan* area core: primary flow within an urban cluster (UC) of 10,000 to 49,999 (large UC)
  4.0 No additional code
  4.1 Secondary flow 30% to 50% to a UA
5 Micropolitan* high commuting: primary flow 30% or more to a large UC
  5.0 No additional code
  5.1 Secondary flow 30% to 50% to a UA
6 Micropolitan* low commuting: primary flow 10% to 30% to a large UC
  6.0 No additional code
7 Small town core: primary flow within UC of 2500 to 9999 (small UC)
  7.0 No additional code
  7.1 Secondary flow 30% to 50% to a UA
  7.2 Secondary flow 30% to 50% to a large UC
8 Small town high commuting: primary flow 30% or more to a small UC
  8.0 No additional code
  8.1 Secondary flow 30% to 50% to a UA
  8.2 Secondary flow 30% to 50% to a large UC
9 Small town low commuting: primary flow 10% to 29% to a small UC
  9.0 No additional code
10 Rural areas: primary flow to a tract outside a UA or UC (including self)
  10.0 No additional code
  10.1 Secondary flow 30% to 50% to a UA
  10.2 Secondary flow 30% to 50% to a large UC
  10.3 Secondary flow 30% to 50% to a small UC

Classification of RUCA:

Urban (RUCA codes 1.0, 1.1, 2.0, 2.1, 3.0, 4.1, 5.1, 8.1, 10.1)

Large town (RUCA codes 4.0, 4.2, 5.0, 5.2, 6.0, 6.1)

Small town (RUCA codes 7.0, 7.2, 8.0, 8.2, 9.0, 9.1, 9.2)

Rural (RUCA codes 10.0, 10.1, 10.2, 10.3)

Social Deprivation Index

Table 1. Domain and Variable Description

Domain	Variables
Income	Percent population less than 100% FPL (population under 0.99/total population)
Education	Percent population 25 y or more with <12 y of education (population with less than high school diploma or 12 y of education/total population)
Employment	Percent nonemployed (not in labor force + unemployed) / (civilian + not in the labor force) for the population 16-64 y
Housing	Percent population living in renter-occupied housing units (renter-occupied housing units/ (owner-occupied housing units + renter-occupied housing units))
	Percent population living in crowded housing units (tenure by occupants per room - a population with ≥1.01 occupants per room in owner-occupied housing units and renter-occupied housing units) / total population
Household characteristics	Percent single-parent households with dependents < 18 y (total single-parent households [male and female] with dependents < 18 y / total population)
Transportation	Percent population with no car (population with no vehicle available/total population)
Demographics	Percent high needs population - (population under 5 y of age + women between the ages of 15-44 y + everyone 65 y and over)/total population

Source: 2015 to 2019 American Community Survey 5-Year Summary File (Sequence Number Table ID Lookup Table).
FPL, federal poverty level.

Table 2. Variable Descriptions, Sequence Number, and Table IDs

Description	Sequence No	Table ID
Population estimate	SF0002	B01001
Percent population below 100% FPL (income in the past 12 mo < 100% FPL)	SF0049	C17001
Percent population with less than 12 y education	SF0042	B15003
Percent nonemployed population (civilian)	SF0075	B23001
Percent unemployed population (civilian)	SF0075	B23001
Percent population in renter-occupied housing units	SF0111	B25003
Percent population in crowded housing units	SF0111	B25044
Percent single-parent household population with children < 18 y	SF0035	B11003
Percent population with no vehicle available	SF0113	B25044
Percent high-needs population (persons aged ≥65 y, women 15-44 y, and children < 5 y)	SF0002	B01001

Source: 2015 to 2019. American Community Survey 5—Year Summary File (Sequence Number Table ID Lookup Table).
FPL, federal poverty level; ID, identification.

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