

The Impact of Persistent Smoking After Surgery on Long-term Outcomes After Stage I Non-small Cell Lung Cancer Resection



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BACKGROUND: Smoking at the time of surgical treatment for lung cancer increases the risk for perioperative morbidity and mortality. The prevalence of persistent smoking in the postoperative period and its association with long-term oncologic outcomes are poorly described.

RESEARCH QUESTION: What is the relationship between persistent smoking and long-term outcomes in early-stage lung cancer after surgical treatment?

STUDY DESIGN AND METHODS: We performed a retrospective cohort study using a uniquely compiled Veterans Health Administration dataset of patients with clinical stage I non-small cell lung cancer (NSCLC) undergoing surgical treatment between 2006 and 2016. We defined persistent smoking as individuals who continued smoking 1 year after surgery and characterized the relationship between persistent smoking and disease-free survival and overall survival.

RESULTS: This study included 7,489 patients undergoing surgical treatment for clinical stage I NSCLC. Of 4,562 patients (60.9%) who were smoking at the time of surgery, 2,648 patients (58.0%) continued to smoke at 1 year after surgery. Among 2,927 patients (39.1%) who were not smoking at the time of surgical treatment, 573 (19.6%) relapsed and were smoking at 1 year after surgery. Persistent smoking at 1 year after surgery was associated with significantly shorter overall survival (adjusted hazard ratio [aHR], 1.291; 95% CI, 1.197-1.392; $P < .001$). However, persistent smoking was not associated with inferior disease-free survival (aHR, 0.989; 95% CI, 0.884-1.106; $P = .84$).

INTERPRETATION: Persistent smoking after surgery for stage I NSCLC is common and is associated with inferior overall survival. Providers should continue to assess smoking habits in the postoperative period given its disproportionate impact on long-term outcomes after potentially curative treatment for early-stage lung cancer. CHEST 2022; 161(6):1687-1696

KEY WORDS: cigarettes; non-small cell lung cancer; smoking; thoracic surgery

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ABBREVIATIONS: aOR = adjusted OR; CDW = Corporate Data Warehouse; HF = Health Factors; ICD = International Classification of Diseases; NSCLC = non-small cell lung cancer; VHA = Veterans Health Administration

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Take-home Points

Study Question: What is the relationship between persistent smoking after surgery and long-term outcomes after non-small cell lung cancer (NSCLC) resection?

Results: Among 7,489 veterans undergoing surgical treatment for clinical stage I NSCLC, persistent smoking was observed in 3,221 patients (43.0%) at 1 year after surgery. Persistent smoking was associated with significantly shorter overall survival.

Interpretation: Persistent smoking is common among veterans with early-stage lung cancer after curative-intent surgery and is associated with inferior overall survival.

Non-small cell lung cancer (NSCLC) is the leading cause of cancer-related mortality in the United States, including among veterans.^{1,2} Approximately 90% of newly diagnosed cases of lung cancer are attributable to cigarette smoking.^{3,4} The gold standard treatment for early-stage NSCLC is surgery, with a subsequent 5-year survival ranging from 60% to 80%.⁵ Continued smoking at the time of surgery is a well-established risk factor for postoperative complications and mortality.^{6,7} Therefore, most professional guidelines recommend aggressive smoking cessation therapy for patients with newly diagnosed lung cancer who smoke.⁸⁻¹⁰ Perioperative smoking cessation interventions are especially important

in the veteran population, which has a disproportionately higher prevalence of smoking.¹¹

Despite the large body of evidence outlining the relationship between smoking and treatment-related adverse events in lung cancer, most cancer registries and surgical databases are static, assessing smoking status at a single preoperative time point, if at all.¹²⁻¹⁴

Consequently, smoking habits in the postoperative period and during extended follow-up are poorly understood. For example, a small study found that nearly half of patients with early-stage lung cancer who smoke at diagnosis continue to smoke within a year after surgery.¹⁵ Furthermore, because long-term smoking habits are not captured routinely in large cancer databases, the association between persistent postoperative smoking habits and oncologic outcomes like disease-free survival and overall survival is poorly understood and is limited to small studies.¹⁶

To address this gap in knowledge, we performed a retrospective cohort study using a cohort of patients from the Veterans Health Administration (VHA) with clinical stage I NSCLC. Our objectives were to describe the prevalence of persistent smoking 1 year after surgery using the granular electronic health records maintained by the VHA and to examine the association between persistent postoperative smoking and long-term oncologic outcomes. We hypothesized that persistent smoking after surgery would be associated with inferior overall and disease-free survival.

Study Design and Methods

Study Population

We performed this retrospective cohort study of adults with clinical stage I NSCLC undergoing surgical treatment in the VHA from 2006

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through 2016. The VHA Informatics and Computing Infrastructure system, which contains clinical and administrative data from multiple platforms in the Corporate Data Warehouse (CDW), was used to generate our initial dataset. NSCLC cases were identified using International Classification of Diseases (ICD) for Oncology, Third Edition codes. Patients were verified as having undergone surgery using ICD, Ninth and Tenth Revisions, procedure codes and Current Procedural Terminology codes. To ensure greater accuracy and validity, we refined the study cohort via additional data abstraction performed by a dedicated team of researchers over a period of nearly 24 months. Exclusion criteria were patients younger than 18 years, patients receiving neoadjuvant chemotherapy or radiotherapy, patients undergoing surgery for recurrent disease, and patients with unavailable smoking data 1 year after surgery. We also excluded individuals who never smoked from the present analysis because this population of patients was exceedingly small in the cohort (< 5%), precluding clinically meaningful analysis. Additionally, given the nature of our analysis, we excluded patients who died within 30 days of surgery as well as patients whose operations led to a diagnosis of pathologic stage IV disease.

The study protocol was approved by the St. Louis VHA Research and Development Committee, and given the deidentified nature

of the analysis, a waiver for consent was granted by the institutional review board. Data were reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Smoking Exposure

In VHA datasets, smoking status typically is determined by using Health Factors (HFs) data, which are maintained within the CDW.¹⁷ These data are collected nationally and are validated against prospective data for determining veteran smoking status.^{17,18} HFs data are compiled from automated prompts, which VHA clinicians must complete on a regular basis, that include information on patient cigarette use.¹⁷ Therefore, these data can be used not only to determine smoking habits at a given time (ie, at the time of surgery), but also to assess changes in smoking status longitudinally (ie, smoking cessation).¹⁹ We assessed smoking status (current vs former) at two time points: the date of surgery and 1 year after the date of surgery. Because the content and frequency of smoking status in HFs can fluctuate,^{19,20} we queried the VHA Informatics and Computing Infrastructure Text Integration Utility data files—which contain free-text documents like progress and consultation notes—to augment the preoperative assessment of smoking status (ie, to assess better if individuals were still smoking on the date of surgery), as described previously by our group.²¹ For the postoperative assessment, HFs data were used without such augmentation because smoking status in the postoperative period is less prone to the temporal limitations of the preoperative assessment. For patients who died within 1 year of surgery, the last recorded smoking status in HFs was used for the analysis.

For subsequent analyses, we defined several terms as follows. *Continued smoking* describes patients who were smoking at the time of surgical treatment and who continued to smoke 1 year after surgery. *Relapsed smoking* describes patients who were not smoking at the time of surgical treatment, but who relapsed and began smoking again at 1 year after surgery. For the survival analyses, we analyzed individuals classified as having continued and relapsed smoking habits together (termed *persistent smoking*) to highlight best the effects of postoperative smoking on long-term outcomes.

We also collected several other variables related to smoking status. Prescriptions for smoking cessation pharmacotherapy (nicotine replacement therapy, varenicline, or bupropion) within 1 year after surgery were assessed using the CDW Pharmacy Outpatient file. We also assessed whether patients followed up with a cardiothoracic surgeon (more than one visit, because patients were assumed to have undergone at least one postoperative visit), oncologist, or primary care physician within 1 year after surgery.

Covariates

We extracted several additional covariates including age, sex, BMI, and comorbidities. Comorbidities were measured from 5 years before surgery to 1 month after surgery and were determined using ICD, Ninth and Tenth Revisions, codes to calculate a composite Charlson/Deyo score.²² Residential zip codes were used to calculate distance from the treating hospital (measured as the straight-line distance between the center of patient zip code and the facility address). Area deprivation index, a county-level measure of socioeconomic deprivation that incorporates several poverty, education, housing, and employment indicators from the US census, also was obtained.^{23,24}

Several oncologic and treatment covariates also were extracted. These included tumor size, histologic findings (adenocarcinoma, squamous cell carcinoma, other), grade, year of operation, hospital caseload (lung cancer treatment volume in the year before surgery at that VHA facility), wait time to surgery (time between radiographic diagnosis and surgery, with delayed surgery defined as a wait time of > 12 weeks²⁵), type of operation (lobectomy, segmentectomy, wedge resection, or pneumonectomy), surgical approach (video-assisted thoracoscopic surgery or thoracotomy), number of lymph nodes assessed (adequacy defined as ≥ 10 based on prior guidelines^{26,27}), and final pathologic stage.

We also extracted several short-term outcomes to include as covariates in our disease free-survival and overall survival analyses. These included length of stay, major postoperative complications (pneumonia, empyema, myocardial infarction, respiratory failure, renal failure, or stroke),^{28,29} and 30-day readmission.

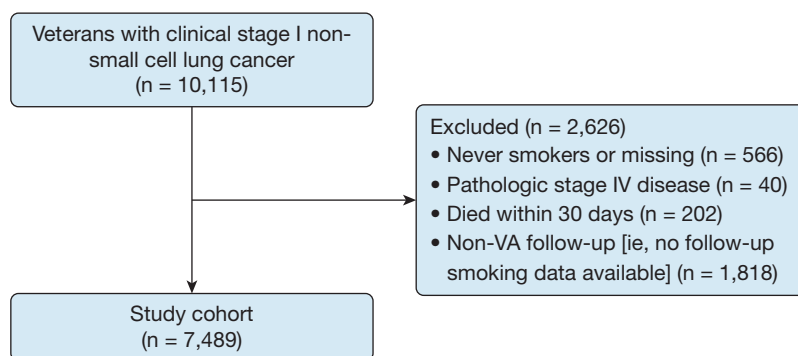
Outcomes

Our primary outcomes of interest were disease-free survival and overall survival. Overall survival was determined using the CDW Vital Status File. Patients were censored at the date of last follow-up (May 1, 2020). Disease-free survival (or time until cancer recurrence) was defined using the CDW Oncology database and was supplemented with additional diagnoses suggestive of recurrence using ICD, Ninth and Tenth Revisions, codes, as described previously in VHA literature and by our group.^{25,30} In particular, patients with any of the following occurrences based on ICD codes also were deemed to demonstrate cancer recurrence: additional chemotherapy or radiation therapy (in the absence of another cancer diagnosis), additional lung resection (in the absence of another cancer diagnosis), malignant pleural effusion, a secondary malignant neoplasm resulting from lung cancer, or lung biopsy (that was followed by additional chemotherapy or radiation therapy).

Statistical Analysis

Cohort characteristics are presented using means \pm SDs for continuous variables and frequencies (proportions) for categorical variables. To compare between groups, two-tailed *t* tests were used for continuous variables and χ^2 tests were used for categorical variables. Factors associated with continued smoking and smoking relapse at 1 year were assessed in multivariate logistic regression models adjusting for the variables specified in the corresponding tables. The association between persistent smoking and overall survival was assessed using Kaplan-Meier curves and a multivariate Cox proportional hazards model (for all-cause mortality), controlling for the aforementioned covariates (available in [supplement](#)). The association between persistent smoking and disease-free survival was assessed using a multivariate competing risk model (Fine and Gray subdistribution hazard function) with recurrence as the outcome and death as a competing event, controlling for the same aforementioned covariates (available in [supplement](#)). Because the occurrence of death precludes the possibility of recurrence in those who die, this time-to-event competing risk model was used for the recurrence analysis and was displayed using a cumulative incidence plot.³¹ Missing data were reported in the univariate analyses (available in [supplement](#)), and complete case analyses was used for the multivariate models (except where missing categories are specified). All analyses were performed using SAS version 9.3 software (SAS Institute).

Figure 1 – Consolidated Standards of Reporting Trials diagram showing study progression.



Results

Study Cohort Characteristics

Among 7,489 patients who underwent surgical treatment for clinical stage I NSCLC, 7,189 patients (96.0%) were men, the mean \pm SD age was 67.0 ± 7.3 years, and 4,562 patients (60.9%) were smoking at the time of surgical treatment (Fig 1). The median wait time between cancer diagnosis and surgery was 62 days (interquartile range, 40-94 days), with 2,282 patients (30.5%) experiencing a delay of longer than 12 weeks.²⁵ Most veterans underwent lobectomy (5,295 patients [70.8%]) and 4,183 patients (55.9%) underwent a thoracotomy. Most patients had received a diagnosis of adenocarcinoma (3,935 patients [52.6%]) with tumor grades of more than I (grade II, 3,688 patients [52.9%]; grade III, 2,320 patients [33.3%]; and grade IV, 102 patients [1.5%]). The median length of stay was 7 days (interquartile range, 4-10 days). The most common complications were pneumonia (411 patients [5.5%]) and cardiorespiratory failure (300 patients [4.0%]). At 30 days after surgery, 567 patients (7.6%) had been readmitted. Additional patient demographics, treatment characteristics, and outcomes of the study cohort are presented in Table 1.

In the year after surgery, 2,666 patients (35.6%) were prescribed smoking cessation pharmacotherapy. In terms of postoperative follow-up in the year after surgery, 4,609 patients (61.5%) were seen by a cardiothoracic surgeon more than once, 3,301 patients (44.1%) were seen by an oncologist, and 7,031 patients (93.9%) were seen by a primary care physician.

Factors Associated With Continued Smoking

Among the 4,562 patients (60.9% of overall cohort) who were smoking at the time of surgical treatment, 2,648 patients (58.0%) continued to smoke at 1 year after surgery (e-Table 1). Factors associated with lower odds of continued smoking were increasing age (for every 1-

unit increase; adjusted OR [aOR], 0.955; 95% CI, 0.944-0.966; $P < .001$) (Table 2), female sex (vs male; aOR, 0.648; 95% CI, 0.452-0.931; $P = .02$), Black race (vs White race; aOR, 0.796; 95% CI, 0.661-0.958; $P = .02$), and higher BMI (for every 1-unit increase; aOR, 0.943; 95% CI, 0.930-0.956; $P < .001$). Factors associated with higher odds of continued smoking were higher Charlson/Deyo score (for every 1-unit increase; aOR, 1.043; 95% CI, 1.005-1.083; $P = .03$), delayed surgery (> 12 weeks between diagnosis and surgery; aOR, 1.197; 95% CI, 1.027-1.395; $P = .02$), undergoing a wedge resection (vs lobectomy; aOR, 1.276; 95% CI, 1.064-1.531; $P = .01$), and receiving cessation pharmacotherapy after surgery (aOR, 1.817; 95% CI, 1.574-2.097; $P < .001$). Of note, continued smoking was not associated with tumor size, final pathologic stage, major complications after surgery, readmission after surgery, or the type of provider performing follow-up (surgeon, oncologist, or primary care provider).

Pack-year smoking history was available for 5,622 patients (75.1%). In a sensitivity analysis using a separate multivariate model, greater pack-year smoking history was associated with slightly higher odds of continued smoking 1 year after surgery (for every 1-unit increase; aOR, 1.003, 95% CI, 1.000-1.005; $P = .03$).

Factors Associated With Smoking Relapse

Among the 2,927 patients (39.1% of overall cohort) who were not smoking at the time of surgical treatment, 573 patients (19.6%) had relapsed and were smoking at 1 year after surgery (e-Table 1). Factors associated with higher odds of smoking relapse were individuals who quit more recently (ie, quitting between diagnosis and surgery vs quitting before diagnosis; aOR, 4.729; 95% CI, 3.711-6.025; $P < .001$) (e-Table 2), higher area deprivation index (for every 1-unit increase; aOR, 1.013; 95% CI, 1.005-1.021; $P < .001$), and higher pathologic stage (eg, II vs I; aOR,

TABLE 1] Characteristics of Veterans With Clinical Stage I NSCLC Undergoing Surgical Treatment in the VHA

Variable	Overall Cohort (N = 7,489)
Demographics	
Age, y	66.95 ± 7.26
Sex	
Male	7,189 (95.99)
Female	300 (4.01)
Race	
White	6,168 (82.36)
Black	1,154 (15.41)
Other	102 (1.36)
Unknown	65 (0.87)
Smoking status (at time of surgical treatment)	
Current	4,562 (60.92)
Former	2,927 (39.08)
BMI, kg/m ²	27.00 (5.40)
Area deprivation index	54.41 ± 14.96
Charlson/Deyo score	7 (5-8)
Smoking cessation pharmacotherapy prescribed after surgery (within 1 y)	2,666 (35.6)
Postoperative appointments (in 1 y after surgery)	
Cardiothoracic surgeon (> 1 visit)	4,609 (61.54)
Oncologist	3,301 (44.08)
Primary care provider	7,031 (93.88)
Treatment characteristics	
Wait time to surgery, d	
Median (IQR)	62 (40-94)
> 12 wk	2,282 (30.47)
Tumor size, Mm	22.96 ± 10.58
Resection	
Lobectomy	5,295 (70.83)
Wedge	1,637 (21.90)
Segment	444 (5.94)
Pneumonectomy	100 (1.34)
Surgical approach	
VATS	2,988 (39.90)
Thoracotomy	4,183 (55.86)

(Continued)

TABLE 1] (Continued)

Variable	Overall Cohort (N = 7,489)
Histologic finding	
Adenocarcinoma	3,935 (52.56)
Squamous cell	2,589 (34.58)
Other	962 (12.85)
Grade	
I	859 (12.33)
II	3,688 (52.92)
III	2,320 (33.29)
IV	102 (1.46)
Pathologic stage	
I	6,373 (85.10)
II	565 (7.54)
III	291 (3.89)
Outcomes	
Length of stay, d	7 (4-10)
Major complications	
Pneumonia	411 (5.49)
MI	67 (0.89)
Empyema	62 (0.83)
Renal failure	82 (1.09)
Respiratory/cardiac failure	300 (4.01)
Stroke	18 (0.24)
30-d readmission	567 (7.57)

Data are presented as No. (%), mean ± SD, or median (IQR). IQR = interquartile range; MI = myocardial infarction; NSCLC = non-small cell lung cancer; VATS = video-assisted thoracoscopic surgery; VHA = Veterans Health Administration.

1.793; 95% CI, 1.216-2.645; *P* = .003). Factors associated with lower odds of smoking relapse were increasing age (for every 1-unit increase; aOR, 0.951; 95% CI, 0.935-0.968; *P* < .001), Black race (vs White race; aOR, 0.660; 95% CI, 0.465-0.937; *P* = .02), higher BMI (for every 1-unit increase; aOR, 0.962; 95% CI, 0.941-0.982; *P* < .001), and delayed surgery (> 12 weeks between diagnosis and surgery; aOR, 0.776; 95% CI, 0.604-0.996; *P* = .05).

Persistent Smoking and Long-term Outcomes

In the entire cohort, persistent smoking was observed in 3,221 patients (43.0%) at 1 year after surgery. Persistent smoking was associated with significantly shorter overall survival (adjusted hazard ratio of all-cause mortality, 1.291; 95% CI, 1.197-1.392; *P* < .001) (e-Table 3), with a median survival of 83.2 months in those

TABLE 2] Factors Independently Associated With Continued Smoking at 1 Y After Surgery (n = 4,562)

Variable	OR	95% CI (Wald)	P Value
Age	0.955	0.944-0.966	< .0001
Sex (female vs male)	0.648	0.452-0.931	.0190
Race (reference, White)			
Black	0.796	0.661-0.958	.0158
Other	0.666	0.369-1.202	.1773
Unknown	0.723	0.363-1.440	.3561
BMI	0.943	0.930-0.956	< .0001
Charlson/Deyo score	1.043	1.005-1.083	.0250
Area deprivation index	1.004	1.000-1.009	.0708
Delayed surgery > 12 wk (yes vs no)	1.197	1.027-1.395	.0215
Resection type (reference, lobectomy)			
Pneumonectomy	1.048	0.546-2.013	.8875
Segmentectomy	1.088	0.801-1.478	.5891
Wedge	1.276	1.064-1.531	.0085
Surgical approach (VATS vs thoracotomy)	1.085	0.937-1.256	.2768
Tumor size (reference, ≤ 10 mm)			
11-20	0.829	0.644-1.067	.1452
21-30	0.813	0.623-1.061	.1276
31-40	0.822	0.612-1.105	.1946
41-50	0.990	0.688-1.424	.9563
Unknown	0.936	0.547-1.603	.8104
Pathologic stage (reference, I)			
II	0.803	0.621-1.040	.0970
III	1.233	0.849-1.791	.2717
Major complication (yes vs no)	0.848	0.676-1.065	.1558
Readmission (yes vs no)	0.845	0.641-1.114	.2330
Smoking cessation pharmacotherapy prescribed after surgery (within 1 y)	1.817	1.574-2.097	< .0001
Postoperative appointments (in 1 y after surgery)			
Cardiothoracic surgeon (> 1 visit)	1.029	0.889-1.191	.7016
Oncologist	1.035	0.897-1.194	.6400
Primary care provider	0.944	0.705-1.263	.6959

Table displays the multivariate model controlling for all covariates. VATS = video-assisted thoracoscopic surgery.

who were not smoking compared with 73.7 months in individuals who persistently smoked (Fig 2). This survival difference was observed most prominently in individuals

who continued smoking as opposed to those who relapsed (e-Figs 1, 2). With a median follow-up of 6.6 years, cancer recurrence was

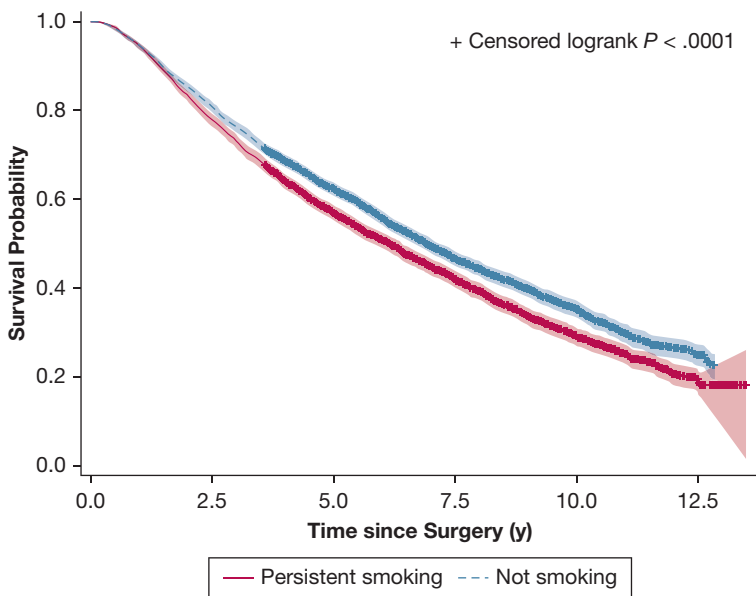


Figure 2 – Graph showing overall survival based on smoking status 1 year after surgical treatment.

detected in 1,850 patients (24.7%). Persistent smoking was not associated with inferior disease-free survival (adjusted hazard ratio, 0.989; 95% CI, 0.884-1.106; $P = .84$) (Fig 3, e-Table 4).

Discussion

This study explored the relationship between persistent postoperative smoking and long-term outcomes in veterans with clinical stage I NSCLC. We found that more than 60% of veterans with early-stage lung cancer smoke at the time of cancer diagnosis. At 1 year after surgery, both continued smoking and smoking relapse

were common. Persistent smoking was associated with significantly shorter long-term survival, but did not influence the risk of cancer recurrence. In aggregate, these findings suggest that persistent smoking after potentially curative lung cancer surgery is an important modifiable factor for long-term survival and should be a key element of cancer survivorship plans.

Cancer survivorship—the experience of living for extended cancer-free periods after curative-intent treatment—is an increasingly common phenomenon in early-stage lung cancer. A major contributing factor to

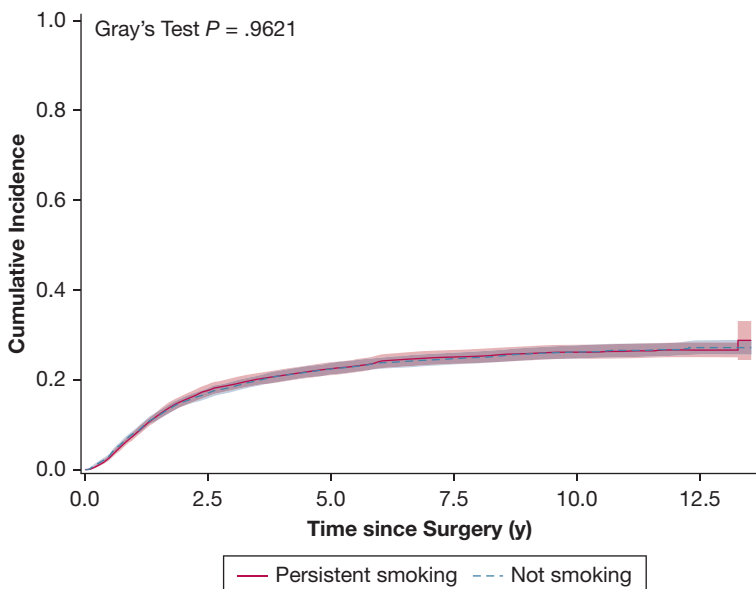


Figure 3 – Graph showing disease-free survival based on smoking status 1 year after surgical treatment.

this is the implementation of lung cancer screening programs and the relative increase in patients with early-stage, potentially curative disease.³² However, a challenge of this survivorship period is the large number of patients who are lost in transition and do not receive appropriate long-term oncologic follow-up care.³³ This has led several organizations, including the American Society for Clinical Oncology and the American College of Surgeons Commission on Cancer, to advocate for so-called survivorship care plans.³⁴ These survivorship care plans are meant to be brief summaries of a patient's treatments, their unique surveillance schedule, and other factors (like warning signs for late treatment effects and healthy lifestyle habits), all of which are designed to improve outcomes during this cancer survivorship period. Despite clear importance, the implementation of survivorship care plans has been poor for a variety of reasons.³⁴ Nonetheless, our data support that smoking cessation should be an integral element of such care plans given the strong relationship between persistent smoking and worse survival.

Most large cancer databases assess preoperative smoking status only at a single time point, if at all, and lack longitudinal smoking data after treatment.^{13,14} Similarly, in administrative datasets where longitudinal data are more readily available, smoking status often is coded unreliably.³⁵ Therefore, changes in preoperative and postoperative smoking status are poorly understood in the context of lung cancer surgery. A prior, single-institution study by Walker and colleagues¹⁵ examined 154 patients with early-stage lung cancer undergoing surgical treatment who smoked within 3 months of surgery; they found that at 12 months after surgery, 36.9% of these patients were still smoking and that this was associated with inferior outcomes. Our study demonstrated that an even higher proportion of veterans who smoked at the time of surgery continued to smoke 1 year after treatment (58.0%). Importantly, we further identified that persistent smoking significantly diminished long-term survival after accounting for tumor-related factors and other comorbidities.

Several factors likely contribute to diminished long-term survival in patients who persistently smoke after surgery. First, it is likely that persistent smoking contributes to accelerated cardiovascular and other smoking-related comorbidities. Although we did assess comorbidities

that were present at the time of surgery, it is likely that these smoking-related comorbidities progress in the follow-up period, leading to higher rates of mortality in patients who continue to smoke. Second, persistent smoking likely is associated with higher risk for other smoking-related malignancies that may contribute to shorter survival in these patients.³⁶ Third, prior studies have demonstrated that the benefits of smoking cessation, especially in reducing the risk of mortality, are realized relatively quickly.^{36,37} This finding should be emphasized to patients so that the treatment experience can be used effectively as a so-called teachable moment.³⁸

A surprising finding was that persistent smoking was not associated with cancer recurrence. Several factors may contribute to this observation. For example, recurrence is relatively uncommon in patients with stage I NSCLC (20%-25%), limiting our study's power. Similarly, surgery in the setting of early-stage disease is potentially curative, negating the risk of smoking-related recurrence. Despite this, it is established that persistent smoking results in higher rates of second primary lung cancers, at a rate of 1% to 2% per year.³⁹ These second lung cancers in addition to other smoking-related malignancies, although not contributing to the incidence of recurrence, likely contribute to the inferior survival in individuals who persistently smoke.

We also assessed several patient- and treatment-related factors and their association with persistent smoking after surgery. Overall, we found through these analyses that it is challenging to identify individuals who are likely to continue smoking in the postoperative period. For example, postoperative smoking habits did not seem to differ based on cancer-related factors like tumor size or stage. Similarly, we did not observe differences in smoking habits in the setting of major complications or readmissions. Smoking habits also were similar among patients who followed up with a surgeon, oncologist, or primary care provider. These results indicate that careful attention must be paid to smoking status of all individuals with a smoking history during cancer follow-up.

This study has several strengths. Most notably, it harnesses well-maintained VHA electronic health records to assess smoking status longitudinally in a homogenous cohort of patients with stage I NSCLC undergoing definitive surgical treatment. Conversely, this study has some limitations. First, smoking status

was not available for all patients at 1 year after surgery. This is related to the variability of the HFs prompts^{19,20} and to the subset of patients who may not receive follow-up care through the VHA. Second, smoking status in this study was determined through historical medical records, and therefore was not validated biochemically. Finally, the VHA serves a unique patient population that is largely male with significant comorbidities and histories of heavy smoking. However, with prior studies showing similar long-term outcomes in veteran and nonveteran populations undergoing lung cancer surgery,⁴⁰ it is likely that our findings will be

applicable generally to the broad population of patients with lung cancer.

Interpretation

In conclusion, persistent smoking after stage I NSCLC resection is common and dramatically worsens long-term survival. Providers—including surgeons—should counsel patients aggressively regarding smoking in the perioperative period and during cancer surveillance because successful cessation interventions can have a disproportionate impact on early-stage lung cancer outcomes.

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