

---

---

# Lack of Adherence to Guideline-Based Imaging Before Subsequent Radiation in Patients with Non–Small Cell Lung Cancer: Impact on Patient Outcomes

Emily Sterbis<sup>1</sup>, Rifei Liang<sup>2</sup>, Premal Trivedi<sup>1</sup>, Jennifer Kwak<sup>1</sup>, Erica Cohen Major<sup>3</sup>, Sana D. Karam<sup>4</sup>, and Rustain L. Morgan<sup>1</sup>

<sup>1</sup>Department of Radiology, University of Colorado Anschutz Medical Campus, Aurora, Colorado; <sup>2</sup>University of Colorado Cancer Center, University of Colorado–Anschutz Medical Campus, Aurora, Colorado; <sup>3</sup>Department of Nuclear Medicine, Edward Hines Jr. VA Hospital, Hines, Illinois; and <sup>4</sup>Department of Radiation Oncology, University of Colorado Anschutz Medical Campus, Aurora, Colorado

---

Lung cancer is the leading cause of cancer death within the United States, yet prior studies have shown a lack of adherence to imaging and treatment guidelines in patients with lung cancer. This study evaluated the use of <sup>18</sup>F-FDG PET/CT imaging before subsequent radiation therapy (RT) in patients with non–small cell lung cancer (NSCLC), as recommended by National Comprehensive Cancer Network guidelines, and whether the use of this imaging modality impacts cancer-specific survival. **Methods:** This was a retrospective study of the National Cancer Institute’s Surveillance, Epidemiology, and End Results program of Medicare-linked data in patients with NSCLC. Hazard ratios and 95% CIs for overall and cancer-specific survival were estimated for patients diagnosed between 2006 and 2015 who underwent either <sup>18</sup>F-FDG PET/CT-based or CT-based imaging before subsequent RT. **Results:** Significant improvement in cancer-specific survival was found in patients who underwent <sup>18</sup>F-FDG PET/CT imaging before subsequent RT, compared with those who underwent CT (hazard ratio, 1.43 [95% CI, 1.32–1.55;  $P < 0.0001$ ]). Although the National Comprehensive Cancer Network recommends <sup>18</sup>F-FDG PET/CT before subsequent RT, 43.6% of patients were imaged with CT alone. **Conclusion:** Many patients with NSCLC are not being imaged according to national guidelines before subsequent RT, and this omission is associated with a lower cancer-specific survival.

**Key Words:** PET/CT; surveillance; radiation therapy; non–small cell lung cancer; guidelines

**J Nucl Med 2023; 64:75–81**  
DOI: 10.2967/jnumed.122.264131

---

**L**ung cancer remains the leading cause of cancer-related death within the United States. The most recent data from 2020 found that lung cancer caused more deaths than breast, prostate, and colorectal cancers combined, accounting for almost 1 in 4 cancer deaths (1). Despite this statistic, there is reason for optimism: during 2016–2017, there was a 2.2% decrease in overall cancer mortality, the largest decline recorded in a single year, with persistent declines in lung cancer mortality (1). Management of non–small

cell lung cancer (NSCLC) is becoming more nuanced with molecular testing to guide therapy based on the patients’ underlying mutations (2). This has led to the idea of limited metastatic burden at the time of diagnosis, also known as oligometastatic disease, and limited progressive disease of a few metastatic sites on systemic therapy, also known as oligoprogressive disease. Either form of limited baseline or progressive metastatic disease can potentially be treated with definitive local ablative therapy, such as minimally invasive surgery, radiation therapy (RT), radiofrequency ablation, or cryoablation. Local ablative therapy has been shown to improve patient outcomes and has the potential to decrease invasive surgeries (3).

Imaging with <sup>18</sup>F-FDG PET/CT can provide additional information to guide treatment for patients with oligoprogressive disease. Multiple prior studies have established the superiority of PET/CT over CT alone for NSCLC staging and treatment planning. Specifically, PET/CT has high sensitivity for tumor, nodal, and metastatic staging (4); can differentiate between recurrent disease and RT changes (5); increases detection of oligoprogressive disease outside the central nervous system (6); improves selection of patients for thoracotomy (7–9); and can change treatment decisions for up to 72% of patients with NSCLC (10). PET/CT also provides prognostic information pertinent to treatment planning. Patients with a higher SUV<sub>max</sub> on pretreatment PET/CT have decreased overall survival and increased recurrence (11–13), and use of baseline <sup>18</sup>F-FDG PET/CT at the time of diagnosis is associated with improved cancer-specific survival (14).

Given these benefits, the National Comprehensive Cancer Network (NCCN) currently recommends that all patients, regardless of stage, be routinely screened for recurrence using CT of the chest, with or without contrast enhancement. If there is evidence of recurrence, <sup>18</sup>F-FDG PET/CT is recommended to evaluate for locoregional recurrence versus distant metastases (15). Prior studies of various cancers, including colon cancer, soft-tissue sarcoma, epithelial ovarian cancer, pancreatic cancer, and NSCLC, have shown that improved adherence to NCCN guidelines leads to improved outcomes in survival (16–20). Research has demonstrated a lack of compliance of imaging and treatment recommendations in patients with lung cancer (14,21,22). We hypothesized that in the case of NSCLC that is being treated with subsequent RT, many patients are not undergoing guideline-recommended imaging and that this lack of adherence is associated with lower patient survival.

---

Received Mar. 16, 2022; revision accepted Jun. 2, 2022.  
For correspondence or reprints, contact Rustain Morgan (rustain.morgan@ucanschutz.edu).  
Published online Jun. 9, 2022.  
COPYRIGHT © 2023 by the Society of Nuclear Medicine and Molecular Imaging.

**TABLE 1**  
 Characteristics by Imaging Modality Before Subsequent RT of NSCLC Patients

Characteristic	Total	CT/CTA alone	Any PET	<i>P</i>
All patients	5,017	2,188	2,829	
Race/ethnicity category				
White NH	4,223 (84.2)	1,786 (81.6)	2,437 (86.1)	<0.0001*
Black NH	337 (6.7)	183 (8.4)	154 (5.4)	
Hispanic	179 (3.6)	80 (3.7)	99 (3.5)	
Other/unknown	278 (5.5)	139 (6.4)	139 (4.9)	
Patient region at diagnosis				
East	1,061 (21.1)	493 (22.5)	568 (20.1)	0.0215*
Midwest	617 (12.3)	285 (13.0)	332 (11.7)	
South	1,510 (30.1)	618 (28.2)	892 (31.5)	
West	1,829 (36.5)	792 (36.2)	1,037 (36.7)	
Facility type				
National Cancer Institute center	605 (12.1)	296 (13.5)	309 (10.9)	0.0179*
Teaching hospital	2,021 (40.3)	873 (39.9)	1,148 (40.6)	
Other/no hospital	2,391 (47.7)	1,019 (46.6)	1,372 (48.5)	
Derived AJCC stage group, sixth edition				
Stage I	1,597 (31.8)	518 (23.7)	1,079 (38.1)	<0.0001*
Stage II	472 (9.4)	160 (7.3)	312 (11.0)	
Stage III	1,511 (30.1)	675 (30.9)	836 (29.6)	
Stage IVA	1,437 (28.6)	835 (38.2)	602 (21.3)	
Initial treatment				
RT	943 (18.8)	385 (17.6)	558 (19.7)	<0.0001*
Surgery	1,217 (24.3)	421 (19.2)	796 (28.1)	
Chemotherapy	659 (13.1)	402 (18.4)	257 (9.1)	
Surgery and RT	112 (2.2)	39 (1.8)	73 (2.6)	
Chemotherapy and RT	1,348 (26.9)	676 (30.9)	672 (23.8)	
Chemotherapy and surgery	488 (9.7)	158 (7.2)	330 (11.7)	
Chemotherapy, surgery, and RT	250 (5.0)	107 (4.9)	143 (5.1)	
Diagnostic imaging category				
CT/CTA alone	531 (10.6)	285 (13.0)	246 (8.7)	<0.0001*
Any PET	4,440 (88.5)	1,885 (86.2)	2,555 (90.3)	
No related imaging	46 (0.9)	18 (0.8)	28 (1.0)	
Histologic subtype of NSCLC				
Adenocarcinoma	2,546 (50.7)	1,157 (52.9)	1,389 (49.1)	<0.0001*
Adenosquamous	120 (2.4)	47 (2.1)	73 (2.6)	
Large cell carcinoma	117 (2.3)	54 (2.5)	63 (2.2)	
Neuroendocrine	89 (1.8)	57 (2.6)	32 (1.1)	
Squamous cell carcinoma	1,542 (30.7)	601 (27.5)	941 (33.3)	
Other/not specified	603 (12.0)	272 (12.4)	331 (11.7)	

\*Statistically significant ( $P < 0.05$ ).

NH = non-Hispanic; AJCC = American Joint Committee on Cancer.

Data are *n* followed by percentage in parentheses.

## MATERIALS AND METHODS

### Data Sources

This was a retrospective study of patients with NSCLC in the Surveillance, Epidemiology, and End Results (SEER) Medicare-linked database. We compared the outcomes of patients who underwent RT

for oligoprogressive or recurrent disease based on whether their most recent imaging was CT or <sup>18</sup>F-FDG PET/CT. SEER, a program of the National Cancer Institute, includes information on patient demographics, tumor characteristics at diagnosis, and treatment information from 18 population-based tumor registries that cover approximately

**TABLE 2**  
Logistic Regression Predicting Whether Patients Received PET

Characteristic	OR	P	Global P
<b>Race/ethnicity category</b>			
White NH (ref)			0.0044*
Black NH vs. White NH	0.688 (0.54–0.88)	0.0023*	
Hispanic vs. White NH	0.958 (0.70–1.32)	0.7944	
Other/unknown vs. White NH	0.752 (0.58–0.98)	0.0336*	
<b>Patient region at diagnosis</b>			
West (ref)			0.0374*
East vs. west	0.799 (0.67–0.95)	0.0111*	
Midwest vs. west	0.856 (0.70–1.05)	0.1390	
South vs. west	0.996 (0.85–1.17)	0.9655	
<b>Derived AJCC stage group, sixth edition</b>			
Stage I (ref)			<0.0001*
Stage II vs. stage I	0.880 (0.70–1.11)	0.2769	
Stage III vs. stage I	0.695 (0.58–0.83)	<0.0001*	
Stage IVA vs. stage I	0.455 (0.38–0.55)	<0.0001*	
<b>Initial treatment</b>			
RT (ref)			<0.0001*
Chemotherapy vs. RT	0.625 (0.50–0.78)	<0.0001*	
Chemotherapy and RT vs. RT	0.827 (0.69–1.00)	0.0464*	
Chemotherapy and surgery vs. RT	1.337 (1.04–1.72)	0.0223*	
Chemotherapy, surgery, and RT vs. RT	0.969 (0.72–1.31)	0.8356	
Surgery vs. RT	1.093 (0.90–1.33)	0.3676	
Surgery and RT vs. RT	1.259 (0.83–1.92)	0.2843	
<b>Diagnostic imaging category</b>			
Any PET (ref)			0.0002*
CT/CTA alone vs. any PET	0.673 (0.56–0.81)	<0.0001*	
No related imaging vs. any PET	1.178 (0.64–2.18)	0.6019	
<b>Histologic subtype of NSCLC</b>			
Adenocarcinoma (ref)			0.0183*
Adenosquamous vs. adenocarcinoma	1.065 (0.72–1.57)	0.7528	
Large cell carcinoma vs. adenocarcinoma	0.920 (0.62–1.35)	0.6718	
Neuroendocrine vs. adenocarcinoma	0.576 (0.36–0.91)	0.0187*	
Squamous cell carcinoma vs. adenocarcinoma	1.176 (1.02–1.35)	0.0212*	
Other/not specified vs. adenocarcinoma	1.148 (0.95–1.39)	0.1537	

\*Statistically significant ( $P < 0.05$ ).

NH = non-Hispanic; AJCC = American Joint Committee on Cancer.

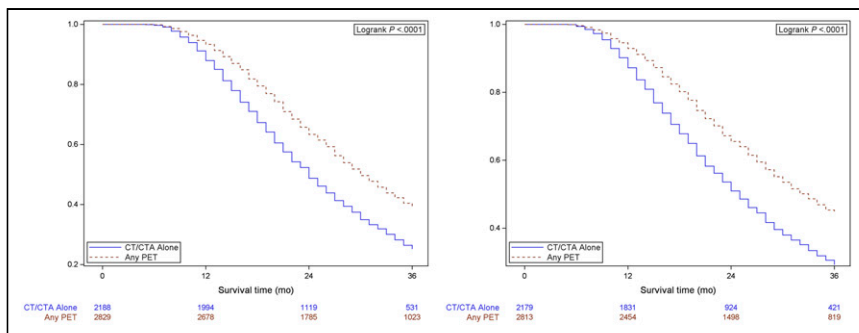
Data in parentheses are 95% CIs.

28% of the U.S. population. Medicare claims provide information on the health services received and on the facility where they were received, and census information is linked to the SEER data for additional geographically based sociodemographic factors (23,24).

#### Cohort Selection

We selected patients aged 66 y or older at diagnosis, whose first primary tumor was NSCLC, diagnosed from 2007 through 2015. Patients were included at this age so there would be at least 1 y of data to identify patients who had cancer before enrolling in Medicare.

We excluded patients who were diagnosed via death certificate or at autopsy, as well as patients who had an unknown diagnosis date. We required continuous enrollment in fee-for-service Medicare parts A and B from 12 mo before through 12 mo after the month of diagnosis (or until death if it occurred within 12 mo) to ensure a complete claims history for comorbidities before diagnosis and for services received after diagnosis. We also excluded patients who had no paid claims in the 12 mo after diagnosis, patients who were stage 0, patients who were missing the census tract, and patients who had an unknown stage, rural measure, or race.



**FIGURE 1.** Impact of imaging modality (CT/CTA alone vs. any PET) on 3-yr overall (left) and cancer-specific (right) survival in patients with NSCLC, according to SEER, 2007–2015.

To best identify patients with disease requiring subsequent RT, we required a specific sequence of events to have occurred after diagnosis. From the cohort, we identified anyone who received initial treatment within 6 mo of diagnosis and had subsequent RT within 36 mo of completion of the initial treatment. A gap of 90 d or more was required to distinguish the initial treatment and subsequent treatment. As we were interested in outcomes by modality of imaging for oligoproliferative disease, we further limited our sample to patients with imaging occurring within 60 d before the subsequent RT. Our final sample with qualifying treatment and imaging included 5,017 patients. All inclusion and exclusion criteria are outlined in Supplemental Figure 1 (supplemental materials are available at <http://jnm.snmjournals.org>). Per NCCN guidelines regarding treatment, this sample could include patients with local or metastatic recurrent disease or patients with progression at a limited number of sites (oligoproliferative disease).

We used the International Classification of Diseases, ninth and 10th revisions; clinical modification codes; current procedural terminology codes; and Healthcare Common Procedure Coding System codes to identify the diagnoses and procedures.

#### Treatment Identification

Initial treatment was defined as chemotherapy, RT, or surgery for NSCLC within 6 mo after diagnosis. We categorized initial treatment as surgery alone, RT alone, chemotherapy alone, surgery and RT, surgery and chemotherapy, chemoradiotherapy, or surgery and chemoradiotherapy. We required at least 90 d to define separate treatment periods; subsequent RT after the initial treatment period was defined as having occurred at least 90 d after initial treatment. We also required this subsequent RT to have occurred within 36 mo of initial treatment. Codes used to identify initial treatment and subsequent RT can be found in Supplemental Table 1.

#### Imaging Identification

Imaging procedures of interest were defined as imaging occurring after initial treatment and within 60 d before subsequent RT. These were categorized into 2 groups: CT or CT angiography (CTA) of the abdomen, chest, and pelvis, and any  $^{18}\text{F}$ -FDG PET either with or without CT/CTA. Initial imaging at the time of diagnosis was also assessed. The imaging codes used in this study can be found in Supplemental Table 1.

#### Statistical Analysis

For comparing baseline characteristics of demographic and diagnostic information,  $\chi^2$  testing was performed to test statistically significant differences in each categorical variable by imaging modality. The categories tested were year of diagnosis, age at diagnosis (66–69, 70–74, or  $\geq 75$  y), race (White, Black, Hispanic, or other/unknown), sex (male or female), marital status (married/partner or single), region, residence (in an urban area or not), socioeconomic status (poverty level and

percentage of individuals with a high school education or less), comorbidities before diagnosis, facility type (National Cancer Institute–designated center, teaching hospital, or other/no hospital), initial derived American Joint Committee on Cancer Stage Group (sixth edition), initial imaging results, histology subtype, and type of initial treatment. The reason for analyzing race is that multiple prior studies have shown that racial and ethnic minorities are not receiving the recommended imaging for their disease. We used Medicare claims from the year before diagnosis to estimate the Charlson comorbidity index according to the National Cancer Institute’s adaptation of the algorithm of Klabunde et al. (25).

Logistic regression was performed to identify predictors of imaging type, adjusting for the covariates included in the univariate table, and odds ratios (ORs) between groups were compared.

Overall survival and cancer-specific survival between imaging modalities was estimated at 36 mo after diagnosis. Overall survival was determined using Medicare-reported dates of death, which are reported through December 2018. However, cancer-specific survival was determined using SEER-reported dates of death, which include cause of death and are through December 2016. Patients living longer than 36 mo were censored at 36 mo.

The Kaplan–Meier method and unadjusted Cox proportional hazards were used for univariate survival analyses. Multivariate cancer-specific survival analyses were completed using Cox proportional-hazards models, adjusting for covariates. The proportional-hazards assumption was evaluated using Schoenfeld residuals, and violations were addressed using time-dependent interaction terms in multivariable models. A forward-stepwise analysis was completed. The base model included demographic characteristics; the stratified model added stage, initial treatment, and facility type to the base model; and the full model included all previous covariates and the imaging modality.

All statistical analyses were performed with SAS, version 9.4 (SAS Institute), and evaluated at a critical  $\alpha$  of 0.05. The study was reviewed and approved by the University of Colorado Institutional Review Board. It was conducted under a data use agreement with the National Cancer Institute.

#### RESULTS

We identified a total of 5,017 patients who underwent subsequent RT for oligoproliferative or recurrent NSCLC after completing initial therapy. Of these patients, 84.2% were non-Hispanic White, 6.7% were Black, 3.6% were Hispanic, and 5.5% were other/unknown. In total, 2,829 (56.3%) patients underwent  $^{18}\text{F}$ -FDG PET/CT before subsequent RT, whereas 2,188 (43.6%) patients had imaging with CT/CTA alone (Table 1). Of note, patients with an initial treatment of surgery demonstrated increased PET/CT use (65.4% had a PET/CT) whereas patients with an initial treatment of chemotherapy had decreased PET/CT use (38.9% had PET/CT) (Table 1; Supplemental Table 2). There was no difference in imaging use between National Cancer Institute centers, teaching hospitals, or other/no hospital (Supplemental Table 3).

There was a significant difference in PET/CT use depending on initial patient stage and initial treatment regimen. Stages III and IV were less likely to be imaged with  $^{18}\text{F}$ -FDG PET/CT than stages I and II (OR, 0.695 [95% CI, 0.58–0.83;  $P < 0.0001$ ] and 0.455 [95% CI, 0.38–0.55;  $P < 0.0001$ ], respectively). Overall, patients

**TABLE 3**  
Multivariate Analysis of Survival at 3-Year Follow-Up

Characteristic	Overall survival			Cancer-specific survival		
	Hazard ratio	<i>P</i>	Global <i>P</i>	Hazard ratio	<i>P</i>	Global <i>P</i>
<b>Age category (y)</b>						
66–69 (ref)			0.0066*			0.0079*
70–74	0.988 (0.90–1.08)	0.7992		0.940 (0.85–1.04)	0.2436	
≥75	1.115 (1.02–1.22)	0.0157*		1.089 (0.99–1.20)	0.0901	
<b>Sex</b>						
Male (ref)			0.0012*			0.0008*
Female	0.886 (0.82–0.95)	0.0012*		0.869 (0.80–0.94)	0.0008*	
<b>Facility type</b>						
National Cancer Institute center (ref)			0.0174*			0.0191*
Other/no hospital	1.151 (1.02–1.30)	0.0205*		1.164 (1.02–1.33)	0.0280*	
Teaching hospital	1.050 (0.93–1.18)	0.4213		1.047 (0.91–1.20)	0.5064	
<b>Derived AJCC stage group, sixth edition</b>						
Stage I (ref)			<0.0001*			<0.0001*
Stage II	1.906 (1.62–2.25)	<0.0001*		1.920 (1.59–2.31)	<0.0001*	
Stage III	2.057 (1.67–2.54)	<0.0001*		2.135 (1.70–2.69)	<0.0001*	
Stage IVA	2.810 (2.11–3.74)	<0.0001*		2.846 (2.08–3.89)	<0.0001*	
<b>Initial treatment</b>						
Radiation (ref)			<0.0001*			<0.0001*
Chemotherapy	0.681 (0.58–0.80)	<0.0001*		0.696 (0.58–0.83)	<0.0001*	
Chemotherapy and RT	0.533 (0.42–0.67)	<0.0001*		0.537 (0.42–0.69)	<0.0001*	
Chemotherapy and surgery	0.278 (0.20–0.38)	<0.0001*		0.272 (0.19–0.38)	<0.0001*	
Chemotherapy, surgery, and RT	0.337 (0.23–0.49)	<0.0001*		0.330 (0.22–0.50)	<0.0001*	
Surgery	0.673 (0.59–0.76)	<0.0001*		0.675 (0.58–0.78)	<0.0001*	
Surgery and RT	0.466 (0.34–0.63)	<0.0001*		0.415 (0.29–0.59)	<0.0001*	
<b>Histologic subtype of NSCLC</b>						
Adenocarcinoma (ref)			<0.0001*			0.0005*
Adenosquamous	1.471 (1.17–1.85)	0.0010*		1.392 (1.07–1.81)	0.0138*	
Large cell carcinoma	1.416 (1.11–1.81)	0.0059*		1.315 (1.00–1.72)	0.0470*	
Neuroendocrine	1.375 (1.02–1.85)	0.0342*		1.455 (1.05–2.01)	0.0232*	
Squamous cell carcinoma	1.719 (1.40–2.11)	<0.0001*		1.644 (1.32–2.05)	<0.0001*	
Other/not specified	1.728 (1.34–2.23)	<0.0001*		1.687 (1.28–2.22)	0.0002*	
<b>Diagnostic imaging category</b>						
Any PET (ref)			<0.0001*			0.0001*
CT/CTA alone	2.089 (1.55–2.81)	<0.0001*		1.986 (1.45–2.73)	<0.0001*	
No related imaging	0.438 (0.27–0.72)	0.0011*		0.448 (0.26–0.77)	0.0039*	
<b>Imaging category before subsequent RT</b>						
Any PET (ref)			<0.0001*			<0.0001*
CT/CTA alone	1.417 (1.32–1.52)	<0.0001*		1.430 (1.32–1.55)	<0.0001*	

\*Statistically significant ( $P < 0.05$ ).

AJCC = American Joint Committee on Cancer.

Hazard ratios are lower confidence limit to upper confidence limit.

who received initial treatment with chemotherapy or chemotherapy and RT were less likely to undergo imaging with  $^{18}\text{F}$ -FDG PET/CT than with RT alone (OR, 0.625 [95% CI, 0.50–0.78;  $P < 0.0001$ ] and 0.827 [95% CI, 0.69–1.00;  $P = 0.0464$ ], respectively).

Conversely, patients who received initial treatment with chemotherapy plus surgery were more likely to have imaging with  $^{18}\text{F}$ -FDG PET/CT (OR, 1.337 [95% CI, 1.04–1.72;  $P = 0.0223$ ]). Patients of Black or other/unknown ethnicity were less likely to have imaging

with PET/CT than White non-Hispanic patients (OR, 0.688 [95% CI, 0.54–0.88;  $P = 0.0023$ ] and 0.752 [95% CI, 0.58–0.98;  $P = 0.0336$ ], respectively). Patients initially imaged with CT/CTA alone were also less likely to have subsequent imaging with PET (OR, 0.673 [95% CI, 0.56–0.81;  $P < 0.0001$ ]) (Table 2).

When survival was compared over a 3-y follow-up period, patients who had undergone CT/CTA alone rather than  $^{18}\text{F}$ -FDG PET/CT before subsequent RT had a lower overall survival (hazard ratio, 1.417 [95% CI, 1.32–1.52;  $P < 0.0001$ ]) and cancer-specific survival (hazard ratio, 1.430 [95% CI, 1.32–1.55;  $P < 0.0001$ ]) (Fig. 1; Table 3) when controlling for initial stage, initial diagnostic imaging, and histologic subtype. Other factors associated with decreased survival included being male, being older, having a histologic subtype other than adenocarcinoma, undergoing initial diagnostic imaging with CT/CTA alone, and having stages II, III, or IV (Table 3, Supplemental Table 4). Overall and cancer-specific survival was increased in the other/unknown race category (hazard ratio, 0.823 [95% CI, 0.70–0.97;  $P = 0.0195$ ] and 0.799 [95% CI, 0.67–0.96;  $P = 0.0162$ ], respectively).

## DISCUSSION

This study demonstrated a significant lack of adherence to guideline-based imaging recommendations, which negatively impacts the survival of patients with NSCLC. Approximately 1 of every 2 patients who undergo subsequent RT does not undergo the recommended pre-RT  $^{18}\text{F}$ -FDG PET/CT examination. This lack of adherence is present throughout all institutions, regardless of patient volume or the frequency of patient encounters.

In general, patients with higher stages of disease, especially stage III or IVA, were less likely to undergo  $^{18}\text{F}$ -FDG PET/CT before subsequent RT. Patients who initially received treatment with chemotherapy or chemotherapy and RT were less likely to be imaged with PET/CT. Patients who initially received chemotherapy with or without RT instead of surgery likely had a higher stage of disease at initial diagnosis. This disparity in the lack of  $^{18}\text{F}$ -FDG PET/CT in patients with higher stages of disease could be a result of provider bias against patients with advanced disease, for whom CT or CTA is considered adequate for monitoring rather than the more sensitive  $^{18}\text{F}$ -FDG PET/CT imaging, which is used more for lower-stage disease that is more carefully evaluated for recurrence. These trends suggest specific areas for improvement in practice patterns, with focused efforts to increase adherence to NCCN guidelines.

The advantage of PET/CT lies in its superior ability to detect metabolically active target sites for RT, which improves disease control and, in turn, survival. Prior studies have suggested that PET/CT improves detection of sites in oligoprogressive disease (6). The survival benefit associated with hybrid imaging was again demonstrated in this study, regardless of disease stage. Patients who underwent  $^{18}\text{F}$ -FDG PET/CT for either initial or subsequent imaging experienced improved overall and cancer-specific survival over a 3-y period compared with CT/CTA alone or other imaging. Greater adherence to NCCN guidelines was associated with improved survival for NSCLC patients.

In addition to institutional practices that may influence PET/CT use, insurance denials are a common barrier to use of advanced diagnostic imaging. Although exact clinical circumstances vary between patients, in general, PET/CT scans are covered under Medicare for the diagnosis, staging, and restaging of NSCLC (26). The population in our study should have met PET/CT insurance coverage criteria for purposes of restaging after recurrence or progression and before subsequent RT.

Our findings are relevant because they support the importance of following current clinical NCCN guidelines and show a lack of guideline adherence in many circumstances. There is an opportunity to improve PET/CT use and possibly cancer-specific survival through increased provider awareness and an active intent to change. Prior studies have suggested routine chart review and audits (27) or the use of a tumor board with a dedicated oncology nurse navigator to improve adherence to NCCN guidelines (28). Our findings suggest that substantial effort is still required to improve adherence on a national scale.

There are several limitations to our study. Our analyses were based on SEER registry data in a Medicare fee-for-service population, with required coverage 12 mo before and after diagnosis, decreasing our sample size and limiting generalizability to all Medicare patients. Application to younger patients or patients with other forms of insurance (or uninsured) requires further study. The SEER data available for analysis include patients treated between 2005 and 2014, which limits our staging analysis to the American Joint Committee on Cancer sixth edition rather than the more recently updated eighth edition. Because the SEER data also include only initial stage, we cannot account for extent of disease at the time of subsequent RT. SEER registries are reported to have a greater economic disadvantage, and greater racial and ethnic diversity, which may limit the generalizability of results to the national population (29). Although our multivariable analysis controlled for numerous independent variables such as age, stage, sex, and facility, there may be unobservable characteristics that also impact the disparate use of imaging (30).

## CONCLUSION

Nearly half of Medicare patients with NSCLC who undergo subsequent RT are not being staged according to NCCN guidelines. There is decreased overall and cancer-specific survival for patients who undergo imaging with CT/CTA alone rather than  $^{18}\text{F}$ -FDG PET/CT. Further research is needed to identify additional factors that contribute to overall survival, causes of current disparities in PET/CT use, and interventions to improve adherence to NCCN guidelines.

## DISCLOSURE

Sana D. Karam is funded by the NIDCR (P50 CA261605-01, R01 DE028529-01, and R01 DE028282-01) and receives clinical trial funding from AstraZeneca and Genentech as well as preclinical funding from Roche for work unrelated to this research. This project was supported by the Population Health Shared Resource of the University of Colorado Cancer Center (P30CA046934). No other potential conflict of interest relevant to this article was reported.

## KEY POINTS

**QUESTION:** Are patients with recurrent NSCLC being imaged according to national guidelines, and if not, is this affecting mortality outcomes?

**PERTINENT FINDINGS:** This retrospective analysis of NSCLC patients in the SEER-Medicare database found that 43.6% of patients did not undergo the guideline-recommended imaging with PET/CT, and patients with CT/CTA alone had a statistically significant decreased overall and cancer-specific survival.

**IMPLICATIONS FOR PATIENT CARE:** The lack of guideline-recommended PET/CT imaging for NSCLC patients affects survival rates.

## REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin*. 2020; 70:7–30.
2. Ettinger DS, Aisner DL, Wood DE, et al. NCCN guidelines insights: non–small cell lung cancer, version 5.2018. *J Natl Compr Canc Netw*. 2018;16:807–821.
3. Kim C, Hoang CD, Kesarwala AH, Schrupp DS, Guha U, Rajan A. Role of local ablative therapy in patients with oligometastatic and oligoprogressive non-small cell lung cancer. *J Thorac Oncol*. 2017;12:179–193.
4. Chao F, Zhang H. PET/CT in the staging of the non-small-cell lung cancer. *J Biomed Biotechnol*. 2012;2012:783739.
5. Hicks RJ, Mac Manus MP, Matthews JP, et al. Early FDG-PET imaging after radical radiotherapy for non-small-cell lung cancer: inflammatory changes in normal tissues correlate with tumor response and do not confound therapeutic response evaluation. *Int J Radiat Oncol Biol Phys*. 2004;60:412–418.
6. Ng TL, Morgan RL, Patil T, Baron AE, Smith DE, Ross Camidge D. Detection of oligoprogressive disease in oncogene-addicted non-small cell lung cancer using PET/CT versus CT in patients receiving a tyrosine kinase inhibitor. *Lung Cancer*. 2018;126:112–118.
7. Maziak DE, Darling GE, Inculet RI, et al. Positron emission tomography in staging early lung cancer: a randomized trial. *Ann Intern Med*. 2009;151:221–228.
8. van Tinteren H, Hoekstra OS, Smit EF, et al. Effectiveness of positron emission tomography in the preoperative assessment of patients with suspected non-small-cell lung cancer: the PLUS multicentre randomised trial. *Lancet*. 2002;359:1388–1393.
9. Viney RC, Boyer MJ, King MT, et al. Randomized controlled trial of the role of positron emission tomography in the management of stage I and II non-small-cell lung cancer. *J Clin Oncol*. 2004;22:2357–2362.
10. Kubota K, Matsuno S, Morioka N, et al. Impact of FDG-PET findings on decisions regarding patient management strategies: a multicenter trial in patients with lung cancer and other types of cancer. *Ann Nucl Med*. 2015;29:431–441.
11. Park HL, Yoo IR, Boo SH, et al. Does FDG PET/CT have a role in determining adjuvant chemotherapy in surgical margin-negative stage IA non-small cell lung cancer patients? *J Cancer Res Clin Oncol*. 2019;145:1021–1026.
12. Tosi D, Pieropan S, Cattoni M, et al. Prognostic value of <sup>18</sup>F-FDG PET/CT metabolic parameters in surgically treated stage I lung adenocarcinoma patients. *Clin Nucl Med*. 2021;46:621–626.
13. Dong M, Liu J, Sun X, Xing L. Prognostic significance of SUVmax on pretreatment <sup>18</sup>F-FDG PET/CT in early-stage non-small cell lung cancer treated with stereotactic body radiotherapy: a meta-analysis. *J Med Imaging Radiat Oncol*. 2017; 61:652–659.
14. Morgan RL, Karam SD, Bradley CJ. Ethnic disparities in PET/CT utilization at diagnosis of non-small cell lung cancer. *J Natl Cancer Inst*. 2020.
15. Ettinger DS, Wood DE, Aisner DL, et al. NCCN guidelines insights: non-small cell lung cancer, version 2.2021. *J Natl Compr Canc Netw*. 2021;19:254–266.
16. Boland GM, Chang GJ, Haynes AB, et al. Association between adherence to National Comprehensive Cancer Network treatment guidelines and improved survival in patients with colon cancer. *Cancer*. 2013;119:1593–1601.
17. Voss RK, Chiang YJ, Torres KE, et al. Adherence to National Comprehensive Cancer Network guidelines is associated with improved survival for patients with stage 2A and stages 2B and 3 extremity and superficial trunk soft tissue sarcoma. *Ann Surg Oncol*. 2017;24:3271–3278.
18. John A, Yang B, Shah R. Clinical impact of adherence to NCCN guidelines for biomarker testing and first-line treatment in advanced non-small cell lung cancer (aNSCLC) using real-world electronic health record data. *Adv Ther*. 2021;38: 1552–1566.
19. Lee JY, Kim TH, Suh DH, et al. Impact of guideline adherence on patient outcomes in early-stage epithelial ovarian cancer. *Eur J Surg Oncol*. 2015;41:585–591.
20. Visser BC, Ma Y, Zak Y, Poultsides GA, Norton JA, Rhoads KF. Failure to comply with NCCN guidelines for the management of pancreatic cancer compromises outcomes. *HPB (Oxford)*. 2012;14:539–547.
21. Schneider CS, Oster RA, Hegde A, Dobelbower MC, Stahl JM, Kole AJ. Nonoperative treatment of large (5–7 cm), node-negative non-small cell lung cancer commonly deviates from NCCN guidelines. *J Natl Compr Canc Netw*. 2021;20:371–377.e5.
22. Shikdar S, Sahu S, Jadhav G, et al. National Comprehensive Cancer Network (NCCN) guideline compliance for lung cancer in a community teaching hospital. *J Clin Oncol*. 2018;36:e18860.
23. Overview of the SEER program. NIH website. <https://seer.cancer.gov/about/overview.html>. Accessed October 12, 2022.
24. SEER-Medicare: brief description of the SEER-Medicare database. NIH website. <https://healthcareelivery.cancer.gov/seermedicare/overview>. Published May 16, 2019. Accessed October 12, 2022.
25. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. *J Clin Epidemiol*. 2000;53:1258–1267.
26. PET scans. CMS website. <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=211&ncdver=3&bc=AAAAEAAAQAA&>. Accessed October 12, 2022.
27. Jazieh A, Alkaiyat MO, Ali Y, Hashim MA, Abdelhafiz N, Al Olayan A. Improving adherence to lung cancer guidelines: a quality improvement project that uses chart review, audit and feedback approach. *BMJ Open Qual*. 2019;8:e000436.
28. Peckham J, Mott-Coles S. Interprofessional lung cancer tumor board: the role of the oncology nurse navigator in improving adherence to national guidelines and streamlining patient care. *Clin J Oncol Nurs*. 2018;22:656–662.
29. Kuo T-M, Mobley LR. How generalizable are the SEER registries to the cancer populations of the USA? *Cancer Causes Control*. 2016;27:1117–1126.
30. Gould MK, Schultz EM, Wagner TH, et al. Disparities in lung cancer staging with positron emission tomography in the Cancer Care Outcomes Research and Surveillance (CanCORS) study. *J Thorac Oncol*. 2011;6:875–883.