Facility-Level Analysis of PET Scanning for Staging Among US Veterans With Non-small Cell Lung Cancer

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Background: PET scanning has been shown in randomized trials to reduce the frequency of surgery without cure among patients with potentially resectable non-small cell lung cancer (NSCLC). We examined whether more frequent use of PET scanning at the facility level improves survival among patients with NSCLC in real-world practice.

Methods: In this prospective cohort study of 622 US veterans with newly diagnosed NSCLC, we compared groups defined by the frequency of PET scan use measured at the facility level and categorized as low (<25%), medium (25%-60%), or high (>60%).

Results: The median age of the sample was 69 years. Ninety-eight percent were men, 36% were Hispanic or nonwhite, and 54% had moderate or severe comorbidities. At low-, medium-, and high-use facilities, PET scan was performed in 13%, 40%, and 72% of patients, respectively ($P < .0001$). Baseline characteristics were similar across groups, including clinical stage based on CT scanning. More frequent use of PET scanning was associated with more frequent invasive staging ($P < .001$) and nonsignificant improvements in downstaging ($P = .13$) and surgery without cure ($P = .12$). After a median of 352 days of follow-up, 22% of the sample was still alive, including 22% at low- and medium-use facilities and 20% at high-use facilities. After adjustment and compared with patients at low-use facilities, the hazard of death was greater for patients at high-use facilities (adjusted hazard ratio [HR], 1.35; 95% CI, 1.05-1.74) but not different for patients at medium-use facilities (adjusted HR, 1.14; 95% CI, 0.88-1.46).

Conclusions: In this study of veterans with NSCLC, markedly greater use of PET scanning at the facility level was associated with more frequent use of invasive staging and possible improvements in downstaging and surgery without cure, but greater use of PET scanning was not associated with better survival.

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Abbreviations: CanCORS = Cancer Care Outcomes Research and Surveillance; NSCLC = non-small cell lung cancer; VHA = Veterans Health Administration

PET scanning is more accurate than CT scanning for identifying malignant mediastinal lymph nodes in patients with non-small cell lung cancer (NSCLC).¹ Guidelines developed by the American College of Chest Physicians and the National Comprehensive Cancer Network recommend that PET scan be used to help stage lung cancer in patients who are candidates for curative treatment.^{2,3} Three randomized controlled trials in patients with potentially resectable NSCLC found that compared with conventional staging, PET scan-based staging reduced the frequency of thoracotomy without cure.⁴⁻⁶ However, in the majority of patients with NSCLC who have unresectable

disease or are medically inoperable, PET scan-based staging strategies have not been evaluated in randomized trials, and few studies have examined use of PET scanning and outcomes in real-world populations. The overuse of tests and procedures has important implications for both patient safety and health-care cost control, and the use of imaging tests for cancer staging is one of the top 25 priorities of the Institute of Medicine for comparative effectiveness research.⁷ In this prospective observational study, we examined the effectiveness of PET scanning by comparing survival and other outcomes among veterans with NSCLC who received care at Veterans Health Administration (VHA)

hospitals that differed considerably in how frequently they used PET scanning.

MATERIALS AND METHODS

To examine the association between use of PET scanning and outcomes among patients with NSCLC, we used data from the Cancer Care Outcomes Research and Surveillance (CanCORS) study, a prospective observational study of practices and outcomes for patients with lung and colorectal cancer.⁸ All patients or an appropriate surrogate provided informed consent. Human subjects committees at Stanford University and all participating sites approved the study. This article was approved by the CanCORS Publications Committee. Additional details about the methods can be found in e-Appendix 1.

Patients

CanCORS used rapid case ascertainment to prospectively enroll incident lung cancer cases in four large, geographically defined regions, five integrated health-care systems, and 13 health-care facilities of the VHA (e-Appendix 1, e-Table 1). Eligible patients were given a diagnosis of lung cancer between September 1, 2003, and October 14, 2005. For this analysis, we included all CanCORS participants with NSCLC who were enrolled at a VHA facility and whose VHA medical records were available. We did not have access to non-VHA records.

Variables

The CanCORS baseline patient survey included items about age, sex, race, ethnicity, insurance coverage, annual household income, and level of education. Professional chart abstractors collected information about comorbidities,^{9,10} tumor size, histology, and stage. Independently, we collected additional information about symp-

toms, signs, imaging tests, procedures, consultations, and outcomes by reviewing the electronic medical records of all VHA CanCORS participants. We collected facility-level information by performing a survey of lung cancer practices that was completed by the VHA CanCORS principal investigator at each site.

To characterize patients by the extent of disease at the earliest possible time in the course of their evaluation, we reviewed electronic transcripts of CT scan reports for evidence of hilar (N1), mediastinal (N2 or N3), or distant (M1) tumor involvement and subsequently classified patients as having N0M0, N1M0, N2/3M0, or M1 disease on the basis of CT scan findings. We used identical methods to classify patients on the basis of PET scan reports.

The main exposure variable of interest was the frequency at which the PET scan was obtained prior to treatment at the facility level. Noting that PET scan use varied widely across VHA facilities during the study period, we classified facilities by frequency of PET scanning as low (<25%), medium (25%-60%), or high (>60%) (e-Appendix 1, e-Table 1) use.

The primary outcome was survival measured from the date of initial suspicion until the date of death or censoring. Other outcomes were use of noninvasive imaging tests; invasive staging procedures; other tests and consultations; and frequency of upstaging, downstaging, and surgery without cure. We determined upstaging and downstaging by comparing stage by CT scan with stage by PET scan or final stage. Similar to the definitions used in two randomized trials, we defined surgery without cure as identification of unresectable disease at the time of surgery or recurrence or death within 1 year of the operation.^{4,6}

Statistical Analysis

For bivariate comparisons, we performed χ^2 tests for categorical variables and Kruskal-Wallis tests for continuous variables. We examined survival by using the Kaplan-Meier method. To adjust for residual differences between groups and identify patient and tumor characteristics that were independently associated with survival, we performed Cox proportional hazards analysis that included all candidate predictor variables, adjusting for stage by CT scan rather than for final stage because more accurate staging is the mechanism by which PET scan is expected to improve survival and because adjusting for this mediating factor would obscure a true association between PET scanning and survival, if one existed. We tested for subgroup effects by entering interaction terms for all variables of interest into multivariate models and by performing selected stratified analyses. We performed sensitivity analyses by developing additional logistic regression models that (1) measured survival from the date of diagnosis instead of the date on which lung cancer was initially suspected, (2) categorized the frequency of PET scanning as low (<25%) vs medium or high ($\geq 25\%$), and (3) included 165 patients with unknown histology.

RESULTS

Of 926 potentially eligible VHA CanCORS participants with lung cancer, we excluded 289 with small cell or unknown histology and 15 with recurrent lung cancer or missing records (Fig 1). The resulting sample included 622 VA CanCORS participants with NSCLC.

Patient, Tumor, and Facility Characteristics

The median age of the sample participants was 69 years (Table 1). Almost all participants were men, and 36% were of Hispanic ethnicity or nonwhite race.

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FIGURE 1. Cohort assembly. CanCORS = Cancer Care Outcomes Research and Surveillance Study; NSCLC = non-small cell lung cancer; VHA = Veterans Health Administration.

Stage distribution by CT scan was N0M0 in 38%, N1M0 in 4%, N2/3M0 in 21%, and M1 in 38%. Almost 40% of VHA CanCORS participants received a PET scan prior to treatment. Stage distribution by PET scan was N0M0 in 44%, N1M0 in 8%, N2/3M0 in 15%, and M1 in 30%. Final stage was local in 33%, regional in 31%, and distant in 35%.

PET scan was obtained prior to treatment in 13%, 40%, and 72% of patients at facilities with low, medium, and high PET scan use, respectively. Across the three types of facilities, sociodemographic, tumor, and facility characteristics were similar, although there were more Hispanics and nonwhites ($P < .0001$) and more patients with squamous histology ($P < .0001$) at low-use facilities (Tables 1, 2). However, the groups were not significantly different with respect to symptoms and signs, comorbidities ($P = .33$), tumor size ($P = .12$), most CT scan findings, and stage by CT scan ($P = .66$).

Imaging Tests, Procedures, and Treatment

As shown in Table 3, the median number of imaging tests, including PET scan, was four per patient at low-, medium-, and high-use facilities ($P = .51$). Invasive mediastinal staging, most often through transbronchial needle aspiration or cervical mediastinoscopy, was per-

formed in 30% of patients and was more commonly used at facilities with high PET scan use ($P < .001$). Per patient, slightly fewer tests for diagnosis and staging were performed at facilities with low PET scan use ($P = .01$). Patients at high-use facilities were somewhat more likely to receive chemotherapy ($P = .06$), but there were no differences in the frequency of surgery or radiotherapy.

Outcomes

Among patients who underwent PET scanning, PET scan stage was higher than CT scan stage in 25%, and PET scan stage was lower than CT scan stage in 27% (Table 4). The frequency of downstaging from CT scan stage to final stage was somewhat greater at facilities with high PET scan use (29%) than those with low (20%) and medium (23%) use, but this difference was not statistically significant ($P = .13$). The frequency of upstaging was not different across facilities characterized by PET scan use ($P = .66$). In 5% of all patients, use of PET scanning resulted in either upstaging or downstaging that changed the stage from surgically amenable to nonsurgically amenable or from nonsurgical to surgical, and this was more common at facilities with high PET scan use compared with those with low and medium use ($P = .002$). Among surgically treated patients, surgery without cure appeared to be more common at facilities with low PET scan use (52%) compared with those with medium (39%) or high (36%) use, but this difference was not statistically significant ($P = .12$).

The median duration of follow-up from the date of diagnosis was 352 days (interquartile range, 141-916 days). Only 22% of the sample was alive at the time of last contact, including 22% of patients at facilities with low and medium PET scan use and 20% at facilities with high PET scan use. Median survival did not differ among patients at low-, medium-, or high-use facilities (Fig 2). After adjustment for sociodemographic, tumor, and facility-level characteristics, the hazard of death was not different for patients at medium-use facilities compared with those at low-use facilities (adjusted hazard ratio, 1.14; 95% CI, 0.88-1.46). However, the hazard of death was greater for patients at high-use than at low-use facilities (adjusted hazard ratio, 1.35; 95% CI, 1.05-1.74). Other factors independently associated with a greater hazard of death were older age, severe comorbidity, lower household income, larger tumor size, higher stage by CT scan, severe signs at presentation, and transfer to or from a VHA CanCORS facility (Table 5).

The association between use of PET scanning at the facility level and survival was not significantly modified by age ($P = .26$), sex ($P = .94$), race/ethnicity ($P = .19$), comorbidity ($P = .24$), or stage by CT scan ($P = .15$).

Table 1—Patient Characteristics

Variable	Total	Low PET Scan Use	Medium PET Scan Use	High PET Scan Use	P Value
No. patients	622	221	245	156	...
No. facilities	13	4	5	4	...
Underwent PET scan	241 (39)	29 (13)	99 (40)	113 (72)	<.0001
Age, y	69 (60-76)	69 (59-76)	67 (60-76)	69 (61-76)	.65
Male sex	610 (98)	215 (97)	244 (100)	151 (97)	.08
Race/ethnicity					<.0001
Non-Hispanic white	395 (64)	113 (51)	170 (69)	112 (72)	
Hispanic or nonwhite	222 (36)	105 (48)	73 (30)	44 (28)	
Unknown	5 (1)	3 (1)	2 (1)	0 (0)	
Symptoms and signs					
Dyspnea	261 (42)	91 (41)	106 (43)	64 (43)	.86
Cough	369 (59)	131 (59)	147 (60)	91 (58)	.95
Hemoptysis	97 (16)	37 (17)	41 (17)	19 (12)	.40
Chest pain	132 (21)	49 (22)	45 (18)	38 (24)	.33
Weight loss	262 (42)	92 (42)	105 (43)	65 (42)	.96
None	68 (11)	28 (13)	21 (9)	19 (12)	.31
Insurance coverage					.18
Private	93 (15)	25 (11)	40 (16)	28 (18)	
Medicare	306 (49)	105 (48)	122 (50)	79 (51)	
Other public or unknown	223 (36)	91 (41)	83 (34)	49 (31)	
Annual household income					.015
< \$20,000	165 (27)	53 (24)	71 (29)	41 (26)	
\$20,000 to < \$40,000	88 (14)	25 (11)	32 (13)	31 (20)	
≥ \$40,000	30 (5)	10 (5)	7 (3)	13 (8)	
Unknown	339 (55)	133 (60)	135 (55)	71 (46)	
Education					.08
Did not graduate high school	92 (15)	33 (15)	31 (13)	28 (18)	
High school graduate	124 (20)	32 (14)	55 (22)	37 (24)	
Vocational school or some college	92 (15)	34 (15)	34 (14)	24 (15)	
College graduate or higher	26 (4)	6 (3)	11 (4)	9 (6)	
Unknown	288 (46)	116 (52)	114 (47)	58 (37)	
Comorbidity					.33
None	64 (10)	23 (10)	22 (9)	19 (12)	
Mild	226 (36)	81 (37)	95 (39)	50 (32)	
Moderate	150 (24)	62 (28)	51 (21)	37 (24)	
Severe	182 (29)	55 (25)	77 (31)	50 (32)	
Tumor size, mm	43 (28-65)	42 (30-68)	40 (28-57)	50 (30-68)	.12
Histology					<.0001
Adenocarcinoma	154 (25)	68 (31)	64 (26)	22 (14)	
Squamous cell carcinoma	227 (37)	99 (45)	75 (31)	53 (34)	
Undifferentiated, large cell, or mixed	241 (39)	54 (24)	106 (43)	81 (52)	
CT scan findings					
Spiculation	132 (21)	47 (21)	49 (20)	36 (23)	.96
Cavitation	35 (6)	16 (7)	6 (2)	13 (8)	.05
Pneumonia	11 (2)	3 (1)	5 (2)	3 (2)	.84
Atelectasis	110 (18)	32 (14)	48 (20)	30 (19)	.30
Multiple nodules or masses	230 (37)	70 (32)	81 (33)	79 (51)	.0002
Pleural effusion	111 (18)	38 (17)	45 (18)	28 (18)	.95
CT scan stage					.66
N0M0	234 (38)	78 (35)	102 (42)	54 (35)	
N1M0	22 (4)	7 (3)	10 (4)	5 (3)	
N2 or N3M0	132 (21)	46 (21)	51 (21)	35 (22)	
Any N M1	234 (38)	90 (41)	82 (33)	62 (40)	
PET scan stage (n = 241)					.40
N0 M0	106 (44)	9 (36)	43 (46)	54 (48)	
N1 M0	18 (8)	3 (12)	9 (10)	6 (5)	
N2 or N3 M0	35 (15)	2 (8)	12 (13)	21 (19)	
Any N M1	73 (30)	11 (44)	30 (32)	32 (28)	
Unknown	9 (4)	4 (14)	5 (5)	0	
Final stage					.47
Local	204 (33)	71 (32)	83 (34)	50 (32)	

(Continued)

Table 1—Continued

Variable	Total	Low PET Scan Use	Medium PET Scan Use	High PET Scan Use	P Value
Regional	195 (31)	59 (27)	80 (33)	56 (36)	
Distant	218 (35)	89 (40)	80 (33)	49 (31)	
Unknown	5 (1)	2 (1)	2 (1)	1 (1)	
Transfer to or from CanCORS site	125 (20)	55 (25)	41 (17)	29 (19)	.08
Transfer from CanCORS before diagnosis	6 (1)	2 (1)	2 (1)	2 (1)	.89
Transfer from CanCORS before treatment	30 (5)	11 (5)	17 (7)	2 (1)	.04
Transfer to CanCORS before diagnosis	62 (10)	28 (13)	14 (6)	20 (13)	.02
Transfer to CanCORS before treatment	27 (4)	14 (6)	8 (3)	5 (3)	.19

Data are presented as No. (%) or median (interquartile range) unless otherwise indicated. CanCORS = Cancer Care Surveillance and Outcomes Research.

In analyses stratified by stage by CT scan, the association between frequent PET scan use and worse survival appeared to be strongest among 234 patients with M1 disease by CT scan, whereas there was no association between the frequency of PET scan use and survival among 234 patients with N0M0 disease (e-Appendix 1).

Sensitivity Analysis

Results of the sensitivity analysis were similar when we measured survival from the date of diagnosis instead of the date on which lung cancer was first suspected, when we combined observations from facilities with medium and high PET scan use and compared them with low-use facilities, and when we included 165 patients with missing information about histology.

DISCUSSION

In this analysis of data from a large, prospective, observational study of lung cancer practices and outcomes, PET scan was obtained prior to treatment in almost 40% of US veterans with NSCLC, but the frequency of PET scan use varied widely across 13 different VHA hospitals. Importantly, baseline sociodemographic and tumor characteristics were remarkably similar for patients treated at different facilities, which enabled us to capitalize on this natural experiment and examine the effectiveness of PET scanning by comparing practices and outcomes across low-, medium-,

and high-use facilities. The most noteworthy finding was that greater use of PET scanning was not associated with better survival. In fact, after adjustment, overall survival appeared to be worse for patients who received care at high-use facilities compared with low-use facilities, suggesting the possibility of overuse of PET scanning at the high-use facilities.

Our conceptual model posited that greater use of PET scanning would improve survival by improving the accuracy of staging, thereby enabling delivery of more-appropriate stage-specific treatment. Although we found that PET scanning resulted in upstaging or downstaging in substantial numbers of patients, it is likely that PET scan stage was incorrect in at least some of these patients, possibly resulting in inappropriate treatment, especially if it was not subsequently confirmed invasively. The greater frequency of invasive staging observed at the high-use facilities mitigates against this possibility but does not exclude it. Guidelines for lung cancer staging emphasize that tissue confirmation of abnormal imaging findings is mandatory unless there is overwhelming evidence of mediastinal or distant metastasis.³

Improving the accuracy of lung cancer staging is necessary but not sufficient to improve survival. PET scanning is unlikely to affect survival in a patient who is not a candidate for potentially curative treatment because the PET scan results will not alter the treatment decision. At least some overuse of PET scanning in this study sample seems likely, given that large numbers

Table 2—Characteristics of Veterans Administration CanCORS Facilities

Variable	Total	Low PET Scan Use	Medium PET Scan Use	High PET Scan Use	P Value
No. facilities	13	4	5	4	...
Case manager present ^a	7 (54)	2 (50)	3 (60)	2 (50)	.94
Time frame for initial workup [?]	4 (31)	1 (25)	1 (20)	1 (25)	.85
Multidisciplinary thoracic oncology clinic [?]	3 (23)	1 (25)	1 (20)	1 (25)	.98
PET or PET/CT scanner available on site [?]	4 (31)	1 (25)	2 (40)	1 (25)	.85
PET scan easy to obtain [?]	9 (69)	3 (75)	3 (60)	3 (75)	.85
PET scan useful for diagnosis and staging [?]	11 (85)	3 (75)	4 (80)	4 (100)	.58

Data are presented as No. (%). See Table 1 legend for expansion of abbreviation.

^aSee e-Appendix 1 for additional information about facility characteristics.

Table 3—Staging Tests

Variable	Total	Low PET Scan Use	Medium PET Scan Use	High PET Scan Use	P Value
No. patients	622	221	245	156	...
No. facilities	13	4	5	4	...
Imaging tests	4 (3-6)	4 (3-6)	5 (3-6)	4 (3-6)	.51
Imaging tests excluding PET	4 (3-6)	4 (3-6)	4 (3-6)	4 (3-5)	.01
Invasive mediastinal staging	184 (30)	49 (22)	70 (29)	65 (42)	<.001
TBNA	103 (17)	21 (10)	49 (20)	33 (21)	.002
EUS-FNA	23 (4)	0	0	23 (15)	<.0001
Mediastinoscopy	69 (11)	30 (14)	24 (10)	15 (10)	.34
Surgical biopsy of mediastinal nodes (separate from resection)	4 (1)	4 (2)	0	0	.03
More than one invasive mediastinal staging test	11 (2)	6 (3)	3 (1)	2 (1)	.41
Biopsy of extrathoracic site	32 (5)	9 (4)	17 (7)	6 (4)	.26
Invasive tests for diagnosis and staging	2 (2-3)	2 (1-2)	2 (2-3)	2 (2-3)	.01

Data are presented as median (interquartile range) or No. (%) unless otherwise indicated. EUS-FNA = endoscopic ultrasound fine needle aspiration; TBNA = transbronchial needle aspiration.

of patients who underwent PET scan had moderate or severe comorbidities or presented with substantial weight loss (e-Appendix 1, e-Table 2).

Improvements in survival with greater use of PET scanning also might not be apparent because with the exception of surgery, treatment-related differences in survival in advanced lung cancer are relatively small in magnitude.¹¹ In the future, the availability of more effective stage-specific treatments might amplify the importance of accurate staging. On the other hand, in the coming era of targeted, personalized therapy for cancer, molecular diagnosis and staging may largely supplant anatomic staging,^{12,13} making currently available staging tests, such as PET scan, less important or even superfluous.

The finding that survival appeared to be worse for patients who received care at facilities with high PET scan use should be interpreted with caution. It is possible that differential sampling across sites resulted in the enrollment of sicker patients at the high-use facilities. However, given the remarkable similarity in patient characteristics across facilities with low, medium, and high PET scan use, the results suggest that more aggressive use of PET scan does not by itself lead to better outcomes, even when accompanied by more aggressive use of invasive staging and a nonsignificant trend toward more frequent use of chemotherapy. In contrast, PET scanning may have led to care that increased mortality or was a marker for more aggressive care associated with worse outcomes.¹⁴

Table 4—Outcomes

Variable	Total	Low PET Scan Use	Medium PET Scan Use	High PET Scan Use	P Value
Change in stage (n = 622)					
PET scan stage > CT scan stage (n = 241, % of those with PET scan)	59 (25)	8 (28)	24 (25)	27 (24)	.91
PET scan stage < CT scan stage (n = 241, % of those with PET scan)	65 (27)	7 (24)	26 (26)	32 (28)	.88
Final stage > CT scan stage	156 (25)	54 (24)	66 (27)	36 (23)	.66
Final stage < CT scan stage	146 (23)	44 (20)	57 (23)	45 (29)	.13
Upstaged by PET scan, resectable to nonresectable stage	19 (3)	3 (1)	7 (3)	9 (5)	.05
Downstaged by PET scan, nonresectable to resectable	15 (2)	1 (<1)	7 (3)	7 (5)	.04
Determination of resectability altered by PET scan	34 (5)	4 (2)	14 (6)	16 (10)	.002
Surgery without cure (n = 214)	92	41	32	19	.12
% who underwent surgery	43	52	39	36	
% total	15	19	13	12	
No. with unresectable disease	12	6	3	3	
No. with recurrence within 1 y	25	15	8	2	
No. who died within 1 y	55	20	21	14	
Alive at end of follow-up (n = 622)	134 (22)	48 (22)	55 (22)	31 (20)	.85
Alive without progressive disease (n = 622)	103 (17)	36 (16)	41 (17)	26 (17)	.99

Data are presented as No. (%) unless otherwise indicated.

FIGURE 2. Cumulative survival from date of initial suspicion to date of last contact among patients who received care at facilities with low, medium, and high PET scan use. CL = confidence limit.

In an observational study that used data from the Surveillance, Epidemiology, and End Results (SEER) tumor registry linked to Medicare claims data, Farjah et al¹⁵ reported that the hazard of death was substantially lower among patients who underwent bimodality or trimodality staging (including PET scanning and invasive staging) compared with those who underwent single-modality staging with CT scan alone. By taking advantage of a natural experiment that (imperfectly) simulated the coin toss of a randomized controlled trial, the present study minimizes the residual confounding that may have biased the results of this previous study.

Properly interpreted, the results do not imply that PET scanning should not be used for staging in NSCLC but, rather, that marginally greater use of PET scan above a relatively low baseline does not appear to add substantial benefits. On the basis of the results of stratified analyses and clinical experience, we believe that PET scanning is potentially most useful in patients at the margin of surgical resectability, including patients with borderline lymphadenopathy; those with larger, central tumors; and those with adenocarcinoma histology who are more likely to have occult metastasis. However, use of PET scan for staging in NSCLC and other cancers is increasing, suggesting that it is being used less rather than more selectively. Of note, the 72% frequency of PET scan use that we observed in high-use VHA facilities is similar to the 65% frequency reported in an analysis of SEER-Medicare records from

2005 to 2007, making the present results highly relevant to current practice.¹⁶⁻¹⁹

Although greater PET scan use at the facility level was not associated with better survival, it did appear to reduce the frequency of surgery without cure. Although not statistically significant, this finding supports the argument that at least in some cases, PET scanning may help to identify occult metastatic disease, thereby avoiding unnecessary surgery. Notably, the absolute reduction of 7% seen in this observational study of actual practice in VHA settings was smaller than the 20% reduction observed in two randomized controlled trials conducted in Europe.^{4,6} The relatively high frequencies of surgery without cure that we observed (52% at low-use facilities and 36% at high-use facilities) were similar to those observed in the PET in Lung Cancer Staging (PLUS) study in which the frequency was 50% in the conventional staging group and 32% in the conventional staging plus PET scan group.⁶

The strengths of the current study are the relatively large, prospectively enrolled, and geographically diverse sample; the collection of detailed sociodemographic and clinical information with limited amounts of missing data; and the use of rigorous analytic methods. Patient characteristics were similar across the three groups of facilities, and we used statistical methods to adjust for any residual differences. In the analyses, we adjusted for CT scan stage and not final stage because improved final staging is the mechanism (mediator) by which

Table 5—Results of Multivariable Cox Proportional Hazards Analysis

Characteristic	HR (95% CI)
Age ≥ 69 vs < 69 y	1.32 (1.06-1.64) ^a
Female vs male sex	0.51 (0.22-1.16)
Nonwhite vs white	1.06 (0.86-1.31)
No vs severe comorbidity	0.92 (0.66-1.28)
Mild vs severe comorbidity	0.67 (0.54-0.85) ^a
Moderate vs severe comorbidity	0.69 (0.54-0.88) ^a
Medicare vs private insurance	0.90 (0.68-1.18)
Did not graduate high school vs college graduate or higher	1.05 (0.60-1.83)
High school graduate vs college graduate or higher	1.25 (0.73-2.14)
Vocational school or some college vs college graduate or higher	0.99 (0.57-1.73)
Annual household income < \$20,000 vs ≥ \$40,000	1.56 (0.91-2.69)
Annual household income \$20,000-\$40,000 vs ≥ \$40,000	1.84 (1.06-3.19) ^a
Tumor size ≥ 43 vs < 43 mm	1.54 (1.24-1.91) ^a
Squamous histology vs adenocarcinoma	1.20 (0.93-1.54)
Undifferentiated, large cell, or mixed histology vs adenocarcinoma	1.13 (0.88-1.45)
CT scan stage N1M0 vs N0M0	1.20 (0.70-2.07)
CT scan stage N2/3M0 vs N0M0	2.06 (1.60-2.65) ^a
CT scan stage M1 vs N0M0	2.36 (1.88-2.96) ^a
Severe symptoms	1.17 (0.92-1.49)
Severe signs	1.80 (1.32-2.45) ^a
Cavitation vs no cavitation	1.16 (0.80-1.69)
Multiple nodules vs no additional nodules	0.98 (0.81-1.18)
Transfer to or from VHA CanCORS site vs no transfer	1.37 (1.12-1.68) ^a
Case manager vs no case manager	1.06 (0.82-1.36)
Time frame for evaluation vs no time frame	1.01 (0.63-1.64)
Multidisciplinary clinic vs no multidisciplinary clinic	1.31 (0.80-2.13)
Medium-PET-scan use facility vs low-PET-scan use facility	1.14 (0.88-1.46)
High-PET scan-use facility vs low-PET-scan use facility	1.35 (1.05-1.74) ^a

HR = hazard ratio; VHA = Veterans Health Administration. See Table 1 legend for expansion of other abbreviation.

^aStatistically significant association between covariate and survival.

the exposure (use of PET scanning) influences the outcome (survival) (e-Fig 1). Adjustment for final stage would obscure any true association between PET scanning and survival, if one in fact did exist. In contrast, we adjusted for stage by CT scan, which is a potential confounder associated with both the exposure and the outcome.

A limitation of potential importance is the use of dedicated PET scanners at the study sites. Although integrated PET/CT scanning is probably more accurate than dedicated PET scanning for staging in NSCLC,²⁰ the relatively modest improvement in accuracy is probably insufficient on its own to translate to better survival. Similarly, the recent introduction and dissemination of minimally invasive staging with endobronchial ultrasound threatens the generalizability of the findings to future practice,²¹ but one could argue that the ability

to locate and sample both enlarged and nonenlarged lymph nodes with endobronchial ultrasound further limits the role of PET scanning in lung cancer staging. Finally, some might question whether the findings apply in non-VHA settings, particularly to nonsmokers and women, who were not represented in the current study. With these two important exceptions, we believe that the results are broadly generalizable to other patient groups and practice settings.

In summary, we found that substantially greater use of PET scanning in patients with NSCLC was associated with more frequent invasive staging, slightly more downstaging, and a nonsignificant reduction in the frequency of surgery without cure. However, markedly greater use of PET scanning was not associated with better survival, suggesting that PET scanning should be reserved for patients who are on the margin of surgical resectability and most likely to benefit.

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Dr Gould: contributed to the study concept and design; data acquisition, analysis, and interpretation; drafting of the manuscript; revision of manuscript for important intellectual content; and final approval of the article.

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