Published in final edited form as:

J Am Coll Radiol. 2016 May ; 13(5): 491–496. doi:10.1016/j.jacr.2015.11.016.

Trends in Use of FDG-PET Imaging in Surveillance of Non-Small Cell Lung and Colorectal Cancer

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Abstract

Background—Surveillance positron emission tomography (PET) following curative intent treatment of non-small cell lung cancer (NSCLC) or colorectal cancer (CRC) is not clearly supported by available evidence or the Choosing Wisely campaign. However, the frequency of PET imaging during the surveillance period is relatively unknown.

Methods—Using SEER-Medicare data, we identified 65,748 patients age 66+ who were diagnosed with Stage I-III NSCLC or Stage I-III CRC during 2001–2009 and who underwent surgical resection. We assessed trends in “any PET” or “PET-only” use 6–18 months post-operatively.

Results—“Any PET” use more than doubled over the study period. 11% of NSCLC patients and 4% of CRC patients diagnosed in 2001 received “any PET” vs. 25% NSCLC and 13% CRC patients in 2009 (both $P < 0.001$). Higher stage disease correlated with higher PET utilization and faster growth in use over the study period. “PET-only” use also increased over the study period, especially in higher stage disease. < 2% of patients diagnosed with Stage IIIA NSCLC in 2001 received “PET-only” vs. 15% of patients diagnosed in 2009 ($P = 0.014$). Similarly, 1% of patients diagnosed with Stage III CRC in 2001 received “PET-only” vs. 8% of patients diagnosed in 2009 ($P < 0.001$).

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Drs. Ciunci, Zafar, and Paulson have no disclosures to report.

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Conclusions—PET utilization during the surveillance period increased between 2001 and 2009. Further research is needed to determine the factors driving use of surveillance PET and to examine relationships between PET and patient outcomes.

Sentence Summary

Between 2001 and 2009, PET utilization during the surveillance period increased in survivors of non-small cell lung cancer or colorectal cancer.

Keywords

Positron Emission Tomography imaging; Surveillance; Colorectal cancer; Non-small cell lung cancer; Choosing Wisely; FDG-PET

Introduction

There are insufficient data to support the use of surveillance positron emission tomography (PET) imaging following curative intent treatment of non-small cell lung cancer (NSCLC) or colorectal cancer (CRC).^{1–5} Accordingly, the American Society of Clinical Oncology and the American Board of Internal Medicine's joint Choosing Wisely campaign, which promotes high-value, high-quality care, recommends against surveillance PET due to lack of proven benefit and the likelihood of false positive results.⁶ For similar reasons the Centers for Medicare and Medicaid have not reimbursed surveillance PET since they initiated coverage of this modality in 2001.⁷ To better understand the frequency of PET utilization during the surveillance period, we examined annual trends in use of PET 6–18 months following resection of locoregional NSCLC (Stage I–IIIA) and CRC (Stage I–III). We focused on the first decade of widespread clinical use of PET (2001–2009), and stratified PET utilization as isolated or in conjunction with separate dedicated computed tomography (CT) imaging.

Methods

We used Survival, Epidemiology, and End Results (SEER)-Medicare data for patients diagnosed with Stage I–IIIA NSCLC or Stage I–III CRC during 2001–2009. We excluded patients without record of surgical resection and those with more than one primary cancer diagnosis. Patients who were enrolled in an HMO or disenrolled from Medicare Part A or B at any point from one year before diagnosis through follow-up were excluded due to incomplete claims data. Finally, we excluded patients less than 66 or more than 99 years of age.

We assessed use of PET imaging in the surveillance period, defined as 181–540 days after surgical resection. To avoid capturing imaging performed in the post-operative period rather than the surveillance period, imaging within 180 days of surgery was excluded. As patients at the end of life may have different patterns of care, we only included patients who survived at least 2.5 years after surgery. Imaging was classified as 1) “any PET” (receipt of PET or integrated PET/CT in conjunction with other, separate CT imaging), and 2) “PET-only” (receipt of PET or integrated PET/CT only, in the absence of other separate CT imaging).

Although patients receiving adjuvant chemotherapy or radiation were not specifically excluded, our analytic period started 6 months after surgical resection when the majority of NSCLC and CRC patients have completed treatment. Furthermore, surveillance PET is not indicated even among NSCLC or CRC patients who are undergoing or have completed adjuvant therapy.

Proportions of patients receiving each category of PET imaging were adjusted for patient age, sex, race/ethnicity, marital status, Charlson comorbidity index, and ZIP-Code-level median household income in 2000, and then calculated by cancer type, diagnosis year, and stage. Equality of adjusted proportions was assessed between diagnosis years with Wald tests. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using STATA software (version 13.1, Stata, Inc., College Station, TX). The study was approved by the Institutional Review Board of the University of Pennsylvania.

Results

7,393 NSCLC patients and 35,050 CRC patients met inclusion criteria. The mean age of NSCLC patients was 73.7 years. Seventy-nine percent had Stage I NSCLC, 13% Stage II, and 9% Stage IIIA. The mean age of CRC patients was 76.8 years. Thirty-five percent had Stage I CRC, 38% had Stage II CRC, and 28% had Stage III CRC. Patient demographics are shown in Table 1.

Figures 1 and 2 show trends in use of PET 6–18 months following surgery for NSCLC and CRC, respectively. Among all patients with NSCLC, 11% of those diagnosed in 2001 received “any PET” vs. 25% of those diagnosed in 2009 ($P < 0.001$). “Any PET” utilization was more common in higher-stage NSCLC patients, with the greatest growth rate demonstrated in Stage III disease. “Any PET” use increased by 2 percentage points per year, on average, among all NSCLC patients and 4 percentage points per year, on average, among Stage IIIA NSCLC patients. Three percent of all NSCLC patients diagnosed in 2001 received “PET-only” vs. 10% of all NSCLC patients diagnosed in 2009 ($P < 0.001$). “PET-only” utilization was also more common in higher-stage NSCLC patients, with the greatest growth demonstrated in Stage III disease. “PET-only” use increased by 1 percentage point per year, on average, among all NSCLC patients and by 2 percentage points per year among Stage IIIA NSCLC patients (Table 2).

Among those patients with CRC, 4% of all patients diagnosed in 2001 received “any PET” vs. 13% of all patients diagnosed in 2009 ($P < 0.001$). “Any PET” utilization was more common in higher-stage CRC patients, with the greatest growth rate demonstrated in Stage III disease. “Any PET” use increased by 1 percentage point per year, on average, among all CRC patients and 2 percentage points per year, on average, among Stage III CRC patients. Less than one percent of all CRC patients diagnosed in 2001 received “PET-only” vs. 4% of all CRC patients diagnosed in 2009 ($P < 0.001$). Over the study period, “PET-only” increased by 1 percentage point per year, on average, among all CRC and Stage III CRC patients (Table 3).

Discussion

In this robust, population-based study of patients with surgically-resected Stage I-III NSCLC or Stage I-III CRC, we found that PET utilization during the first year of the surveillance period was not infrequent. In contrast to routine surveillance CT imaging, routine surveillance PET imaging is not indicated by guidelines for either NSCLC or CRC. Nevertheless, PET use more than doubled during 2001–2009, with more use and faster growth among patients with higher-stage disease relative to lower-stage disease. In fact, in the last three years of the study (2007–2009), nearly 50% of Stage IIIA NSCLC and 25% of Stage III CRC patients received a PET scan during the first year of the surveillance period. Among both NSCLC and CRC patients, “any PET” use more than doubled over the study period. “PET-only” use also increased significantly over the study period, more than tripling in both cohorts of patients, but overall was used less frequently than “any PET.”

The overall increase in PET use during the study period may have been driven by multiple factors. We are not aware of any studies documenting trends in surveillance testing during the study period. However, if overall use of surveillance testing for NSCLC and CRC increased during the study period, then increased “any PET” use may reflect follow-up evaluation of abnormal surveillance test results. A second possible driver is the increased availability of, and patient and provider familiarity with, PET imaging over the study period.^{8,9} Given the wide availability and increased awareness of PET, providers may have ordered PET for both diagnostic and surveillance indications. Finally, physicians may have ordered PET because they believed that it was an appropriate or superior surveillance modality, particularly in patients at higher risk for recurrence.¹⁰

It is difficult to determine from claims data whether increased PET use over the study period was appropriate or inappropriate. Increased rates of “any PET” may be a manifestation of increased imaging among all cancer patients during 2001–2009.¹¹ It is plausible that some of the PET scans in this cohort were performed appropriately to evaluate abnormalities in preceding surveillance imaging, carcinoembryonic antigen values (in CRC patients), or other findings suggestive of cancer recurrence, though we cannot determine this from claims. A prior study of Medicare claims for patients with six different types of cancer, including NSCLC and CRC, found an 18% annual increase in the use of PET from 2004–2008. In about 50% of cases in that study, body CT preceded the use of PET.¹² Although that study included patients at various points in cancer care from diagnosis through treatment, surveillance, and recurrent disease and thus cannot be directly compared to our study, it does similarly demonstrate a continued increase in PET use several years after the modality first became a covered service for patients with NSCLC and CRC.

Higher PET use and faster growth in use among patients with higher-stage disease may suggest appropriate utilization; patients with higher disease stage will have more recurrences that require evaluation. However, it may also suggest inappropriate use if providers order surveillance PET because they believe PET is superior to CT as surveillance in patients at higher risk for recurrence. In contrast, increased use of PET during the study period among patients with Stage I disease, who are at low risk for cancer recurrence, suggests inappropriate use. Similarly increased “PET-only” imaging, that is, PET or PET/CT

performed in the absence of separate CT imaging, suggests that PET may have replaced guideline-based CT surveillance imaging rather than being used to further evaluate abnormalities seen on surveillance CT, also implying potential inappropriate utilization of PET. Many benign conditions, such as radiation fibrosis after NSCLC treatment, are not easily distinguished from recurrent cancer based on CT imaging alone. Providers may feel that PET-only surveillance “saves a step” by eliminating the need to follow an abnormal CT scan with PET for further evaluation, yet guidelines do not support PET-only surveillance.

Despite the lack of guideline support for the use of surveillance PET in NSCLC and CRC, there is a growing body of literature that suggests the need for prospective data to address this issue. One retrospective study has shown that PET/CT has superior sensitivity, specificity and accuracy than conventional CT for the diagnosis of local recurrence and distant metastasis in patients with previously treated CRC.¹³ In NSCLC, a number of relatively small retrospective studies have shown that PET/CT has improved sensitivity for detecting recurrences, even in asymptomatic patients¹⁴ compared with conventional CT.^{15,16} Another study demonstrated that NSCLC patients with positive PET/CT scans in the surveillance setting have significantly reduced overall survival compared with patients who have negative PET/CT scans.¹⁷ However, none of these studies have evaluated associations between routine surveillance PET and clinically-meaningful patient outcomes such as overall survival.

Our findings are important given the health-related and economic costs associated with PET imaging during surveillance. In addition to higher imaging costs associated with PET, false positive tests may result in unnecessary invasive procedures, incorrect diagnoses, and overtreatment with chemotherapy, radiation, or surgery. Although the Choosing Wisely campaign was not initiated until 2013, CMS did not reimburse for surveillance PET during our study period. Our results indicate that PET use during surveillance increased among patients with NSCLC and CRC. Further research is needed to determine the factors driving use of PET imaging during surveillance and to carefully examine relationships between surveillance PET and patient outcomes.

Acknowledgments

Dr. Veenstra discloses research funding (to the University of Michigan) from Pfizer.

Dr. Vachani discloses research funding (to the University of Pennsylvania) from Integrated Diagnostics, Allegro Diagnostics, Janssen Research and Development, and Viomics, Inc. He previously served on the scientific advisory board for Allegro Diagnostics until September, 2014.

Dr. Epstein serves as consultant to Medicus Economics.

Funding/Support: This study was supported by the NCI Cancer Center Support Grant (P30 CA016520); Abramson Cancer Center Population Science Pilot Project

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Take-Home Points

- Neither clinical care guidelines nor the Choosing Wisely support the use of surveillance positron emission tomography (PET) imaging following curative intent treatment of non-small cell lung cancer (NSCLC) or colorectal cancer (CRC).
- The use of PET imaging, both with and without separate CT imaging, significantly increased among patients with resected NSCLC and CRC from 2001–2009.
- Some PET imaging during the surveillance period may represent appropriate follow-up of clinical symptoms or test results concerning for disease recurrence, though some PET imaging likely represents inappropriate use and replacement of guideline-recommended conventional CT.
- High quality, prospective studies are needed to determine the role of PET imaging in routine surveillance for patients with NSCLC and CRC treated with curative intent.

Figure 1. Adjusted PET Surveillance in Non-Small Cell Lung Cancer, by Disease Stage, 2001–2009

Models adjust for patient age, sex, race/ethnicity, marital status, Charlson comorbidity index, and ZIP-Code level median household income in 2000. In these stacked area graphs, the red crosshatches indicate “PET only” and the blue stripes indicate PET with additional imaging. Their sum indicates “any PET.”

Figure 2. Adjusted PET Surveillance in Colorectal Cancer, by Disease Stage, 2001–2009

Models adjust for patient age, sex, race/ethnicity, marital status, Charlson comorbidity index, and ZIP-Code level median household income in 2000. In these stacked area graphs, the red crosshatches indicate “PET only” and the blue stripes indicate PET with additional imaging. Their sum indicates “any PET.”

Table 1.

Patient Demographics, by Disease Type

Characteristic	All Patients (n=42,443)	Non-Small Cell Lung Cancer (n=7393)	Colorectal Cancer (n=35,050)	P Value
Age				<0.001
66–70	9935 (23%)	2422 (33%)	7513 (21%)	
71–75	10,710 (25%)	2354 (32%)	8356 (24%)	
76–80	10,191 (24%)	1738 (24%)	8453 (24%)	
81–85	7327 (17%)	731 (10%)	6596 (19%)	
>85	4280 (10%)	148 (2%)	4132 (12%)	
Sex				<0.001
Male	23,468 (55%)	3391 (46%)	20,077 (57%)	
Female	18,975 (45%)	4002 (54%)	14,973 (43%)	
Race				<0.001
White	35,830 (84%)	6491 (88%)	29,339 (84%)	
Black	2636 (6%)	355 (5%)	2281 (7%)	
Hispanic	1714 (4%)	194 (3%)	1520 (4%)	
Asian	1576 (4%)	266 (4%)	1310 (4%)	
Unknown	548 (1%)	87 (1%)	461 (1%)	
Missing	139 (0.3%)	0 (0%)	139 (0.4%)	
Marital Status				<0.001
Unmarried	19,639 (46%)	2996 (41%)	16,643 (47%)	
Married	22,804 (54%)	4397 (59%)	18,407 (53%)	
Charlson Comorbidity Index				<0.001
0	24,604 (58%)	4004 (54%)	20,600 (59%)	
1	10,152 (24%)	2008 (27%)	8144 (23%)	
2	3664 (9%)	730 (10%)	2934 (8%)	
3	2292 (5%)	425 (6%)	1867 (5%)	
Missing	1731 (4%)	226 (3%)	1505 (4%)	
Median Household Income *				<0.001
Low	13,887 (33%)	2050 (28%)	11,837 (34%)	
Medium	13,954 (33%)	2441 (33%)	11,513 (33%)	
High	14,544 (34%)	2892 (39%)	11,652 (33%)	
Missing	58 (0.1%)	10 (0.1%)	48 (0.1%)	

Data shown are n (%). Proportions may not add to 100% because of rounding.

* ZIP-code level median household income, in tertiles.

Table 2:

Proportions of NSCLC Patients Undergoing “any PET” and “PET-only” in Surveillance Year 1 (6–18 months after surgical resection), by Year of Diagnosis

Year of Diagnosis	Overall		Stage IIIA	
	“Any PET”	“PET-only”	“Any PET”	“PET-only”
2001	11.0%	2.6%	14.2%	< 2.0%
2002	13.2%	2.2%	24.2%	6.3%
2003	17.0%	3.5%	34.1%	3.6%
2004	21.4%	5.0%	44.7%	7.9%
2005	22.9%	6.2%	35.4%	9.5%
2006	22.7%	6.1%	37.8%	10.6%
2007	25.3%	7.5%	52.9%	14.8%
2008	25.3%	7.9%	48.9%	15.3%
2009	24.7%	10.0%	41.2%	14.9%
2001 vs. 2009 (P)	<0.001	<0.001	0.004	0.014
Avg. annual increase (percentage points) *	1.9	0.9	3.9	1.9
N	7,393		660	

Proportions are adjusted for patient age, sex, race/ethnicity, marital status, Charlson comorbidity index, and ZIP-Code level median household income in 2000.

* P<0.001 for all average annual increases.

Table 3:

Proportions of CRC Patients Undergoing “any PET” and “PET-only” in Surveillance Year 1 (6–18 months after surgical resection), by Year of Diagnosis

Year of Diagnosis	Overall		Stage III	
	“Any PET”	“PET-only”	“Any PET”	“PET-only”
2001	3.9%	0.3%	8.7%	0.9%
2002	5.6%	0.6%	10.9%	0.9%
2003	6.7%	0.9%	13.0%	1.3%
2004	8.5%	1.3%	16.4%	2.6%
2005	10.7%	2.5%	18.2%	4.3%
2006	11.8%	3.5%	20.9%	6.8%
2007	12.5%	4.2%	22.7%	6.0%
2008	13.3%	4.8%	24.6%	8.7%
2009	12.5%	4.4%	27.4%	8.3%
2001 vs. 2009 (P)	<0.001	<0.001	<0.001	<0.001
Avg. annual increase (percentage points) *	1.3	0.7	2.3	1.1
N	35,050		9,653	

Proportions are adjusted for patient age, sex, race/ethnicity, marital status, Charlson comorbidity index, and ZIP-Code level median household income in 2000.

* P<0.001 for all average annual increases.