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Influence of Surveillance PET/CT on Detection of Early Recurrence Following Definitive Radiation in Stage III Non-Small Cell Lung Cancer

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Abstract

Purpose—There is little data to support the use of varying imaging modalities in evaluating recurrence in non-small cell lung cancer (NSCLC). We compared the efficacy of surveillance PET/CT vs. CT scans of the chest in detecting recurrences following definitive radiation for NSCLC.

Materials/Methods—We retrospectively analyzed 200 patients treated between 2000–2011 that met the inclusion criteria of stage III NSCLC, completion of definitive radiation treatment, and absence of recurrence within the initial 6 months. These patients were then grouped based on the use of PET/CT imaging during post-radiation surveillance. Patients who received 1 PET/CT scans within 6 months of the end of radiation treatment were placed in the PET-group while all others were placed in the CT-group. We compared survival times from the end of treatment to the date of death or last follow-up utilizing log-rank tests. Multivariate analysis was conducted to identify factors associated with decreased survival.

Results—In the entire cohort, median event-free survival (EFS) was 26.7 months, and median overall survival (OS) was 41.2 months. The CT-group had a median EFS of 21.4 months vs. 29.4 months for the PET-group ($p=0.59$). There was no difference in OS between the CT- and PET-groups (median OS of 41.2 and 41.3 months, respectively, $p=0.59$). There was also no difference in local recurrence-free survival or distant metastases-free survival between the CT-only and PET-

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high groups ($p=0.92$ and $p=0.30$, respectively). Similarly, on multivariate analysis, stratification into the PET-group was not associated with improved EFS (HR: 0.90, 95% CI: 0.61–1.34, $p=0.60$) or OS (HR: 1.2, 95% CI: 0.83–1.7, $p=0.34$).

Conclusions—In stage III NSCLC patients treated with definitive radiation and without early recurrence, PET/CT scan surveillance did not result in decreased time to detection of locoregional or distant recurrence or improved survival.

Keywords

lung cancer; CT; PET/CT; radiation; recurrence

Introduction

Lung cancer remains the leading cause of cancer mortality in the United States and has a 5 year survival rate of 17%¹. This is due both to the aggressive nature of the disease and its proclivity to recur following definitive treatment with surgery or radiation. Consequently, intensive surveillance may be necessary to detect recurrence². Despite this, there is no consensus recommendation regarding the optimal post-treatment surveillance imaging modality or sequencing. Current National Comprehensive Cancer Network (NCCN) guidelines for non-small cell lung cancer (NSCLC) recommend a chest CT every 6–12 months following completion of treatment for 2 years followed by annual low-dose chest CT surveillance³. Furthermore, routine surveillance PET/CT imaging is not recommended, predominantly due to the lack of data demonstrating benefit⁴. However, PET/CT has quickly received widespread adoption during the initial staging evaluation and has become commonly used in the post-treatment surveillance window to assess for disease recurrence both locally and distantly due to reported improvements in sensitivity and specificity in disease recurrence detection^{5, 6}.

Unfortunately, PET/CT imaging is costly and, thus, its potential overuse is subject to increasing scrutiny given the national trend in improving oncologic care efficiency and cost effectiveness. Consequently, studies that inform when PET/CT should be used in the post-treatment surveillance are needed. The limited analyses currently available have included small patient numbers and suboptimal comparison groups^{7–10}. Therefore, further analysis is needed to determine the role of PET/CT scan in surveillance for locally advanced NSCLC compared to CT scan with contrast, as recommended in national guidelines³.

The aims of the current study were as follows: 1) determine if there are systematic differences between those patients that undergo CT vs. PET/CT surveillance after definitive radiation therapy (RT) for locally advanced NSCLC, 2) compare patterns of failure in those patients that undergo each of these surveillance regimens, and 3) assess survival based on surveillance approach. We hypothesized that PET/CT surveillance would detect disease earlier, due to the increased sensitivity of this imaging modality and more comprehensive nature of full body scanning, and that this earlier detection would lead to increased survival outcomes due to initiation of salvage therapy in the context of smaller volume disease.

Materials and Methods

Patients and Imaging Data

Following institutional review board approval, patients were selected from a clinical database of patients with pathologically confirmed NSCLC treated with definitive radiation therapy to a dose of 60 Gy at a single tertiary cancer center. Radiation treatment was begun from January 2000 to January 2011. Patient confidentiality was maintained in accordance to the Health Insurance Portability and Accountability Act. 494 consecutively treated patients met the aforementioned criteria (Figure 1a). For the final cohort we used the following inclusion criteria: 1) stage III disease, 2) no events or deaths less than 6 months following treatment, and 3) at least 2 surveillance scans must have been acquired. The first criteria was used to generate a population that was treated in a uniform fashion. The latter two criteria were adopted to ensure both sufficient follow-up time and surveillance imaging to identify trends in a population of patients with a potentially long disease-free interval. For example, some patients who relapsed or died within the first 6 months following definitive radiation treatment either had none or only one surveillance scan. Many patients did not accumulate multiple post-treatment scans and, as a result, did not develop a pattern of surveillance imaging. Consequently, the imaging patterns in this group are highly heterogeneous and challenging to interpret. After applying the above inclusion criteria, 200 patients were subsequently found to be eligible for analysis.

Imaging and relapse data were retrospectively collected from electronic medical records for patients who met the aforementioned criteria. All CT and PET/CT scans obtained following the completion of definitive radiation therapy were recorded. Of note, routine chest CT imaging for lung cancer patients at our institution extends to the level of the adrenal glands, which detects extrathoracic metastatic lesions in the upper abdomen.

Assessing Surveillance Methods

Over the past 10 years, there has been heterogeneity among the multiple treating physicians at our institution with regard to the choice of post-RT imaging. Two primary surveillance strategies are used. The first approach is CT scan at every surveillance visit, every 3–6 months for the first 5 years and annually thereafter. The second approach is alternating PET/CT and CT scans for 1–2 years (since it is the biggest risk period), reserving PET/CT for abnormal findings on CT scan. Our objectives were first to compare patient, disease, and treatment characteristics between the two groups, and then to examine the treatment strategies according to the detection of recurrence and overall survival.

As an initial step, scans taken prior to 1 month post-treatment and those taken after disease relapse were excluded as these are not relevant to surveillance imaging. We then examined the distribution of post RT images over time, to determine if there was a consistent pattern over an extended period that could be adequately evaluated (Figure 1b). This analysis revealed that the ratio of CT to PET/CT dramatically increases over time reflecting the practice of omitting routine PET/CT in those patients who do not have local or distant failure in the initial 2 years following definitive radiation. Consequently, in order to compare a predominantly CT-based surveillance strategy to a PET/CT-based one, we elected to

categorize patients into two distinct groups by focusing on surveillance imaging patterns immediately following definitive treatment. To categorize patients into these groups, the first two scans performed following radiation treatment were examined. If a PET/CT was performed during one of the initial two scans, the patient was categorized into the PET/CT-group, while patients that only received CTs as their initial two scans were categorized into the CT-group. Critical to the current analysis was the absence of a systematic difference between patients that receive PET/CT and CT scan. To demonstrate that there was not a systematic difference between those patients that received PET/CT vs. CT, we compared multiple characteristics between groups.

Statistical Methods

Survival curves were calculated using the Kaplan-Meier method. Univariate and multivariate odds ratios associating relevant clinical variables were calculated via logistic regression. Variables analyzed included demographic data, stage (IIIA vs IIIB), performance status, and chemotherapy. All tests were considered significant at $p < 0.05$. Analyses were performed using either SAS version 9.3 or JMP version 12 (SAS Institute, Cary, NC).

Results

Patient Characteristics and Comparison Between PET/CT and CT Groups

A total of 200 patients with stage III NSCLC who were treated with definitive radiation met our study inclusion criteria. Table 1 summarizes the baseline patient characteristics. Median age for the entire cohort was 65 years (range, 34–83). Median follow-up for alive patients was 59.4 months (range, 14.5–125.3). 91.5% of patients received concurrent chemotherapy with radiation therapy. 47% of patients had stage IIIA disease, and 53% had stage IIIB disease. A total of 102 patients experienced a recurrence (defined as locoregional or distant failure).

We then stratified the patient population into CT- ($n=95$) and PET/CT-groups ($n=105$) based on the nature of the imaging obtained for each patient following the end of RT (detailed above in Materials and Methods). Table 2 summarizes patient characteristics stratified on the CT- and PET/CT-based surveillance imaging groups. The two groups were well balanced with respect to age, performance status, race, stage, and concurrent chemotherapy treatment. Of note, 29.5% of patients in the PET/CT group received induction chemotherapy versus 52.5% in the CT group ($p < 0.01$). Conversely, 37.1% of patients in the PET/CT group received adjuvant chemotherapy as opposed to 16.8% in the CT-group ($p < 0.01$). However, there were similar TNM staging and gross tumor volumes (GTV) between the 2 comparison groups (Table 2). Consequently, the significance of the PET/CT group receiving more adjuvant chemotherapy and the CT-group receiving more neoadjuvant chemotherapy is unclear.

Patterns of Failure Between CT and PET/CT Groups

We next examined the patterns of failure between the two patient cohorts. There were 52 recurrences in the CT-group and 50 in the PET/CT-group (54.7% and 47.6% of their respective cohorts), which reflects the similarity of disease characteristics between the two

populations ($p=0.33$, Table 3). There were 28 and 23 primary tumor failures in the CT- and PET/CT-groups, respectively ($p=0.26$). The PET/CT group did have more lymph node recurrences detected (10 vs 3), but this did not meet statistical significance ($p=0.09$). A similar trend was observed with respect to extrathoracic lymph node recurrence, with 7 failures in the PET/CT-group as opposed to 3 in the CT-group ($p=0.34$). Conversely, the CT-group detected more bone metastases as opposed to the PET/CT-group, though this did not meet statistical significance (7 vs 2, $p=0.09$). Overall, the specific patterns of failure were proportionally similar between the two groups, and no significant differences were observed with any of the patterns of failure (Table 3). However, the small patient numbers above may have disguised a potential benefit of PET/CT in discerning lymph node metastasis and CT in identifying bone metastasis.

Survival Comparison Between PET/CT and CT Surveillance Groups and Inclusion of Covariates

Median event-free survival (EFS) for the entire cohort was 26.7 months and median overall survival (OS) was 41.2 months. Outcomes were subsequently stratified on surveillance imaging group (Figure 2a–d). There was no statistical difference in OS between the two groups (median OS: CT-group, 41.2 months; PET/CT-group, 41.3 months; Figure 2a, $p=0.59$). Similarly, there was no statistical difference in EFS ($p=0.59$), local-regional failure-free survival (LRFS, $p=0.92$), or distant metastases-free survival (DMFS, $p=0.30$) between the two surveillance groups (Figure 2b–d). Consequently, the above results suggest that post-radiation treatment surveillance in stage III NSCLC patients with routine PET/CT imaging affords no benefit with respect to local or distant relapse detection or associated survival benefit over CT imaging.

We next generated a multivariate model to assess whether covariates of interest, including surveillance group stratification, were associated with clinical endpoints. Similar to the aforementioned log-rank tests, stratification to the PET/CT imaging group was not associated with differences in clinical endpoints, including OS, EFS, LRFS, and DMFS (Table 4). KPS >80 , stage IIIB disease, and the use of concurrent chemotherapy also were not associated with changes in clinical outcome (Table 4). Interestingly, squamous histology was associated with decreased OS (vs other histology, HR: 1.64, 95% CI: 1.13–2.35, $p=0.01$) and LRFS (HR: 2.47, 95% CI: 1.47–4.17, $p<0.01$). Conversely, squamous histology was associated with increased DMFS (HR: 0.42, 95% CI: 0.21–0.78, $p<0.01$).

Discussion

This study examines whether a PET/CT-based strategy carries any benefit in detecting both locoregional and distant recurrence over a CT-based strategy in stage III NSCLC patients who are treated with definitive radiation and do not experience disease recurrence within 6 months. Given the improved sensitivity and specificity of PET/CT over CT, we hypothesized that we would observe earlier detection of both local and distant recurrence, which could then lead to rapid deployment of salvage therapies, for which multiple randomized clinical trials have demonstrated a survival benefit^{11, 12}. In this context, our pertinent findings were as follows. First, we found that treatment characteristics were similar between the two

groups, as were the patterns of failure (Tables 2 and 3). Second, the PET/CT-based group had similar OS, EFS, LRFS, and DMFS rates as the CT-based group in a cohort of stage III NSCLC patients treated with definitive radiation therapy (Figure 2 and Table 4). This suggests that a PET/CT-based surveillance strategy confers no additional benefit in clinical outcomes in this patient population despite its improved sensitivity and specificity.

This non-randomized comparative effectiveness study was subject to confounding that could have altered the results due to selection bias in assigning patients to a given surveillance strategy (e.g. if higher risk patients were routinely selected to undergo PET/CT surveillance). However, we do not believe that this imbalance occurred in the current patient cohort for two reasons. First, we assessed for systematic differences in the patient, disease, and treatment characteristics of these two groups. If the surveillance regimen was strongly correlated with prognostic factors, this association would have been evident in this comparison. However, none of the many prognostic factors that we assessed corresponded with surveillance approach, and thus we concluded that, as we hypothesized, these choices were being made according to individual physician preference among the multiple (approximately 25) medical and radiation oncologists at our institution. Second, even in the scenario where higher risk patients were more frequently allocated to the PET/CT regimen (for factors for which we could not account in our comparison), we would anticipate higher recurrence in this group and lower survival. As noted above, recurrence and survival patterns were very similar.

There is accumulating evidence that PET/CT has improved sensitivity and specificity over standard CT in detecting NSCLC recurrence, though there have been few reports comparing the two directly ^{6, 13, 14}. Antonious et al. found that PET/CT imaging performed 6 months following treatment for lung cancer was a prognostic marker for overall survival (OS) and identified recurrence over 40% of the time even when there was no suspicion for recurrence ⁷. However, the benefit of PET/CT imaging over standard CT imaging was not compared. Another report compared PET/CT and CT imaging in lung cancer surveillance in stage I patients following lobectomy, and PET/CT imaging indeed was more sensitive and specific ⁸. However, in this study PET/CT was compared to the non-contrast CT obtained during PET imaging; therefore, it is possible that the use of a contrast CT would have mitigated this benefit. In a prospective study of 100 NSCLC patients, PET/CT imaging obtained 3 months following treatment detected more instances of progressive disease than CT alone and enabled rapid initiation of salvage therapy ¹⁰. However, this included small patient numbers, did not address the role of PET/CT in long-term surveillance of advanced stage NSCLC patients, and did not report long-term outcomes. Overall, there have been few studies examining this issue and most have had small patient numbers and typically involve patients in the post-operative setting. Consequently, our study is unique in its relatively large size and examination in the post-radiation treatment setting.

Given the dearth of evidence, current NCCN guidelines do not recommend the use of PET/CT in the post-treatment surveillance period ³. Our data appears to support this recommendation. However, our findings that PET/CT does not confer any benefit in early detection of disease recurrence is surprising. Indeed, there have been multiple reports that tumor metabolism as determined by PET/CT has significant prognostic value in the post-

radiation setting^{15–20}, though these studies do not address whether serial PET/CT imaging in the post-treatment setting confers additional prognostic benefit. Our hypothesis for our unexpected findings is that close surveillance with CT scans (every 3–4 months for the first 2 years) can detect abnormalities that can then be further evaluated with PET/CT. A contributing factor may be the extension of chest CT scans at our institution to the upper abdomen, which capture the adrenal glands and liver, two common sites of metastasis²¹. Therefore, patients are likely not presenting with substantially greater volume of disease to influence survival, and the advantage of PET/CT over CT in terms of sensitivity and specificity may be less robust in this study.

Other than the limitations inherent in any retrospective analysis, there are constraints on the interpretation of the results in this study. First, the results are partially dependent on the quality of the imaging modalities and interpretations of them at the institutional level. Second, neither of these strategies addresses the detection of brain metastases, which are common in lung cancer. However, routine brain imaging is not recommended in patients with stage III disease, and therefore was not directly related to the current study. Finally, the choice of PET/CT vs. CT scan, while not due to any known factors, was also not likely completely random and was in some patients based on clinical gestalt, which can be difficult to tease out. Other than the approaches we used to limit selection bias outlined above, we also attempted to further decrease heterogeneity and potential confounding factors by limiting our analysis to stage III patients and the post-treatment surveillance window to the 18 month period following radiation treatment. The latter was done as PET/CT utilization dramatically decreased eighteen months post-treatment. Our design also excluded those who failed less than six months after treatment, as these patients did not accumulate multiple post-treatment scans. This exclusion, in addition to the single institution nature of the study, likely explains the finding that the median OS of 41.2 months in the study cohort is superior to the reported median OS of 28 months in the 60 Gy arm of RTOG 0617²², despite similar treatments. While these exclusion criteria allowed for a homogeneous study population to allow for assessment of long-term surveillance trends, they also limit the generalizability of our conclusions.

In conclusion, we report the largest series to examine the differences between post-treatment imaging surveillance in stage III NSCLC patients following definitive radiation treatment. We have found that there were no differences in patterns of failure or survival outcomes between the two strategies. While we are currently performing an analysis to further elucidate the cost effectiveness of surveillance regimens, our data provide the best evidence to date that supports the current NCCN guidelines that recommend CT-only surveillance in this context.

References

1. Society AC. Cancer Facts & Figures 2015. 2015:1–52.
2. Westeel V, Choma D, Clement F, et al. Relevance of an intensive postoperative follow-up after surgery for non-small cell lung cancer. *Ann Thorac Surg*. 2000; 70:1185–1190. [PubMed: 11081867]
3. Network NCC. Non-Small Cell Lung Cancer. 2015.

4. Rubins J, Unger M, Colice GL. American College of Chest P. Follow-up and surveillance of the lung cancer patient following curative intent therapy: ACCP evidence-based clinical practice guideline (2nd edition). Chest. 2007; 132:355S–367S. [PubMed: 17873180]
5. Fischer BM, Mortensen J. The future in diagnosis and staging of lung cancer: positron emission tomography. Respiration. 2006; 73:267–276. [PubMed: 16679747]
6. Jimenez-Bonilla JF, Quirce R, Martinez-Rodriguez I, et al. Diagnosis of recurrence and assessment of post-recurrence survival in patients with extracranial non-small cell lung cancer evaluated by 18F-FDG PET/CT. Lung Cancer. 2013; 81:71–76. [PubMed: 23597930]
7. Antoniou AJ, Marcus C, Tahari AK, Wahl RL, Subramaniam RM. Follow-up or Surveillance (18)F-FDG PET/CT and Survival Outcome in Lung Cancer Patients. J Nucl Med. 2014; 55:1062–1068. [PubMed: 24777290]
8. Dane B, Grechushkin V, Plank A, Moore W, Bilfinger T. PET/CT vs. non-contrast CT alone for surveillance 1-year post lobectomy for stage I non-small-cell lung cancer. Am J Nucl Med Mol Imaging. 2013; 3:408–416. [PubMed: 24116349]
9. van Loon J, Grutters JP, Wanders R, et al. 18FDG-PET-CT in the follow-up of non-small cell lung cancer patients after radical radiotherapy with or without chemotherapy: an economic evaluation. Eur J Cancer. 2010; 46:110–119. [PubMed: 19944595]
10. van Loon J, Grutters J, Wanders R, et al. Follow-up with 18FDG-PET-CT after radical radiotherapy with or without chemotherapy allows the detection of potentially curable progressive disease in non-small cell lung cancer patients: a prospective study. Eur J Cancer. 2009; 45:588–595. [PubMed: 19046631]
11. Fossella FV, DeVore R, Kerr RN, et al. Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small-cell lung cancer previously treated with platinum-containing chemotherapy regimens. The TAX 320 Non-Small Cell Lung Cancer Study Group. J Clin Oncol. 2000; 18:2354–2362. [PubMed: 10856094]
12. Shepherd FA, Dancey J, Ramlau R, et al. Prospective randomized trial of docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy. J Clin Oncol. 2000; 18:2095–2103. [PubMed: 10811675]
13. Onishi Y, Ohno Y, Koyama H, et al. Non-small cell carcinoma: comparison of postoperative intra- and extrathoracic recurrence assessment capability of qualitatively and/or quantitatively assessed FDG-PET/CT and standard radiological examinations. Eur J Radiol. 2011; 79:473–479. [PubMed: 20547021]
14. Takenaka D, Ohno Y, Koyama H, et al. Integrated FDG-PET/CT vs. standard radiological examinations: comparison of capability for assessment of postoperative recurrence in non-small cell lung cancer patients. Eur J Radiol. 2010; 74:458–464. [PubMed: 19398291]
15. Machtay M, Duan F, Siegel BA, et al. Prediction of survival by [18F]fluorodeoxyglucose positron emission tomography in patients with locally advanced non-small-cell lung cancer undergoing definitive chemoradiation therapy: results of the ACRIN 6668/RTOG 0235 trial. J Clin Oncol. 2013; 31:3823–3830. [PubMed: 24043740]
16. Roy S, Pathy S, Kumar R, et al. Efficacy of 18F-fluorodeoxyglucose positron emission tomography/computed tomography as a predictor of response in locally advanced non-small-cell carcinoma of the lung. Nucl Med Commun. 2016; 37:129–138. [PubMed: 26544097]
17. Na F, Wang J, Li C, Deng L, Xue J, Lu Y. Primary tumor standardized uptake value measured on F18-Fluorodeoxyglucose positron emission tomography is of prediction value for survival and local control in non-small-cell lung cancer receiving radiotherapy: meta-analysis. J Thorac Oncol. 2014; 9:834–842. [PubMed: 24787963]
18. Xiang ZL, Erasmus J, Komaki R, Cox JD, Chang JY. FDG uptake correlates with recurrence and survival after treatment of unresectable stage III non-small cell lung cancer with high-dose proton therapy and chemotherapy. Radiat Oncol. 2012; 7:144. [PubMed: 22929048]
19. Lopez Guerra JL, Gladish G, Komaki R, Gomez D, Zhuang Y, Liao Z. Large decreases in standardized uptake values after definitive radiation are associated with better survival of patients with locally advanced non-small cell lung cancer. J Nucl Med. 2012; 53:225–233. [PubMed: 22241911]

20. Jeong JU, Chung WK, Nam TK, et al. Early metabolic response on 18F-fluorodeoxyglucose-positron-emission tomography/computed tomography after concurrent chemoradiotherapy for advanced stage III non-small cell lung cancer is correlated with local tumor control and survival. *Anticancer research*. 2014; 34:2517–2523. [PubMed: 24778069]
21. Quint LE, Tummala S, Brisson LJ, et al. Distribution of distant metastases from newly diagnosed non-small cell lung cancer. *Ann Thorac Surg*. 1996; 62:246–250. [PubMed: 8678651]
22. Bradley JD, Paulus R, Komaki R, et al. Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a randomised, two-by-two factorial phase 3 study. *The lancet oncology*. 2015; 16:187–199. [PubMed: 25601342]

Clinical Practice Points

- There is little data to support the use of PET/CT in routine surveillance of locally-advanced NSCLC patients who complete definitive radiation and do not fail within the initial 6 months.
- To address this knowledge gap, we report the largest series to evaluate the relative benefit of PET/CT surveillance over CT alone in stage III NSCLC following radiation treatment.
- Our study suggests that routine PET/CT surveillance confers no additional benefit over CT alone in detecting local or distant failure.
- These findings will be of interest to radiation, medical, and surgical oncologists in helping guide how best to follow locally-advanced NSCLC patients after definitive therapy. Currently, national guidelines do not endorse the use of PET/CT in this setting, and the data presented in this study supports this recommendation.

Figure 1a:

Figure 1b:

Figure 1.

A) Study diagram depicting initial patient cohort followed by exclusion criteria. B) Post-treatment CT:PET/CT ratio over time.

Figure 2a: **Figure 2b:**

Figure 2c: **Figure 2d:** **Figure 2.**

A) Overall survival, B) Event-free survival, C) Local recurrence-free survival, and D) Distant metastasis-free survival stratified based on imaging group.

Table 1

Baseline patient and treatment characteristics

Characteristics	All Patients (n=200)
Sex	
Male	108 (54.0%)
Female	92 (46.0%)
Age at diagnosis (years, median [range])	65 (34–83)
Karnofsky performance status score	
<70	5 (2.5%)
70	24 (12.0%)
80	99 (49.5%)
>90	72 (36.0%)
Race	
White	173 (86.5%)
Black	20 (10.0%)
Other	7 (3.95%)
Chemotherapy	
Neoadjuvant	81 (40.5%)
Concurrent	183 (91.5%)
Adjuvant	55 (27.5%)
Tumor histology	
Adenocarcinoma	71 (35.5%)
Squamous	79 (39.5%)
NOS	50 (25.0%)
T status (AJCC 6 th edn)	
T1	32 (16.0%)
T2	73 (36.5%)
T3	31 (15.5%)
T4	61 (30.5%)
N status (AJCC 6 th edn)	
N0	19 (9.5%)
N1	14 (7.0%)
N2	115 (57.5%)
N3	51 (25.5%)
Stage (AJCC 6 th edn)	
IIIA	94 (47.0%)
IIIB	106 (53.0%)

AJCC 6th edn, American Joint Committee on Cancer Staging Manual, published in 2002.

Table 2

Patient and treatment characteristics by surveillance group

Characteristics	CT-group (n=95)	PET/CT-group (n=105)	P value
Sex			0.07
Male	45 (47.4%)	63 (60.0%)	
Female	50 (52.6%)	42 (40.0%)	
Age at diagnosis (years, median)	66	65	0.81
Gross tumor volume (cc, median)	91.7	87.6	0.95
Karnofsky performance status score			0.17
<70	0 (0.0%)	5 (4.8%)	
70	13 (13.7%)	11 (10.5%)	
80	51 (53.7%)	48 (45.7%)	
>90	31 (32.6%)	41 (39.1%)	
Race			0.32
White	81 (85.3%)	92 (87.6%)	
Black	12 (12.6%)	8 (7.6%)	
Other	2 (2.1%)	5 (4.8%)	
Concurrent Chemotherapy			0.64
No	9 (9.5%)	8 (7.6%)	
Yes	86 (90.5%)	97 (92.4%)	
Neoadjuvant Chemotherapy			<0.01
No	45 (47.4%)	74 (70.5%)	
Yes	50 (52.6%)	31 (29.5%)	
Adjuvant Chemotherapy			<0.01
No	79 (83.2%)	66 (62.9%)	
Yes	16 (16.8%)	39 (37.1%)	
Tumor histology			0.75
Adenocarcinoma	32 (33.7%)	39 (37.1%)	
Squamous	37 (39.0%)	42 (40.0%)	
NOS	26 (27.4%)	24 (22.9%)	
T status (AJCC 6 th edn)			0.59
T1	17 (17.9%)	15 (14.3%)	
T2	34 (35.8%)	39 (37.1%)	
T3	11 (11.6%)	20 (19.1%)	
T4	32 (33.7%)	29 (27.6%)	
N status (AJCC 6 th edn)			0.32
N0	10 (10.5%)	9 (8.6%)	
N1	10 (10.5%)	4 (3.8%)	
N2	52 (54.7%)	63 (60.0%)	
N3	23 (24.2%)	28 (26.7%)	
Stage (AJCC 6 th edn)			0.45
IIIA	42 (44.2%)	52 (49.5%)	

Characteristics	CT-group (n=95)	PET/CT-group (n=105)	P value
IIIB	53 (55.8%)	53 (50.5%)	
Sites of First Recurrence			0.64
Local Recurrence	22 (23.2%)	25 (23.8%)	
Distant Metastases	24 (23.2%)	19 (18.1%)	
Both	8 (8.4%)	6 (5.7%)	
None	43 (45.3%)	55 (52.4%)	

AJCC 6th edn, American Joint Committee on Cancer Staging Manual, published in 2002.

Table 3

Patterns of failure by imaging group

	CT (n=95)	PET/CT (n=105)	P value
Total Recurrences	52	50	0.33
Local Recurrences			
Primary tumor	28	23	0.26
Lymph node	3	10	0.09
Distant Metastases			
Contralateral lung	8	8	1.0
Pleura	1	3	0.62
Adrenal	2	1	0.61
Bone	7	2	0.09
Liver	3	0	0.11
Extrathoracic LN	3	7	0.34
Other	1	0	0.48

Table 4

Multivariate analyses for covariates of interest with respect to outcome

Covariates	Overall Survival			Event-Free Survival			Locoregional Failure-Free Survival			Distant Metastasis-Free Survival		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
PET/CT (vs CT)	1.2	0.83–1.7	0.34	0.90	0.61–1.34	0.60	1.10	0.66–1.84	0.71	0.76	0.44–1.30	0.32
KPS >80 (vs 80)	0.74	0.50–1.07	0.11	1.14	0.76–1.70	0.52	1.32	0.78–2.20	0.29	0.68	0.37–1.20	0.18
Stage IIIB (vs IIIA)	1.0	0.73–1.48	0.84	1.15	0.78–1.71	0.49	1.04	0.63–1.74	0.86	1.15	0.68–1.99	0.60
Squamous histology (vs other)	1.64	1.13–2.35	0.01	1.07	0.70–1.60	0.76	2.47	1.47–4.17	<0.01	0.42	0.21–0.78	<0.01
Concurrent chemo (vs No concurrent)	0.75	0.43–1.46	0.38	0.99	0.52–2.13	0.98	1.05	0.48–2.76	0.91	1.03	0.42–3.44	0.95