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Value of fourth and subsequent post-therapy follow-up ^{18}F -FDG PET/CT scans in patients with breast cancer

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Abstract

Objective—To evaluate the accuracy and value of the fourth and subsequent post-therapy follow-up fluorine-18 fluorodeoxyglucose (^{18}F -FDG) PET/computed tomography (CT) scans in the clinical assessment of breast cancer patients.

Materials and methods—Ninety-two female patients, with a total of 426 fourth and subsequent follow-up PET/CT scans, were retrospectively included. Patients were followed for a median of 23.7 months (range, 0.7–124.4) from the fourth follow-up PET/CT. The diagnostic accuracy of PET/CT, its impact on clinical assessment, patients' management, and survival outcome were established.

Result—Of the 426 follow-up PET/CT scans, 264 (62%) were interpreted as positive and 162 (38%) were interpreted as negative. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the fourth and subsequent follow-up PET/CT scans were 97.7, 98.1, 98.8, 96.3, and 97.9%, respectively. Fourth and subsequent follow-up PET/CT were useful in excluding a tumor in 13.4% (39/292) of patients with a clinical suspicion of recurrence and identifying suspected recurrence in 10.5% (14/134) of patients without previous clinical suspicion. A change in management was noted in 6.7% (9/134) of scan times when the scans were performed without previous clinical suspicion of recurrence or therapy response and was 27.7% (81/292) when the scans were performed with clinical suspicion. Overall survival differed significantly between patients with all negative follow-up scans ($n = 23$) and those who had at least one positive follow-up scan ($n = 69$) (hazard ratio of 4.65, $P < 0.001$).

Conclusion—The fourth and subsequent PET/CT scans performed after the completion of primary treatment led to a change in management in 27.7% of patients when the scans were

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Conflicts of interest

There are no conflicts of interest.

performed with clinical suspicion and only in 6.7% of patients when performed without clinical suspicion or context.

Keywords

accuracy; breast cancer; follow-up; PET/CT; survival

Introduction

Breast cancer is the most common malignancy and the leading cause of cancer-related death in women [1]. Despite advances in the treatment of breast cancer, depending on the initial extent of the disease, 20–30% of patients will develop loco regional or distance recurrence [2,3]. Advances in chemotherapy, hormone therapy, and HER-2-targeted therapy have led to a modest improvement in the survival of patients with recurrent breast cancer [4].

Surveillance and follow-up in breast cancer patients remains a controversial topic. The National Comprehensive Cancer Network guidelines for breast cancer follow-up (version 3, 2014) [5] recommend performing an annual mammography and regular history/physical examinations every 4 to 6 months for the first 5 years after primary therapy and annually thereafter. The guideline did not recommend performing routine bone scans, computed tomography (CT), MRI, PET scans, or ultrasound examinations in the asymptomatic patient [5]. However, diagnostic imaging methods, such as PET/CT, have been found to be highly sensitive in the detection of recurrence [2]. Moreover, follow-up PET/CT scans provide information that influences patient management and improves prognostic prediction in patients with suspected recurrent breast cancer [3].

In 2013, the Center for Medicare and Medicaid Services declared that three fluorine-18 fluorodeoxyglucose (^{18}F -FDG) PET scans are covered [§ 1862(a) (1) (A)] when used to guide subsequent management of patients after completion of initial anticancer therapy. The Local Medicare Administrative Contractor will determine the coverage of any additional ^{18}F -FDG PET/CT scans [6–8] on the basis of medical necessity. We have reported that the fourth and subsequent follow-up ^{18}F -FDG PET/CT scans performed after treatment completion added value to the clinical assessment and management plan in patients with lung cancer as well as colorectal cancer [6, 8]. The aim of the present study is to evaluate the accuracy, added value to clinical assessment, impact on management on the basis of clinical context, and association with overall survival (OS) outcome of fourth and subsequent post-therapy ^{18}F -FDG PET/CT scans in patients with breast cancer.

Materials and methods

Eligible patients and follow-up

This IRB-approved retrospective study was carried out under a waiver of informed consent. Guidelines of the Health Insurance and Portability and Accountability Act were followed. Medical records of 837 patients with biopsy-proven breast cancers who underwent a PET/CT scan between 2000 and 2012 in our center were retrospectively reviewed. Of these, a total of 99 (11.8%) patients had more than three follow-up ^{18}F -FDG PET/CT studies after

completion of the primary treatment. Seven patients had a history of other malignancies and the follow-up PET/CT scans were performed for restaging of both breast cancer and the other malignancies; therefore, these seven patients were excluded. The remaining 92 patients were included in the study. Of these 92 patients, 30 patients were also included in our previous study [1]. A total of 426 fourth and subsequent follow-up PET/CT scans (median $\pm$ SD: 6 ± 3.9 , range: 4–20 follow-up scans per patient) were included. The scans were performed because of two indications: (a) clinical suspicion of disease recurrence/metastasis or for therapy response assessment in recurrent setting (b) as part of routine follow-up, at the clinician's discretion, without clinical suspicion for disease recurrence or metastases or therapy response assessment. All patients included in the study were followed until death or those who survived were censored to the last date of follow-up at our institution. The median follow-up period of the patients included in the study from the fourth follow-up PET/CT study was 23.7 months (SD = 27.8, range = 0.7–124.4 months).

PET/CT study protocol

PET/CT studies were carried out as per the institutional clinical protocol. All patients fasted for at least 4 h before the scans and had blood glucose levels lower than 200 mg/dl at the time of ^{18}F -FDG injection. After administration of a 5.55 MBq/kg (0.068 mCi/lb) dose of ^{18}F -FDG, with a maximum of 647.5 MBq (17.5 mCi), the patients rested for about 60 min. PET/CT imaging was performed either using a Discovery LS (two-dimensional) or Discovery VCT (three-dimensional) (GE Healthcare, Waukesha, Wisconsin, USA). Whole-body scanning was performed while the patients were supine and their arms were above their head. The scan was performed 3 min per bed position and the images were in a 128×128 matrix. The PET images were reconstructed using a two-dimensional and three-dimensional ordered-subsets expectation maximization algorithm both with and without CT-based attenuation correction. CT images (120 kV; 20–200 mAs; 8.0 noise index) were in a 512×512 matrix (beam collimation = 128×0.6 mm, pitch = 0.8). Slice thickness was 3 mm and field of view was 50 cm. These methods are similar to those reported in our previously published studies [8,9].

^{18}F -FDG PET/CT image analysis

The ^{18}F -FDG PET/CT images were read at the time of the imaging as per the routine imaging review protocol in the hospital by board-certified nuclear medicine physicians. Scan reports were retrospectively categorized as negative, indeterminate, or positive. Positive reports clearly indicated disease recurrence or metastases related to the primary breast cancer. Indeterminate reports indicated some ^{18}F -FDG avidity; however, it did not clearly identify or rule out disease, and the report impression included indefinite terms for example 'indeterminate' or 'cannot exclude recurrence' [9]. Negative scan reports clearly excluded the possibility of disease. For analysis purposes, the indeterminate scans were categorized as 'negative'.

The scan request forms and the last clinical note of the treating physician requesting the study were reviewed carefully and the scans were categorized according to the previous clinical suspicion of the disease into two groups: those without previous clinical suspicion of

disease or recurrence at the time of scan and those performed secondary to clinical suspicion of disease or recurrence or therapy response assessment [8–10] at the time of the scan.

Measures of accuracy and change in management

The accuracy of the fourth and subsequent follow-up PET/CT studies was validated by either a pathologic examination of suspected lesion (when biopsy was performed) or clinical follow-up (when the patients were followed up clinically without performing a biopsy). The clinical follow-up information was obtained after a careful review of medical and imaging records for 6 months from the date of the PET/CT study as a reference standard.

The management modality and treatment details immediately before and after each scan were documented from electronic medical records and the change in management after each scan was established. The impact of each follow-up ^{18}F -FDG PET/CT scan result on the treatment strategy for each individual patient was assessed. The treatment impact was categorized into six groups: (a) the patients received no treatment before the scan and the treating physician continued to observe the patient without treatment after the scan (no treatment to no treatment), (b) the patients received a specific cancer treatment before the scan and the treating physician continued the same treatment after the scan (treatment to continue the same treatment), (c) the patients received no treatment before the scan and the treating physician started new treatment after the scan (no treatment to new treatment), (d) the patients received a specific cancer treatment before the scan and the treating physician changed the treatment modality/regimen after the scan (treatment to change in treatment), (e) the patients received a specific cancer treatment before the scan and the treating physician discontinued the treatment after the scan (treatment to stop the treatment), and (f) the patient's management after the scan was unknown (treatment change unknown). We have described these classifications in our previous studies [6,8].

Outcome measures

OS was defined as the time (months) interval between the date of the fourth or subsequent follow-up PET/CT scan and the date of death. The date of scan was recorded from the electronic medical record of each patient and the date of death was extracted from the electronic medical records and a public registry of death [11]. The survival data for patients who were alive were censored at the last follow-up date at our institution. For patients who had all negative scans, the time to event was calculated from the fourth follow-up scan. For patients who had at least one positive scan, the time to event was calculated from the first positive scan.

Statistical analysis

The descriptive feature of variable was presented using mean $\pm$ SD or median and range. This study focused on the evaluation of the accuracy and impact of fourth and subsequent follow-up ^{18}F -FDG PET/CT scans on treatment as well as assessment of the relationship between these scan results and OS of patients with breast cancer. The accuracy of late follow-up PET/CT scans was calculated using the classic 2×2 table and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the accuracy of the late follow-up PET/CT scan in patients with breast cancer was reported. The

impact of scan results (positive or negative) on the treatment of breast cancer (six classified categories) was evaluated using χ^2 analysis. Cox regression analysis was carried out to calculate the survival probabilities. First, a univariate Cox regression analysis was carried out for each parameter: age, race, histology (ductal, lobular, other), primary tumor characteristics (estrogen receptor, progesterone receptor, Her2neu status, grade, stage), primary treatment modality, clinical suspicion before the PET/CT scan, PET scan result, and the PET/CT scan impact on treatment. A multivariate Cox regression analysis was carried out and those variables with a significant P -value (< 0.05) in the univariate analysis were included. Survival curves were constructed using the Kaplan–Meier analysis and the OS between patients with at least one positive fourth and subsequent follow-up scan and patients with all negative fourth and subsequent follow-up scans was compared using a log rank test. Statistical significance was set at two-tailed P -value less than 0.05 for all tests. SPSS 15.0 (SPSS Inc., Chicago, Illinois, USA) software was used to carry out all the statistical analyses [6,9].

Results

Patient characteristics

The median $\pm$ SD age of these 92 included female patients was 58.5 ± 13 years. During a median follow-up of 23.7 months (SD = 27.8; 25–75% quartile: 11.1–42.9), 48 patients (52.2%) survived and 44 patients (47.8%) died.

Patient demographics, tumor characteristics (histology, estrogen receptor, progesterone receptor, Her2neu status, grade, stage), treatment details, clinical suspicion of recurrence before the follow-up scan, and the PET/CT results are presented in Table 1. A total of 426 fourth and subsequent follow-up scans were obtained from these 92 patients. The number of follow-up scans per patient ranged from four to 20 scans (average of 4.6 scans per patient). Forty-seven (51.1%) patients had four to six follow-up scans, 27 (29.3%) patients had seven to 10 follow-up scans, and 10 (19.6%) patients had 11 or more follow-up scans (Fig. 1). Of all fourth and subsequent follow-up scans, 160/426 (37.6%) were performed in the first 6 years after the completion of the initial treatment, 161/426 (37.8%) of the fourth and subsequent follow-up scans were performed within 6–12 years after the completion of the initial treatment, and 104/426 (24.4%) were performed after 12 years of treatment completion.

Accuracy of fourth and subsequent follow-up PET/CT

Of a total of 426 fourth and subsequent follow-up scans, the reference standard was available for 423 scans, including histopathological confirmation (19 scans) and 6-month clinical follow-up (404 scans). Three scans that did not contain any information to confirm the results of PET/CT (neither pathologic report nor follow-up clinical information) were excluded from the accuracy analysis. Of the total 423 late follow-up scans with available confirmation data, 261 (61.7%) were positive and 162 (38.3%) were negative (including 24 indeterminate scans). A total of 258 out of 261 positive scans were confirmed as true positive (TP), whereas three turned out to be false positive (FP) by biopsy and/or clinical follow-up. A total of 156 out of 162 negative scans were confirmed as true negative (TN) by

the 6-month clinical follow-up, whereas six scans (all originally interpreted as indeterminate scans) turned out to be false negative (FN). The sensitivity, specificity, PPV, NPV, and accuracy of the fourth and subsequent follow-up PET/CT in patients with breast cancer were 97.7, 98.1, 98.8, 96.3, and 97.9%, respectively.

In addition, a subgroup analysis was carried out on the basis of a previous clinical suspicion of recurrence before the PET/CT scan. The sensitivity, specificity, PPV, NPV, and accuracy of the fourth and subsequent followup ^{18}F -FDG PET/CT when performed with previous clinical suspicion were 98, 95.1, 99.2, 88.6, and 97.6%, respectively. The sensitivity, specificity, PPV, NPV, and accuracy of the fourth and subsequent follow-up ^{18}F -FDG PET/CT when performed without a clinical suspicion of recurrence were 93.3, 99.2, 93.3, 99.2, and 98.5%, respectively.

Value of follow-up PET/CT for clinical assessment

Of the 426 scans, 134 (31.5%) were obtained for routine follow-up without previous clinical suspicion of disease. Among the 134 routine follow-up scans, 12% (16/134) were read as positive scans and suggested disease recurrence (TP: 14, FP: 1, no confirmation data available: 1). The remaining 88% (118/134) of routine scans were negative for disease (TN: 117, FN: 1 indeterminate scan). In the context of clinical assessment, excluding the false-positive scans, PET/CT identified recurrence or metastasis in 10.5% (14/134) of scans performed without previous clinical suspicion.

Of the 426 scans, 292 (68.5%) were obtained with previous suspicion of disease recurrence. Among these 292 follow-up scans with previous suspicion of disease recurrence, 85% (248/292) were read as positive scans and suggested disease recurrence (TP: 244, FP: 2, no confirmation data available: 2). The remaining 15% (44/292) of scans with previous suspicion were negative for disease (TN: 39, FN: 5 and all were indeterminate scans). In the context of clinical assessment, excluding the false-negative scans, PET/CT ruled out disease in 13.4% (39/292) of scans performed with previous clinical suspicion (Table 2).

Impact of follow-up PET/CT on patient management

The impact of each follow-up PET/CT study on the patient's treatment plan was also evaluated by a careful review of the electronic medical records before and after the studies. Table 3 summarizes the impact of scan results on treatment. Of the 426 scans, 71 (16.7%) scans led to no change in treatment and the patients continued to be on follow-up with observation without any treatment before or after the scan. A total of 260 (61%) scans led to no change in treatment and the same treatment plan was continued as before (PET/CT showed good response to the treatment and the treatment regimen was not altered). Therefore, patient management was not changed after 331 (77.7%) scans.

However, PET/CT results led to a change in the patients' management in 90/426 (21%) scans. This includes the initiation of new treatment (24 scans, 5.6%), change in the previous treatment regimen (64 scans, 15%), and stopped treatment (two scans, 0.4%). The treatment impact was not known in 5/426 (1.2%) scans because of the lack of information in the electronic medical records. The χ^2 analysis showed that there was a significant difference

between the follow-up scan results and the impact on the treatment of patients with breast cancer ($P < 0.001$).

In the context of clinical suspicion, the fourth and subsequent follow-up PET/CT scans led to a change in the management of patients in 6.7% (9/134) of scan times when the scans were performed without previous clinical suspicion of recurrence and the rate of change in management was 27.7% (81/292) when the scans were performed with a clinical suspicion of recurrence.

Patient outcome

Cox regression models—For evaluation of OS, Cox regression models (univariate and multivariate) were used. In univariate Cox regression analysis, clinical suspicion ($P = 0.007$), scan result ($P = 0.001$), and impact on treatment ($P < 0.001$) were associated significantly with OS. However, using multivariate Cox regression analysis and adjusting for other factors, only the PET/CT scan result ($P = 0.019$) remained significantly associated with the OS (Table 4).

Kaplan–Meier survival analysis—Of the 92 patients included in the study, 69 had at least one positive fourth or subsequent PET/CT scan for recurrence (41 patients deceased and 28 survived) and all of the follow-up scan results of the remaining 23 patients were negative (three patients died and 20 survived). The median survival time in the positive scan group was 22.5 months (25–75% quartile: 10–37.7 months), whereas the median survival in the negative scan group was 40.4 months (25–75% quartile: 20–73.4 months). The Kaplan–Meier analysis on the basis of the PET/CT scan results showed that these differences were statistically significant [hazard ratio = 4.65 (95% confidence interval 1.3–16.8), log rank $P < 0.001$] (Fig. 2).

Discussion

The aim of this study was to evaluate the value of the fourth and subsequent ^{18}F -FDG PET/CT scans in the follow-up of patients with breast cancer, performed after the completion of primary treatment with or without a clinical suspicion of disease or recurrence. Our results showed that the fourth and subsequent ^{18}F -FDG PET/CT follow-up scans have 97.9% accuracy in detecting recurrence or ruling out tumor recurrence in patients who were treated for primary breast cancer. These scans add value to clinical assessment by identifying disease in studies carried out without previous clinical suspicion of disease and ruling out disease in studies carried out with previous suspicion of disease recurrence. In addition, these late follow-up scans have a significant impact on the treatment plan of these patients during the follow-up period. Those patients with all negative fourth and follow-up PET/CT scans survived significantly longer compared with those patients with at least one positive scan.

Our results show that late follow-up PET/CT scans show high performance in detecting recurrence in patients with breast cancer. The sensitivity, specificity, PPV, NPV, and accuracy of the fourth and subsequent follow-up ^{18}F -FDG PET/CT in patients with breast cancer were 97.7, 98.1, 98.8, 96.3, and 97.9%, respectively. Previous studies have also

reported high performance of the PET/CT scan in the detection of recurrence in patients with breast cancer. Manohar *et al.* [12] evaluated 111 patients with breast cancer who underwent PET/CT because of a clinical suspicion of recurrence and they showed that follow-up PET/CT scan had a sensitivity, specificity, PPV, and NPV of 98.7, 85.3, 92.5, and 97.2%, respectively, in detecting recurrent disease. Moreover, Murakami *et al.* [13] reported the overall sensitivity, specificity, PPV, NPV, and accuracy of PET/CT for follow-up of patients with suspected recurrent breast cancer to be 96, 91, 92, 95, and 94%, respectively. A meta-analysis by Isasi *et al.* [14] evaluated 18 studies (a total of 808 patients with recurrent breast cancer) and indicated that the pooled sensitivity of a PET/CT scan was 90%, with a false-positive rate of 11%. According to the previous studies, the sensitivity of conventional imaging for the detection of all recurrence lesions was less than that of the PET/CT scan [15–18]. Therefore, in the context of accuracy, PET/CT appears to be an effective surveillance tool and our results highlight the effective diagnostic performance of fourth and subsequent follow-up PET/CT in following patients with breast cancer.

The present study showed that fourth and subsequent follow-up PET/CT results have an impact on the clinical assessment of patients with breast cancer in about 24% (10.5 and 13.4%) of scan times. These scans are useful in excluding tumor in 13.4% of patients with a clinical suspicion of recurrence and identifying suspected recurrence in 10.5% of patients with no previous clinical suspicion. Previous studies have shown that PET/CT scans can rule out disease recurrence in a range of 15.2 to 42.5% when there is a clinical suspicion of recurrence before the scan (high tumor marker, clinical sign and symptom, radiographic sign of recurrence) [13,19]. Chang *et al.* [20] assessed the value of a PET/CT scan in 71 patients with a clinical suspicion of recurrent breast cancer and 69 patients without a clinical suspicion of recurrence and reported that the PET/CT scan actually ruled out disease in 38% of patients with a clinical suspicion of recurrence and identified suspected recurrence in 10.1% of patients with no previous clinical suspicion. Our results show that although the impact of late (fourth and subsequent) follow-up PET/CT scans is less than early follow-up scans, it still has a considerable effect (24%) on the clinical assessment of patients with breast cancer.

We found that the fourth and subsequent follow-up PET/CT scans led to a change in the overall management of patients in 21% (90/426) of scan times, more for patients with clinical suspicion of recurrence (81/292, 27.7%) than in asymptomatic patients (9/134, 6.7% of scans). Our result is in agreement with a previous study by Chang *et al.* [20], which showed a change in the planned management of 30% of breast cancer patients after PET/CT, including 49% of patients with suspected recurrence and 10% of asymptomatic patients. Previous studies have largely focused on evaluating the impact of follow-up PET/CT scan on the management of patients with breast cancer when there was a clinical suspicion of recurrence. The follow-up PET/CT scan could alter the therapeutic plan in about 32–57% of patients with breast cancer when there was a suspicion of recurrence [3,19 – 21]. Grahek *et al.* [22] evaluated the impact of a PET/CT scan on the management of patients with recurrent breast cancer and reported that a PET/CT scan led to a change in management in 44% of patients. Similarly, Manohar *et al.* [12] showed that PET/CT scans led to a change in the modality of treatment in 41% of patients with recurrent breast cancer. The wide difference between our results and the previous studies is likely because previous studies included only

patients with a clinical suspicion of recurrence and included follow-up scans without considering the number of follow-up scans. However, in the present study, we included all of the late (fourth and subsequent) follow-up PET/CT scans (with or without previous clinical suspicion of recurrence).

The present study shows that the fourth and subsequent follow-up PET/CT scan results are associated with the OS and prognosis of patients with breast cancer. The survival rate of those who had a positive late follow-up scan is lower than for patients with all negative late follow-up scans. Multiple previous studies have shown that staging and therapy assessment PET/CT scans provided information for prognosis stratification of patients with breast cancer [23–25]. However, very few studies have evaluated the value of a follow-up PET/CT scan on the survival of patients with breast cancer. Cochet *et al.* [3] reported that follow-up PET/CT findings predicted the survival of patients with a suspicion of recurrent breast cancer, whereas conventional imaging was not a significant predictor of survival in these patients.

This study was carried out retrospectively and the limitations of a retrospective study must be considered. The clinical indication of the study was retrospectively recorded from the patient medical records, which could potentially have led to underestimation of the clinical suspicion before PET/CT scans. A public registry and the patient medical records at our hospital were used to determine the date of death for patients. There may be a time lag between death and public registry update, which may have resulted in loss of accurate mortality data. However, in patients who were alive, the OS was censored to their last date of follow-up at our institution and this could have affected the results of survival. We used OS rather than cancer-specific survival as this is a more valuable end point and is used most commonly. Patients had up to 20 follow-up scans and a patient-level analysis would be more valuable than a scan-level analysis.

Conclusion

Our study showed that the fourth and subsequent followup ^{18}F -FDG PET/CT study adds value to clinical assessment, has an impact on treatment planning, and predicts prognosis in patients with breast cancer. The change in the management of scans performed in the appropriate clinical context was significantly greater than the scans performed without clinical suspicion. Hence, fourth and subsequent scans without an appropriate clinical context should be avoided.

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Fig. 1.

Percentage of patients who had more than three follow-up PET/CT scans. The number of follow-up scans per patient ranged from four to 20 scans. Forty-seven (51.1%) patients had four to six follow-up scans, 27 (29.3%) patients had seven to 10 follow-up scans, and 10 (19.6%) patients had 11 or more follow-up scans. CT, computed tomography.

Fig. 2. Kaplan–Meier analysis on the basis of the PET/CT scan results. CT, computed tomography.

Table 1

Characteristics of the patients included in the study

Characteristics	Survived (N = 48)	Died (N = 44)	P-value
Age (mean $\pm$ SD)	57 $\pm$ 13	59 $\pm$ 12	0.4
Race			
White	41	35	0.7
Black	4	6	
Other	3	3	
Histology			
Ductal	27	20	0.2
Lobular	3	6	
Other	4	3	
Unknown	14	15	
ER			
Negative	10	12	0.5
Positive	31	28	
Unknown	7	4	
PR			
Negative	17	17	1
Positive	23	23	
Unknown	8	4	
HER2neu			
Negative	24	27	0.05
Positive	12	4	
Unknown	12	13	
Grade			
1	2	1	0.7
2	7	9	
3	9	12	
Unknown	30	22	
Stage			
1	6	5	0.1
2	8	8	
3	5	11	
4	10	4	
unknown	19	16	
Treatment			
CT	1	3	0.6
RT	0	1	
Sx	10	22	
CRT	4	8	
Sx + CT	11	19	

Characteristics	Survived (<i>N</i> = 48)	Died (<i>N</i> = 44)	<i>P</i> -value
Sx + RT	6	13	
Sx + CRT	16	9	
Clinical suspicion			
Without suspicion	19	8	0.02*
With suspicion	29	36	
Scan result			
All negative	20	3	< 0.001*
At least one positive	28	41	
Follow-up (median) (months)	30.7	14.7	0.003*

CRT, chemoradiotherapy; CT, chemotherapy; ER, estrogen receptor; PR, progesterone receptor; RT, radiotherapy; Sx, surgery.

Table 2

Fourth and subsequent follow-up PET/CT results were valuable in excluding tumor in 13.4% of patients with a clinical suspicion of recurrence and identifying suspected recurrence in 10.5% of patients with no previous clinical suspicion

Scan type	Scan result (%)			
	True positive	True negative	False positive	False negative
Without suspicion	10.5	88	0.75	0.75
With suspicion	84.1	13.4	0.68	1.72

CT, computed tomography.

Table 3

Impact of follow-up PET/CT on patient management

Scan impact on breast cancer treatment	Scan result		Total (N = 426) [n (%)]
	+	–	
No treatment to no treatment	5	66	71 (16.7)
Treatment to continue same treatment	166	94	260 (61)
No treatment to new treatment	24	0	24 (5.6)
Treatment to change in treatment	64	0	64 (15)
Treatment to treatment stopped	0	2	2 (0.4)
Treatment change unknown	5	0	5 (1.2)

+, positive scan;

–, negative scan;

CT, computed tomography.

Table 4

Univariate and multivariate Cox regression analyses

Cox model	Variables	HR	95% CI	P
Univariate	Age	1.01	0.9–1.04	0.1
	Race	1.03	0.6–1.7	0.9
	Histology	1.16	0.7–1.7	0.5
	ER	0.91	0.4–1.8	0.8
	PR	1.07	0.5–2	0.8
	Her2neu	0.37	0.1–1	0.06
	Grade	1.13	0.5–2.3	0.7
	Stage	1	0.7–1.4	0.9
	Primary treatment	0.9	0.7–1	0.2
	Clinical suspicion	2.9	1.3–6.2	0.007*
	Scan result	7.6	2.3–24.8	0.001*
	Treatment impact	1.6	1.2–2.1	< 0.001*
Multivariate	Clinical suspicion	1.5	0.6–1.4	0.3
	Scan result	4.65	1.3–16.8	0.019*
	Treatment impact	1.3	0.9–1.8	0.08

CI, confidence interval; ER, estrogen receptor; HR, hazard ratio; PR, progesterone receptor.

* Statistically significant.