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ORIGINAL ARTICLE

The Effects of Preoperative ^{18}F-FDG PET/CT in Breast Cancer Patients in Comparison to the Conventional Imaging Study

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Purpose: There have been recent studies of the ^{18}F-fluorodeoxyglucose positron emission tomography and computed tomography (^{18}F-FDG PET/CT) in the staging, detection, and follow-up of the breast cancer occurrence and recurrence. There was controversy concerning the use of ^{18}F-FDG PET/CT for staging primary breast cancer. In this study, we investigated the potential effects of ^{18}F-FDG PET/CT in the initial assessment of patients with primary breast cancer. **Methods:** From January 2008 to December 2009, 154 consecutive biopsy-proven invasive breast cancer patients were enrolled in this study. Patients underwent conventional imaging studies including mammography, breast ultrasonography (USG), and magnetic resonance imaging for local assessment, and plain chest X-ray, liver USG, and bone scan to rule out distant metastasis. All 154 patients underwent ^{18}F-FDG PET/CT in the initial assessment. **Results:** ^{18}F-FDG PET/CT did not detect primary breast lesions in 16 patients with a sensitivity of 89.6% and detected only 5 multiple lesions (12.5%) out of 40 cases. Histologically confirmed axillary lymph node (LN) metastases were in 51 patients, and the sensitivity and specificity of ^{18}F-FDG PET/CT to detect metastatic axilla were 37.3% and 95.8%, respectively; whereas the corresponding estimates of USG were 41.2% and 93.7%, respectively. Eleven extra-axillary LN metastases were found in eight patients, and seven lesions were detected by ^{18}F-FDG PET/CT only. The sensitivity and specificity of ^{18}F-FDG PET/CT in detecting distant metastasis were 100% and 96.4%, respectively; whereas the sensitivity and specificity of the conventional imaging were 61.5% and 99.2%, respectively. **Conclusion:** ^{18}F-FDG PET/CT cannot be recommended as a primary diagnostic procedure in breast cancer, but it has the potential to be used as an additional imaging tool for the detection of axillary metastasis, distant metastasis, and extra-axillary LN metastasis. ^{18}F-FDG PET/CT cannot solely replace the conventional diagnostic procedure in primary breast cancer. The best approach may be the combination of different imaging modalities.

Key Words: *Breast, Carcinoma, Computed tomography, Diagnostic imaging, Positron-emission tomography*

INTRODUCTION

Breast cancer is the most common malignancy in the female population of the Western countries, and is the second common newly diagnosed malignancy in the Korean women. In Korea, the number of early breast cancer detection has increased due to the development of the screening programs, but the detection rate of advanced breast cancer has not decreased. The thorough evaluation of the metastasis is important in making decisions on and managing this type of advanced breast cancer.

According to the National Comprehensive Cancer Network guidelines, the following imaging tests can be used to diagnose and stage locally advanced breast cancer: bilateral mammography (MMG), breast ultrasonography (USG) as necessary, chest imaging if the patient had no symptoms or other abnormal staging studies, and breast magnetic resonance imaging (MRI), bone scintigraphy (BS), abdominal and/or pelvic computed tomography (CT), USG, and MRI if the patients had symptoms or other abnormal staging studies.

The ^{18}F-fluorodeoxyglucose positron emission tomography

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and computed tomography (^{18}F-FDG PET/CT) have recently been introduced in the staging of the breast cancer. However, most studies include women with recurrent or metastatic disease, or study the use of ^{18}F-FDG PET or ^{18}F-FDG PET/CT in the evaluation response [1-4]. Recently, some studies have emerged which deal with the added value of using the ^{18}F-FDG PET/CT over the conventional testing for staging primary breast cancer [5-8]. Research shows that the ^{18}F-FDG PET/CT cannot replace the sentinel node biopsy for evaluating axillary lymph node (LN) status, because ^{18}F-FDG PET/CT showed the low negative predictive value in detecting axilla. But a consistently high specificity in detecting metastatic axillary LNs was demonstrated, and it may be helpful in preventing unnecessary sentinel node biopsies for the patients with positive axilla results from the ^{18}F-FDG PET/CT. Also the ^{18}F-FDG PET/CT had the advantage of identifying internal mammary and mediastinal LNs metastasis, and it can be used in detecting bone metastasis as a complementary method. In 32% to 58% of patients, ^{18}F-FDG PET/CT created a change in the therapeutic plans for the breast cancer clients. The FDG uptake values also correlated with the prognosis in some studies [1,2,5-8].

At this time, the ^{18}F-FDG PET/CT is not a routine imaging modality for early breast cancer staging. Rather, the ^{18}F-FDG PET/CT is recommended as an adjunctive evaluation method of distant metastasis and regional LN in advanced breast cancer. In South Korea, ^{18}F-FDG PET/CT is covered by the medical insurance in the diagnosed cancer patients, and many primary breast cancer patients have undergone the exam on initial staging. At the center, we used bilateral MMG, breast USG, MRI, chest X-ray, BS, abdominal and/or pelvic USG as initial conventional staging methods of newly diagnosed breast cancer. In this study, we evaluated the diagnostic role of ^{18}F-FDG PET/CT in newly diagnosed breast cancer in comparison to the conventional imaging methods. The first aim of this study was to evaluate the diagnostic role of ^{18}F-FDG PET/CT in the detection of primary tumors and the pathologic axillary LNs and distant metastasis including bone, lung, liver, and soft tissues. The second aim of this study was to evaluate whether ^{18}F-FDG PET/CT can replace the conventional imaging for the detection of distant metastases.

METHODS

Study patients

We retrospectively reviewed the 154 consecutive patients with invasive breast cancer who were newly diagnosed at the Department of Surgery, Eulji University Hospital from January 1, 2008 to December 31, 2009. Patients with invasive breast cancer who were diagnosed with excisional biopsy were excluded in this study, because of the nonvisualization of primary tumor. Most patients underwent MMG, breast USG, and core needle biopsy to confirm the presence of breast cancer. The majority of the patients underwent conventional preoperative staging procedures, including the biochemistry for the liver function, the conventional imaging procedures (including chest X-ray, bilateral MMG, breast USG, breast MRI, BS, abdominal, and/or pelvic USG), and tumor markers (including CEA, CA 15-3). The axillary and internal mammary LNs are defined as abnormal, if any LN has a cortex of more than 2 mm in size, or if there were morphologic LN changes. The ^{18}F-FDG PET/CT was studied in all 154 patients before the initiation of any therapy, in order to evaluate the usefulness of the exam. We reviewed the medical record of each patient for clinical information including age at diagnosis, follow-up status, and outcome information. Pathological parameters were evaluated including the tumor size, LN metastasis, hormone receptor status, nuclear grade, c-erbB-2, and p53 status. The breast cancer stage was classified according to the TNM criteria of the American Joint Committee on Cancer (AJCC), 6th edition. The protocol for the study was approved by the Institutional Review Board (approval number, 09-06) of the Eulji University Hospital.

^{18}F-FDG PET/CT imaging and image interpretation

All patients were studied with the ^{18}F-FDG PET/CT after the results of the core needle biopsy. All examinations were performed using a Discovery 690 PET/CT scanner (General Electric Medical System, Milwaukee, USA). The PET/CT was performed 60 minutes after the injection of 5.55 MBq of fluorodeoxyglucose (FDG) per kilogram of body weight. A helical non-enhanced CT scan was acquired from the top of the skull base to mid-thigh in normal breathing. Immediately after the CT, a PET was performed covering the same axial field of view of the body. PET emission data were acquired at the 2 minutes per bed position. The blood glucose measurements obtained before the scanning were lower than 180 mg/dL. The PET images were generated by using a standard three-dimensional VPFX time-of-flight reconstruction algorithms with the CT-based attenuation correction.

All PET/CT images were read directly from the screen of the computer workstation. The region of interest was drawn on the fused PET/CT image to measure the peak standardized uptake value (SUV) of the breast lesions. In this study, SUV = (peak kBq/mL in region of interest)/(injected activity/g of body weight). Except for the primary tumor sites, all foci with pathologic uptake higher than the liver activity were reported as positive and suspicious, if the uptake was focal and related

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to the anatomical structures or pathological findings on the corresponding CT slices. More diffuse pathological uptake was reported as the nonmalignant inflammatory change, and reported as negative.

Reference standard

Histopathologic results were used as the final standard. If the tissue or cell diagnosis was unattainable, additional images and clinical follow-up studies were used to evaluate the clinical significance of other lesions detected on ^{18}F-FDG PET/CT.

Statistical analysis

The concordance between conventional imaging and ^{18}F-FDG PET/CT was evaluated using the SPSS software statistical package version 13.0, for Windows (SPSS Inc., Chicago, USA). The negative predictive value, positive predictive value, sensitivity, and specificity of ^{18}F-FDG PET/CT were calculated by the standard methods. Univariate analyses were carried out using the Pearson chi-square test. Statistical significance was defined as p-value < 0.05.

RESULTS

Patient characteristics

The median age of the study population at diagnosis was 52 years (range, 30-81 years). The ductal histology was the most prevalent type in 141 patients (91.5%), and the lobular histology was prevalent in four patients (2.7%). The remaining nine patients (5.8%) had other histology including the mucinous, tubular, and medullary type. Sixty-five patients (42.2%) had stage I disease, 51 patients (33.1%) had stage II disease, and 21 patients (13.6%) had stage III disease. Thirteen patients (8.4%) had stage IV disease. The details on the distribution of the clinicopathological factors in the study cohort are listed in Table 1. Mastectomy was performed in 74 patients (50.4%), and 72 patients (49.6%) underwent the breast-conserving surgery.

Table 1. Clinicopathologic characteristics of 154 patients

Characteristic	No. (%)
Age (yr)*	52 (30-81)
Tumor size (cm)	
≤2	89 (57.7)
>2, ≤5	51 (33.1)
>5	14 (9.1)
Lymph node metastasis	
Negative	95 (61.7)
Positive	59 (38.3)
Distant metastasis	
Negative	142 (92.2)
Positive	12 (7.8)
AJCC stage	
I	69 (44.8)
IIA-IIB	51 (33.2)
IIIA-IIIC	21 (13.6)
IV	13 (8.4)
Histology	
Ductal	141 (91.5)
Lobular	4 (2.6)
Others	9 (5.8)
Operation method	
Mastectomy	74 (50.4)
Breast-conserving surgery	72 (49.6)

AJCC = American Joint Committee on Cancer.
*Median (range).

^{18}F-FDG PET/CT in the detection of primary tumor and axilla

Table 2 shows the diagnostic abilities of USG, MRI, and ^{18}F-FDG PET/CT on the evaluation of primary tumors and axillary LNs. Breast USG detected primary lesions in 153 out of 154 patients. Out of 132 patients who were studied with breast MRI, the breast MRI did not detect primary breast lesions in two patients. ^{18}F-FDG PET/CT did not detect primary breast lesions in 16 (10.4%) patients. On the evaluation of primary lesions in the diagnosed breast cancer, the sensitivity of USG, MRI, and ^{18}F-FDG PET/CT was 99.4%, 98.5%, and 89.6%, respectively. ^{18}F-FDG PET/CT detected all primary breast lesions with the tumor size above 2 cm. But in 89 patients with a T1 lesion, ^{18}F-FDG PET/CT detected only 73 (81.0%) primary breast lesions. When the differentiate T1 lesion was above 1 cm or below 1 cm, PET/CT detected 17 (70.8%) primary breast lesions below 1 cm and 56 (86.2%) primary breast lesion above 1 cm. Among the 16 lesions with negative primary on

Table 2. Results of the USG, MRI, and ^{18}F-FDG PET/CT evaluation of primary lesion and axillary region

	USG		MRI		^{18}F-FDG PET/CT	
	Pos.	Neg.	Pos.	Neg.	Pos.	Neg.
Primary tumor						
+	153	1	130	2	138	16
Sensitivity (%)		99.3		98.4		89.6
Multiple lesion						
+	32	8	29	8	5	35
-	9	105	13	82	1	113
Sensitivity (%)		80.0		78.4		12.5
Specificity (%)		92.1		86.3		99.1
Axillary LN metastasis						
+	21	30	16	24	19	32
-	6	89	11	78	4	91
Sensitivity (%)		41.2		40.0		37.3
Specificity (%)		93.7		87.6		95.8

USG = ultrasound; MRI = magnetic resonance imaging; ^{18}F-FDG PET/CT = ^{18}F-fluorodeoxyglucose positron emission tomography and computed tomography; Pos. = positive; Neg. = negative; LN = lymph node.

^{18}F-FDG PET/CT, 15 patients had ductal histology and one patient had metaplastic carcinoma. All four patients with lobular carcinoma showed ^{18}F-FDG PET/CT-positive primary lesions. The postoperative histology revealed multifocal tumors in 40 case out of 154 cases (26.0%). The sensitivity of breast USG, breast MRI, and ^{18}F-FDG PET/CT in the detection of multiple lesions were 80.0%, 81.1%, and 12.5%, respectively, and the specificity was 92.1%, 86.3%, and 99.1%, respectively.

Out of 146 patients who underwent axillary surgery, the pathologic examination confirmed metastases in 51 cases (34.9%). The USG assessment showed suspicious LNs in 27 patients, with the pathologic examination of 21 patients among the 27 showing confirmed node positivity. Axilla USG had a sensitivity of 41.2% and specificity of 93.7%. ^{18}F-FDG PET/CT indicated axillary involvement in 23 cases, and histology confirmed positivity in 19 patients, with the sensitivity of 37.3% and specificity of 95.8%. ^{18}F-FDG PET/CT did not detect any micrometastases, and only two cases of the axillary LN metastases were detected by ^{18}F-FDG PET/CT only. Out of 129 patients who were studied with MRI, MRI detected suspicious lesions in 27 patients, and histology confirmed it in 16 patients (sensitivity, 40.0%; specificity, 87.6%). ^{18}F-FDG PET/CT showed comparable sensitivity in comparison with USG and MRI, but showed relatively high specificity in detecting metastatic axilla.

^{18}F-FDG PET/CT in the detection of extraaxillary LNs

In eight patients (5.2%), extraaxillary LNs were detected by ^{18}F-FDG PET/CT. Table 3 shows the patients with extraaxillary LN metastasis detected on the ^{18}F-FDG PET/CT. Three patients showed multiple anatomical localizations of extraaxillary LN involvement. Lymph nodes outside the axilla on ^{18}F-FDG PET/CT were localized in the supraclavicular (2 LNs), internal mammary (2 LNs), mediastinal (3 LNs), paraaortic (1 LN), and inguinal (1 LN), pelvic (1 LN), and deep cervical (1 LN). Out of these 11 extraaxillary LN lesions, seven lesions were not detected by initial conventional imaging. Further enhanced chest and abdomen-pelvis CT and inguinal USG were studied in ^{18}F-FDG PET/CT-only lesions. The mediastinal lesions in two patients were not detected in additional enhanced chest CT. The inguinal lesions were revealed as reactive LN on fine needle aspiration cytology. Out of 11 suspected extraaxillary LN lesions, eight were not verified by the histopathological examination, because the surgery did not include the resection of these LN regions, but all eight lesions may have had metastasis.

^{18}F-FDG PET/CT in the detection of distant organ metastasis

On the initial ^{18}F-FDG PET/CT evaluation, 13 patients showed high FDG uptake in distant organ. Out of 13 ^{18}F-FDG PET/CT positive patients, eight patients with FDG uptake on the distant organ (5 bone, 2 lung, 1 liver) showed concordant findings on the conventional studies as well. One patient with bone metastasis was detected by ^{18}F-FDG PET/CT only (Figure 1). ^{18}F-FDG PET/CT showed small suspicious ^{18}FDG positive lesions on right sacrum and ileum, which were equivocal findings on the initial bone scan. The lesions thought to be lytic bone metastases on the bone MRI and follow-up study of 6 months showed increased size of lesions. In contrast, ^{18}F-FDG PET/CT showed false positive findings in four patients. Three patients had the ovary uptake that was revealed as benign functional cyst on the laparoscopic biopsy. One patient

Table 3. Results of eight patients with extraaxillary LN metastasis on ^{18}F-FDG PET/CT

Pt.	Age	Sites of extraaxillary LN	SUV	Conventional imaging	Tumor size (cm)	Distant organ metastasis	Results of pathologic evaluation	Results of extraaxillary LN	Follow-up duration (mo)
1	39	Mediastinal	5.14	Not identified	2.5	Bone	NA	Positive	42
2	51	SCN	6.40	Identified	3.8	Liver	NA	Positive	8*
3	39	IM	4.76	Positive	3.25	-	NA	Positive	43†
		Deep cervical	1.71	Not identified			NA	Positive‡	
4	54	Inguinal, pelvic	4.08	Not identified	2.3	-	Reactive§	False positive	38
			3.20	Not identified					
5	49	Mediastinal	5.36	Not identified	Inflammatory cancer	-	NA	Positive	31*
6	65	Paraaortic, mediastinal	4.79	Not identified	3.8	-	NA	Positive‖	47
			4.05	Not identified			NA		
7	31	SCN	5.53	Positive	Inflammatory cancer	Bone	NA	Positive	26
8	63	IM	2.42	Positive	2.7	-	Metastasis	Positive	23

LN = lymph node; ^{18}F-FDG PET/CT = ^{18}F-fluorodeoxyglucose positron emission tomography and computed tomography; Pt. = patient; SUV = standardized uptake value; SCN = supraclavicular; IM = internal mammary; NA = not available.
*Expired; †Recurrence on contralateral axilla in 24 months; ‡The size of deep cervical LN was increased; §Revealed as reactive LN on fine needle aspiration cytology; ‖Disappeared in 40 months.

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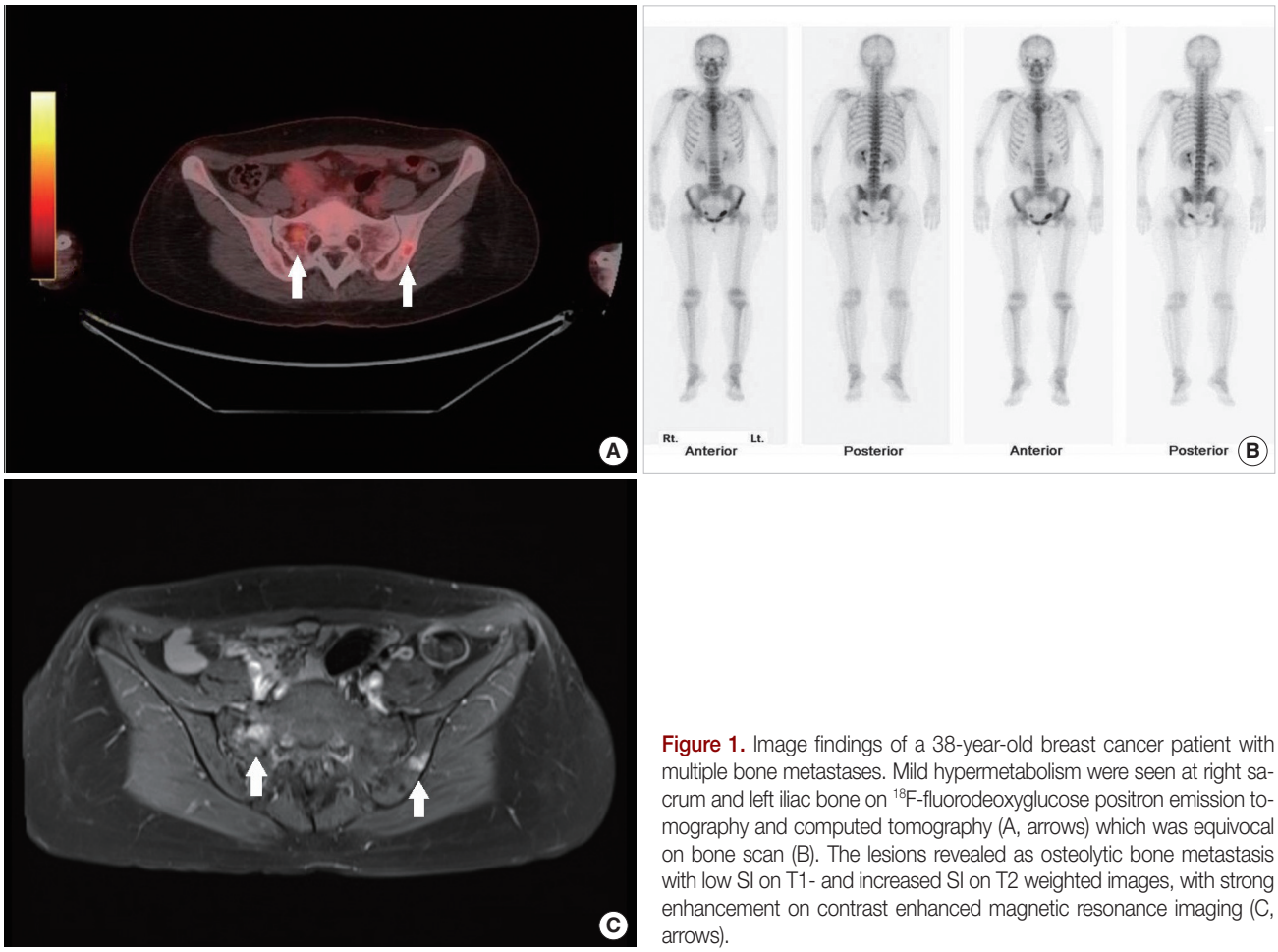

Figure 1. Image findings of a 38-year-old breast cancer patient with multiple bone metastases. Mild hypermetabolism were seen at right sacrum and left iliac bone on ^{18}F-fluorodeoxyglucose positron emission tomography and computed tomography (A, arrows) which was equivocal on bone scan (B). The lesions revealed as osteolytic bone metastasis with low SI on T1- and increased SI on T2 weighted images, with strong enhancement on contrast enhanced magnetic resonance imaging (C, arrows).

had the lung uptake that was revealed as an inflammatory nodule by a serial follow-up chest CT with 21 months clinical follow-up period.

On the conventional studies, nine patients showed positive findings. Of those, eight patients showed concordant findings with the ^{18}F-FDG PET/CT results. One patient with suspicious intramedullary metastasis on the left fibula as found in the bone scan, and had a negative finding on the ^{18}F-FDG PET/CT, revealed as benign bone tumor a discovered in the bone biopsy. When all distant metastasis were encountered, including extraaxillary LNs, 13 patients were revealed as having distant metastases. The overall sensitivity and specificity in detecting distant metastases of the ^{18}F-FDG PET/CT were 100% and 96.4%, respectively; whereas the sensitivity and specificity of the conventional imaging were 61.5% and 99.2%, respectively.

DISCUSSION

In the present study, we compared the diagnostic ability of ^{18}F-FDG PET/CT and conventional imaging in 154 newly diagnosed breast cancer patients. If ^{18}F-FDG PET/CT can cover all diagnostic staging by one study, other unnecessary conventional imaging studies can be omitted.

In various studies, the role of ^{18}F-FDG PET/CT in detecting the primary breast lesion showed some limitations. Segaert et al. [9] reported a 97% detection rate in stage IIB and III breast cancer. Inokuchi et al. [10] reported that the ^{18}F-FDG PET/CT was 80% sensitive in the detection of primary breast cancer, and especially less sensitive in small sized, low grade tumor. It has previously been reported that the accuracy of ^{18}F-FDG PET/CT is affected by the tumor size. It may also be affected by the histology with a more intense FDG-uptake in the high-grade lesions than those with an aggressive behavior, which therefore may have prognostic consequences [11]. Our study results were that the ^{18}F-FDG PET/CT detected the primary breast lesion in 138 (89.6%) patients, and all primary tumors above 2 cm were detected by ^{18}F-FDG PET/CT. However ^{18}F-FDG PET/CT showed less sensitivity in the detection of tumor sizes less than 20 mm (81.0%), especially the tumors less than 10 mm (70.8%). As most patients in the study had the ductal

histology, we cannot identify the diagnostic ability of ^{18}F-FDG PET/CT regarding histology.

Multiplicity is the predisposing factor in local recurrence after breast-conserving surgery, and there are many approaches to finding the most powerful imaging studies in detecting multiplicity. Most often, MRI has been thought to be the sensitive study in multiplicity, but in this study, USG was the most sensitive study in comparison to MRI and ^{18}F-FDG PET/CT. There are many contradictory results of other studies, showing the high sensitivity of ^{18}F-FDG PET/CT [6,12]. This study did not find the diagnostic roles of ^{18}F-FDG PET/CT in differentiating multiple tumors and a single tumor, with the low sensitivity of 12.5%. Breast USG was the most sensitive study in detecting primary lesions and evaluating multiplicity. Because breast MRI showed comparable results with USG and ^{18}F-FDG PET/CT showed many false negative cases, it was seen unnecessary to detect the primary lesion and multiplicity with MRI or ^{18}F-FDG PET/CT. As this study involves the pathologically confirmed breast cancer cases, we cannot evaluate the specificity of multiple diagnostic modalities in detecting primary breast cancer.

In this study, the ^{18}F-FDG PET/CT was 37.3% sensitive and 95.8% specific for detecting metastatic axilla. Several studies have reported low sensitivities of ^{18}F-FDG PET/CT for the detection of axillary metastasis, ranging from 37% to 85%. The ^{18}F-FDG PET/CT was less sensitive for the detection of small (< 10 mm) sized metastatic LN (29.4%), and could not detect micrometastasis [10,13-15]. But others reported the high sensitivity and specificity of ^{18}F-FDG PET/CT in detecting axilla, and that ^{18}F-FDG PET/CT could modify the TNM staging in 47% [12]. Relatively, ^{18}F-FDG PET/CT showed high specificity in most studies. Another study compared sentinel lymph node biopsy (SLNB) and ^{18}F-FDG PET/CT in detecting occult axillary metastasis and reported low sensitivity (37%) of ^{18}F-FDG PET/CT, but acceptable specificity and positive predictive values (96% and 88%, respectively) [14]. They concluded that the high specificity of ^{18}F-FDG PET/CT indicates that patients who have the ^{18}F-FDG PET/CT-positive axilla should have the ALND rather than the SLNB for axillary staging. This study was not able to conduct a direct comparison, as we omitted axillary dissection in SLN-negative patients; however, the ^{18}F-FDG PET/CT showed the relatively high specificity in detecting axilla than other studies. As a result, in patients with ^{18}F-FDG PET/CT-positive axilla, we can omit the time-consuming SLNB rather perform an immediate axillary dissection. But there is a possibility that our results may lead to more false positive patients who may undergo axillary lymph node dissection (ALND) unnecessarily. There were four patients with false positive ^{18}F-FDG PET/CT in this study. LN biopsy under USG-guided localization may be helpful in those patients, and they would not undergo unnecessary ALND. In this study, there were many false negative cases of ^{18}F-FDG PET/CT in detecting axilla. As such, although the positive axillary ^{18}F-FDG PET/CT is a good predictor of axillary disease and correlates well with SLNB, the relatively poor sensitivity must considered in treatment planning. The SLNB needs to be performed carefully in those patients. To increase the sensitivity of ^{18}F-FDG PET/CT in assessing the primary lesion and axilla, some reported the increased sensitivity when the exam was studied in the prone position. In prone position, the tumor can be more clearly distinguished from adjacent structures and offers a more extensive evaluation of the axillary fat and its lymph nodes. The low sensitivity of ^{18}F-FDG PET/CT in local assessment can be increased by these protocols, and more studies will be needed [16].

^{18}F-FDG PET/CT was especially important in our series in detecting disease of extraaxillary nodal regions, such as supraclavicular, internal mammary, and mediastinal lesions. Bernsdorf et al. [17] reported that ^{18}F-FDG PET/CT solely detected six cases of distant metastasis and 12 cases of extraaxillary LN involvement, in comparison of the conventional imaging in early breast cancer above 2 cm. Because they studied MMG, breast USG, chest X-ray, and blood samples on conventional staging, ^{18}F-FDG PET/CT could be only diagnostic modality of the metastasis work up. This study included the abdomen USG and bone scan on the initial conventional studies, and the results showed some small advantages of ^{18}F-FDG PET/CT in comparison to the previous study's results. In our patients, we detected seven extraaxillary LNs by ^{18}F-FDG PET/CT only. In the present study, most suspected extraaxillary LNs on ^{18}F-FDG PET/CT only were not verified by histopathological examination, because the surgery did not include the resection of these lymph node regions. However most patients with extraaxillary LN metastasis detected by ^{18}F-FDG PET/CT only were in the advanced stage, and all were thought to have metastases. The only false positive lesion is in the inguinal and pelvic uptake in patients with stage IIA disease. It showed a benign reactive finding with intact fatty hilum on the inguinal USG and was revealed as benign reactive lymphadenopathy on the fine needle aspiration cytology. Out of these ^{18}F-FDG PET/CT-positive extraaxillary LN lesions, two mediastinal lesions were not detected in further enhanced chest CT imaging. Although these lesions cannot change the treatment plan because of the advanced stage of the disease, we cannot detect these lesions without ^{18}F-FDG PET/CT. In one patient, the only metastatic lesions were paraaortic LN and mediastinal LNs. She had stage IIB disease without the ^{18}F-FDG PET/CT, and after ^{18}F-FDG PET/CT, her stage was increased to stage

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IV and we started chemotherapy.

Because of the small number of cases of the internal mammary LN metastasis, we cannot identify the role of ^{18}F-FDG PET/CT as superior. But the presence of positive internal mammary lymph nodes represent N3 breast cancer, thus their identification has important prognostic and staging implications. This is relevant, because patients with undiagnosed disease in internal mammary chain are likely to have worse prognosis than those without malignant involvement of these nodes. The superiority of ^{18}F-FDG PET/CT in the detection of extraaxillary LN metastasis has been reported by others [1]. They concluded to design a prospective study using the histopathology for confirmation, and to validate the value of the PET-CT in the diagnosis of internal mammary LN involvement. But clinically, there are many difficulties in the pathologic identification of all suspicious extraaxillary LNs, and discussion is needed on the advantages and disadvantages of the pathologic identification of extraaxillary nodal lesions.

In many studies, ^{18}F-FDG PET/CT seems to be more effective than the conventional imaging methods in detecting occult distant metastasis, and effective in detecting pleural and abdomino-pelvic metastasis [12,18]. In this study, the ^{18}F-FDG PET/CT showed a higher sensitivity than the conventional imaging in the detection of distant organ metastases. Although ^{18}F-FDG PET/CT had superior sensitivity in detecting distant metastases, it showed low specificity as compared to conventional imaging. Four false negative cases included three ovary and one lung uptake. All three patients with ovarian uptake were young premenopausal patients. In many studies, the increased FDG uptake in the ovaries indicated malignancy in postmenopausal patients. In the premenopausal patients, however, the increased ovarian uptake could be either malignant or functional with low sensitivity [19,20]. The ovary uptake may be false positive, according to the menstrual cycle. Around the time of ovulation may be the increased ^{18}F-FDG uptake in the normal ovaries of premenopausal women, and in our series, the false positive cases may derived from the uptake of corpus luteum or fallopian tube. In many cases, the detection of a dominant functional ovarian cyst on a CT and discussing the menstrual cycle phase with the patient may assist in differentiating the physiologic from the malignant ^{18}F-FDG ovarian uptake. In pulmonary lesions, most benign pulmonary nodules do not accumulate FDG. However, active granulomatous infections like tuberculosis and sarcoidosis can demonstrate increased FDG uptake [21,22]. In our study, one FDG positive pulmonary nodule was thought to be an inflammatory nodule on the serial follow-up that showed no change in shape and size on the chest CT and decreased FDG uptake in the serial ^{18}F-FDG PET/CT.

Many studies have found that ^{18}F-FDG PET/CT is more efficient than bone scintigraphy in detecting lytic and mixed bone metastases and bone marrow involvement, but it sometimes lacks sensitivity to sclerotic bone metastasis, and a multimodality approach is suggested [18,23]. In our study, five metastatic bone lesions were detected by ^{18}F-FDG PET/CT and the bone scan. One patient was detected as having bone metastasis by ^{18}F-FDG PET/CT only. The patient revealed a lytic bone metastasis on the bone MRI. One patient with suspicious intramedullary metastasis in the bone scan, who showed negative finding on the PET-CT, was revealed as having the benign bone tumor on the bone biopsy. No consensus has yet been established regarding the best modality for diagnosing breast cancer bone metastasis and for assessing its response to treatment. The best approach is likely the combination of the different imaging modalities, being aware of the strengths and weaknesses of each technique.

The National Comprehensive Cancer Network 2012 Report concludes that ^{18}F-FDG PET/CT is not indicated in the staging of clinical stage I, II, or operable III breast cancer. The report stated that ^{18}F-FDG PET/CT is most helpful in situations where the standard staging studies are equivocal or suspicious, especially in the locally advanced or metastatic disease. ^{18}F-FDG PET/CT may also be helpful in identifying the unsuspected regional nodal disease and/or distant metastases in locally advanced breast cancer, when used in addition to the standard staging studies. Our study had some limitations in differentiating the diagnostic ability of ^{18}F-FDG PET/CT and conventional imaging studies, because there was a wide range in the stages of the patients and many early stage breast cancer cases. The advantage of our study was that it showed the diagnostic role of ^{18}F-FDG PET/CT in consecutive primary breast cancer patients. In the study, the ^{18}F-FDG PET/CT showed low sensitivity in primary breast lesions, and it showed some advantages in locoregional staging and identifying distant metastasis over the conventional imaging studies.

In conclusion, the use of ^{18}F-FDG PET/CT had low sensitivity than the conventional studies in detecting primary lesions and axilla. The ^{18}F-FDG PET/CT showed some advantages in detecting the uncovered extraaxillary nodal metastasis and distant organ metastasis. In primary breast cancer, ^{18}F-FDG PET/CT cannot solely replace the conventional diagnostic procedure in primary breast cancer, with the potential to be useful as an additional imaging tool for the staging and management of the disease.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests

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