Bone Scan or ^{18}F -Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography; Which Modality Better Shows Bone Metastases of Breast Cancer?

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Keywords

Breast cancer · Bone metastasis · FDG PET/CT · Bone scintigraphy

Summary

Background: In this multicenter study, we aimed to compare concurrent ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) and bone scan results of breast cancer patient. **Patients and Methods:** 162 patients with breast cancer (158 female, 4 male; mean age 50.6 years) were included in the study. FDG PET/CT examination was performed in all patients, and concurrent bone scintigraphy in 68 patients. The results of FDG PET/CT and bone scan were compared. **Results:** 132 of the 162 patients were operated on because of breast cancer. 89 patients had metastasis, and 4 had recurrent disease according to FDG PET/CT results. Metastatic sites in order of frequency were lymph nodes, bone, lung, liver, adrenal gland, local skin or muscle, brain, and peritoneum (peritonitis carcinomatosa). The sensitivity, specificity, accuracy, and negative and positive predictive value of bone scintigraphy versus FDG PET/CT were 96 vs. 100%, 100 vs. 98%, 100 vs. 83%, 100 vs. 100%, and 90 vs. 100%, respectively. **Conclusion:** Although the 2 modalities were in concordance with each other, in 5 (21%) cases, FDG PET/CT could not show bone metastasis which were detected on bone scintigraphy. Hence, bone scintigraphy was superior to FDG PET/CT in the determination of bone metastasis derived from breast cancer. However, FDG PET/CT should be considered for soft tissue metastasis.

Schlüsselwörter

Mammakarzinom · Knochenmetastasen · FDG PET/CT · Knochenszintigraphie

Zusammenfassung

Hintergrund: Ziel dieser multizentrischen Studie war es, die Ergebnisse gleichzeitig erstellter ^{18}F -Fluorodesoxyglucose-Positronen-Emissions-Tomographie/Computertomographie (FDG PET/CT)-Studien und knochenszintigraphischer Untersuchungen von Mammakarzinompatienten zu vergleichen. **Patienten und Methoden:** 162 Mammakarzinompatienten (158 weiblich, 4 männlich; mittleres Alter 50,6 Jahre) wurden in die Studie aufgenommen. FDG PET/CT-Studien wurden bei allen Patienten durchgeführt, und 68 wurden gleichzeitig knochenszintigraphisch untersucht. Die Ergebnisse beider Modalitäten wurden verglichen. **Ergebnisse:** 132 der 162 Patienten wurden auf Grund eines Mammakarzinoms operiert. 89 Patienten hatten Metastasen, und 4 Patienten hatten laut FDG PET/CT ein Rezidiv. Metastasen wurden entsprechend der Häufigkeit des Auftretens in folgenden Organsystemen gefunden: Lymphknoten, Knochen, Lunge, Leber, Nebenniere, lokale Haut oder Muskel, Gehirn und Peritoneum (Peritonealkarzinose). Die Sensitivität, Spezifität und Genauigkeit sowie der negative und positive Vorhersagewert der Knochenszintigraphie versus FDG PET/CT waren 96 vs. 100%, 100 vs. 98%, 100 vs. 83% sowie 100 vs. 100% und 90 vs. 100%. **Schlussfolgerung:** Obgleich beide Modalitäten weitestgehend miteinander übereinstimmten, konnte das FDG PET/CT bei 5 (21%) Patienten Metastasen, die in der Knochenszintigraphie sichtbar waren, nicht darstellen. Die Knochenszintigraphie war demnach dem FDG PET/CT bei der Detektion von Knochenmetastasen eines Mammakarzinoms überlegen. FDG PET/CT sollte dennoch bei Weichteilmetastasen in Erwägung gezogen werden.

Introduction

Breast cancer is one of most common malignancies and a serious life-threatening condition. Appropriate staging of breast cancer is important in order to save patients from unnecessary treatments and interventions. Bone is one of the most common distant metastatic sites. Recent reports point out that ^{18}F -fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F -FDG PET/CT) can show distant metastatic disease and change patient management in almost half of all breast cancer patients [1, 2]. Superiority of FDG PET/CT for staging of breast cancer over conventional imaging methods is widely accepted [3, 4]. No direct comparison of ^{18}F PET/CT and ^{18}F FDG PET/CT has been made in the detection of bone metastasis of breast cancer. However, the comparison of these 2 modalities in various cancers has shown them to be complementary [5]. Also, it is expected that ^{18}F imaging will replace bone scan for the detection of breast cancer bone metastasis in the future [5]. Hybrid imaging is certainly superior in the detection of bone metastasis. A recent study has indicated superiority of single-photon emission computed tomography (SPECT)/CT over bone scan and SPECT alone for the detection of bone metastasis in breast cancer patients [6]. Additionally, magnetic resonance imaging (MRI) has been found to be superior to bone scan especially for vertebral metastasis and therefore is recommended for patients with equivocal findings in the vertebral region [7]. Variations according to the either osteolytic or osteoblastic nature of bone metastasis of breast cancer make the diagnosis more complex. Osteolytic metastasis can be more clearly demonstrated by FDG PET/CT, while bone scan can show osteoblastic lesions with greater sensitivity [8, 9]. In this study, we aimed to compare the diagnostic efficacy of FDG PET/CT and bone scan in the detection of bone metastasis in breast cancer patients.

Metastatic site	Patients, n
Lymph node	60
Bone	49
Lung	26
Liver	17
Other	13

Stage	Patients, n
I	63
II	33
III	5
IV	61

Metastatic site	Patients, n	
	PET/CT	CT
Lymph node	9	4
Lung	3	4
Liver	7	6
Adrenal	2	1

Table 1. Distribution of metastatic sites in FDG PET/CT

Table 2. Patient distribution according to stage

Table 3. Positivity of soft tissue metastasis in PET/CT and simultaneous contrast-enhanced CT

Patients and Methods

A total of 162 breast cancer patients (158 female, 4 male; mean age 50.6 years) were retrospectively evaluated. FDG PET/CT examination was performed in all patients, and concurrent bone scan in 68 patients.

FDG PET/CT

All patients fasted for at least 8 h prior to the FDG PET/CT examination and had normal plasma glucose levels. FDG PET/CT was performed with the Siemens Biograph 6 PET/CT system (Siemens AG, Munich, Germany). CT slices and PET emission data were acquired from the skull to mid thigh. Imaging was started approximately 60 min after injection of 370–550 MBq (10–15 mCi; according to body weight) ^{18}F FDG. Oral contrast was administered at the same time as ^{18}F FDG, but no intravenous contrast was performed. Low-dose CT was performed for attenuation correction. CT, PET, and fusion images at transaxial, coronal, and sagittal planes were interpreted visually.

Bone Scan

Subsequent bone scan was performed in 68 patients. 550–1,000 MBq (15–30 mCi; according to body weight) Tc-99m methylene diphosphonate (MDP) were administered intravenously, followed by a saline infusion. Anterior-posterior projection whole body bone scans with spot planar images and SPECT imaging ($n = 5$) were performed after a 2–3 h delay following injection. Imaging was performed with a GE Infinia Dual Head SPECT Gamma Camera (GE Healthcare Israel Ltd., Tirat Hacarmel, Israel) equipped with low-energy high-resolution collimators. Increased asymmetrical tracer uptake at unusual sites was considered metastatic. Equivocal bone scan results ($n = 10$ patients) were confirmed with other imaging methods (CT or MRI) because low-dose CT without intravenous contrast administration in FDG PET/CT was not performed for diagnostic purposes. Interpretation of FDG PET/CT and bone scan results was performed by experienced physicians. Each of the 2 centers interpreted its own images, and no-cross reading was performed. The results of FDG PET/CT and bone scan were compared according to reference standard clinical or imaging follow-up in a patient-based analysis. The sensitivity, specificity, accuracy, and negative and positive predictive values were calculated.

Results

A total of 132 of the 162 patients were operated on because of breast cancer. 89 patients had metastasis, and 4 had recurrent disease according to FDG PET/CT results. Metastatic sites in order of frequency were lymph nodes, bone, lung, liver, adrenal gland, local skin or muscle, brain, and peritoneum (peritonitis carcinomatosa) (table 1). Patients were staged according to PET/CT findings, and the number of patients in each stage is summarized in table 2. A subgroup of these patients also had simultaneous contrast-enhanced CT and comparison with FDG PET/CT results according to the true-positive patients (table 3). Of the 162 patients who received FDG PET/CT, 49 had bone metastasis. 24 of these patients also had a bone scan with 1 (4%) false-negative case. Among the 68 patients who were evaluated by both bone scan and FDG PET/CT, 5 (20%) of the scintigraphically positive patients showed no bone metastasis on FDG PET/CT (figs. 1 and 2). 10 patients who had suspicious findings on bone scan were confirmed to have non-metastatic uptake by morpho-

Fig. 1. **A** Whole body bone scan in anteroposterior projection of a patient with sacral metastasis. **B** Coronal, sagittal, transaxial projection CT, PET and fusion images, and maximum-intensity projection (MIP) images showing no bone metastasis.

Fig 2. **A** Whole body bone scan in anteroposterior projection of a patient with local invasion at the left manubrium sterni and metastasis at the occipital bone of the cranium. **B** Coronal, sagittal, transaxial projection of SPECT images with metastatic uptake at the junction of the right sacroiliac joint and the iliac bone. **C** Coronal, sagittal, transaxial projection CT, PET and fusion images, and maximum-intensity projection (MIP) images showing no bone invasion at the left manubrium sterni. **D** Coronal, sagittal, transaxial projection CT, PET and fusion images, and MIP images without signs of bone metastasis at the right sacroiliac joint and adjacent bone tissue

	Sensitivity, %	Specificity, %	Accuracy, %	NPV, %	PPV, %
Bone scan	96	100	100	98	100
FDG PET/CT	83	100	100	90	100

NPV = Negative predictive value; PPV = positive predictive value.

Table 4. Diagnostic efficacy of bone scan and FDG PET/CT

logical imaging methods (CT or MRI). These lesions had no FDG uptake, and neither CT nor MRI showed metastasis; degenerative changes in the vertebral region and traumatic changes of the ribs were the final interpretation in these patients. The sensitivity, specificity, accuracy, and negative and positive predictive values of both bone scan and FDG PET/CT are summarized in table 4.

Discussion

In this study, we observed bone metastasis in 49 (30%) of 162 breast cancer patients who were referred for FDG PET/CT. That way bone metastasis should be excluded in all breast cancer patients. Other studies also confirm that among patients who are referred for FDG PET/CT, occult distant metastasis can be shown in a significant percentage of patients, which influences the management of those patients [10].

CT has been largely replaced by FDG PET/CT for staging of breast cancer patients. Comparative studies involving both imaging methods show that PET is superior to conventional imaging procedures, especially for distant metastasis [4]. A study concerned with the preoperative staging of breast cancer patients showed that the sensitivity and specificity of FDG PET/CT (100 and 98%, respectively) are higher than those of conventional methods (60 and 83%, respectively) for distant metastasis [3]. In the same study, it was found that bone scan had a lower sensitivity for osteolytic bone metastasis [11]. Yap et al. [2] showed that PET changed the staging in 36% and the treatment modality in 60% of their patients, mostly by showing additional distant metastasis. In contrast to this important diagnostic efficacy of FDG PET/CT, there are some reports about false-negative scans in osteoblastic metastasis [12, 13]. In our study, we also observed that bone scan is superior to FDG PET/CT in detecting bone metastasis. Although FDG PET/CT is an important method for post-operative follow-up and treatment monitoring, further prospective comparative studies are needed to show the superiority of FDG PET/CT in the detection of bone metastasis [14, 15]. A comparative study indicated that the sensitivity of FDG PET/CT for detecting bone metastasis is similar to that of bone scans, and F18 fluoride imaging is more sensitive [16]. In a lesion-based analysis, Hahn et al. [17] found FDG PET/CT to be superior to bone scan in the detection of bone metastasis of breast cancer, with higher sensitivity and equal specific-

ity. A recent study by Morris et al. [18] concluded that while FDG PET/CT can find bone metastasis, it is not clear whether it can replace bone scan. The authors also reported that a high percentage of their patients had non-osseous metastasis, and addressed the value of FDG PET/CT in that regard. In our study, 72% of patients had extra-osseous metastasis. Additionally Morris et al. [18] performed bone biopsies in 28 patients, which was not possible in our study. While FDG PET/CT yielded no equivocal results, follow-up bone scans and additional CT/MRI were performed in 10 patients with suspicious findings on bone scan to decide in these circumstances.

Guidelines recommend bone scan as a screening method but to perform FDG PET/CT to confirm negative or equivocal findings [19]. Since most bone metastases in breast cancer patients are osteolytic, and FDG PET/CT is more successful in the detection of osteolytic bone metastasis, it may be considered as effective. However, because of the 15–20% osteoblastic bone metastases, there is concern about false-negative cases which could not be determined by FDG PET/CT [20]. An analysis based on osteolytic and osteoblastic bone metastasis of breast cancer has shown that FDG PET/CT has limitations in osteoblastic disease [21]. Since there are reports that have determined osteoblastic metastasis in 30% and mixed type in 15% in a lesion-based analysis, PET has limited ability to show all metastatic lesions [22, 23]. There is also a case report with progressive osteoblastic metastasis without any uptake on FDG PET/CT [24].

Limitations of our study are its retrospective nature and the lack of biopsy results. Additionally, SPECT imaging was performed in only 5 patients. However, we observed that SPECT imaging shows more lesions than planar bone scan in patients with bone metastasis. In our opinion, SPECT imaging would be an important tool for lesion-based analysis. Our results demonstrated the clinical significance and superiority of bone scan in showing bone metastasis of breast cancer in a large study population. Although FDG PET/CT is an important method for breast cancer patient evaluation, it may be insufficient as a sole method to determine bone metastasis. Future prospective studies are warranted to confirm these results.

Disclosure Statement

The authors declare no conflicts of interest.

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