Clinical Imaging 38 (2014) 109–114

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: http://www.clinicalimaging.org

Role of ^{18}F-FDG PET/CT in differentiation of a benign lesion and metastasis on the ribs of cancer patients

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ARTICLE INFO

Article history:
Received 23 April 2013
Received in revised form 27 October 2013
Accepted 19 November 2013

Keywords:
PET/CT
SUVmax
Rib
Metastasis

ABSTRACT

Objective: Incidental 18-Fluoro-2-deoxyglucose positron emission tomography (^{18}F-FDG) uptake in the ribs is a relatively common finding on positron emission tomography/computed tomography (PET/CT) images of cancer patients. This study examined the role of ^{18}F-FDG PET/CT in differentiating between benign lesions and metastases on the ribs.

Methods: This study included 264 lesions in 172 PET/CT cases with underlying malignancy showing newly developed indeterminate ^{18}F-FDG rib uptake between June 2009 and May 2010. Patients with more than five FDG rib uptakes or hematologic malignancy were excluded. Malignancy was confirmed either histologically or by imaging studies, and clinical follow-up with serial images was at least 6 months. The maximum standardized uptake value (SUVmax) of the rib lesion was recorded. The FDG uptake patterns (focal or segmental; discrete or non-discrete) and CT findings (evidence of fracture, soft tissue lesions, osteoblastic and/or osteolytic lesions) were recorded.

Results: There were 206 benign lesions and 58 metastases. The SUVmax was significantly higher in the metastatic group (3.0±1.8) than in the benign group (2.5±1.1), (P=.014). For the differential diagnosis between benign and metastatic lesions, the best SUVmax cut-off was determined to be 2.4. Significant indicators for metastasis were a segmental FDG uptake pattern (OR=10.262, 95% CI 4.151–25.371), presence of an osteoblastic/-lytic lesion (OR=22.903, 95% CI 10.468 to 50.108) and the absence of fractures on CT (OR=291.629, 95% CI 39.09–2175.666).

Conclusion: SUVmax alone is not sufficient to differentiate benign and metastatic rib lesions in cancer patients. The diagnostic accuracy can be further increased when findings of the CT part of PET/CT are considered.

1. Introduction

18-Fluoro-2-deoxyglucose positron emission tomography (^{18}F-FDG) and computed tomography (CT) scanning have been used worldwide to stage various malignancies, such as those of the head and neck, breast, lung, and esophagus, and also in colorectal cancer, lymphoma, and melanoma [1].

Whole-body ^{18}F-FDG positron emission tomography (PET)/CT scans often show many unexpected findings outside the primary region of abnormality. Although FDG uptake can suggest the presence of a malignancy, it is also observed in normal physiological states and in benign pathologies such as inflammation. These characteristics of FDG uptake often pose a diagnostic challenge for nuclear-medicine physicians, especially in patients with underlying malignancies [2,3].

In addition to the spine, pelvic bones, and the femur, the ribs are a common site of bone metastases [4]. Baxter and colleagues found that in patients with known extraskeletal malignancies, solitary rib lesions are frequently malignant (41%) [5]. However, rib fractures commonly cause FDG uptake that can be misinterpreted as osseous metastatic disease [6]. We have encountered many such examples of indeterminate FDG uptake in the ribs of patients with malignancy, and differentiating between the possible causes is difficult.

A number of studies has been conducted to evaluate the SUVmax of bone lesions in the differential diagnosis of benign and metastatic lesions [7,8]. Taira and colleagues showed that the positive predictive value (PPV) was 81% when only the PET portion of PET/CT scans was assessed for bone metastases, while the PPV was 98% when both PET and CT components were evaluated [9]. However, the prevalence of metastasis and the difference in image patterns between benign lesions and metastasis on PET/CT scans have not been studied extensively in rib lesions demonstrating indeterminate FDG uptake.

Thus, the first aim of this study was to evaluate the prevalence of metastasis in indeterminate FDG uptake by the ribs on PET/CT scans of patients with underlying malignancy. Second, we sought to determine the key PET and CT imaging findings for differentiation of benign lesions and metastases.

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http://dx.doi.org/10.1016/j.clinimag.2013.11.011

2. Materials and methods

2.1. Patient population

The subjects included in this retrospective study were patients with underlying malignancies who had new indeterminate FDG uptake in the ribs on PET CT imaging between June 2009 and May 2010. FDG uptakes without definite findings of metastasis were regarded as indeterminate FDG uptake. Patients with hematologic malignancies, including lymphoma, were excluded. More than five newly discovered instances of FDG uptake were also excluded from the study.

This study was approved by the institutional review board at our institution. Informed consent was waived due to the retrospective design of this study.

2.2. ^{18}F-FDG PET/CT imaging

All patients fasted for at least 6 h before the PET/CT study. ^{18}F-FDG (370–555 MBq) was injected intravenously, and scanning began 60 min later. None of the patients had a blood glucose level greater than 130 mg/dl before the injection. No intravenous contrast agent was administered. Studies were acquired on combined PET/CT in-line systems, either Biograph Duo or Biograph Truepoint (Siemens Medical Solutions, Knoxville, TN, USA). The first scan, a whole-body image from the orbitomeatal line to the upper thigh, was performed 1 h after ^{18}F-FDG injection. Six to eight bed positions were used and the acquisition time was 2 min per bed position. All patients were in a supine position with their arms raised. CT began at the orbitomeatal line and progressed to the proximal thigh (120 kV, 50 mAs and 5 mm slice thickness; 130 kV, 80 mAs and 5 mm slice thickness). PET followed immediately, over the same body region. The CT data were used for attenuation correction, and images were reconstructed using a standard ordered-subset expectation maximization algorithm (OSEM two iterations, eight subsets). Axial spatial resolution was 6.5 or 4.5 mm at the center of the field of view.

2.3. Interpretation

All FDG PET/CT images were reviewed with fusion software (Syngo; Siemens Medical Solutions, Knoxville, TN, USA) that provided multiplanar reformatted images and displayed PET images with attenuation correction, CT images, and PET/CT fusion images.

Two nuclear-medicine physicians reviewed the images and reached a consensus. For semiquantitative analysis, the regions of interest were delineated on transaxial images around the areas with increased FDG uptake, and the maximum standardized uptake value (SUVmax), which is widely used to quantify FDG uptake, was calculated. The SUVmax was calculated using the attenuation-corrected images, the amount of FDG injected, the body weight of each patient, and the cross-calibration factors between ^{18}F-FDG PET and the dose calibrator.

We analyzed the findings of PET- and CT-imaging studies separately. The pattern of FDG uptake was categorized as segmental or focal and discrete, or non-discrete, on PET images. The segmental FDG uptake pattern was defined as having an FDG-uptake length at least twice that of the width. The discrete uptake pattern was defined as the margin of FDG uptake that was clearly delineated on PET images, regardless of SUVmax. To analyze CT images further, we searched for evidence of the involvement of soft tissue, the presence of osteoblastic or osteolytic lesions, and evidence of fracture in lesions that demonstrated FDG uptake. The presence of fracture lines or callus formation was interpreted as evidence of fracture. CT images were analyzed in the bone-setting window.

The final diagnosis was made and confirmed histologically (either through biopsy or surgery), through correlation with other imaging studies [CT, magnetic resonance imaging (MRI)] within 4 weeks, follow-up (FU) imaging studies (PET/CT, serial CT), and patients' clinical data over at least 6 months. For diagnosis of a benign lesion, the patient had to remain asymptomatic and/or the lesions had to remain stable or regress without treatment and appear definitely benign in subsequent imaging and clinical investigations for at least 6 months. A lesion was considered malignant either upon demonstration of progression in subsequent imaging studies, or when it regressed following systemic chemotherapy similar to concomitant bone metastases.

2.4. Statistical analysis

All statistical analyses were performed using SPSS for Windows software, version 13.0 (SPSS, Chicago, IL, USA). The statistical difference between the SUVmax of benign lesions and metastases was analyzed using Student's t test. The association between the variables in PET and CT images and metastasis was investigated using chi-square tests.

The diagnostic performance and optimum SUV cut-off points were determined using a receiver operating characteristic (ROC) curve. A value of $P<.05$ was considered to indicate statistical significance.

3. Results

Among 9872 PET/CT scans, the final number of patients enrolled in the study was 172 (1.9%), with a total of 264 lesions (109 males, 63 females; mean age±S.D., 61±16 years). Of these patients, 161 had solitary malignancies and 11 had two or more malignancies. The most common primary cancers observed in the study group were those of the GI tract and lung (Table 1). The average clinical follow-up period was 11.1 months (range 6–18.7 months).

Of the 264 lesions, 58 were diagnosed as metastases (21.9%). Of the 58 metastases, two lesions were confirmed by biopsy, and the remaining 56 were confirmed using other imaging studies and clinical data. Two-hundred and six lesions were found to be benign, and of these one was confirmed by histopathology, 13 by correlation with other imaging studies, and the remaining 192 by FU-imaging studies and clinical data. There were no cases in which a single patient had both metastasis and benign lesions.

The mean±S.D. SUVmax values of the benign lesions and metastases were 2.5±1.1 and 3.0±1.8, respectively, and the difference was statistically significant ($P=.014$) (Fig. 1). In ROC curve analysis, the area under the curve was 0.607 when an SUVmax of 2.4 was used as the cutoff for the differential diagnosis, with 60.3% sensitivity and 56.3% specificity (Fig. 2). Lesions with an SUVmax value higher than 2.4 demonstrated a statistical correlation with metastasis as compared with lesions with an SUVmax value lower than 2.4 (OR=1.961; 95% CI, 1.083–3.552; $P=.025$).

Twenty-five lesions (9.5%) demonstrated segmental FDG uptake, while focal FDG uptake was observed in 239 (90.5%). The rate of metastases was higher for lesions showing a segmental uptake pattern (68%) than for those showing a focal uptake pattern (17.2%) ($P<.001$). The odds ratio for metastasis was 10.262 for lesions showing

Table 1
Underlying malignancy in patients included in study

Primary malignancy	No of patients (%)
GI tract	48 (27.9)
Lung	36 (20.9)
Breast	28 (16.2)
Thyroid	11 (6.4)
HCC	8 (4.8)
Others	41 (23.8)
Total	172 (100)