Original Article

The value of delayed ^{18}F FDG-PET imaging in diagnosis of solitary pulmonary nodules: a preliminary study on 28 patients

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Objective: The aim of this study was to investigate whether adding delayed phase imaging can improve diagnostic ability of ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) in evaluating solitary pulmonary nodules (SPNs).

Materials and methods: 28 patients with SPNs received dual-phase ^{18}F-FDG PET at 1h and 2h after ^{18}F-FDG injection during Feb 2009 to Jun 2011were included in this retrospective study. Their final diagnosis was confirmed by pathological examination in 27 cases and clinical follow-up in 1 case. The standardized uptake value (SUV) of early and delayed phases of all lesions was measured.

Results: The 28 SPNs included 9 benign lesions and 19 malignant lesions. Using SUV ≥2.5 as a criteria for malignancy, the sensitivity, specificity, and accuracy were 52.6%, 55.6% and 53.6% respectively at early phase; 68.4%, 55.6% and 64.3% respectively at early and delayed phases combined. Combined early and delayed phase scans combined picked up 3 additional malignant lesions from the 14 lesions with an initial SUV value less than 2.5, and there was no additional false positive result with the benign lesions.

Conclusion: Adding delayed phase scanning resulted in correct diagnosis of three malignant lesions with an initial SUV value less than 2.5. Delayed phase scanning can be recommended in the SPNs with SUV less than 2.5 at early phase.

Key Words: Solitary pulmonary nodules; ^{18}F-FDG; SUV

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Introduction

Diagnosis and management of solitary pulmonary nodules (SPNs) is a complex process and remains a challenge for both radiologists and physicians, even though CT and positron emission tomography (PET) or PET-CT are wildly used in evaluating these pulmonary lesions (1). The differential diagnosis of SPNs is extensive, including granuloma, hamartoma lung cancer, and metastasis (2). Once a SPN was detected, the first and most important goal of radiological evaluation is to noninvasively differentiate benign from malignant lesions as accurately as possible, because SPNs may be malignant and lung cancer has an overall mortality rate of up to 85% (3). On the other hand, malignant lesions account for only 60-80% of resected pulmonary nodules (4). ^{18}F-fluorodeoxyglucose PET (^{18}F-FDG PET) has been reported to be useful in characterizing SPNs (5,6). In the evaluation of an SPN, an SUV of ≥2.5 is frequently used as a criterion for malignancy. However, FDG is not a tumor-specific radiotracer, increased FDG uptake can be seen not only in malignancy but also seen in benign SPNs, while some malignant tumors, such as bronchoalveolar carcinoma and well differentiated adenocarcinoma, may exhibit only minimally increased activity (7-9). Many studies found that the FDG uptake value of a considerable amount of benign and malignant lesions overlaps (10-11). Some authors show that dual-time point imaging could improve the accuracy of FDG PET in the evaluation of lung lesions (12-15). The aim of this study was to assess whether adding delayed phase imaging can improve the

accuracy of FDG PET in the evaluation of SPNs.

Materials and methods

Patients

Our institutional review board approved this retrospective study and waived informed consent. Twenty-eight patients with SPNs, receiving a dual-phase FDG PET from February 2009 to June 2011 in our institution, were enrolled in this study. There were 19 men and 9 women with age range of 33-85 years and average of 65.2 years. The final diagnosis was confirmed from pathologic examination (n=26), biopsy pathology (n=1), or repeated radiographic examination and clinical follow-up for more than 24 months (n=1).

FDG PET scan

All scans were obtained on a dedicated whole-body PET/CT scanner (Biograph 64; Siemens). Before examination, informed consent for PET was obtained from all patients. At the time of FDG injection, all patients were instructed to fast for more than 6 hours and had fasting blood glucose levels of less than 140 mg/dL. The early phase image acquisition for the whole-body scan started at a mean time point of 60 minutes (range: 60-80 minutes) after injection of 5.18 MBq/kg of FDG per body weight. Patients were told to stay in a supine position in a solitary quiet environment for approximately 1 h waiting for the delayed imaging. Whole-body emission scan used 5 to 7 bed positions. PET used three dimensional (3D) acquisition. Acquisition time was 1.5-2.5 min per bed position. CT parameters were: effective amperage settings of 80-100 mAs; a tube voltage of 120 kV; a matrix of 512×512; a section thickness of 5 mm; and a reconstruction interval of 3 mm. Scanning was performed with the patients supine with arms raised above their heads. Delayed scan included one bed position in the thorax 110-150 minutes after tracer injection. A transmission scan was obtained with both sets of images for attenuation correction.

Image interpretation

All PET/CT images were reviewed at a workstation with fusion software (syngo, Siemens) that displayed maximum intensity projection (MIP) PET images and multiplanar reformatted PET, CT and PET/CT fusion images. Two experienced diagnostic radiologists viewed the images in consensus. For semi-quantitative analysis, the maximal SUV of FDG was measured from both the early and delayed phase images by placing regions of interest (ROI) over the nodule that had the highest perceptible FDG uptake by visual analysis.

The accuracy for differentiating malignant nodules from benign nodules was calculated for the early, and early and delayed phases combined using SUV ≥2.5 as a criteria for malignancy, and clinical outcome served as reference standard.

Results

The 28 SPNs included 9 benign and 19 malignant nodules. In the nine benign nodules, there were 2 tuberculomas, 2 inflammatory granulomas, 3 non-specific inflammations, 1 cryptococcal infection, and 1 case of benign lesion without histropathologic evidence, which was regarded as benign by >24 months clinical follow-up. The malignant group consisted of 2 squamous cell carcinomas, 16 adenocarcinomas and one bronchoalveolar carcinoma containing a small amount of adenocarcinoma cells.

The sensitivity, specificity, and accuracy of the early phase in distinguishing malignancy from benign were 52.6%, 55.6% and 53.6%, respectively; while early and delayed phases combined achieved 68.4%,55.6% and 64.3%, respectively. Among the 14 nodules with SUV less than 2.5 at the early phase, SUV of 3 malignant lesions became higher than 2.5 at the delayed phase (*Figure 1*), while such change was not noted in the benign lesions (*Figure 2*). On the other hand, no lesions with SUV of 2.5 or higher at early phase experienced the change of SUV decreasing to less than 2.5 in the delayed phase. Therefore, combined early and delayed phase scans added three correct diagnosis cases in malignant lesions, while there was no additional false positive result with the benign lesions.

Discussion

Chest radiograph and CT screening have increased the detection of SPNs, but imaging evaluation of SPNs is a common diagnostic dilemma. It is essential to distinguish malignancy from benign nodules, because correct diagnosis can not only have small malignant SPNs resected at early stage to improve patients' life quality and survive, but also avoid a benign node being unnecessary resected and reduce inappropriate invasive diagnostic investigation. With ^{18}F-FDG PET, an SUV greater than 2.5 has been widely used as a diagnostic criteria of malignancy in evaluating SPNs with a sensitivity of 92-96% and a specificity of 77-90% (16-23).

However, SUV of benign and malignant lesions may have overlaps. Some malignant tumors, such as bronchoalveolar carcinoma and well differentiated adenocarcinoma, may exhibit only minimally increased activity, while some inflammatory lesions, such as pulmonary tuberculosis, can have high FDG uptake (7,8,10,11). Therefore, dual phase ^{18}F-FDG PET has been proposed to evaluate pulmonary diseases, especially in the lesions with initial SUV less than 2.5 (9,12-15). The reported results varied. Some studies showed

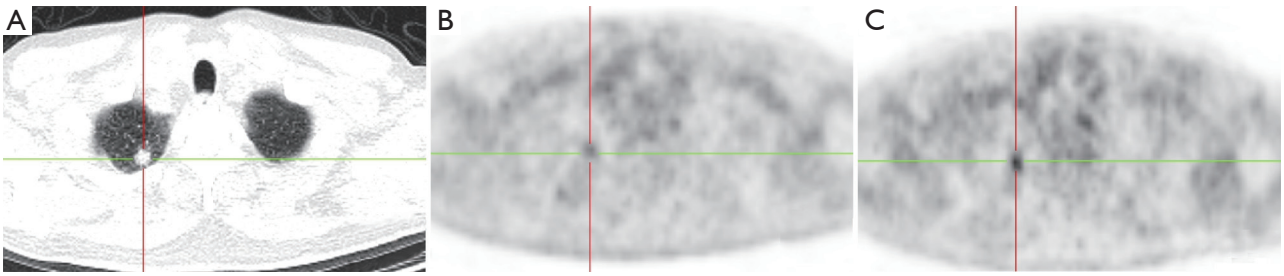

Figure 1 One 75-year-old man with a lung adenocarcinoma. A. Axial CT image shows a 1.2-cm-diameter SPN in right upper lobe apical segment. B. SUV of the nodule (cross) at initial phase was 2.43. C. At delayed phase, SUV of the nodule (cross) increased to 2.90

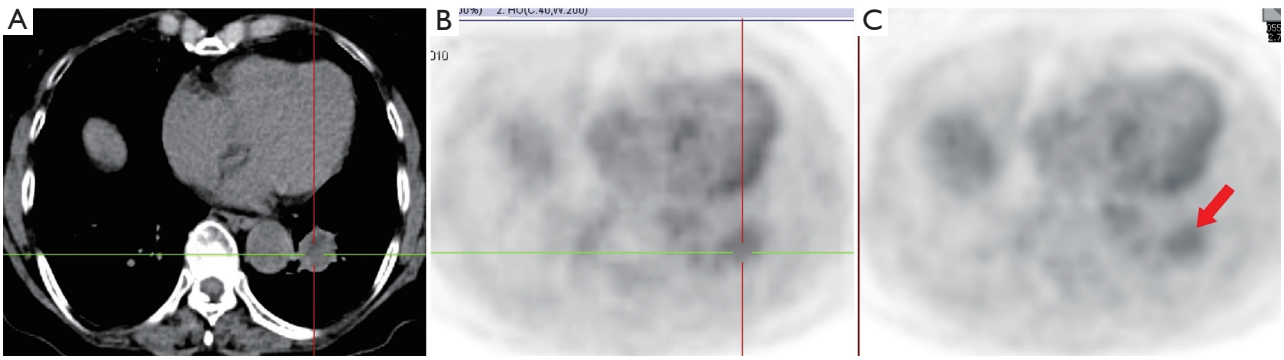

Figure 2 One 75-year-old woman with an indeterminate benign node which is confirmed by 24 months follow-up. A. CT shows a 2.6-cm-diameter pulmonary nodule in left lower lobe beside thoracic aorta. B. Early phase PET image shows SUV of the node (cross) being 2.04. C. Delayed phase image demonstrates SUV of the node (arrow) being 1.85

that dual phase imaging could improve the accuracy of PET in distinguishing between benign and malignant disease due to that malignancies tend to retain the tracer (12-14), but some studies' results did not support this finding (9,24,25). Chen *et al*. used dual-phase FDG PET to evaluate pulmonary nodules with an initial SUV less than 2.5 and found that dual phase FDG PET could not improve the diagnosis performance of PET on pulmonary diseases in geographic regions with high risk of granulomatous inflammation (9).

In our study, we added a 120-minute delayed imaging to the initial imaging at 60 minutes in 28 patients to evaluate SPNs. The aim of our study was to examine whether adding delayed phase imaging can improve diagnosis ability of PET in assessment of SPNs. Using SUV ≥2.5 as the criteria for malignancy, combined early phase and delayed phase scans obtained an accuracy of 64.3% (sensitivity: 68.4%; specificity: 55.6%), which was slight higher than the accuracy of 53.6% (sensitivity: 52.6%; specificity: 55.6%) at the early phase scan only. Our results were consistent with what Chen and his colleagues reported (9). However, in our series, three malignant SPNs with initial SUV less than 2.5 were measured with SUV higher than 2.5 at delayed phase, while no benign lesions experienced such changes and no malignancy with SUV more than 2.5 at initial imaging alternated their SUV to less than 2.5. Therefore, the early and delayed phase combined added three true positive cases, and the sensitivity increased without sacrifice of specificity. Considering benefits of the three patients obtained, it's worthy to carry out the delayed phase imaging in those SPNs with initial SUV less than 2.5 at the early phase.

False-positive result occurred in 4 benign nodules in our series which had resulted in an unnecessary lobectomy or wedge resection. These nodules were incorrectly considered to be malignancy because they all showed high uptake of FDG (SUV >2.5) at early phase. Similar false-positive findings have been reported (9,26-27). The result indicated delayed phase FDG PET imaging may not eliminate unnecessary invasive procedures for benign lesions completely, and positive SPNs should be cautiously interpreted.

In summary, three patients with malignant SPNs benefited from adding delayed phase imaging in our present study group of 28 SPNs. Considering advantage the correct diagnosis brought to the three patients, delayed phase scanning can be recommended in the SPNs with SUV less than 2.5 at early phase.

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