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Research Article

PET and CT features differentiating infectious/inflammatory from malignant mediastinal lymphadenopathy: A correlated study with endobronchial ultrasound-guided transbronchial needle aspiration

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Abstract

Purpose: To explore the advantages of differentiating inflammatory from malignant thoracic lymph nodes by integrating their features on positron emission tomography (PET) and computed tomography (CT).
Material and method: Following institutional review board approval, PET and CT parameters of thoracic lymph nodes were examined based on their pathologic diagnosis via endobronchial ultrasound-guided transbronchial needle aspiration. The standardized uptake value (SUV) of PET and CT findings of the long- and short-axis diameters, axial short to long diameter ratios (S/L), and measured nodal CT values of the lymph nodes were compared and analyzed statistically.
Results: A total of 124 lymph nodes from 70 patients were studied. The inflammatory and malignant lymph nodes differed significantly in their SUV ($P = 0.008$), short-axis diameters (SAD, $p < 0.001$), long-axis diameters (LAD, $p = 0.002$) and S/L ratios ($p < 0.001$). They did not differ significantly in non-contrast enhanced CT values ($p = 0.304$). The sensitivities, specificities, positive predictive values, negative predictive values, diagnostic accuracies and diagnostic odds ratios (DOR) were: 1) elevated SUV alone - 95.31% (61/64), 20% (12/60), 55.96% (61/109), 80% (12/15), 58.87% (73/124), and 5; 2) combined SUV + SAD - 89.06%, 53.33%, 67.06%, 82.05%, 71.77%, and 9.31; 3) combined SUV + S/L ratio - 87.5%, 93.33%, 93.33%, 87.5%, 90.32%, and 98, respectively.
Conclusion: Increased SUV, SAD, LAD, and S/L ratio are accurate PET/CT parameters to characterize inflammatory or malignant lymph nodes. SUV has high sensitivity but low specificity, low positive and negative predictive values, and low DOR. The SUV + SAD and SUV + S/L ratios have higher specificity, positive and negative predictive values, diagnostic accuracy and DOR.

Keywords: PET/CT; Positron emission tomography; Computed tomography; Mediastinal lymph nodes; EBUS

1. Introduction

Enlarged thoracic (hilar and mediastinal) lymph nodes are common clinical scenarios. Lymph nodes may be enlarged due to benign causes such as inflammation or infection, or due to malignancy especially metastatic lymphadenopathy. It is crucial to differentiate inflammatory from malignant lymph node under many clinical situations. For example, the nodal status can dictate the course of therapy and prognosis of lung cancer. Although CT has been widely used for the preoperative evaluation of tumor size and adjacent structural details, numerous studies have shown the limited reliability of CT in lymph node staging [1,2]. CT diagnostic criteria using an

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upper limit of 1.0 cm or more for malignancy can overlook early or partial malignant infiltration of the node, and a number of reviews and meta-analyses have shown this limited reliability of CT in lymph node staging [3]. 18F-Fluorodeoxy glucose positron emission tomography−computed tomography (18F-FDG-PET) can detect malignant lymph nodes of even normal size, thus overcoming one of the major limitations of CT. However the diagnostic value of PET has also been reduced by its low spatial resolution. Infection or inflammation can also cause high FDG uptake leading to false positivity [4]. Integrated PET and CT (PET/CT) had been found to outperform CT or PET alone as it provides structural and functional information of disease status at the same time [5] although tissue diagnosis remains the gold standard.

Endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) is a proven accurate technique for histological diagnosis of thoracic lymph nodes [6]. However, this procedure is invasive in nature, which cannot be performed on patients who have other comorbidities. There is no single non-invasive imaging method that was fairly conclusive in evaluating potential chest nodal involvement in otherwise operable lung cancer patient under routine clinical conditions [7].

The aim of this study was to retrospectively analyze the different PET and CT features of suspicious thoracic lymph nodes sampled by EBUS-TBNA and to explore the advantages of combining the most predictive parameters of PET and CT to derive better diagnostic parameters in differentiating inflammatory from malignant thoracic lymph nodes.

2. Materials and methods

2.1. Patients

Following institutional research and ethical review board approval and HIPAA compliance, a total of 70 consecutive patients with hilar and mediastinal lymphadenopathy detected on chest CT were enrolled in the study. There were 39 males and 31 females with mean age of 62.45 ± 14 years (range 20−93years). The radiological and pathological data of those 70 patients who underwent both PET/CT exams and EBUS-TBNA procedures for hilar and mediastinal lymph nodes sampling were retrospectively analyzed.

2.2. PET/CT

All PET/CT studies were acquired in the same PET center using a combined in-line PET/CT system (Discovery RX; GE Healthcare, USA), within 3 weeks from the EBUS-TBNA.

Patients fasted for at least 6 h before the exam; the scanning was performed 60 min after IV administration of 18F-FDG (4.5−5.5 MBq/kg). Scanning was performed from the base of the skull to the pelvis with patients in supine position. To obtain a precise anatomic correlation between PET and CT images, scanning was performed with the arms in the overhead position for both PET and CT. Coronal and transverse data sets were reconstructed. Diagnostic non-contrast-enhanced CT was initially performed at 120 KV and with automatic current adjustment (maximum, 300 mA) according to the patient's weight. The axial CT images (in 5 mm thickness) were reconstructed using B30f kernel for mediastinal algorithm. Images were transferred to PACS workstations for detailed analysis. Nuclear medicine board certified specialists from nuclear medicine department interpreted the PET images while the CT images were interpreted by board certified radiologists. Abnormal 18F-FDG uptake was defined as accumulation outside the normal anatomic structures and of greater intensity than background activity inside the normal structures. Any abnormally elevated visual focus of 18F-FDG uptake over that of the background was deemed to represent tumor tissue. The uptake of the radiotracer was also assessed semi-quantitatively using the standardized uptake value (SUV) method.

According to the result of most authors [7,8], hilar and/or mediastinal lymph nodes were considered positive for malignant if they showed increased FDG uptake (SUV thresholds: SUV >2.5). CT images were evaluated in respects of LADs and SADs of the lymph nodes, their axial S/L ratios, nodal locations and average CT HUs (Hounsfield unit). A currently accepted upper limit of SAD >1.0 cm [9] was used for malignancy positivity. According to our previous study, the axial S/L ratio >0.7 was the most accurate positive predictor for malignancy.

2.3. EBUS-TBNA

After PET/CT and/or CT identification of the lymph nodes in question, their locations were correlated by EDUS through a bronchofibervideoscope (Olympus Exera). Subsequent cytological specimens were collected via EBUD-TBNA with 22-gauge needle, and core biopsies were obtained using 19-gause needle. On-site evaluation of biopsy sample adequacy was performed by an experienced cytotechnologist. In many patients, multiple passes were performed to ensure sample adequacy. Core-biopsy samples were sent for frozen-section with final pathology diagnosis made at our institution. When malignant tumor cells were confirmed, the sampled nodes were labeled as positive for malignancy or metastatic nodes. Inflammatory/infectious lymphadenopathy were diagnosed with characteristic histology findings without the presence of tumor cells. If neither malignant cell no inflammatory changes were found in lymph node sampling, the specimens were labeled as non-diagnostic and the data were excluded. None-enlarged lymph nodes were not sampled and were not included in this study. Some lymph node levels are difficult for EBUS to gain access, such as paraesophagaeal nodes or aortopulmonary window nodes which are also excluded from this study.

3. Statistical analysis

Data analysis was performed using SPSS statistical software (IBM SPSS Statistics 20; Chicago, IL, USA). Continuous variables were analyzed using one-way ANOVA, and