Original Article

Dual-time-point positron emission tomography findings of benign mediastinal fluorine-18-fluorodeoxyglucose uptake in tuberculosis-endemic region

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ABSTRACT

Background: We performed dual-time-point positron emission tomography imaging in patients without evidences of mediastinal lymph node metastasis to investigate the characteristics of benign mediastinal fluorine-18-fluorodeoxyglucose (FDG) uptake. **Materials and Methods:** One-hundred and eighteen mediastinal lesions of 24 patients were included for this study. On the early and delayed positron emission tomography images, size, attenuation, maximum standardized uptake value (SUV) and retention indices (RI) were recorded for lymph node characterization. **Results:** The mean SUV on the early and delayed scan of 118 lymph nodes was 3.3 ± 1.2 and 4.2 ± 1.7, respectively. The mean RI was $26.4 \pm 24.5\%$. Higher FDG uptake was observed in patients with calcified nodules and bilateral FDG uptake and in lymph nodes with calcification or short-axis diameter larger than 10 mm. **Conclusion:** In tuberculosis-endemic area, the increments of SUV or RI were frequently observed in benign mediastinal lymph nodes, and these values might not be the accurate indicators of malignant disease for mediastinal FDG uptake.

Keywords: Dual-time-point imaging, fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography, mediastinal lymph node, tuberculosis

INTRODUCTION

Fluorine-18-fluorodeoxyglucose (FDG) uptakes in benign inflammatory lymph nodes of mediastinum are frequently observed even in patients with non-thoracic tumor, especially in regions with a high prevalence of granulomatous disease such as tuberculosis (TB).[1] Therefore, mediastinal FDG uptake in patients with non-thoracic tumor is difficult to interpret, and this becomes a major problem when analyzing single-session positron emission tomography (PET) or dual-time-point positron emission tomography imaging (DTPI) in TB-endemic regions such as Korea. Several studies have explored the usefulness of DTPI using FDG in improving detection and staging of lung malignancy, distinguishing malignant from benign lesions.[2-4] However, there are a few reports about the DTPI findings of benign mediastinal FDG uptake in patients with non-thoracic tumor. To apply the DTPI for various kinds of cancer and enhance the diagnostic performance of DTPI, a descriptive study about DTPI findings of benign mediastinal lymph nodes is required.

In this study, we performed DTPI in patients without evidences of mediastinal lymph node metastasis to investigate the characteristics of benign mediastinal FDG uptake.

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MATERIALS AND METHODS

Patients

Between the period of six months, PET scans of patients with non-thoracic tumor were reviewed by a nuclear medicine physician, and if mediastinal FDG uptake was detected, additional PET scan was performed for thorax on the same day. Patients with a history of thoracic malignancy such as lung, breast or esophagus cancer were excluded. Patients with metastatic disease

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of non-thoracic tumor in mediastinal lymph nodes were also excluded. As a result, 118 mediastinal lesions of 24 patients (17 males and 7 females; mean age 68.1 years) were included for this study. Patients had variable non-thoracic tumors (gastric cancer, *n*=9; rectosigmoid cancer, *n*=8; colon cancer, *n*=3; hepatocellular carcinoma, *n*=2; thyroid cancer, *n*=1; skin cancer, *n*=1). One patient had a history of treatment for pulmonary TB 15 years ago. All patients were radiologically followed up for at least 12 months to confirm that mediastinal FDG uptakes were benign (mean follow-up period 22.4±5.1 months) using chest computed tomography (CT) or FDG PET/CT. One patient had undergone thoracotomy during the follow-up period, and histopathologic examinations of mediastinal lymph nodes confirmed benign disease. This study was approved by the ethics committee of our institution.

PET/CT imaging

FDG was prepared using a cyclotron (RDS-111, CTI Cyclotron Systems, Inc., Korea) and automated synthesis apparatus. The radiochemical and chemical purity of the product was assayed by analytic high-performance liquid chromatography and thin-layer chromatography and was consistently >99% by both assays. The measured specific activity of the FDG was >740 GBq/mmol at the end of synthesis. Patients fasted for at least 6 hours before FDG PET/CT. The early PET/CT scans were started 50–60 mins after the administration of 296–444 MBq FDG using an integrated PET/CT system (Biograph Sensation 16, Siemens Medical Systems), and the delayed PET/CT scans were performed at 102.5±26.4 mins (range 60–130 mins) after early scan. The axes of both systems were mechanically aligned to coincide optimally. CT data were acquired first and the following parameters were used: tube rotation time 0.5 second per revolution, 120 kV, 140 mA, reconstructed slice thickness 5 mm. No contrast medium was used for the CT examination. After the acquisition of CT data had been completed, the table top with the patient automatically advanced into the PET sensitive field of view and acquisition of PET data was started in three-dimensional mode with the patient in exactly the same position on the table. Scanning was performed in one bed position for 3 mins. The attenuation correction was automatically completed using corresponding CT data.

Image analysis

All PET/CT images were reviewed by two experienced nuclear medicine physicians by means of consensus. For each patient, CT component of PET/CT was reviewed for evaluating the presence of fibrostreaky lesions or calcified nodules in lungs. On the early PET/CT scans, all visually recognizable hypermetabolic lesions of the mediastinal lymph nodes were included for lymph node based analysis. The following values of early PET/CT were recorded: maximum standardized uptake value (SUVe), short-axis diameter, Hounsfield unit (HU) and the presence of calcification. HU was measured within the non-calcified area of lymph node, and if HU was over 70, the lymph node was considered as having high attenuation. When the patient had hypermetabolic lesions on both sides of the mediastinal lymph nodes, the patient was considered as having bilateral lymph node uptakes, irrespective of the lymph node stations.[5,6] Then, maximum standardized uptake values on the delayed PET/CT (SUVd) were recorded, and retention indices (RI) were calculated for each mediastinal lymph node on the basis of the following equation: (SUVd − SUVe)/SUVe × 100. RI means the increment of SUV on the delayed scan compared with early scan.

Statistical analysis

Where applicable, data were presented as mean ± SD. Data were analyzed using descriptive statistics, and changes in continuous variables were analyzed using the independent samples *t*-test. To analyze the correlation among values, bivariate correlation was used. Results with $P<0.05$ were considered significant.

RESULTS

Among the 24 patients, 5 (20.8%) had fibrostreaky lesions and 8 (33.3%) had calcified nodules on the lungs. Twenty patients (83.3%) had bilateral FDG uptakes of the mediastinal lymph nodes. The mean SUVe and SUVd of 118 lymph nodes was 3.3±1.2 and 4.2±1.7, respectively. The mean RI was 26.4±24.5% [Table 1].

The patients who had calcified pulmonary nodules had significantly higher SUVe, SUVd and RI values than those without calcified nodules (SUVe: 3.8±1.4 vs. 3.0±0.9; SUVd: 5.1±2.1 vs. 3.7±1.2; and RI: 35.7±30.7 vs. 21.1±18.3%). The patients who had bilateral FDG uptake had significantly higher SUVe, SUVd and RI values than those without it (SUVe: 3.4±1.1 vs. 2.5±1.2; SUVd: 4.3±1.7 vs. 2.8±1.5; and RI: 27.3±24.9 vs. 13.4±14.5%). However, these values were not significantly different between the patients with and without fibrostreaky pulmonary lesions (SUVe: 3.5±1.0 vs. 3.3±1.2; SUVd: 4.2±1.2 vs. 4.2±1.8; and RI: 24.2±27.2 vs. 27.0±23.8%) [Table 2].

On the lymph node based analysis, SUVe and SUVd were significantly higher in the lymph nodes with calcification or short-axis diameter larger than 10 mm. RI did not correlate with the presence of calcification or short-axis diameter of lymph nodes. SUVe, SUVd and RI were not significantly different between lymph nodes with and without high attenuation [Table 3]. There was a strong positive correlation between SUVe and SUVd ($\gamma=0.865$, $P<0.01$) and evident positive correlation between RI and SUVd ($\gamma=0.493$, $P<0.01$). However, there was no significant correlation between SUVe and RI ($\gamma=0.024$, $P=0.793$) [Figure 1].

Table 1: Characteristics of benign mediastinal lymph nodes on the dual-time-point PET/CT (*n*=118)

Characteristics	Mean	SD	Minimum	Maximum
SUVe	3.33	1.16	1.51	8.09
SUVd	4.21	1.69	1.49	10.95
RI (%)	26.41	24.51	−9.67	139.34
Size (mm)	7.8	2.2	4.1	15.1
HU	74.6	17.4	34	122

SD: standard deviation; SUVe and SUVd: maximum standardized uptake value of early and delayed PET/CT: respectively; RI: retention indices; HU: hounsfield unit

Table 2: Retention indices and maximum standardized uptake values of benign mediastinal lymph nodes according to the presence or absence of calcified pulmonary nodules, fibrostreaky lesions and bilateral FDG uptakes

		SUVe	SUVd	RI
Calcified pulmonary nodules	Present (*n*=43)	3.8±1.4*	5.1±2.1*	35.7±30.7*
	Absent (*n*=75)	3.0±0.9	3.7±1.2	21.1±18.3
Fibrostreaky pulmonary lesions	Present (*n*=26)	3.5±1.0	4.2±1.2	24.2±27.2
	Absent (*n*=92)	3.3±1.2	4.2±1.8	27.0±23.8
Bilateral mediastinal FDG uptake	Present (*n*=110)	3.4±1.1*	4.3±1.7*	27.3±24.9*
	Absent (*n*=8)	2.5±1.2	2.8±1.5	13.4±14.5

Data presented as mean±SD; *Statistically significant compared to the corresponding absent value (*P*<0.05) ; FDG: fluorine-18-fluorodeoxyglucose; SUVe: maximum standardized uptake value ; SUVd: maximum standardized uptake values on the delayed; RI: retention indices

Table 3: Retention indices and maximum standardized uptake values of benign mediastinal lymph nodes according to the short-axis diameter and presence or absence of calcification within lymph node and high attenuation (>70 HU)

		SUVe	SUVd	RI
Short-axis diameter	≥10 mm (*n*=20)	4.6±1.7*	5.9±2.3*	27.9±19.2
	<10 mm (*n*=98)	3.1±0.8	3.9±1.3	26.1±25.5
Calcification within lymph node	Present (*n*=20)	3.8±1.4*	5.1±2.2*	31.5±25.4
	Absent (*n*=98)	3.2±1.1	4.0±1.5	28.7±23.6
High attenuation	Present (*n*=66)	3.5±1.3	4.5±1.9	28.1±23.9
	Absent (*n*=52)	3.1±1.0	3.9±1.4	24.2±25.3

Data presented as mean±SD; *Statistically significant compared to the corresponding value (*P*<0.05); FDG: fluorine-18-fluorodeoxyglucose; SUVe: maximum standardized uptake value; SUVd: maximum standardized uptake values on the delayed; RI: retention indices

DISCUSSION

In this study, we had performed DTPI in patients without evidences of mediastinal lymph node metastasis to investigate the characteristics of benign mediastinal FDG uptake. The mean SUVe, SUVd and RI of 118 lymph nodes were 3.3±1.2, 4.2±1.7, and 26.4±24.5%, respectively. Yen *et al*. had reported that the mean SUVe, SUVd and RI of 81 benign mediastinal lymph nodes were 3.6±1.3, 4.3±1.8 and 19.0±35.4%, respectively, in their study evaluating the value of DTPI for staging of lung cancer.[7] These values are comparable with those obtained in our study.

In one-third of primary pulmonary TB cases, the lung infiltrates leave some kind of parenchymal scar, such as a nodule (tuberculoma), which can calcify forming the Ghon focus or an area of fibrosis.[8] So, we had compared SUVe, SUVd and RI between patients with calcified pulmonary nodules or fibrostreaky lesions and those without it. Karam *et al*. had reported that foci of bilateral uptake limited to the hilar regions are likely to be related to a benign etiology.[9] In our study, bilateral FDG uptakes of the mediastinal lymph nodes were observed in 20 patients (83.3%), and SUVe, SUVd and RI were significant higher in these patients.

It has been shown that for CT, a threshold of 10 mm short-axis diameter has the best trade-off between sensitivity and specificity.[10] In our study, SUVe and SUVd were significantly higher in the lymph nodes with short-axis diameter larger than 10 mm. This might be partly caused by partial volume averaging

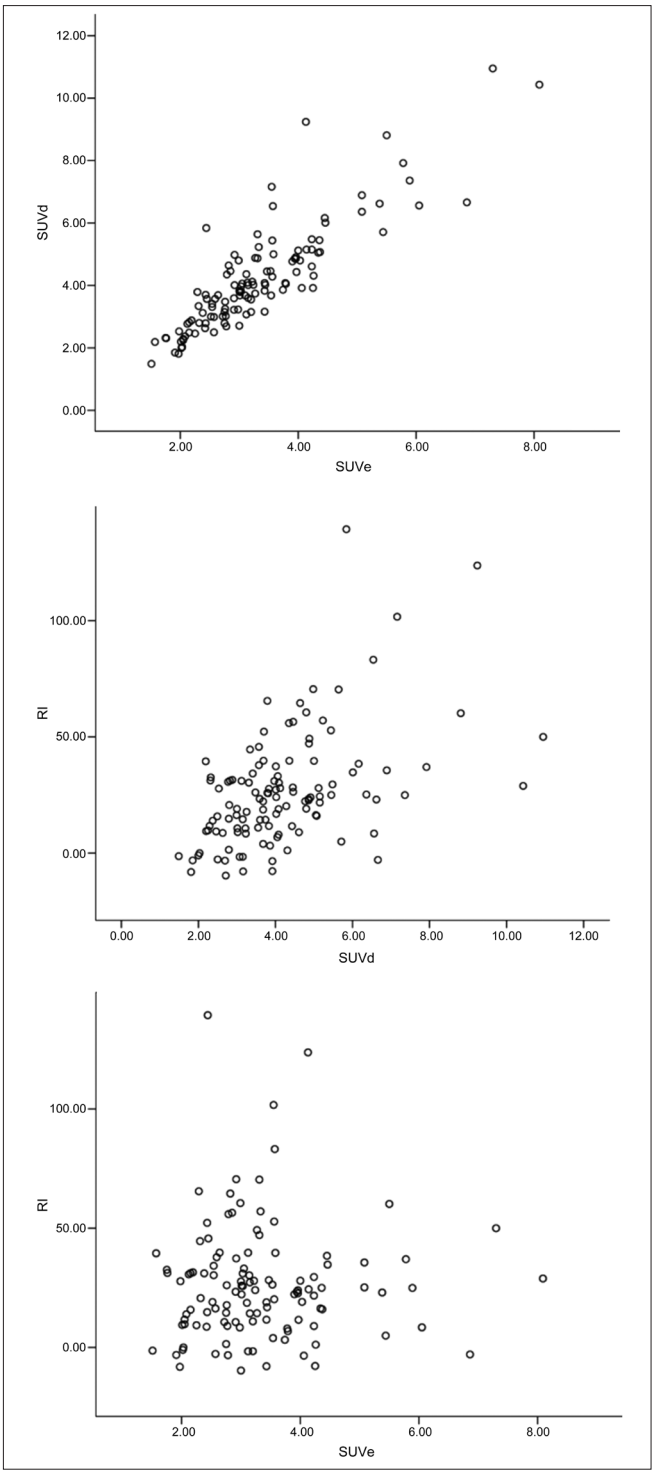

Figure 1: Correlations among retention indices (RI) and maximum standardized uptake values (SUVe and SUVd) of benign mediastinal lymph nodes presented as scatter plots

effects due to the limited resolution of the system in smaller lymph nodes.[11] Several studies had reported that lymph nodes with calcification or high attenuation should be considered as benign irrespective of FDG uptake.[12-14] Also, the association of a parenchymal calcification due to primary with calcified hilar nodes is known as a Ranke complex, a finding highly indicative of prior primary TB.[8]

Kubota *et al.* reported that most malignant lesions, including primary lung cancer, mediastinal node metastasis and lymphoma, showed higher FDG uptake at 2 hours than at 1 hour after injection of FDG, while normal tissue including lung and mediastinum, and benign lesions except for sarcoidosis, showed lower uptake at 2 hours than at 1 hour after injection, and that a delayed scan of FDG PET provided better sensitivity than an early scan.[15] Discordant to their report, in our study, mediastinal lymph nodes with some of the aforementioned features representing benign disease showed higher FDG uptake at delayed scan than early scan. The results of our study might suggest that the increments of SUV or RI are not the reliable indicators to discriminate malignant disease from benign mediastinal FDG uptake in the TB-endemic area.

The first limitation of our study is lack of histopathologic confirmation of mediastinal lymph nodes. However, surgery or biopsy of benign mediastinal lymph nodes was clearly unnecessary and these invasive procedures could be substituted by long-term imaging follow-up. The second limitation is that we had evaluated patients with non-thoracic tumors. The mediastinal FDG uptake is more clinically important in patients with thoracic malignancies, as medaistinal nodes are frequently involved. Therefore additional study including patients with thoracic malignancy has been planned by the authors.

CONCLUSION

In the present study, we had performed DTPI in patients without evidences of mediastinal lymph node metastasis to investigate the characteristics of benign mediastinal FDG uptake. In TB-endemic area, the increments of SUVe, SUVd or RI were frequently observed in benign mediastinal lymph nodes, and these values might be not the reliable indicators to discriminate malignant disease from benign mediastinal FDG uptake in the TB-endemic area.

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