Original Article
The role of FDG PET/CT in evaluation of mediastinal masses and neurogenic tumors of chest wall

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Abstract: We evaluated the efficiency of FDG PET/CT for the differentiation of malignant from benign mediastinal masses and neurogenic tumors of chest-wall. Methods: The 88 patients with chest wall-mediastinal masses who underwent examination before operation were retrospectively reviewed. Size, CT density (HU mean) and SUVmax of mediastinal and chest wall lesions were determined. Statistical differences of these parameters were compared between groups by Mann-Whitney U test. Receiver-operating characteristic curve (ROC) analysis with respect to SUVmax was performed to determine the best cutoff value for differentiating benign from malignant masses. Results: The overall sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of PET/CT in detection of malignancy were 90%, 55.17%, 67%, 50.94% and 91.43%, respectively. The SUVmax, HU mean and size were higher in malignant cases (P < 0.05). To distinguish benign and malignant lesions, the cut off value of SUVmax was 4.67. The lesion SUVmax was significantly associated with the lesion size and lesion HU mean values (P < 0.05). The value of SUVmax and HU mean were higher in solid benign lesions than those of cystic benign lesions (P < 0.05). The lesion size was higher in cystic lesions (P = 0.000). The mean SUVmax was significantly higher in invasive thymomas than those of non-invasive forms (P = 0.029). Conclusion: FDG PET/CT may be complementary to conventional imaging methods for the evaluation of mediastinal and chest wall masses. PET/CT may reduce unnecessary invasive investigations for diagnosis in patients with nonavid or low avid FDG lesions. However confirmatory tissue sampling is required to confirm PET positive findings for the definite diagnosis.

Keywords: FDG PET/CT, castleman disease, schwannoma

Introduction
Mediastinal and chest-wall masses are caused by benign or malign, solid or cystic conditions. The differential diagnosis of these lesions is a common problem. Although, conventional radiological methods can provide detailed information about their morphology such as size, location, tissue characteristics and extent of mediastinal tumors [1], none of these morphological imaging techniques can reliably differentiate benign tumours from malignant ones [2]. The glucose analogue 2-Deoxy-2-[18F] Fluoro-D-Glucose (FDG) preferentially accumulates in most malignant tumors, reflecting increased glycolytic rate in these tumors [3]. Use of 18F-FDG Positron emission tomography (PET)/Computed Tomography (CT) is recommended in a variety of tumor types by NCCN guidelines [4], and may be helpful for further evaluation of patients with mediastinal tumours. The objective of this study is: 1) to evaluate visual FDG PET/CT characteristics of mediastinal tumours; 2) to determine whether quantitative evaluation of FDG PET/CT images can differentiate benign mediastinal tumours from malignant ones; 3) to document the usefulness of FDG PET/CT in differentiation non-invasive thymic epithelial tumors from invasive forms.

Material and methods

Patients
We retrospectively reviewed medical database of 88 patients with mediastinal and chest wall
PET/CT in mediastinal masses

PET/CT imaging was performed with a dedicated PET/CT scanner (Biograph LSO HI-REZ PET/CT; Siemens, Medical Solutions, Knoxville, TN, USA) by the same method that was described in a previous study [5].

FDG PET/CT analysis

All PET/CT images were evaluated qualitatively by two experienced nuclear medicine physician and one radiologist who were uninformed about the pathological diagnosis of masses. PET/CT findings were interpreted as positive for malignancy if the FDG uptake of lesion was greater than the uptake of mediastinal blood pool [6]. Lesion with FDG uptake equal to or less than the mediastinum was defined as negative.

Statistical analysis

The sensitivity, specificity, accuracy, positive predictive value, and negative predictive values of FDG PET/CT for detecting mediastinal and chest wall malignancy were calculated with using the pathological results as a reference standard. Statistical differences of $SUV_{max}$, attenuation value (HU mean) and lesion diameter were analysed on the groups by Mann-Whitney U test. Receiver-operating characteristic curve (ROC) analysis with respect to $SUV_{max}$ was performed to determine the best cutoff value for differentiating benign lesions from malignant lesions.
malignant ones. A P-value less than 0.05 was considered statistically significant.

Results

Patient characteristics

Detailed characteristics of the study population was presented in Table 1. Among the 88 patients, 83 patients had mediastinal lesion and 5 patients had chest wall lesion. Seventy-four of the 88 patients underwent surgical resection and the remaining 14 patients underwent biopsy. Of 88 cases, 58 (66%) were benign and 30 (34%) were malignant. Fifteen of 58 benign lesions were in cystic (4 bronchogenic cyst, 4 pericardial cyst, 4 thymic cyst, 1 parathyroid cyst, 1 gastroenteric cyst and 1 benign mature cystic teratoma).

The remaining 43 of 58 benign lesions were solid. The majority of mediastinal lesions were thymic disorders (51/88, 57.95%), followed by neurogenic tumors (15/88, 17.04%) (Table 2).

Qualitative analyses

Three of 30 (10%) malignant cases (2 invasive thymomas and 1 thymic carcinomas) were false-negative on FDG PET (Table 2). There were 26 benign mediastinal and chest-wall lesions showing positive FDG uptake. Also, false-positive rate was high in non-invasive thymomas (8/11, 72.7%), Castleman diseases (4/5, 80%), Schwannomas (10/13, 76.9%), and thymic hyperplasia (3/9, 33.3%). There was one case of benign paraganglioma with false-positive FDG uptake. The images of false-positive, false-negative, true-positive, and true negative-cases were shown in Figure 1. The overall sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) of PET/CT in detection of malignancy were 90%, 55.17%, 67%, 50.94% and 91.43%, respectively.

Quantitative analysis

Comparison of quantitative PET/CT indices in mediastinal and chest-wall lesions was shown in Table 3. The $SUV_{max}$, HU mean and size were higher in malignant cases ($P = 0.002$, $P = 0.000$, and $P = 0.014$ respectively). We found a cut-off value of 4.67 for $SUV_{max}$ to discriminate benign lesions from malignant ones with a sensitivity and specificity of 73.7% and 75.9%, respectively (AUC 0.876, 95% CI 0.805-0.948, $P < 0.0001$) (Figure 2). A positive correlation between lesion diameter and $SUV_{max}$ value in all lesions was found in this study. This correlation...
**Table 3.** Comparison of quantitative PET/CT indices in mediastinal lesions

<table>
<thead>
<tr>
<th></th>
<th>Malignant vs. benign lesions (n = 88)</th>
<th>Benign solid vs. cystic lesions (n = 58)</th>
<th>Invasive vs. noninvasive thymoma (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Malignant (n = 30)</td>
<td>Benign (n = 58)</td>
<td><strong>P value</strong></td>
</tr>
<tr>
<td>Size in mm (mean ± SD)</td>
<td>69.8 ± 32.1</td>
<td>56.3 ± 27.5</td>
<td>0.014*</td>
</tr>
<tr>
<td>SUV&lt;sub&gt;max&lt;/sub&gt; (mean ± SD)</td>
<td>8.7 ± 4.8</td>
<td>3.3 ± 2.2</td>
<td>0.002*</td>
</tr>
<tr>
<td>HU mean (mean ± SD)</td>
<td>51.6 ± 19.9</td>
<td>34.4 ± 32.1</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

HU = Hounsfield unit, *P < 0.05.
There was no significant difference in the lesion size between noninvasive and invasive thymomas (P = 0.300). The mean $\text{SUV}_{\text{max}}$ was significantly higher in invasive thymomas (P = 0.029).

The values of $\text{SUV}_{\text{max}}$ and HU mean were higher in solid benign lesions than those of cystic benign lesions (P = 0.000 and P = 0.032, respectively). The lesion size was higher in cystic lesions (P = 0.000).

Discussion

PET/CT had a limited specificity (55.17%) due to high false-positive PET results caused from Castleman diseases, benign neurogenic tumors, thymic hyperplasia and noninvasive thymomas in our study. Castleman disease (CD) is a rare lymphoproliferative disorder. There are recognized mainly two histologic types; hyaline-vascular and plasma cell variants [7]. We found that mild to moderate FDG uptake on patients with CD concordance with literature [7, 8]. $\text{SUV}_{\text{max}}$ was higher in a patient with plasma cell variant (6.75) than in hyaline vascular variants (range 2.94-4.06, mean 3.75 ± 0.9) in our limited study. The plasma cell variant of the disease is usually multicentric and more aggressive than the hyaline vascular forms [7]. The value of FDG PET/CT in prediction of histologic types may be evaluated with large sample size studies.

Schwannoma, which is a benign peripheral nerve sheath tumor. Differential diagnosis cannot be made between schwannomas and malignant peripheral nerve sheath tumors based on value $\text{SUV}_{\text{max}}$ because of high FDG uptake can be seen in schwannomas [9]. Authors showed that uptake of FDG in patients with schwannoma was correlated with vascular endothelial growth factor/vascular permeability factor (VEGF/VPF) [10]. We found that intense FDG uptake in malignant paraganglioma ($\text{SUV}_{\text{max}} = 24.13$) and moderate uptake ($\text{SUV}_{\text{max}} = 5.92$) in benign paraganglioma. Increased FDG uptake of paraganglioma might be associated with specific mutations on the genes of B, C, and D subunits of the mitochondrial complex II enzyme succinate dehydrogenase [11, 12]. We suggest that PET/CT may be helpful in detection of schwannoma and paraganglioma.

We found high PET/CT sensitivity rates for identification of the malignancy (90%). All of 15 mediastinal cystic masses had true-negative PET findings. There were cases of a retrosternal goiter, thymolipoma, parathyroid adenoma and esophageal leiomyoma with true-negative PET results in our study. For evaluation of these lesions, PET/CT may have be complementary role to the CT for planning a management strategy. PET/CT may reduce unnecessary invasive investigations for diagnosis in patients with nonavid or low avid FDG lesions.
Among 30 malignant cases, there were 3 false-negative cases (2 invasive thymomas and 1 thymic carcinoma). Different results were obtained about effectiveness of PET/CT in predicting tumor invasiveness of thymomas in several studies. Some investigators reported that inability of FDG SUV to predict thymoma invasiveness [13-15]. However Kubota et al. and Sung et al. showed that higher FDG uptake in invasive thymoma than in noninvasive form [16, 17]. Similarly, we found that the mean SUVmax was significantly higher in invasive thymomas. Shibata et al. reported that the cutoff value of SUVmax was 6.3 for predicting type C thymoma (thymic carcinoma) with a sensitivity of 1.0 and a specificity of 0.92 [14]. All type C thymomas (n = 3) had an FDG-SUV ≥ 6.3. But we found 4 of totally 9 thymic carcinomas (44.4%) had an FDG-SUV > 6.3. We assumed that thymic carcinomas tends to have high FDG uptake but in the presence of low FDG uptake thymic carcinomas and invasive thymomas cannot be excluded.

Kubato et al. reported that mean FDG uptake of malignant mediastinal tumors was significantly higher than that of benign tumors, with cutoff line was about 3.5 by DUR (differential uptake ratio; synonym SUV) [16]. Similarly, our study showed significant difference between SUVmax of malignant and benign lesions, with optimal cut off was 4.67. We suggest that SUVmax can be a useful marker for discriminating malignant tumors from benign ones.

In conclusion, FDG PET/CT may be complementary to conventional imaging methods for the evaluation of mediastinal and chest wall masses. PET/CT may reduce unnecessary invasive investigations for diagnosis in patients with nonavid or low avid FDG lesions. However confirmatory tissue sampling is required to confirm PET positive findings for the definite diagnosis. Thymomas with high SUVmax have high potential to be invasive.

Disclosure of conflict of interest

None.

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