Utility of $^{18}$F-fluorodeoxyglucose positron emission tomography for distinguishing between the histological types of early stage thymic epithelial tumours

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Abstract

OBJECTIVES: Recent studies have shown the usefulness of $^{18}$F-fluorodeoxyglucose positron emission tomography (FDG-PET) in differentiating between World Health Organization (WHO) histological subgroups of thymic epithelial tumours. However, these reports may have included many advanced cases of these lesions (Masaoka stage III or IV) of high-risk subtypes. The objective of our present study was to assess the usefulness of FDG-PET for distinguishing the histological subtypes of early stage thymic epithelial tumours (Masaoka stage I or II).

METHODS: Twenty patients who had undergone an FDG-PET examination prior to treatment and had been diagnosed with an early stage thymic epithelial tumour between July 2005 and July 2011 were enrolled in the present study. All patients underwent a total thymectomy. This cohort was divided into two groups according to the WHO histological classification of their lesion, i.e. low-risk tumours (types A, AB or B1) in one group and high-risk tumours (types B2, B3 or thymic carcinoma) in the other. Focal FDG accumulation was evaluated by determining the maximum standardized uptake value (SUV-max).

RESULTS: The patient cohort for this study included 13 men and 7 women ranging in age from 26 to 70 years (mean 55 years). The low-risk group included seven cases (type A, 0; type AB, 7; type B1, 0), and the high-risk group comprised 13 cases (type B2, 7; type B3, 3; thymic carcinoma, 3). The SUV-max values of the low-risk and high-risk tumours were 3.09 ± 0.51 and 6.19 ± 3.13, respectively, and this was a significant difference. For the differential diagnosis of low-risk and high-risk tumours, sensitivity and specificity were 92.3% and 83.3%, respectively, when an SUV-max of 3.5 was used as a cutoff.

CONCLUSIONS: FDG-PET is a useful method for distinguishing histological types of early stage thymic epithelial tumours.

Keywords: Thymic epithelial tumours • $^{18}$F-fluorodeoxyglucose positron emission tomography

INTRODUCTION

Thymic epithelial tumours remain the predominant lesions that arise in the anterior mediastinum. It is also widely accepted that the tumour stage is the most important prognostic factor for these cases [1]. In addition, many studies have shown that the World Health Organization (WHO) histological classification also constitutes an independent prognostic factor for this disease [2, 3].

$^{18}$F-fluorodeoxyglucose positron emission tomography (FDG-PET) is widely used to differentiate benign from malignant lesions in various organs. Recent studies have shown that there is increased FDG accumulation in high-risk thymic epithelial tumours when compared with low-risk tumours and that FDG-PET is a useful method for differentiating the histological subgroups of these lesions [4–8]. Most of the thymic epithelial tumour cohorts analysed in previous studies are likely to have included numerous advanced stage tumours of a high-risk subtype, and the proportion of invasive tumours tends to increase in accordance with the subtypes, i.e. from low-risk tumours (types A, AB and B1) to high-risk tumours (types B2, B3 and thymic carcinoma) [9, 10]. However, there have been no previous studies of thymic epithelial tumours that have limited their scope to early stage lesions and compared the FDG-PET findings for low-risk and high-risk tumours.

The objective of our present study was to assess the usefulness of FDG-PET for distinguishing the histological subtypes of early stage thymic epithelial tumours (i.e. Masaoka stage I and II).
MATERIALS AND METHODS

This study was approved by the institutional review board of Shinshu University and written informed consent was obtained from all patients for the FDG-PET study.

Patient population

Twenty patients who had been diagnosed with an early stage thymic epithelial tumour (Masaoka stage I or II) and had undergone an FDG-PET examination prior to treatment between July 2005 and July 2011 were enrolled in the present study. All patients received a total thymectomy at Shinshu University Hospital (Matsumoto, Japan) and were divided into two study groups based on the WHO histological classification of their lesions, i.e. low-risk tumours (types A, AB or B1) or high-risk tumours (types B2, B3 or thymic carcinoma).

FDG-PET imaging

PET scanning was performed at a single centre in Aizawa Hospital (Matsumoto, Japan) using a dedicated instrument (Advance Nxi, GE, Milwaukee, WI, USA) in a two-dimensional imaging mode. Emission scans were obtained with a 2–3 min acquisition time per table position, requiring six or eight table positions to cover the area from the pelvis floor to the head. Following emission scanning, transmission scans of the same area were obtained with a 1–2 min acquisition time per table position. The PET image set was reconstructed using the ordered subset expansion maximization algorithm with segmented attenuation correction, and the resulting resolution was ≈4.3 mm full-width at half-maximum.

After at least 4 h of fasting, the patients were intravenously injected with 5 MBq/kg (maximum, 370 MBq) of $^{18}$F-FDG and rested for 1 h before receiving a whole-body scan. Focal FDG accumulation was evaluated via the maximum standardized uptake value (SUV-max).

Statistical analysis

All of the data generated in this study are presented as the mean ± standard deviation. Comparisons of the data obtained for the two patient groups were performed using the unpaired t-test. Statistical significance was set at $P < 0.05$.

RESULTS

Representative computed tomography (CT) and FDG-PET images from patients in each of the tumour groups are shown in Figs 1 and 2.

Clinical characteristics of the patients

The patient cohort in this study included 13 men (65%) and 7 women (35%) ranging in age from 26 to 70 years (mean 55 years). Using the WHO histological classification system to type the thymic epithelial tumours in these subjects, seven of these cases were assigned to the low-risk group (type A, 0; type AB, 7; type B1, 0), and the remaining 13 patients were placed in the high-risk group (type B2, 7; type B3, 3; thymic carcinoma, 3). There were no significant differences between the two groups in terms of age, sex or tumour size (Table 1).

Table 1: Clinical characteristics of the patients enrolled in this study

<table>
<thead>
<tr>
<th></th>
<th>Low-risk tumours</th>
<th>High-risk tumours</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60.1 ± 6.3</td>
<td>52.2 ± 15</td>
<td>0.199</td>
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<tr>
<td>Sex (male/female)</td>
<td>4/3</td>
<td>9/4</td>
<td>0.564</td>
</tr>
<tr>
<td>Tumour size (cm)</td>
<td>5.4 ± 3</td>
<td>4.9 ± 2.4</td>
<td>0.684</td>
</tr>
<tr>
<td>Masaoka stage (I/II)</td>
<td>3/4</td>
<td>2/11</td>
<td>0.195</td>
</tr>
<tr>
<td>SUV-max</td>
<td>3.09 ± 0.51</td>
<td>6.19 ± 3.13</td>
<td>0.019*</td>
</tr>
</tbody>
</table>

*Denotes significant difference between the two groups ($P < 0.05$). SUV-max: the maximum standardized uptake value.
The SUV-max values of the low-risk and high-risk tumour groups were 3.09 ± 0.51, and 6.19 ± 3.13, respectively. This is a significant difference (Fig. 3).

**Differential diagnosis of a low-risk or high-risk thymic epithelial tumour**

The usefulness of the SUV-max value for the differential diagnosis of low-risk or high-risk thymic epithelial tumour was evaluated. Sensitivity and specificity were 92.3% and 83.3%, respectively, when an SUV-max of 3.5 was used as a cutoff. The area under the curve was measured at 0.92 using receiver-operating characteristic analysis (Fig. 4).

**DISCUSSION**

In our present study, the SUV-max of high-risk thymic epithelial tumours was found to be higher than that of the corresponding low-risk tumours and this demonstrated the usefulness of FDG-PET in differentiating between these lesions at an early stage. Previously, some reports had already shown the usefulness of FDG-PET in differentiating between WHO histological types, particularly between thymomas and thymic cancers at all tumour stages [4–8]. However, these studies are likely to have included many advanced cases with high-risk tumours. Sasaki et al. [6] have reported no difference in the FDG uptake between invasive and non-invasive thymoma. Based on our own preliminary data (not published) however, the SUV-max in thymic carcinoma increases with advanced tumour stage (II; 7.1 ± 1.5; III, IV; 12 ± 4.6; n = 3, 6, respectively). In our present study, we thus examined thymic epithelial tumours at early stages only to reduce the influence of tumour stage on the measurements.

As for the differential diagnosis of low-risk or high-risk thymic epithelial tumours using the SUV-max, Inoue et al. have described in their previous retrospective study of 46 patients with thymic epithelial tumours that sensitivity and specificity were 78.3% and 91.3%, respectively, when 4.5 was used as a cutoff, and that this information is a useful prognostic indicator [5]. In our present study, the SUV-max cutoff value of 3.5 appeared to be useful (sensitivity and specificity were 92.3% and 83.3%, respectively). The reason for the differences in these cutoff values is unclear, but it is possible that tumour invasiveness could influence these results because the former study included many advanced stage tumours (Masaoka stage III or IV) in the high-risk tumour group (83%).

In our current study cohort, all patients underwent a total thymectomy which is widely accepted in the treatment of stage I and II thymomas. Some authors have reported several cases of multiple thymoma and recommended an extensive thymectomy even for stage I thymomas to avoid recurrence from tumour remnants [11]. On the other hand, some authors have recommended a thoracoscopic subtotal or partial thymectomy for stage I and II thymomas [12, 13]. There is a general consensus in the literature that complete resection of the tumour should be performed [14–16], but there is as yet no consensus on the appropriate level of thymic resection in cases of a thymic epithelial tumour without myasthenia gravis. It must be noted that the validity of performing a subtotal thymectomy is unclear at this time, but it is possible that a limited resection might be indicated in the future for low-risk stage I or II thymomas. Taken together, the current evidence indicates that FDG-PET does not have any direct benefit in terms of deciding the treatment strategy for thymic lesions, but suggests that this method has the potential to determine the appropriate level of thymic resection for a given patient.

Our current study has several noteworthy limitations. First, the small number of patients analysed and the retrospective nature of the analysis may have affected our results. Second, there was an imbalance between the histological subtypes in our cohort. In the low-risk group, there were no patients with a type A or B1 tumour, and this may have been a selection bias. Third, the observation period was short and no prognostic evaluations were undertaken.

**CONCLUSION**

FDG-PET has utility in distinguishing the histological types of early stage thymic epithelial tumour.

Conflict of interest: none declared.
REFERENCES