Dual-time-point F-18 FDG PET/CT for the prediction of the WHO grade of malignancy in thymic tumours

Poster No.: C-0609
Congress: ECR 2015
Type: Scientific Exhibit
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Keywords: Cancer, Diagnostic procedure, PET-CT, PET, Thorax, Oncology, Mediastinum
DOI: 10.1594/ecr2015/C-0609

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Aims and objectives

The World Health Organization (WHO) histologic classification system for thymic epithelial neoplasm (TEN) was proposed in 1999 and updated in 2004 [1] and has been widely adapted for independent prognostic factors [2, 3]. This classification system recognizes six types of thymoma: type A, AB, B1, B2, B3, and type C (thymic carcinoma).

F-18 fluorodeoxyglucose (FDG) positron emission tomography/ computed tomography (PET/CT) has been proposed as an advanced non-invasive imaging methods for evaluating TENs and the previous studies investigated the correlations between FDG uptake and the WHO histological classification [4 - 7]. In these analyses, PET images had been analyzed with qualitative or semiquantitative analyses, such as the calculation of the maximum standardized uptake value (SUVmax) on single-time-point F-18 FDG PET scans. However, F-18 FDG injected activity and time between injection and PET acquisition were quite different among the studies. In contrast, only one study have evaluated the diagnostic performance of dual-time-point (DTP) F-18 FDG PET/CT, which were performed at 60 minutes and 3 hours after tracer injection [8].

The aim of the present study was to investigate the diagnostic capacity of DTP F-18 FDG PET/CT with 90 minutes early- and 2 hours delayed scans as a predictor of the WHO classification based malignancy grade in TEN.
Methods and materials

Patients

Between August 2006 and September 2014, a total of 36 patients met the following conditions for inclusion in the present retrospective study (22 men, 14 women; age [mean ± SD] 60.22 ± 14.73; range 21-86 years): patients diagnosed with TEN, who underwent F-18 FDG PET/CT before biopsy or surgery at an adjacent imaging center, without any received therapy before PET/CT study, DTP PET/CT scan available. TEN were classified using the WHO criteria and graded into three risk groups: type A, AB, and B1 = low-risk thymoma (LR); B2, B3, and C = high-risk thymoma (HR); and thymic carcinoma (CA), by pathologists who were unaware of the PET results [A, B].

F-18 FDG PET/CT

PET image acquisition started 90 min after injection of FDG (early-phase) and 2 hours after the injection (delayed-phase) with the patient in a relaxed supine position using an integrated PET/CT scanner (Biogtaph LS/Sensation 16, Siemens, Munchen, Germany) at an adjacent imaging center. Patients fasted for at least 5 h, after which blood glucose levels were determined to ensure a level of <140 mg/dL. Patients then received an intravenous injection of 3.7 MBq/kg (1.0 × 10-4 Ci/kg) body weight FDG. The patients were asked to remain resting on a reclining chair to minimize FDG consumption by the muscles just before scans. First, a total-body low-dose CT scan for calculation of attenuation correction was performed, using a standardized protocol involving 140 kV, 12 to 14 mAs, a tube-rotation time of 0.5 s per rotation, a pitch of 0.8, a section thickness of 3 mm, and scan field from head up to the mid-thigh level (consisting of 7-8 bed positions with 2.4 min per table position) was performed. The PET images were reconstructed with an ordered-subset expectation maximization (OSEM) iterative reconstruction algorithm. Integrated, coregistered PET/CT images were obtained using a workstation (PET Viewer, AZE), which enabled image fusion and analysis.

Image data analysis

Two nuclear physicians unaware of the histological results interpreted all F-18 FDG PET/CT findings by consensus. For semiquantitative analysis of FDG uptakes, the standardized uptake value (SUV) was adopted. SUVs were calculated using lean body
mass as follows: SUV = radioactivity in regions of interest (ROI) (Bq/ml) / injected radioactivity (Bq)/lean body mass (kg). To minimize partial-volume effects, the maximum SUV (SUVmax) within ROIs was used. The SUVmax measurements of TEN were obtained both on early phase (SUV1) and on delayed phase (SUV2). Furthermore, we calculated RI-SUVmax from SUVmax according to the following formula: RI-SUVmax (%) = (SUV2 [delayed phase] - SUV1 [early-phase]) × 100 /SUV1 (early phase). Circular ROIs were drawn to encompass TEN contour on transaxial images. On CT images, the longaxis diameters of the nodal lesions detected on PET/CT were calculated.

Statistical Analysis

Differences in SUVmax and RI-SUVmax were analyzed with the Mann-Whitney U test using the Statview 5.0 (SAS Institute Inc., Berkeley, CA). Moreover, Receiver Operating Characteristic (ROC) curve analyses were performed to determine SUVmax values for thymic carcinoma in both early- and delayed-phases that maximized sensitivity and specificity. Discrimination was measured with the use of area under the curve (Az). We used Labroc 5 (CE Metz, Chicago, IL) to calculate ROC curves. A P-value < .05 was considered a statistically significant difference for all analyses.
Results

Patients and tumour Characteristics

A total of 36 patients met criteria for analysis. Histopathologically, seventeen (47%) had be classified to LR (type A: 5 patients, type AB: 5 patients, and type B1: 7 patients), nine (25%) had be classified to HR (typeB2: 6 patients, type B3: 3 patients), ten (28%) had be classified to CA. The tumor size ranged from 15 to 85 mm with a mean of 51.71 mm in LR, from 19 to 79 mm with a mean of 43.44 mm in HR, from 32 to 100 mm with a mean of 71.50 mm in CA in long-axis diameter. Significant difference was identified in tumor size between HR and CA (p=0.0178). There were no significant differences in the size of lesions between LR and HR (p=0.4664) and LR and CA (p=0.063).

Maximum Standardized Uptake Values and Retention Index of SUVmax

Table 1 shows SUV1, SUV2, and RI-SUVmax values for all of the study groups. Median SUVmax values were 4.15 (range, 1.50-8.63) for SUV1 and 4.55 (range, 2.02 -9.23) for SUV2 in LR thymomas, 3.17 (range, 1.88-6.88) for SUV1 and 3.52 (range, 2.17-7.41) for SUV2 in HR thymomas, and 5.49 (range, 2.75 - 9.89) for SUV1 and 6.28 (range, 2.93-12.59) for SUV2 in thymic carcinomas. Ten of 17 LR thymomas, seven of 9 HR thymomas, and nine of 10 thymic carcinomas showed higher SUVmax values on 2-h delayed-phase than on 90-min early-phase. There were no significant differences between the SUV1 and SUV2 for all study groups.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>LR thymoma</th>
<th>HR thymoma</th>
<th>Thymic carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUV1</td>
<td>4.15 ± 0.426</td>
<td>3.17 ± 0.513</td>
<td>5.49 ± 0.742</td>
</tr>
<tr>
<td>SUV2</td>
<td>4.55 ± 0.454</td>
<td>3.52 ± 0.575</td>
<td>6.28 ± 0.893</td>
</tr>
<tr>
<td>RI-SUVmax (%)</td>
<td>1.70 ± 4.896</td>
<td>7.70 ± 3.138</td>
<td>6.40 ± 3.019</td>
</tr>
</tbody>
</table>

LR, low-risk; HR, high-risk; SUV, standardized uptake value;

RI, retention index.

The data represent median ± standard error of mean.
The SUV1 was significantly higher in thymic carcinomas than in both LR thymomas (p = 0.349) and in HR thymomas (p = 0.0142). No significant difference was identified in SUV1 between LR and HR thymomas (p = 0.1693). The SUV1 was significantly higher in thymic carcinomas than in all thymomas (p = 0.011) (Fig. 1 on page 7).

The SUV2 was significantly higher in thymic carcinomas than both in LR thymomas (p = 0.0308) and in HR thymomas (p = 0.0142). No significant difference was identified in SUV2 between LR and HR thymomas (p = 0.1531). The SUV2 was significantly higher in thymic carcinomas than in all thymomas (Fig. 2 on page 7).

Median RI-SUVmax was 1.70% (range, -6.10 to 77.00%) in LR thymomas, 7.70% (range, -14.80 to 15.40%) in HR thymomas, and 6.40% (range, -6.20 to 27.30%) in thymic carcinomas. No significant difference was found in RI-SUVmax between LR and HR thymomas (P = 0.5004), LR thymomas and thymic carcinomas (p = 0.2801), and HR thymomas and thymic carcinomas (p = 0.8701).

ROC Curves and Cut-Off Values for SUVmax and RI-SUVmax

Figure 3 and 4 shows the ROC curves obtained to determine the appropriate cut-off values of SUV1 (Fig. 3 on page 8) and SUV2 (Fig. 4 on page 9). For SUV1, the cut-off value yielding the highest accuracy was 4.775, with a sensitivity of 76.2% and specificity of 65.0%. For SUV2, the cut-off value was 4.75, yielding a sensitivity of 78.8% and specificity of 61.6%. The area under the ROC curve (Az) between early and delayed scans were same level (each 0.7844).
Fig. 1: A correlation between the maximum standardized uptake value (SUVmax) on 90-min early scan and classified risk group.

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**Fig. 2:** A correlation between the maximum standardized uptake value (SUVmax) on 2-h delayed scan and classified risk group.

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**Fig. 3:** ROC curve obtained to determine the appropriate cut-off value of SUV1.

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Fig. 4: ROC curve obtained to determine the appropriate cut-off value of SUV2.

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Conclusion

F-18 FDG PET/CT may differentiate thymomas from thymic carcinomas with moderate accuracy on both 90-min early and 2-h delayed phases. RI - SUVmax would not be useful predictor for the WHO malignancy in TENs in DTP F-18 FDG PET/CT with 90-min and 2-h scans.
References


