Therapeutic effect of metabolic parameters measured by 18F-FDG-PET/CT in patients with Rheumatoid Arthritis.

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Aims and objectives

Rheumatoid arthritis (RA) is a systemic disease characterized by chronic synovial inflammation and joint damage. Assessment of the inflammatory activity of RA is important for the prediction of future articular destruction. Anti-TNF-# antibody has proved to stop progression of joint damage, therefore, the therapeutic monitoring of this agent is currently of great interest. The usefulness of 18F-FDG-PET has been well established for the diagnosis, staging, and evaluation of therapy for various types of cancer throughout the whole body, and recently, FDG uptake in patients with RA has been shown to represent the activity of synovial inflammation [1-4]. The purpose of this study was to evaluate the utility of 18F-FDG-PET/CT and contrast enhanced MRI (CMR) in assessing joint inflammatory activity change in RA patients before and after the treatment with anti TNF # antibody.
Fifteen patients with RA were enrolled (2 males, 13 females, aged 33-72 years; average 58.5 years old). Patients visited our University hospital during the period from April 2008 to June 2013. 18F- FDG PET /CT and clinical assessment before and 6 months after the treatment with anti-TNF-# antibody were performed. Anti TNF-# antibody was given to all patients. Infliximab was administered intravenously at a dose of 3 mg/kg in weeks 0, 2, and 6, with subsequent doses at 8-week intervals. For PET/CT imaging, patients were injected with 5 MBq/kg of 18F-FDG after fasting for six hours. Sixty minutes after the administration of FDG, whole-body images were obtained using PET/CT scanners (Biograph 16; Siemens Medical Solutions). FDG uptake was evaluated by the maximum standardized uptake value (SUV max) and metabolic tumor volume (MTV). MTV was measured using Volume Viewer software, which provides an automatically delineated volume of interest (VOI) using an isocontour threshold method based on the SUV. Using the threshold SUV, VOIs of the lesions were automatically generated. For the assessment of CMR, post contrast fat-suppressed T1WI (TR/TE=440/10 msec) was used. Within the selected area of interest, volume of enhancement on each slice was calculated by multiplying the enhancing area by slice thickness, and summed up. Pre and post treatment FDG uptake as expressed by SUV max change ratio (rSUV) and MTV change ratio (rMTV) were compared with that of enhancement area in CMR change ratio (rCMR).
Results

Totally 15 patients were evaluated and paired t test are performed before and after therapeutic changes of SUV max, MTV and CMR (Table 1). In 16 patients, the results of therapeutic response evaluation for FDG and MRI showed agreement, while disagreement was noted in 2 patients. Significant correlation (P=0.0129, r=0.61) was noted in rCMR and rSUV, whereas, rMTV showed no correlation with rCMR (Figure 1, 2). In responder case, SUV max significantly decreased in the right shoulder joint, and MTV and CMR decreased as well (Figure 3). In case 2, SUV max and the other parameters also decreased significantly (Figure 4).

In recent years, attention has been focused on how early the active treatment of RA should be started. Anti TNF-# antibody is a molecular-targeted agent for RA. RA inflammation is classified into two different types: inflammation based on immune abnormality and nonspecific inflammation. The latter centers on granulocytes, which produce granulation tissue that directly acts on bone destruction. Inhibiting the nonspecific activity of granulation tissue as well as active production of cytokine and protein-cutting enzyme in the tissue, such as TNF, is expected to cure RA by restraining bone destruction. 18F- FDG-PET/CT may have advantages over MRI or US, because 18F- FDG-PET can evaluate activity of inflammation of all joints in a single scan. Latest reports, MTV is a volumetric measurement of tumour cells with high glycolytic activity [5]. PET parameters that can serve as useful indices for determining therapeutic response or predicting prognosis are volume-based metabolic parameters such as MTV in lung cancer [6]. The results of this study showed that rSUV correlated with rCMI in response to the therapy. The evaluation using SUVmax also covers swelling or painful joints, which may bring different views depending on examiners. These results suggest that the efficacy of anti-TNF-# antibody can be readily evaluated in patients with early active RA by using SUVmax to assess arthritis and may be able to evaluate objective inflammatory activity as a noninvasive tool and, furthermore, it could make more accurate evaluation than MTV. Despite it's widely used and practical application, SUVmax is far from excellent.
### Table 1

<table>
<thead>
<tr>
<th>Patient No</th>
<th>age</th>
<th>sex</th>
<th>rSUV</th>
<th>rMRI</th>
<th>rPETV CAR</th>
<th>rMRI</th>
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<tr>
<td>1</td>
<td>72</td>
<td>F</td>
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<td>0.23</td>
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<td>0.85</td>
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<td>3</td>
<td>64</td>
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<td>0.73</td>
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<td>4</td>
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<td>71</td>
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<td>15</td>
<td>69</td>
<td>F</td>
<td>0.83</td>
<td>0.68</td>
<td>0.00</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Before and after therapeutic changes of SUV max, MTV and CMR

**Fig. 1**

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Correlation between rSUV and rCMR

Figure 1

p<0.05

Fig. 2

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Correlation between rMTV and rCMR

Figure 2

Fig. 3

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Case 1

<table>
<thead>
<tr>
<th>Region</th>
<th>Right (Rt)</th>
<th>Left (Lt)</th>
<th>SUV max Reduction</th>
</tr>
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<tbody>
<tr>
<td>Shoulder</td>
<td>6.17</td>
<td>4.78</td>
<td>1.73</td>
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<tr>
<td>Elbow</td>
<td>2.93</td>
<td>2.72</td>
<td>1.54</td>
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<tr>
<td>Hip</td>
<td>3.41</td>
<td>3.36</td>
<td>1.01</td>
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<tr>
<td>Knee</td>
<td>2.30</td>
<td>2.85</td>
<td>1.39</td>
</tr>
</tbody>
</table>

**MTV**
- 79.3 \(\rightarrow\) 0.83

**CMR**
- 57.5 \(\rightarrow\) 13.4

**CRP**
- 5.11 \(\rightarrow\) 0.78

Figure 3
Fig. 4

Case 2

- SUVmax
  - Shoulder: Rt 2.20 → 1.83, Lt 1.95 → 1.20
  - Elbow: Rt 1.10 → 0.75, Lt 2.00 → 0.67
  - Hip: Rt 1.56 → 1.28, Lt 1.79 → 1.64
  - Knee: Rt 1.83 → 0.96, Lt 2.34 → 1.13

- MTV: 4.36 → 1.95
- CMR: 10.3 → 7.0
- CRP: 4.84 → 0.01

Fig. 5

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Conclusion

18F-FDG-PET/CT may have alternative value to evaluate effectiveness of therapy for RA and by taking the advantage of the possible single whole body image acquisition, it may be conveniently used on behalf of CMR.
References


