The Assessment of Biological Treatment in Patients with Rheumatoid Arthritis Using FDG-PET/CT

+1 Okamura K; +2 Yonemoto Y; +2 Arisaka Y; +1 Takeuchi K; +1 Kaneko T; +1 Kobayashi T; +1 Takagishi K

+1 Department of Orthopaedic Surgery, Gunma University Graduate School of Medicine, Gunma, Japan
+2 Department of Diagnostic Radiology and Nuclear Medicine, Gunma University Graduate School of Medicine, Gunma, Japan
kokamura@med.gunma-u.ac.jp

ABSTRACT INTRODUCTION:
18F fluorodeoxyglucose (FDG) positron emission tomography (PET) can be used to image synovial inflammation in patients with rheumatoid arthritis (RA). Recent advances in medical biology and pharmaceutical engineering have provided new drugs, such as tumor necrosis factor (TNF) inhibitors, anti-interleukin-6 receptor antibodies, and anti-CD20 antibodies for the treatment of RA patients. Clinical application of novel therapies for RA has stimulated increased interest in the radiological assessment of the disease activity of RA.

Because no complete response leads patient who have been undergoing these biological therapies to discontinue the treatment, which has high costs and possible side effects, monitoring of the specific biological response to the therapies might be helpful for the clinicians to determine suitable treatments. Therefore, the development of molecular imaging methods would be beneficial, especially in RA patients.

One of the merits of PET is that it enables quantitative measurement of metabolic activity. 18F-FDG PET studies have been proposed to assess the metabolic activity measured quantitatively by the standardized uptake value (SUV). In particular, lesions in patients with RA.

In the present study, we evaluated whether the FDG uptake of the affected joints represented by the SUV correlated with the clinical assessment of patients with RA. In addition, we wanted to evaluate if there was a correlation between the differences in the SUV and the improvement of the clinical findings in RA patients receiving anti-TNF therapies.

METHODS:

Patients - RA patients who underwent anti-TNF therapies in our hospital were assessed using whole-body FDG-PET/CT. The FDG-PET and clinical assessments were performed prior to, and 6 months after the initiation of the therapies. Clinical assessments included the erythrocyte sedimentation rate (ESR), white blood cell (WBC) count, and serum concentrations of CRP, matrix metalloproteinase (MMP)-3, and rheumatoid factor (RF). The activity of inflammation was evaluated using both the disease activity score (DAS) and the DAS28-CRP. The DAS28 was calculated based on the results of 28 tender joints count (TJC), 28 swollen joints count (SJC), and the ESR. The DAS28-CRP was calculated using the TJC, SJC, and CRP. The institutional review board of the hospital approved this study, and informed consent was obtained from each patient.

PET images - Whole-body 18F-FDG PET was performed following intravenous injection of 18F-FDG (5 MBq/kg) after fasting for more than 6 hours. Patients were scanned from the head to the toe in the arms-down position. PET images were interpreted by experienced physician specializing in nuclear medicine and increased 18F-FDG uptake in bilateral shoulder, elbow, wrist, hip, knee and ankle joints was recorded.

Data analysis - For the semiquantitative analysis, functional images of the standardized uptake value (SUV) were produced using attenuation-corrected transaxial images, injected doses of 18F-FDG, patient's body weight, and the cross-calibration factor between PET and dose calibrator. SUV was defined as follows: SUV = Radioactive concentration in the region of interest (ROI) [MBq/g] / Injected dose (MBq) / Patient's body weight. ROIs were manually drawn at each joint on the SUV images. ROI analysis was conducted by a nuclear physician with the aid of corresponding CT scans. The maximal SUV in the ROI was used as a representative value for the assessment of 18F-FDG uptake.

For the assessment of therapeutic response, the difference in the total of the maximal SUV of each joints and DAS28 were presented as delta SUV (ΔSUV) or delta DAS28 (ΔDAS28) for each patient.

RESULTS:

Forty-two patients (10 male, 32 female; average age: 55.67 (18-74) years) who underwent anti-TNF therapies (infliximab (IFX) for 17 patients, etanercept (ETN) for 14 patients and adalimumab (ADA) for 11 patients), were assessed. The average disease duration of these patients was 11.7 (6.6-49) years.

Before treatment, the sum of the SUVmax among the measured joints (total SUVmax), was correlated with the DAS28 (r=0.532, p=0.001), DAS28-CRP (r=0.529, p=0.001), ESR (r=0.506, p=0.001), CRP (r=0.385, p=0.012) and the number of tender/swollen joints (r=0.416, p=0.007 vs. 0.467, p=0.002), respectively.

The ΔSUV, the difference in the total SUVmax before and after treatment, significantly correlated with the ΔDAS28 (r=0.498, p=0.001), ΔDAS28-CRP (r=0.517, p=0.001), ΔESR (r=0.485, p=0.001), ΔCRP (r=0.437, p=0.003) and the difference of the number of tender/swollen joints (r=0.447, p=0.003 vs. 0.525, p=0.001), respectively.

DISCUSSION:

Several previous studies have evaluated whole-body FDG joint uptakes based on the visual assessment score, i.e., the visual uptake score. Goerres et al. assessed seven RA patients prior to and 12 weeks after IFX treatment using FDG PET imaging-based total joint scores, and concluded that visual assessment of the FDG uptake showed a significant correlation with the clinical evaluation of disease activity performed by the rheumatologist in patients undergoing anti-inflammatory treatment.

Although rheumatologists usually examine patients by calculating scores such as the DAS28 or DAS28-CRP, which include subjective items, to assess the treatment response, whole-body imaging with FDG-PET seems to provide an alternative and objective evaluation method, or at the very least, an additional tool to provide assistance with the evaluation. With regard to this point, the SUVs might be able to provide a better description for the joint FDG uptake than visual uptake scores.

Hence, in the present study, we evaluated the FDG uptake using SUVs, not visual uptake scores.

It has so far been reported that the SUVs obtained from 18F-FDG PET assessment of rheumatoid synovitis were correlated with MRI findings, with the SUVs being closely correlated with the volume of the enhancing pannus. In addition, Beckers et al examined 356 joints of 21 patients and showed that 18F-FDG PET imaging could assess the metabolic activity of synovitis and measure the disease activity of the RA. The authors of that study also assessed 16 knees in 16 patients with active RA with PET, MRI and US at baseline and 4 weeks after initiation of anti-TNF-α treatment, and semi-quantitative analyses of the synovial uptake of FDG using the SUVs were performed.

While SUVs apparently reflect the results of the clinical evaluation, the SUVs noted above were based on monoarthric assessments, and none of the previous reports evaluated whole-body FDG-PET/CT to assess the clinical conditions or treatment responses of patients. Therefore, in this study, to provide a semiquantitative analysis and to focus on the potential utility in clinical practice, we conducted whole-body FDG-PET/CT and used the SUVmax to determine the FDG uptake. The difference in the total SUVmax between studies before and after anti-TNF therapies might reflect the changes in the disease activity resulting from the medication, because these values were significantly correlated with the differences in the DAS28 and DAS28-CRP.

In conclusion, the FDG uptake observed in the inflamed RA joints may reflect the disease activity. FDG-PET might play an important role in the evaluation of the biological treatment for RA.

SIGNIFICANCE:

18F FDG-PET can image the extent of inflammation in patients with RA. FDG-PET might play an important role in evaluating the response of RA patients to biological treatment.