The clinical assessment of rheumatoid arthritis using FDG-PET/CT

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ABBREVIATION INTRODUCTION:
F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) can be used to image synovial inflammation in patients with rheumatoid arthritis (RA). Recently, clinical application of novel therapies for RA, such as tumor necrosis factor-α (TNF-α) inhibitor and anti-interleukin-6 receptor antibody, has been introduced. The radiological assessment of disease activity changes of patients who underwent these therapies will help the clinicians to obtain more information about the patients and to decide drug withdrawal or change of medication. It is considered that FDG-PET scan is generally very expensive, however, the information from FDG-PET about patients during biological treatments helps discontinue these treatments with incomplete response despite its high costs and with possible side effects such as malignant lymphoma.

In this study, we evaluated if the FDG uptake of the affected joints represented by SUV correlated with the clinical assessment of patients with RA. In addition, we would like to evaluate if there was a correlation between the difference of SUV and improvement of clinical findings in RA patients undergoing anti TNF therapies.

METHODS:

Patients- RA patients who underwent anti-TNFα therapies in our hospital were assessed using whole-body FDG-PET/CT. Imaging and clinical assessments were performed prior to, and 6 months after the initiation of treatment with anti-TNFα therapies. Disease activity score (DAS28 and DAS28-CRP) were recorded and white blood cell (WBC), matrix metalloproteinase (MMP), and rheumatoid factor (RF) were examined in all patients. 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. Data acquisition was done by 3D-mode at 60 minutes using PET-CT machine (Biograph 16, Siemens Medical Solutions Inc.). Patients were scanned from the head to the toes in the arms-down position. Attenuation correction of the PET images was performed using CT, followed by the reconstruction using an ordered subsets expectation-maximization algorithm into 128x128 matrix. 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 mean value of the maximal SUV of each joints and DAS28 were presented as delta SUV (ΔSUV) or delta DAS28 (ΔDAS28) for each patient as follows: ΔSUV = mean SUVpre − mean SUVpost, ΔDAS28 = DAS28pre − DAS28post . mean SUVpre, mean SUVpost, DAS28pre and DAS28post represent the mean SUV before treatment, the mean SUV after treatment, DAS28 before treatment and DAS28 after treatment, respectively. Additionally, in the following result section, Δ that placed ahead of each examined items mean the difference of the value between before and after the treatment.

Statistics- Spearman’s rank correlation test was used for the analysis of possible relationships among the different parameters recorded in this study. SPSS v 11.0 software (SPSS Inc, Chicago, IL) was used for the analysis. P values less than 0.05 were considered significant.

RESULTS SECTION:

23 patients (2 men, 21 women; average age: 57.6(20-74) years) who underwent anti-TNFα therapies, infliximab(IFX) for 16 patients and etanercept(ETN) for 7 patients, were assessed. The average disease duration of these patients was 12.82 (1-49) years. The average of meanSUV pre and meanSUV post were 2.14 (1.14-3.30) and 1.64 (0.94-2.62). DAS28pre, DAS28-CRPPre, DAS28post and DAS28-CRPPost were 5.38 (3.47-7.20), 4.42 (2.39-6.52), 3.80 (2.20-5.33) and 2.60 (1.18-4.03).

The average of SUVmax among measured joints, the sum of these joints(total SUV max), correlated with DAS28 (r=0.692, p<0.001), DAS28-CRP (r=0.637, p<0.001), ESR (r=0.577, p<0.001), CRP (r=0.441, p=0.002), MMP-3 (r=0.403, p=0.006) and RF (r=0.459, p=0.002).

There were correlations between Δ SUV and Δ DAS28 (r=0.668, p<0.001), Δ SUV and Δ DAS28-CRP (r=0.690, p<0.001), Δ SUV and Δ ESR (r=0.460, p=0.027) and Δ SUV and Δ MMP-3 (r=0.455, p=0.029), respectively. Δ WBC was not significantly correlated with the Δ SUV (r = 0.277, p = 0.200), and Δ CRP with Δ SUV (r = 0.279, p = 0.198).

DISCUSSION:

In recent years, F-18 FDG-PET can be used to image inflammation in patients with arthritis. F-18 FDG-PET imaging has been used to assess the metabolic activity of synovitis in patients with RA and to evaluate the disease activity of RA. Several reports indicated that there was a significant correlation between the visual assessment of FDG uptake, i.e., visual uptake score and clinical evaluation of disease activity. Furthermore, PET findings have been correlated with MRI and US assessments of the pannus in patients with RA as well as with the classical serum parameter of inflammation, CRP, and MMP-3.

Recent advancement in the medical biology and pharmaceutical engineering allows use of new drugs such as tumor necrosis factor-α (TNF-α) inhibitor, anti-interleukin-6 receptor antibody. Clinical application of novel therapy for RA has stimulated increased interest in the radiological assessment of disease activity. One of the merits of PET is quantitative measure of metabolic activity. A few studies have been performed to examine the possible role of 18F-FDG PET to see the disease activity of RA. Previous studies have evaluated FDG joint uptakes based on visual assessment score, i.e., visual uptake score. So, in this study, we evaluated if the FDG uptake of the affected joints represented by SUV correlated with the clinical assessment of patients with RA. In addition, we would like to evaluate if there was a correlation between the difference of SUV and improvement of clinical findings in RA patients undergoing anti TNF therapies.

Goorjes et al assessed seven RA patients prior to, and 12 weeks after IFX treatment using FDG PET total joint score and concluded that visual assessment of FDG uptake showed a significant correlation with clinical evaluation of disease activity in patients undergoing anti-inflammatory treatment. Kubota et al demonstrated the visual FDG uptake score might be useful for evaluating arthritis in large joints. They studied the total FDG score was significantly correlated with the CRP level, however the total SUVmax and the CRP level were weakly, but not significantly, correlated.

In this study, for the semiquantitative analysis and focusing on the utility in clinical practice, we used SUVmax for the grade of FDG uptake. There were the correlations between total SUVmax and clinical findings (DAS28, DAS28-CRP, ESR, CRP, MMP-3 and RF). The difference of the mean SUVmax between before and after anti-TNFα therapies was significantly correlated with the difference of DAS28 and DAS28-CRP, respectively.

Consequently, FDG-uptake observed in the inflamed RA joints may reflect disease activity. FDG-PET might play an important role in the evaluation of treatment for RA and the expectation of the disease prognosis.