**INTRODUCTION**

Takayasu arteritis (TAK) is a large-vessel vasculitis characterized by inflammation of the aorta and its major branches. For its treatment, it is important to detect active inflammation early in the disease and treat it accordingly before the occurrence of irreversible structural vessel damage, such as stenosis or aneurysmal change. However, assessing the disease activity of TAK is challenging as clinical symptoms and laboratory data do not precisely reflect the actual inflammation of the arterial wall, which makes it difficult to effectively monitor and treat the disease.

**Materials and Methods:** Patients with TAK who underwent 18F-FDG PET/CT during the clinically inactive state of the disease between 2006 and 2019 were included. Clinically inactive disease was defined as a status not fulfilling the National Institutes of Health (NIH) criteria for active disease in TAK. Relapse was defined as recurrence of clinically active disease after a clinically inactive period, requiring change in the treatment regimen. Vascular uptake on 18F-FDG PET/CT was assessed using target/background ratio (TBR), calculated as arterial maximum standardized uptake value (SUV)/mean SUV in venous blood pool. Multivariable Cox regression analysis was performed to identify factors associated with relapse.

**Results:** A total of 33 patients with clinically inactive TAK were included. During a median observation period of 4.5 (0.9–8.1) years, relapse occurred in 9 (27.3%) patients at median 1.3 (0.7–6.9) years. Notably, TBR [1.5 (1.3–1.8) vs. 1.3 (1.1–1.4), \( p = 0.044 \)] was significantly higher in patients who relapsed than in those who did not. On multivariable Cox regression analysis, the presence of NIH criterion 2 [adjusted hazard ratio (HR): 7.044 (1.424–34.855), \( p = 0.017 \)] and TBR [adjusted HR: 11.533 (1.053–126.282), \( p = 0.045 \)] were significantly associated with an increased risk of relapse.

**Conclusion:** Vascular uptake on 18F-FDG PET/CT and the presence of NIH criterion 2 are associated with future relapse in patients with clinically inactive TAK.

**Key Words:** PET/CT, inactive, relapse, Takayasu arteritis
take on $^{18}$F-FDG PET/CT. Although previous studies have reported that clinically inactive patients with vascular uptake on $^{18}$F-FDG PET/CT exist,\textsuperscript{7-10} the clinical significance of vascular uptake on $^{18}$F-FDG PET/CT in patients with clinically inactive TAK remains unclear. Given that TAK is an inflammatory disease that primarily affects vessels (large vessels in particular),\textsuperscript{1} vascular uptake on $^{18}$F-FDG PET/CT during the clinically inactive state of the disease might be associated with future relapse. In this study, we aimed to evaluate whether vascular uptake on $^{18}$F-FDG PET/CT during clinically inactive disease in patients with TAK are associated with disease relapse.

**MATERIALS AND METHODS**

**Patients**

Patients with TAK who underwent an $^{18}$F-FDG PET/CT between 2006 and 2019 at two tertiary referral hospitals were retrospectively screened for inclusion. All patients fulfilled the American College of Rheumatology 1990 criteria for the classification of TAK.\textsuperscript{11} Patients with clinically active disease at the time of $^{18}$F-FDG PET/CT were excluded, and the remaining patients who had clinically inactive disease at the time of $^{18}$F-FDG PET/CT were included for the analysis. All of the included patients underwent $^{18}$F-FDG PET/CT for further evaluation of disease activity, despite the clinically inactive disease state. The timing of $^{18}$F-FDG PET/CT was at the investigator’s discretion. None of the patients had experienced relapse prior to the date of $^{18}$F-FDG PET/CT. The following data at the time of $^{18}$F-FDG PET/CT were reviewed: age, sex, disease duration, presence of hypertension, diabetes mellitus, and dyslipidemia, smoking status (current smoker or not), body mass index, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), vascular involvement pattern according to the Hata classification,\textsuperscript{14} and current use of glucocorticoids and immunosuppressants (methotrexate or azathioprine).

This study was conducted in accordance with the Declaration of Helsinki, and was approved by the Institutional Review Board of Gangnam Severance Hospital (approval no. 3-2019-0423). The requirement for informed consent was waived owing to the retrospective nature of this study.

**Definition of clinically inactive disease and relapse**

Clinically inactive disease was defined as a status not meeting the National Institutes of Health (NIH) criteria for active disease in TAK.\textsuperscript{2} According to the NIH criteria, new onset or worsening of two or more of the following criteria indicates active disease: criterion 1, systemic features such as fever or arthralgia; criterion 2, elevated ESR; criterion 3, features of vascular ischemia or inflammation; and criterion 4, typical angiographic features.\textsuperscript{1} The NIH criterion 4 was assessed based on CT or magnetic resonance angiography that was performed at the closest date (within 1 month in all cases) to the date $^{18}$F-FDG PET/CT was performed. Due to the heterogeneity of angiographic modalities, worsening of angiographic features was confined to worsening of luminal changes in the affected vessels. The fulfillment of each criterion at the time of $^{18}$F-FDG PET/CT was retrospectively reviewed. Relapse was defined as a recurrence of clinically active disease (based on the NIH criteria) after a period of clinically inactive disease, necessitating an increase in the prednisone dose of $\geq 10$ mg/day from the basal dose and/or the addition of glucocorticoid-sparing therapy. The retrospective observation period was from the time of $^{18}$F-FDG PET/CT to the last follow-up date or the occurrence of relapse, whichever came first.

**$^{18}$F-FDG PET/CT**

$^{18}$F-FDG PET/CT scans were obtained using a dedicated PET/CT scanner [Discovery STE (GE Healthcare, Chicago, IL, USA) or Biograph 40 TruePoint (Siemens Medical Systems, Erlangen, Germany)], as previously described.\textsuperscript{15} The dose of $^{18}$F-FDG was 5.5 MBq/kg. The images were interpreted by a nuclear physician who was blinded to the clinical data. As used in previous studies,\textsuperscript{16,17} the target/background ratio (TBR) was assessed as a parameter of vascular uptake. TBR was calculated as arterial maximum standardized uptake value (max SUV)/mean SUV in background reference tissue. The arterial max SUV was defined as the highest value in a slice-by-slice analysis of the entire aorta and its major branches. The mean SUV in background reference tissue was measured in venous blood pool.

**Statistical analysis**

The patient characteristics are summarized as median (interquartile range) for continuous variables and as number (%) for categorical variables. For comparison between patients who did and did not experience relapse, the Mann-Whitney U-test was performed for continuous variables and Fisher’s exact test was used for categorical variables. Multivariable Cox proportional hazard regression analysis with a stepwise backward elimination procedure was used to identify factors associated with relapse. The proportional hazard assumption was confirmed by examination of log [−log (survival)] curves and by testing Schoenfeld partial residuals, which revealed no relevant violation. Factors with a $p$ value of $<0.05$ in univariable analysis were included in multivariable analysis. To assess the predictive accuracy and determine the cut-off value of TBR that best predicts relapse, we performed a receiver-operating characteristic (ROC) analysis. Relapse-free survival rates were analyzed using the Kaplan-Meier survival analysis and were compared using the log-rank test. All analyses were performed using the SPSS software (version 25.0; IBM Corp., Armonk, NY, USA).

**RESULTS**

**Patient characteristics**

A total of 33 patients with TAK who underwent $^{18}$F-FDG PET/CT...
CT during the clinically inactive state of the disease were identified. The characteristics of patients at the time of $^{18}$F-FDG PET/CT are summarized in Table 1. The median patient age was 49.0 (38.0–55.0) years, and majority of the patients were female (30 of 33, 90.9%). The median disease duration of TAK at the time of $^{18}$F-FDG PET/CT was 4.0 (1.0–10.0) years. During a median observation period of 4.5 (0.9–8.1) years, relapse occurred in 9 (27.3%) patients at a median of 1.3 (0.7–6.9) years. The median values of arterial max SUV, mean SUV in blood pool, and TBR were 2.3 (1.9–2.9) g/mL, 1.7 (1.5–2.3) g/mL, and 1.4 (1.2–1.6), respectively.

### Comparison between patients who did and did not experience relapse

Patients who experienced relapse had longer disease duration [10.0 (3.5–16.5) years vs. 3.5 (0.8–5.8) years, $p=0.029$], higher ESR [26.0 (19.0–32.5) mm/h vs. 18.0 (10.8–20.0) mm/h, $p=0.010$] and CRP [3.2 (0.8–4.3) mg/L vs. 1.0 (0.6–1.3) mg/L, $p=0.049$], more commonly fulfilled NIH criterion 2 (77.8% vs. 16.7%, $p=0.002$), and less commonly fulfilled NIH criterion 4 (0.0% vs. 50.0%, $p=0.012$), compared to patients who did not experience relapse. Notably, the TBR [1.5 (1.3–1.8) vs. 1.3 (1.1–1.4), $p=0.044$] was significantly higher in patients who experienced relapse than in those who did not (Fig. 1). On the other hand, there was no significant difference in age ($p=0.766$), sex distribution ($p>0.999$), BMI ($p=0.453$), type of vascular involvement (type I, $p=0.394$; type IIA, $p=0.555$; type IIB, $p=0.651$; type III, $p=0.273$; and type V, $p=0.690$), fulfillment of NIH criterion 1 ($p=0.477$) and NIH criterion 3 ($p=0.477$), arterial max SUV ($p=0.486$), mean SUV in IVC ($p=0.166$), use and dose of glucocorticoids ($p>0.999$ and $p=0.648$, respectively), and use of methotrexate ($p>0.999$) and azathioprine ($p=0.477$) between the two groups (Table 2).

Among the total 33 patients with clinically inactive TAK, one patient with a TBR of 1.6 was newly administered prednisolone at a dose of 10 mg/day based on the $^{18}$F-FDG PET/CT result. No disease relapse was noted in this patient during the observation period.

### Factors associated with relapse

On univariable analysis, ESR [unadjusted hazard ratio (HR): 1.112, 95% confidence interval (CI): 1.035–1.195, $p=0.004$], CRP (unadjusted HR: 1.573, 95% CI: 1.005–2.460, $p=0.047$), presence of NIH criterion 2 (comparison with absence of NIH criterion 2) (unadjusted HR: 8.210, 95% CI: 1.688–39.927, $p=0.009$), and TBR (unadjusted HR: 14.751, 95% CI: 1.484–146.663, $p=0.022$) had a $p$ value of <0.05. Among these variables, ESR and CRP were not included in the multivariable analysis owing to multicollinearity with NIH criterion 2. On multivariable analysis,

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**Table 1. Characteristics of the 33 Patients with Clinically Inactive TAK**

| Characteristic                                      | Description                  | Median (IQR)       |
|-----------------------------------------------------|------------------------------|-------------------|
| Age at $^{18}$F-FDG PET/CT, yr                      |                              | 49.0 (38.0–55.0)  |
| Female sex                                          |                              | 30 (90.9)         |
| Disease duration, yr                                |                              | 4.0 (1.0–10.0)    |
| Hypertension                                        |                              | 16 (48.5)         |
| Diabetes mellitus                                   |                              | 2 (6.1)           |
| Dyslipidemia                                        |                              | 14 (42.4)         |
| Smoking                                             |                              | 3 (9.1)           |
| BMI, kg/m²                                          |                              | 22.2 (21.6–24.8)  |
| ESR, mm/h                                           |                              | 19.0 (11.5–24.0)  |
| CRP, mg/L                                           |                              | 1.0 (0.6–2.8)     |
| Type of vascular involvement                        |                              |                   |
| I                                                    |                              | 8 (24.2)          |
| IIA                                                  |                              | 4 (12.1)          |
| IIB                                                  |                              | 8 (24.2)          |
| III                                                  |                              | 1 (3.0)           |
| IV                                                   |                              | 0 (0.0)           |
| V                                                    |                              | 12 (36.4)         |
| NIH criterion 1                                      |                              | 2 (6.1)           |
| NIH criterion 2                                      |                              | 11 (33.3)         |
| NIH criterion 3                                      |                              | 2 (6.1)           |
| NIH criterion 4                                      |                              | 12 (36.4)         |
| Fulfillment of no NIH criteria                      |                              | 6 (18.2)          |
| Fulfillment of one NIH criterion                     |                              | 27 (81.8)         |
| Arterial max SUV, g/mL                              |                              | 2.3 (1.9–2.9)     |
| Mean SUV in blood pool, g/mL                        |                              | 1.7 (1.5–2.3)     |
| TBR                                                 |                              | 1.4 (1.2–1.6)     |
| Medications at $^{18}$F-FDG PET/CT                   |                              |                   |
| Glucocorticoid                                      |                              | 13 (39.4)         |
| Glucocorticoid dose*, mg/d                          |                              | 0.0 (0.0–5.0)     |
| Methotrexate                                        |                              | 7 (21.2)          |
| Azathioprine                                        |                              | 2 (6.1)           |

TAK, Takayasu arteritis; $^{18}$F-FDG PET/CT, $^{18}$F-fluorodeoxyglucose positron emission tomography/computed tomography; IQR, interquartile range; BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NIH, National Institutes of Health; SUV, standardized uptake value; TBR, target/background ratio.

Data are presented as median (IQR) or n (%).

*Equivalent to prednisolone. †Median dose: 10.0 (IQR 7.5–15.0) mg/week.

Both patients received 100 mg/d.
the presence of NIH criterion 2 (comparison with absence of NIH criterion 2) (adjusted HR: 7.044, 95% CI: 1.424–34.855, \( p = 0.017 \)) and TBR (adjusted HR: 11.533, 95% CI: 1.053–126.282, \( p = 0.045 \)) were significantly associated with an increased risk of relapse (Table 3).

**DISCUSSION**

In this study, we demonstrated that the vascular uptake on \(^{18}\)F-FDG PET/CT, as assessed by TBR, and the presence of NIH criterion 2 during the clinically inactive state of the disease in TAK are associated with an increased risk of relapse. This finding has an important clinical implication, as it may aid in identifying patients with inactive disease who are at a higher risk of relapse.

Tezuka, et al.\(^{16}\) compared \(^{18}\)F-FDG uptake between patients with relapsed TAK (defined as active disease while receiving immunosuppressants) and patients with inactive TAK who were...
Fig. 2. Receiver-operating characteristic curves for (A) TBR and (B) combination of TBR and NIH criterion 2 in predicting relapse. TBR, target/background ratio; NIH, National Institutes of Health; AUC, area under the curve.

Table 3. Factors Associated with Relapse

|                               | Univariable analysis |                         | Multivariable analysis |                         |
|--------------------------------|----------------------|-------------------------|------------------------|-------------------------|
|                                | HR (95% CI)          | p value                 | HR (95% CI)            | p value                 |
| Age at \(^{18}\)F-FDG PET/CT, yr| 0.957 (0.903–1.014)  | 0.134                   |                        |                         |
| Female (vs. male) sex          | 1.067 (0.131–8.695)  | 0.952                   |                        |                         |
| Disease duration, yr           | 1.056 (0.997–1.119)  | 0.062                   |                        |                         |
| Hypertension                   | 1.512 (0.400–5.714)  | 0.542                   |                        |                         |
| Diabetes mellitus              | 2.262 (0.271–18.858) | 0.451                   |                        |                         |
| Dyslipidemia                   | 1.038 (0.256–4.212)  | 0.958                   |                        |                         |
| Smoking                        | 1.278 (0.159–10.296) | 0.818                   |                        |                         |
| BMI, kg/m\(^2\)               | 0.897 (0.688–1.170)  | 0.423                   |                        |                         |
| ESR, mm/h                      | 1.112 (0.035–1.195)  | 0.004*                  |                        |                         |
| CRP, mg/L                      | 1.573 (1.005–2.460)  | 0.047*                  |                        |                         |
| Type I (vs. non-type I)        | 0.265 (0.033–1.137)  | 0.213                   |                        |                         |
| Type II A (vs. non-type II A)  | 0.042 (0.009–24640.130) | 0.641                |                        |                         |
| Type II B (vs. non-type II B)  | 1.289 (0.321–5.174)  | 0.720                   |                        |                         |
| Type III (vs. non-type III)    | 9.155 (0.952–88.046) | 0.055                   |                        |                         |
| Type IV (vs. non-type IV)      | N/A                  | N/A                     |                        |                         |
| Type V (vs. non-type V)        | 1.588 (0.424–5.938)  | 0.492                   |                        |                         |
| Presence of NIH criterion 1 (vs. absence of NIH criterion 1) | 1.682 (0.206–13.710) | 0.627                   |                        |                         |
| Presence of NIH criterion 2 (vs. absence of NIH criterion 2) | 8.210 (1.688–39.927) | 0.009                   | 7.044 (1.424–34.855) | 0.017                |
| Presence of NIH criterion 3 (vs. absence of NIH criterion 3) | 1.521 (0.187–12.380) | 0.695                   |                        |                         |
| Presence of NIH criterion 4 (vs. absence of NIH criterion 4) | 0.022 (0.000–5.447)  | 0.174                   |                        |                         |
| Fulfillment of one NIH criterion (vs. fulfillment of no NIH criteria) | 3.204 (0.393–26.104) | 0.277                   |                        |                         |
| Use of glucocorticoid          | 1.413 (0.376–5.316)  | 0.609                   |                        |                         |
| Dose of glucocorticoid         | 0.993 (0.904–1.091)  | 0.884                   |                        |                         |
| Use of methotrexate            | 0.797 (0.163–3.896)  | 0.779                   |                        |                         |
| Use of azathioprine            | 3.116 (0.347–27.951) | 0.310                   |                        |                         |
| Arterial max SUV, g/mL         | 1.457 (0.999–2.124)  | 0.050                   |                        |                         |
| Mean SUV in blood pool, g/mL   | 1.187 (0.545–2.583)  | 0.666                   |                        |                         |
| TBR                            | 14.751 (1.484–146.683)| 0.022                   | 11.533 (1.053–126.282) | 0.045                |

HR, hazard ratio; CI, confidence interval; \(^{18}\)F-FDG PET/CT, \(^{18}\)F-fluorodeoxyglucose positron emission tomography/computed tomography; BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NIH, National Institutes of Health; SUV, standardized uptake value; TBR, target/background ratio.

*ESR and CRP were not included in multivariable analysis.
receiving immunosuppressants, and showed that 18F-FDG uptake was higher in the former group than in the latter group, suggesting that 18F-FDG PET/CT is a useful tool in detecting active disease even during immunosuppressant treatment. Our data add to the previous finding that 18F-FDG PET/CT can be useful not only for detecting the occurrence of relapse but also for stratifying the risk of relapse in patients during clinically inactive disease. Similar to our present study, a previous prospective cohort study consisting of patients with large-vessel vasculitis showed that high 18F-FDG PET/CT activity during clinical remission is associated with a future clinical relapse.20 However, both TAK and giant cell arteritis (GCA) were included in that study, and only one patient with TAK was included in the high 18F-FDG PET/CT activity group.21 Therefore, it was unclear whether the previous finding still applies when confined to patients with TAK. Our study suggests that higher 18F-FDG PET/CT activity during remission is associated with future relapse, even when confined to patients with TAK.

While vascular uptake on 18F-FDG PET/CT during the clinically inactive state of the disease may indicate subclinical vasculitis, it may also represent atherosclerosis.19 Due to the lack of histologic data in our study, it was difficult to determine whether the uptake in the vascular wall was due to subclinical vasculitis or atherosclerosis. With respect to atherosclerosis in inflammatory rheumatic diseases, ESR and CRP, as markers of systemic inflammation, are positively associated with atherosclerosis, suggesting that inflammation is a major contributor to accelerated atherosclerosis.21,22 On the other hand, acute phase reactants poorly reflect the histologically-proven actual vascular inflammation.22 Therefore, assessment of the correlation between TBR and acute phase reactants could aid in speculating the cause of vascular uptake. In the present study, there was no significant correlation between TBR and ESR (γ=0.055, p=0.762), as well as between TBR and CRP (γ=-0.167, p=0.353) (data not shown in the results). Given the lack of correlation of TBR with ESR and CRP, we presume that the vascular uptake observed in 18F-FDG PET/CT favors subclinical vasculitis, rather than atherosclerosis, attributed to the inflammation. In any case, it is important to perceive patients with vascular uptake on 18F-FDG PET/CT during the clinically inactive state of the disease as high-risk patients for disease relapse.

A previous study has shown that in some patients with GCA, which also is a large-vessel vasculitis, vascular uptake on 18F-FDG PET/CT does not completely resolve even after treatment.23 Furthermore, a recent study consisting of patients with large vessel vasculitis showed that when treatment was reduced, 18F-FDG PET/CT activity worsened, despite no change in clinical and serologic disease activity.24 Considering the association between vascular uptake on 18F-FDG PET/CT and the risk of relapse, as observed in our study, it could be helpful to perform 18F-FDG PET/CT in patients with clinically inactive disease and tailor treatment accordingly. In our study, although limited by the small number, one patient with a relatively high TBR (TBR=1.6, which corresponds to the upper quartile among the total population) on 18F-FDG PET/CT received increased medication despite clinically inactive disease state and remained relapse free, supporting the potential usefulness of adjusting treatment based on 18F-FDG PET/CT findings.

The presence of NIH criterion 2 (new or worsening elevation of ESR) during the clinically inactive state of the disease was also associated with the risk of relapse. The median value of ESR in patients fulfilling NIH criterion 2 was 26.0 (23.0–30.0) mm/h (data not shown in the results). Considering the normal range of ESR (0–15 mm/h for male and 0–20 mm/h for female), ESR was only modestly increased in patients who fulfilled NIH criterion 2. Our data suggest that ESR increments during the clinically inactive state of the disease, even in small amounts, might indicate an increased risk of future relapse. However, among the nine patients who relapsed, two patients did not fulfill NIH criterion 2 at the time of 18F-FDG PET/CT. One of these two patients had high TBR (TBR=2.1, which corresponds to the top 3.0% among the total population), suggesting that 18F-FDG PET/CT results can identify patients at higher risk of relapse who otherwise would have not been identified using NIH criterion 2 alone. Therefore, TBR can be used as a complementary parameter with NIH criterion 2 in predicting the risk of relapse. Notably, combination of TBR and NIH criterion 2 as a composite parameter had an excellent predictive accuracy (AUC=0.903).

New or worsening of angiographic feature (i.e. NIH criterion 4) during apparent clinical remission is common (up to 61%) in TAK.2 We also observed that substantial proportion of patients (12 of 33, 36.4%) fulfilled NIH criterion 4 during the clinically inactive state of TAK. Interestingly, the presence of NIH criterion 4 was more common in patients who did not experience relapse compared to those who experienced relapse. Although an exact explanation for this observation remains unclear, it could be speculated that the presence of NIH criterion 4 indicates an end-stage sequelae, and therefore, is less likely to relapse. Similar observation has been reported in a prospective study consisting of 60 patients with TAK, in which a subgroup of patients who had new angiographic feature during clinical

Fig. 3. Comparison of relapse-free survival between patients with high TBR and low TBR. TBR, target/background ratio.

Number at risk

|          | TBR  | TBR  | TBR  | TBR  |
|----------|------|------|------|------|
| Low TBR  | 20   | 14   | 9    | 5    |
| High TBR | 13   | 7    | 6    | 3    |

| Time (yr) | 0.0 | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 |
|-----------|-----|-----|-----|-----|-----|-----|
| Low TBR   | 0.0 | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 |
| High TBR  | 0.0 | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 |

| TBR        | Low TBR | High TBR | p  |
|------------|---------|----------|----|
| Relapse-free survival probability | 0.092 | 0.0019 | 0.019 |

| Time (yr) | Number at risk | TBR  | TBR  | TBR  | TBR  |
|-----------|----------------|------|------|------|------|
| 0.0       | 20             | 2.0  | 1.9  | 1.7  | 1.5  |
| 0.2       | 14             | 2.1  | 2.0  | 1.8  | 1.6  |
| 0.4       | 9              | 2.2  | 2.1  | 1.9  | 1.7  |
| 0.6       | 5              | 2.3  | 2.2  | 2.0  | 1.8  |
| 0.8       | 6              | 2.4  | 2.3  | 2.1  | 1.9  |
| 1.0       | 3              | 2.5  | 2.4  | 2.2  | 2.0  |

**Table 3.** Comparison of relapse-free survival between patients with high TBR and low TBR. TBR, target/background ratio.
remission had a lower relapse rate (27.3%) than the total study population (45%). These suggest that the presence of NIH 4 criterion during clinically inactive state might be associated with a lower risk of relapse. However, the presence of NIH criterion 4 did not show a significant association with the risk of relapse in Cox regression analysis; therefore, it cannot be concluded that the presence of NIH criterion 4 is associated with a lower risk of relapse.

We defined clinically inactive disease as a status not meeting the NIH criteria for active disease in TAK, as used in previous studies. Therefore, patients who fulfilled none of the NIH criteria for active disease in TAK, as used in previous studies, were defined as having clinically inactive disease. Third, the NIH criteria are suboptimal as a tool for detecting pathologically proven active disease. Nevertheless, owing to the lack of a gold standard for assessing disease activity in TAK, several studies have similarly used the NIH criteria for defining active disease.

In conclusion, we found that TBR on 18F-FDG PET/CT and the presence of NIH criterion 2 during the clinically inactive state of the disease could be associated with future relapse. These indicators may help clinicians in identifying patients who are at a higher risk of relapse during the clinically inactive state of the disease, leading to closer monitoring and earlier adjustment of treatment in patients with TAK.

**Author Contributions**

Conceptualization: Min-Chan Park. Data curation: all authors. Formal analysis: all authors. Investigation: Oh Chan Kwon and Min-Chan Park. Methodology: Oh Chan Kwon and Min-Chan Park. Project administration: all authors. Resources: all authors. Software: Oh Chan Kwon and Min-Chan Park. Supervision: Min-Chan Park. Validation: Oh Chan Kwon and Min-Chan Park. Visualization: Oh Chan Kwon and Min-Chan Park. Writing—original draft: Oh Chan Kwon and Min-Chan Park. Writing—review & editing: Oh Chan Kwon and Min-Chan Park. Approval of final manuscript: all authors.

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