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Statins reduce relapse rate in Takayasu arteritis ☆

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ABSTRACT

Background: To investigate the effect of statins on relapse of Takayasu arteritis (TAK), which frequently occurs after achievement of remission.
Methods: We conducted a retrospective study on TAK patients with active disease, diagnosed between 2012 and 2017. Relapse was defined as recurrence of active disease after achieving remission. Demographic and clinical parameters of patients who experienced relapse were compared to those who did not. To identify factors associated with relapse, significant factors identified in this comparison were included in a multivariate Cox regression analysis. Inverse probability of treatment weighting (IPTW)-adjusted analysis was used to evaluate the influence of statins on relapse.
Results: Of the total 74 TAK patients, 40 (54.1%) patients received statins, whereas 34 (45.9%) patients did not. Relapse was observed in 36 (48.6%) patients of the total 74 TAK patients. Compared with patients who did not experience relapse, patients who experienced relapse were younger (44.5 ± 13.5 years vs 34.1 ± 12.6 years, $p = 0.001$), had lower prevalence of hypertension (63.2% vs 38.9%, $p = 0.037$), more commonly had carotidynia (7.9% vs 27.8%, $p = 0.025$), had higher LDL-cholesterol (84.8 ± 18.8 mg/dl vs 100.5 ± 26.1 mg/dl, $p = 0.010$), and were less commonly taking statins (71.1% vs 36.1%, $p = 0.003$). The use of statins was significant in multivariate Cox regression analysis (adjusted hazard ratio 0.260, 95% confidence interval 0.120–0.563, $p = 0.001$). Furthermore, IPTW-adjusted analysis confirmed that statin use was associated with a lower risk of relapse (IPTW-adjusted hazard ratio 0.153, 95% confidence interval 0.038–0.616, $p = 0.008$).
Conclusion: In TAK, statins can be beneficial in reducing relapse rate after achieving remission.

1. Introduction

Takayasu arteritis (TAK) is a chronic inflammatory disease characterised by large vessel vasculitis mainly involving the aorta and its major branches [1]. In later stages of the disease, stenosis or aneurysmal change can occur in the affected vessels [2]. The basis of treatment is to interrupt active inflammation before significant vessel damages occur, the mainstream of treatment being glucocorticoid [3–5]. Additional immunosuppressive agents such as methotrexate (MTX), azathioprine (AZA), mycophenolate mofetil, cyclophosphamide and leflunomide can be used in glucocorticoid-resistant cases, or when remission cannot be maintained with acceptable doses of glucocorticoids [6–10]. Despite the use of glucocorticoid and adjunctive immunosuppressive agent, relapse is common after achieving remission; up to 96% [11].

Statins, the 3-hydroxy-methylglutaryl-coenzyme A inhibitors, have a lipid-lowering effect and are widely used for primary and secondary prevention of cardiovascular diseases [12,13]. In addition to their lipid-lowering effect, statins also have anti-inflammatory and immunomodulatory effects [14]. On this basis, some studies have shown possible beneficial effect of statins on inflammatory and autoimmune diseases; reduced incidence and disease activity of rheumatoid arthritis [15,16], and delayed progression of disease in murine systemic lupus erythematosus model [17].

Moreover, statins restore nitric oxide (NO) production in endothelial cells, which is essential in preserving vascular structure and function, and thereby improve endothelial function [18]. Given this favorable effect of statins on endothelial function, statins may be beneficial in vasculitis. However, to date, no studies have addressed the effect of statins on TAK.

Considering the high relapse rate despite use of glucocorticoid and adjunctive immunosuppressive agents in TAK patients [11], identifying additional medications that may possibly aid in sustaining remission is important. Statins, by having favorable effects on endothelial cells [18] and anti-inflammatory/immunomodulatory effects as well [14], may potentially be one such possibility. In this study, we aimed to evaluate whether use of statins affects relapse rate in patients with TAK.

☆ Authorship: All authors had access to the data and contributed sufficiently to writing the manuscript to be included as authors.

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2. Methods

2.1. Patients

Patients who were newly diagnosed with TAK at a tertiary referral hospital in Seoul, South Korea between January 2012 and October 2017 were included. All patients met the 1990 American College of Rheumatology (ACR) classification criteria for TAK [19]. Only patients with active disease at the time of diagnosis were included. Active disease was defined as two or more of the following criteria: fever or other systemic features; elevated erythrocyte sedimentation rate (ESR); symptoms or signs of vascular ischemia or inflammation such as claudication, absent pulse and carotidynia; and typical angiographic lesions [3]. Patients were initially treated with 40 to 60 mg/day of glucocorticoid (prednisolone or its equivalent). The initial dose of glucocorticoid was maintained until reversible symptoms improved and acute phase reactants normalised; usually 2 to 4 weeks. Thereafter, the dose of glucocorticoid was tapered down according to the physicians' discretion. Immunosuppressive agents (MTX and/or AZA) were added in glucocorticoid-refractory and/or glucocorticoid-dependent cases. Remission was defined as absence of clinical and laboratory evidence of active vascular lesions for >6 months while receiving glucocorticoid in a dose (prednisolone or its equivalent) of <10 mg/day [11].

We retrospectively reviewed the following baseline data: age, sex, time from disease onset to diagnosis, presence of hypertension and diabetes mellitus, clinical features attributable to TAK (claudication, decreased pulse, blood pressure difference of >10 mmHg between arms, bruit and carotidynia), laboratory data (ESR, C-reactive protein (CRP), total cholesterol, triglyceride, high density lipoprotein (HDL)-cholesterol and low density lipoprotein (LDL)-cholesterol), and type of vascular lesion distribution according to Hata's classification [20]. The follow-up data collected included time to remission, cumulative dose of glucocorticoid used from diagnosis to remission, immunosuppressants added to achieve remission, occurrence of relapse, time from remission to relapse. Use of glucocorticoid and immunosuppressants at the end of follow-up, mortality and new interventions performed during the follow-up were also reviewed.

According to the use of statins, patients were categorised as statin users or statin non-users. Statin users were defined as patients who had taken statins at the time of TAK diagnosis and continued to take them throughout the follow-up period. Statin non-users were defined as patients who had never taken statins. Patients who did not fit into these categories were not included. For statin users, the type and dosage of statins were reviewed.

This study was approved by the Institutional Review Board of Asan Medical Center in Seoul, South Korea (IRB No: 2017-0857). The requirement for informed consent was waived due to the retrospective nature of the study.

2.2. Definition of relapse

Relapse was defined as the recurrence of active disease (two or more of the following criteria: fever or other systemic features; elevated erythrocyte sedimentation rate (ESR); symptoms or signs of vascular ischemia or inflammation such as claudication, absent pulse and carotidynia; and typical angiographic lesions [3]) after achieving remission (absence of clinical and laboratory evidence of active vascular lesions for >6 months while receiving glucocorticoid in a dose of <10 mg/day [11]). Isolated elevation of ESR and/or CRP itself was not considered to be relapse.

2.3. Statistical analysis

For comparison between two groups, Student's *t*-test and Mann-Whitney test were used for continuous variables, and Chi-square test and Fisher's exact test were used for categorical variables. Multivariate Cox proportional hazard regression analysis with stepwise backward elimination was performed to identify factors associated with relapse. The proportional hazards assumption was confirmed by examining the log [−log (survival)] curves and by testing for Schoenfeld partial residuals. No relevant violations were identified. Factors with a p value < 0.05 in the comparative analysis were entered into the multivariate Cox proportional hazard regression analysis. For variables included in the multivariate analysis, no multicollinearity was detected among variables. In analysing the effect of statins on relapse of TAK, the inverse probability of treatment weighting (IPTW) was performed to further exclude the influence of confounders. SPSS software (SPSS version 20.0, Armonk, NY, IBM Corporation) was used to conduct all analyses.

3. Results

3.1. Patients' characteristics

A total of 74 patients who fulfilled the 1990 ACR classification criteria for TAK [19] and the criteria for active disease [3] were identified. The mean age of the patients was 39.5 ± 14.0 years and female were predominant (87.8%). Time from disease onset to diagnosis was median 3.0 (2.0–5.3) months. Hypertension and diabetes mellitus were present in 38 (51.4%) and 9 (12.2%) patients, respectively. The most common clinical feature attributable to TAK was blood pressure difference of >10 mm Hg between arms (86.5%), followed by decreased brachial pulse (59.5%). ESR and CRP were elevated; ESR 62.7 ± 31.0 mm/h and CRP 1.49 (range: 0.65–3.28) mg/dl. Serum concentrations of total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol were 177.2 ± 30.6 mg/dl, 110.4 ± 40.6 mg/dl, 53.3 ± 14.4 mg/dl and 99.8 ± 21.4 mg/dl, respectively. The most common type of vessel involvement was type V (45.9%).

Median follow-up time was 35.8 (range: 14.2–75.2) months. Remission was achieved in all patients in a median of 10.2 (range: 9.1–12.4) months. Cumulative dose of glucocorticoid (prednisolone or its equivalent) used from diagnosis to remission was median 4.68 (range: 3.19–6.31) g. MTX and AZA were added in 49 (66.2%) and 14 (18.9%) patients, respectively. Relapse after achieving remission occurred in 36 (48.6%) patients, in a median time of 9.8 (range: 3.9–23.8) months. At the end of follow-up, the daily dose of glucocorticoid used was median 2.5 (range: 0.0–5.0) mg/day. MTX and AZA were used in 70 (94.6%) and 17 (23.0%) patients, respectively. During the follow-up, death was not observed, and 7 (19.4%) of the 36 relapsed patients underwent intervention (percutaneous transluminal angioplasty, 5 patients; stent placement, 2 patients).

3.2. Comparison between statin users and statin non-users

Forty (54.1%) patients were statin users and 34 (45.9%) patients were statin non-users. Among statin users, 22 patients received atorvastatin (10–20 mg/day), 13 patients received rosuvastatin (5–10 mg/day), 4 patients received simvastatin (10–20 mg/day) and 1 patient received pitavastatin (4 mg/day). Comparison between statin users and statin non-users is shown in Table 1. Patients taking statins were older (47.2 ± 11.6 years vs 30.3 ± 10.8 years, $p < 0.001$), had higher prevalence of hypertension (67.5% vs 32.4%, $p = 0.003$), less commonly had carotidynia (7.5% vs 29.4%, $p = 0.014$), and had lower ESR (55.7 ± 27.8 mm/h vs 71.0 ± 32.8 mm/h, $p = 0.034$), lower CRP (1.00 (0.29–2.15) mg/dl vs 2.25 (0.81–5.39) mg/dl, $p = 0.009$) and lower LDL-cholesterol (80.8 ± 17.5 mg/dl vs 109.9 ± 21.3 mg/dl, $p < 0.001$). Furthermore, patients taking statins had lower relapse rate, compared with patients not taking statins (32.5% vs 67.6%, $p = 0.003$) (Table 1).

3.3. Factors associated with relapse

Compared with patients in whom relapse did not occur, patients in whom relapse occurred were younger (44.5 ± 13.5 years vs 34.1 ± 12.6 years, $p = 0.001$), had lower prevalence of hypertension (63.2% vs 38.9%, $p = 0.037$), more commonly had carotidynia (7.9% vs 27.8%, $p = 0.025$), had higher LDL-cholesterol (84.8 ± 18.8 mg/dl vs 100.5 ± 26.1 mg/dl, $p = 0.010$), and were less commonly taking statins (71.1% vs 36.1%, $p = 0.003$) (Table 2). These factors were included in the multivariate Cox proportional hazard regression analysis. Multivariate analysis revealed that carotidynia was associated with risk of relapse (adjusted hazard ratio 2.603, 95% confidence interval 1.121–6.047, $p = 0.026$), whereas use of statins was inversely associated with risk of relapse (adjusted hazard ratio 0.260, 95% confidence interval 0.120–0.563, $p = 0.001$) (Table 3). Furthermore, adjustment with propensity score using IPTW confirmed that use of statins was associated with lower risk of relapse (IPTW-adjusted hazard ratio 0.153, 95% confidence interval 0.038–0.616, $p = 0.008$) (Table 4).

4. Discussion

In this study, we found that the use of statins was associated with a reduced risk of relapse in TAK patients. Previous studies have explored variables related to relapse of TAK [21,22]. Comarmond et al. [21], reported that male sex, elevated CRP level, and carotidynia were associated with relapse of TAK. Similarly, we observed higher risk of relapse in patients with carotidyina. Another study reported that age > 40 years, incipient disease, and use of cyclophosphamide and hydroxychloroquine

Table 1
Comparison of baseline characteristics between statin users and statin non-users.

	Total (N = 74)	Statin users (N = 40)	Statin non-users (N = 34)	p value
Age (years)	39.5 (±14.0)	47.2 (±11.6)	30.3 (±10.8)	<**0.001**
Female	65 (87.8%)	36 (90.0%)	29 (85.3%)	0.724
Time from disease onset to diagnosis (months)	3.0 (2.0–5.3)	2.5 (2.0–6.0)	3.0 (2.0–5.0)	0.580
Hypertension	38 (51.4%)	27 (67.5%)	11 (32.4%)	**0.003**
Diabetes mellitus	9 (12.2%)	7 (17.5%)	2 (5.9%)	0.166
Clinical features				
Claudication	26 (35.1%)	17 (42.5%)	9 (26.5%)	0.150
Decreased pulse	44 (59.5%)	24 (60.0%)	20 (58.8%)	0.918
BP difference > 10 mm Hg	64 (86.5%)	34 (85.0%)	30 (88.2%)	0.745
Bruit	34 (45.9%)	17 (42.5%)	17 (50.0%)	0.519
Carotidynia	13 (17.6%)	3 (7.5%)	10 (29.4%)	**0.014**
Laboratory data				
ESR (mm/h)	62.7 (±31.0)	55.7 (±27.8)	71.0 (±32.8)	**0.034**
CRP (mg/dl)	1.49 (0.65–3.28)	1.00 (0.29–2.15)	2.25 (0.81–5.39)	**0.009**
Total cholesterol (mg/dl)	177.2 (±30.6)	171.3 (±26.3)	186.4 (±34.8)	0.076
Triglycerides (mg/dl)	110.4 (±40.6)	113.4 (±36.4)	105.7 (±46.7)	0.471
HDL-cholesterol (mg/dl)	55.3 (±14.4)	55.3 (±14.5)	55.4 (±14.6)	0.978
LDL-cholesterol (mg/dl)	99.8 (±21.4)	80.8 (±17.5)	109.9 (±21.3)	<**0.001**
Hata's classification				
Type I	14 (18.9%)	8 (20.0%)	6 (17.6%)	0.724
Type IIA	9 (12.2%)	4 (10.0%)	5 (14.7%)	
Type IIB	17 (23.0%)	11 (27.5%)	6 (17.6%)	
Type III	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Type IV	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Type V	34 (45.9%)	17 (42.5%)	17 (50.0%)	
Follow-up data				
Time to remission (months)	10.2 (9.1–12.4)	9.9 (9.0–12.2)	10.6 (9.4–13.2)	0.231
Glucocorticoid (g)[a]	4.68 (3.19–6.31)	4.48 (2.88–5.97)	4.98 (3.44–6.70)	0.290
Methotrexate	49 (66.2%)	27 (67.5%)	22 (64.7%)	0.800
Azathioprine	14 (18.9%)	7 (17.5%)	7 (20.6%)	0.735
Relapse	36 (48.6%)	13 (32.5%)	23 (67.6%)	**0.003**
Medication at end of follow-up				
Glucocorticoid (mg/d)[b]	2.5 (0.0–5.0)	2.5 (0.0–5.0)	2.5 (0.0–5.0)	0.982
Methotrexate	70 (94.6%)	39 (97.5%)	31 (91.2%)	0.328
Azathioprine	17 (23.0%)	8 (20.0%)	9 (26.5%)	0.510

Abbreviations: BP; blood pressure, ESR; erythrocyte sedimentation rate, CRP; C-reactive protein, HDL; high density lipoprotein, LDL; low density lipoprotein.
P values < 0.05 are indicated in bold.
[a] Cumulative dose used from diagnosis to remission, prednisolone or its equivalent.
[b] Prednisolone or its equivalent.

Table 2
Comparison between non-relapsed and relapsed patients.

	Non-relapsed (N = 38)	Relapsed (N = 36)	p value
Age (years)	44.5 (±13.5)	34.1 (±12.6)	**0.001**
Female	33 (86.8%)	32 (88.9%)	>0.999
Time from disease onset to diagnosis (months)	3.0 (2.0–6.3)	2.5 (2.0–4.0)	0.197
Hypertension	24 (63.2%)	14 (38.9%)	**0.037**
Diabetes mellitus	6 (15.8%)	3 (8.3%)	0.481
Clinical features			
Claudication	12 (31.6%)	14 (38.9%)	0.510
Decreased pulse	22 (57.9%)	22 (61.1%)	0.778
BP difference > 10 mm Hg	32 (84.2%)	32 (88.9%)	0.737
Bruit	19 (50.0%)	15 (41.7%)	0.472
Carotidynia	3 (7.9%)	10 (27.8%)	**0.025**
Laboratory data			
ESR (mm/h)	62.2 (±31.7)	63.3 (±30.6)	0.872
CRP (mg/dl)	1.06 (0.27–2.45)	1.72 (0.84–5.25)	0.065
Total cholesterol (mg/dl)	170.9 (±26.4)	184.1 (±33.7)	0.093
Triglycerides (mg/dl)	110.4 (±42.1)	110.3 (±39.5)	0.988
HDL-cholesterol (mg/dl)	54.8 (±13.6)	55.9 (±15.4)	0.766
LDL-cholesterol (mg/dl)	84.8 (±18.8)	100.5 (±26.1)	**0.010**
Hata's classification			
Type I	8 (21.1%)	6 (16.7%)	0.940
Type IIA	4 (10.5%)	5 (13.9%)	
Type IIB	9 (23.7%)	8 (22.2%)	
Type III	0 (0.0%)	0 (0.0%)	
Type IV	0 (0.0%)	0 (0.0%)	
Type V	17 (44.7%)	17 (47.2%)	
Statin use	27 (71.1%)	13 (36.1%)	**0.003**
Follow-up data			
Time to remission (months)	10.0 (9.1–12.1)	10.2 (9.0–13.1)	0.689
Glucocorticoid (g)[a]	4.48 (3.12–5.60)	4.93 (3.52–6.86)	0.270
Methotrexate	25 (65.8%)	24 (66.7%)	0.936
Azathioprine	9 (23.7%)	5 (13.9%)	0.282
Medication at end of follow-up			
Glucocorticoid (mg/d)[b]	2.5 (0.0–5.0)	2.5 (0.0–5.0)	0.615
Methotrexate	36 (94.7%)	34 (94.4%)	>0.999
Azathioprine	10 (26.3%)	7 (19.4%)	0.482

Abbreviations: BP; blood pressure, ESR; erythrocyte sedimentation rate, CRP; C-reactive protein, HDL; high density lipoprotein, LDL; low density lipoprotein.
P values < 0.05 are indicated in bold.
[a] Cumulative dose used from diagnosis to remission, prednisolone or its equivalent.
[b] Prednisolone or its equivalent.

were associated with lower risk of relapse [22]. However, use of statins was not addressed in those studies. This study is clinically meaningful in that it is the first study to provide data on the influence of statins on relapse of TAK.

Interestingly, previous study has suggested hypocholesterolemia (total cholesterol < 150 mg/dl) as a predictor of relapse of TAK [23]. In our cohort, the proportion of patients with hypocholesterolemia (total cholesterol < 150 mg/dl; as defined by Fukui et al. [23]) did not differ between statin users and statin non-users (7 (17.5%) vs 4 (11.8%), p = 0.489). Further, the level of total cholesterol did not differ between statin users and statin non-users as shown in Table 1. Therefore, we assume that the effect of statins observed in our study is independent from baseline cholesterol levels.

Statins exert immunomodulatory effects through the repression of T cell activation [24,25]. Statins effectively repress the induction of class II major histocompatibility complex (MHC) protein and gene expression by interferon-γ (IFN-γ) and, therefore, act as direct repressors of class II MHC-mediated T cell activation [24]. Furthermore, statins also exert beneficial effect by suppressing particular type of immune response [25]. Previous studies have shown effect of statins on suppressing Th1 response [26,27]. In an animal model of central nervous system autoimmune disease, statins suppressed the secretion of Th1 cytokines such as

Table 3
Multivariate Cox proportional hazard regression analysis estimating risk of relapse.

	Adjusted hazard ratio	95% Confidence interval	p value
Age > 40 years	0.558	0.236–1.320	0.184
Hypertension	0.720	0.301–1.721	0.459
Carotidynia	2.603	1.121–6.047	**0.026**
LDL-cholesterol	1.007	0.987–1.029	0.487
Statin use	0.260	0.120–0.563	**0.001**

Abbreviation: LDL; low density lipoprotein.
Covariates: age > 40 years (yes/no), hypertension (yes/no), carotidynia (yes/no), LDL-cholesterol (continuous), and statin use (yes/no).
P values < 0.05 are indicated in bold.

Table 4
Influence of use of statins on relapse.

	IPTW Adjusted hazard ratio	95% confidence interval	p value
Statin use	0.153	0.038–0.616	**0.008**

Abbreviation: IPTW; inverse probability of treatment weighting.
P values < 0.05 are indicated in bold.

interleukin-2 (IL-2), IL-12, IFN-γ and tumor necrosis factor-α (TNF-α) [26]. Similarly, in patients with acute coronary syndrome, Th1/Th2 ratio was significantly decreased by use of statins [27]. In addition, previous studies have shown that statins also regulate the differentiation of Th17 cells and inhibit secretion of IL-17 by directly inhibiting the expression of retinoic acid-related orphan nuclear hormone receptor C, which is the transcription factor that controls IL-17 production in $CD4^+$ T lymphocytes [28,29].

Although the exact pathogenesis of TAK is poorly understood, cell-mediated cytotoxicity has been suggested as the pathogenic mechanism of TAK, based on increased numbers of γδ T lymphocytes, natural killer cells and cytotoxic T lymphocytes in aortic tissue [30]. $CD4^+$ T lymphocytes are also known as critical cellular players in vasculitic lesion [31]. Several studies have suggested that Th1 and Th17 cells are involved in the pathogenesis of TAK [32,33]. Expansion of Th1 and Th17 cells were observed in sera and vascular lesions from TAK patients, which correlated with disease activity, suggesting Th1 and Th17 immunity as an important pathogenic mechanism in TAK [32]. Considering this pathogenesis of TAK, the suppressive effect of statins on Th1 and Th17 cells might possibly explain the reduced relapse observed in our study. In particular, considering that glucocorticoid decreases Th1 cytokines but not Th17 cytokines in TAK [32], the effect of statins on reducing relapse rate of TAK when added to glucocorticoid might be attributable to the regulation of Th17 cells.

Although no previous studies have investigated effects of statins in TAK, several studies have evaluated effects of statins in giant cell arteritis, which is also a large vessel vasculitis [34–36]. The use of statins was associated with lower incidence of giant cell arteritis [34]. However, use of statins did not have glucocorticoid sparing effect [35], and did not have significant benefit in reducing frequency of relapses in giant cell arteritis [36]. Giant cell arteritis shares many pathogenic principles with TAK in that T lymphocytes, antigen-presenting cells, and macrophages are fundamental to both diseases [31]. In spite of this pathogenic similarity, we observed a reduced relapse rate in TAK patients using statins, which contrasts the previous study in giant cell arteritis patients [36]. This discrepancy may be attributable to differences in ethnicity. In our study, all patients included were Asian. Due to the differences in the metabolism of statins at the level of hepatic enzymes and drug transporters, efficacy of low doses of statins in Asians are comparable to that of high doses of statins in Caucasians [37]. Therefore, although statin users in our study received low to moderate doses of statins, which is similar to the doses used in the previous studies on giant cell arteritis [35,36], the effect is equivalent to high dose statins in Caucasians (high dose statins: atorvastatin 80 mg/day or rosuvastatin 20–80 mg/day or simvastatin 40–80 mg/day [38]).

Our study has several limitations. First, as we did not include patients who were started on statins after the diagnosis of TAK, patients with a high cholesterol level were excluded and possibility of bias exists. Second, this was a retrospective study. Although we observed that the use of statins is significantly associated with reduced relapse rate, causality cannot be clearly stated. Third, the sample size was relatively small, and thus, we were unable to analyse the dose-response relationship between statin dose and relapse rate. Fourth, ischaemic complication is another important issue in TAK; however, we were unable to analyse the effect of statins on ischaemic complication due to small number of events (data not shown). A prospective controlled trial with larger sample size will help clarify this complication.

In conclusion, we showed that statins significantly reduced the risk of relapse in TAK patients receiving background glucocorticoid and/or immunosuppressants. Considering that relapse is common in TAK, patients with TAK may potentially benefit from taking statins.

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Conflict of interest

The authors declare that there are no conflicts of interest in relation to this article.

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