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Improved Prognosis of Takayasu Arteritis Over the Past Decade

– Comprehensive Analysis of 106 Patients –

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Background: We aimed to describe the recent clinical characteristics of Takayasu arteritis (TA).

Methods and Results: We enrolled 106 consecutive TA patients and compared the clinical characteristics of patients with TA onset before 1999 and after 2000, patients with onset at age less than 39 years and more than 40 years, patients with monophasic and relapsing-remitting clinical course, and patients with and without human lymphocyte antigen (HLA)-B52 allele. Among the patients with TA onset after 2000, the time from onset to diagnosis had decreased; the frequency of occlusion in aortic arch branches and the complication of moderate or severe aortic regurgitation (AR) had decreased, and the maximum dose of prednisolone and the use of immunosuppressive agents had increased. In patients with onset at age more than 40 years, the complications of coronary artery lesions and hypertension had increased, and the incidence of moderate or severe AR had decreased. In the relapsing-remitting group, the maximum dose of prednisolone and the use of immunosuppressive agents had increased, and the mean dose reduction rate of prednisolone was significantly high. There was no significant difference between patients with and without HLA-B52 allele.

Conclusions: The prognosis of TA patients has improved over the past decade, which may be related to early diagnosis because of the development of noninvasive diagnostic imaging tools and improved medical treatments. (*Circ J* 2012; **76:** 1004–1011)

Key Words: HLA-B52; Immunosuppressive therapy; Takayasu arteritis

Takayasu arteritis (TA) is a rare nonspecific inflammatory disease with unknown cause, predominantly affecting the aorta and its main branches, coronary arteries, and pulmonary arteries.[1,2] It induces a variety of nonspecific inflammatory symptoms (systemic and local) and ischemic symptoms related to stenotic lesions or thrombus formation. Further progression of TA causes destruction of the media of the arterial wall, leading to aneurysms or rupture of the involved arteries.[3]

The disease is more common in young women in Asia and the Middle East than in Europe and North America, although precise data of its prevalence and characteristics are not available.[4–6] The true incidence and prevalence of TA is underestimated, and many patients remain undiagnosed or wait for a long time before the correct diagnosis is made.[5,6]

There have been recent improvements in the diagnosis and treatment of TA, owing to the development of noninvasive diagnostic imaging tools and the use of immunosuppressive agents; however, only a relatively small amount of data is available to indicate the prognostic changes in TA in recent years.

In this study, we aimed to clarify the clinical characteristics of TA in a Japanese population, and to investigate changes in TA patient characteristics over the past decade (2000–2010). In addition, in our cohort we studied the clinical features of patients with late onset TA (age >40 years), patients with relapsing-remitting clinical course, and patients with the human lymphocyte antigen (HLA)-B52 allele.

Methods

Patient Selection

We retrospectively enrolled 106 consecutive patients with TA who had visited the Department of Cardiovascular Medicine at Tokyo Medical and Dental University Hospital (Tokyo, Japan) between 2000 and 2010. The diagnosis was confirmed according to the criteria of the Japanese Circulation Society

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Table 1. Clinical Characteristics of TA

	Total	Onset before 1999	Onset after 2000	P value
n	106	71	35	
Sex (F/M)	102/4	70/1	32/3	0.10
Age (years)	49.3±17.9	57.9±14.1	33.0±11.8	<0.0001
Age at onset (years)	26.9±11.8	26.7±11.9	27.3±11.7	0.81
Delay in diagnosis (years)	3.3±5.0	5.2±6.1	1.2±2.3	0.0005
Duration of disease (years)	22.2±15.5	30.9±11.7	5.7±3.2	<0.0001
HLA-B52 (+) (%)*	51.7	43.3	69.0	0.02
Hypertension (%)	45.3	56.3	22.9	0.001
Dyslipidemia (%)	26.4	35.2	8.6	0.005
Diabetes mellitus (%)	9.4	12.7	2.9	0.16
Diagnostic imaging tools (%)				
Ultrasound	20.6	6.1	34.3	0.006
CTA	51.5	24.2	77.1	<0.0001
MRA	39.7	21.82	57.1	0.003
PET	10.3	0	20.0	0.01
DSA	42.6	78.8	8.6	<0.0001
Medical treatment				
Use of glucocorticoids (%)	79.2	70.4	97.1	0.0007
Maximum dose of prednisolone (mg)†	29.6±16.6	22.4±14.4	38.9±14.6	<0.0001
Use of immunosuppressive agents (%)	18.9	7.0	42.9	<0.0001
Surgical treatments (%)	22.6	22.5	22.8	0.97

*Among 89 patients out of 106. †Among patients treated with glucocorticoids.
TA, Takayasu arteritis; HLA, human lymphocyte antigen; CTA, computed tomography angiography; MRA, magnetic resonance angiography; PET, positron emission tomography; DSA, digital subtraction angiography.

Guideline for Management of Vasculitis Syndrome (2008).[2]

Study Design

We focused on patient data, including clinical history of TA, signs and symptoms at onset, vascular involvement, and medical and surgical treatments. Patients were classified according to the angiographic classification of the International TA Conference in Tokyo 1994 on the basis of the distribution of the lesions as follows: Type I (branches of the aortic arch), Type IIa (ascending aorta, aortic arch and its branches), Type IIb (ascending aorta, aortic arch and its branches, and thoracic descending aorta), Type III (thoracic descending aorta, abdominal aorta, and/or renal arteries), Type IV (abdominal aorta and/or renal arteries), and Type V (combined features of Types IIb and IV), with subcategorization according to the presence/absence of lesions in the coronary and pulmonary arteries.[7] We compared the clinical characteristics of patients according to the year of onset and age at onset.

Disease activity was determined according to National Institutes of Health criteria, which define the clinical status on the basis of 4 elements: systemic features, elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) level, features of vascular ischemia or inflammation, and angiographic changes.[1] The active phase was defined as new onset or worsening of 2 or more of these features. A marked decrease in symptoms and/or improved clinical findings indicated partial remission or smoldering disease, and complete resolution of all clinical features or their stabilization in the case of fixed vascular lesions was indicative of remission.[1] Among the patients who developed TA after 2000, we classified the patient activity profiles into 2 groups: a monophasic group that showed no clinical evidence of relapse after the induction of remission, and a relapsing-remitting group that showed relapses during the course of glucocorticoid treatment. The mean dose reduction rate of prednisolone ([initial dose of prednisolone – dose at relapse or at the last reduction]/duration until relapse or the last reduction) was calculated for the 2 groups. We performed multiple linear regression stepwise analysis to evaluate the relative contribution of each variable to the clinical course.

HLA typing was performed in 89 of the 106 TA patients, using peripheral white blood cells and a polymerase chain reaction sequencing-based method (Medical & Biological Laboratory Co Ltd, Nagoya, Japan). We investigated the prevalence of the HLA-B52 allele, and the effect of its presence on the clinical characteristics of TA.[8,9]

This study was approved by the Ethics Review Board at Tokyo Medical and Dental University.

Statistical Analysis

Continuous data are presented as mean with standard deviation, and categorical data are presented as numbers (percent). The means were compared by independent t-test or Mann-Whitney U test, and the proportions were compared by Mantel-Haenszel chi-square test or Fisher's exact test as appropriate. The area under the receiver-operating characteristics (ROC) curve was computed to determine the diagnostic and prognostic values and to determine optimal cutoff values. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were determined for the relevant cutoff values. Relapse rates were analyzed by the log-rank test and survival curves were calculated using Kaplan-Meier estimates. Multiple linear regression stepwise analysis was performed to examine the association of multiple variables of interest at the same time as independent variables to show the relative contribution of each of these variables to the clinical course. Only the variables with $P<0.20$ were included in the final fitted model.

Table 2. Vascular Involvement in TA Patients

	Total	Onset before 1999	Onset after 2000	P value
Angiographic classification (%)				
Type I	35.9	31.0	45.7	0.14
Type IIa	9.4	4.2	20.0	0.01
Type IIb	8.5	11.3	2.9	0.26
Type III	0.9	1.4	0	1.0
Type IV	1.9	2.8	0	1.0
Type V	43.4	49.3	31.4	0.08
Branches of the aortic arch (%)				
Any lesion	95.3	95.8	94.3	1.0
Irregularity or stenosis	85.9	81.7	94.3	0.14
Occlusion	40.6	49.2	22.9	0.005
Dilatation	24.5	23.9	25.7	0.87
Thoracic aorta (%)				
Any lesion	41.5	40.8	42.8	0.89
Irregularity or stenosis	25.5	28.2	20.0	0.33
Occlusion	0	0	0	1.0
Dilatation	23.6	23.9	22.9	0.87
Abdominal aorta (%)				
Any lesion	31.1	32.4	28.6	0.72
Irregularity or stenosis	25.5	25.4	25.7	0.90
Occlusion	1.9	2.8	0	1.0
Dilatation	5.7	7.0	2.9	0.66
Coronary artery lesions (%)	8.5	11.3	2.9	0.27
Pulmonary artery lesions (%)	4.7	2.8	8.6	0.33
Renal artery lesions (%)	21.7	26.8	11.4	0.06
Moderate or severe AR (%)	22.6	28.2	11.4	0.04
Dialysis (%)	1.9	2.8	0	1.0
Loss of vision (%)	2.8	4.2	0	0.55
Death (%)	2.8	4.2	0	0.55

TA, Takayasu arteritis; AR, aortic regurgitation.

Table 3. Surgical Treatments for TA Patients

Procedure/Site of procedure	Patients	Procedures	Restenosis	Aneurysm formation	Follow-up (years)
Bypass	14	20	7 (35.0%)	0	10.6±9.6
Subclavian or axillary artery		6			
Coronary artery		5			
Carotid artery		4			
Iliofemoral artery		3			
Renal artery		2			
Balloon angioplasty and stenting	6	8	3 (37.5%)	0	9.3±7.9
Coronary artery		3			
Renal artery		2			
Subclavian artery		1			
Carotid artery		1			
Iliac artery		1			
Endarterectomy	1	2	1 (50%)	0	9.5±0.7
Carotid artery		1			
Iliac artery		1			
Aortic replacement					
Aortic aneurysm	4	4		1 (25%)	5.3±3.0
Aortic stenting					
Aortic aneurysm	1	1	0	0	2
Aortic valve replacement					
AR	1	1		0	23

Abbreviations see in Table 2.

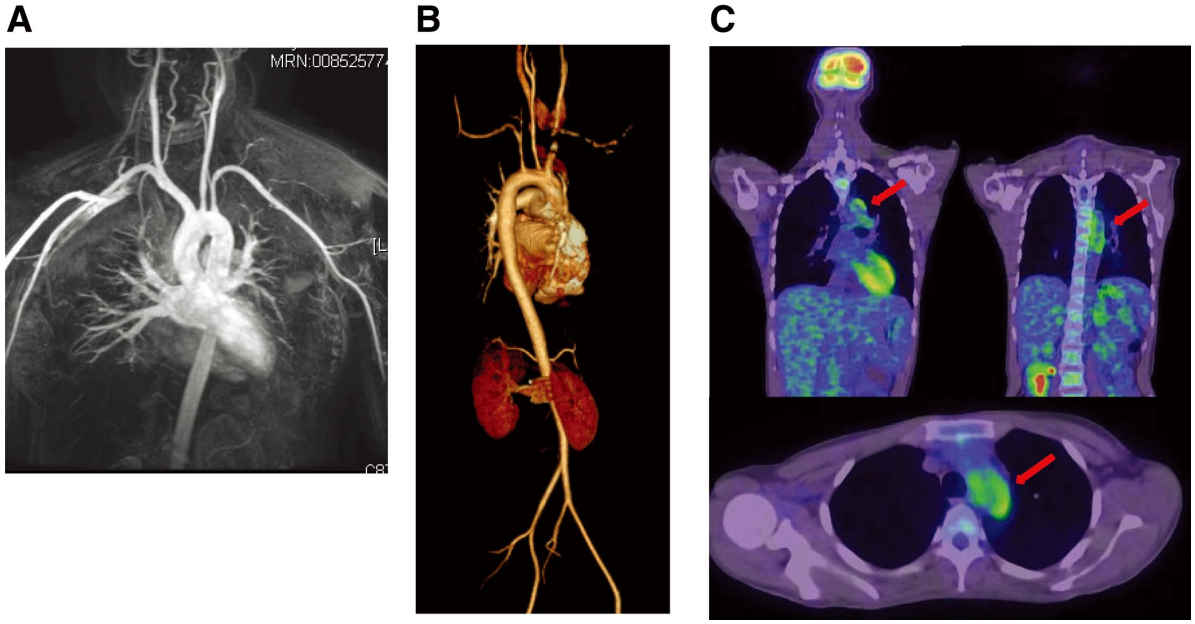

Figure 1. Representative case diagnosed by ^{18}F-FDG PET/CT in the prestenotic stage. A 21-year-old woman experienced fever of unknown origin for 4 months. CRP and ESR levels were elevated to 8.73mg/dl and 114mm/h, respectively. MRA (**A**) and CTA (**B**) showed no abnormalities. However, since vascular bruit was heard over her right neck, ^{18}F-FDG PET/CT (**C**) was performed and showed significant uptake in the aortic arch and descending aorta (arrows). On the basis of these findings, she was diagnosed with TA. CRP, C-reactive protein; CTA, computed tomography angiography; ESR, erythrocyte sedimentation rate; ^{18}F-FDG PET/CT, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; MRA, magnetic resonance angiography; TA, Takayasu arteritis.

Table 4. Differences in TA Patients With Late Onset

	Onset age <39	Onset age >40	P value
n	92	14	
Sex (F/M)	89/3	13/1	0.43
Age at onset	23.2±7.3	49.9±7.9	<0.0001
Delay in diagnosis (years)	3.6±5.3	1.2±1.3	0.18
HLA-B52 (+) (%)*	54.6	40.0	0.51
Hypertension (%)	39.6	76.9	0.02
Dyslipidemia (%)	23.9	42.8	0.11
Diabetes mellitus (%)	8.7	14.2	0.60
Angiographic classification (%)			
Type I	36.3	35.7	0.97
Type IIa	8.8	14.3	0.62
Type IIb	9.9	0	0.60
Type III	0	7.1	0.13
Type IV	2.2	0	1.0
Type V	42.9	42.9	1.0
Coronary artery lesions (%)	5.9	28.6	0.02
Pulmonary artery lesions (%)	4.7	7.1	0.54
Renal artery lesions (%)	19.1	33.3	0.23
Moderate or severe AR (%)	26.7	0	0.04
Dialysis (%)	2.2	0	1.0
Loss of vision (%)	2.2	7.1	0.36
Death (%)	3.3	0	1.0
Maximum dose of prednisolone (mg)†	29.6±16.2	28.9±20.5	0.90
Use of immunosuppressive agent (%)	18.5	21.4	0.73
Surgical treatments (%)	19.4	40.0	0.09

*Among 89 patients out of 106. †Among patients treated with glucocorticoids.
Abbreviations see in Tables 1,2.

Table 5. Differences in TA Patients With Activity Profiles

	Monophasic	Relapsing-remitting	P values
n	11	24	
Sex (F/M)	11/0	21/3	0.54
Age at onset	28.8±10.1	25.7±12.1	0.47
Delay in diagnosis (years)	0.6±0.4	1.6±2.7	0.23
Inflammatory markers at diagnosis			
CRP (mg/dl)	5.7±3.6	7.2±6.4	0.55
ESR (mm/h)	101.1±21.8	84.2±37.7	0.29
HLA-B52 (+) (%)*	55.6	75.0	0.39
Hypertension (%)	9.1	33.3	0.22
Dyslipidemia (%)	0	8.3	0.11
Diabetes mellitus (%)	0	4.2	1.0
Angiographic classification (%)			
Type I	63.6	37.5	0.15
Type IIa	9.1	25.0	0.39
Type IIb	0	4.2	1.0
Type III	0	0	1.0
Type IV	0	0	1.0
Type V	27.3	33.3	1.0
Coronary artery lesions (%)	0	4.2	1.0
Pulmonary artery lesions (%)	9.1	8.3	1.0
Renal artery lesions (%)	18.2	8.3	0.58
Moderate or severe AR (%)	18.2	8.3	0.58
Use of glucocorticoids (%)	90.9	100	0.31
Initial dose of prednisolone (mg)†	29.5±15.4	39.1±15.4	0.10
Maximum dose of prednisolone (mg)†	29.5±15.4	42.2±14.8	0.03
Mean dose reduction rate of prednisolone (mg/month)†	1.1±1.1	4.0±3.5	0.02
Use of immunosuppressive agent (%)	0	62.5	0.0005
Surgical treatments (%)	27.3	20.8	0.69

*Among 29 patients out of 35. †Among patients treated with glucocorticoids.
CRP, C-reactive protein; ESR, erythrocyte sedimentation rate. Other abbreviations see in Tables 1,2.

In all statistical tests, P<0.05 was considered significant. The analyses were performed using JMP 9.0 for Windows (SAS Institute Japan Ltd, Tokyo, Japan).

Results

Patient Characteristics (Table 1)

In total, 7% of the patients developed TA after the age of 50. The most common signs and symptoms of TA before diagnosis were systemic, such as fever (temperature >37.0°C; 53%) and easy fatigability (39%), followed by ischemic signs/symptoms from branches of aortic arch lesions such as decrease/lack of pulse in the radial artery (38%), difference in blood pressures of left and right arms (37%), and neck bruit (30%).

Vascular Involvement (Table 2)

More than 90% of the patients had some lesions in the branches of the aortic arch. Three patients died during the observation period: 1 died of pulmonary hypertension (age 68), 1 was sudden cardiac death (age 40), and 1 died of cancer (age 58).

Medical Treatments

During the overall disease course, 79% of the patients were treated with glucocorticoids. Immunosuppressive agents were prescribed to patients who were resistant to glucocorticoids and to patients in whom glucocorticoid withdrawal was difficult (19%). In the case of these patients, methotrexate was the most commonly used first-line immunosuppressive agent (50%), followed by cyclosporine A (35%); however, the immunosuppressive agent was changed in 12 patients (60%) because of resistance to the agent or adverse effects. An anti-tumor necrosis factor (TNF)-α agent was administered to 4 patients after failure of treatment with 3 or more immunosuppressive agents, and all of them showed remission without significant adverse effects, except for 1 patient who developed tuberculosis. Antiplatelet agents were used in 67% of the patients and oral anticoagulants in 10% of the patients.

Surgical Treatments

Surgical treatment was indicated for patients with hemodynamically significant lesions, mainly for those who showed clinical features of cerebral ischemia, ischemia of extremities limiting activities of daily living, coronary artery disease, renovascular hypertension with resistance to hypertensive drugs, progressive enlargement of an aortic aneurysm, and severe aortic regurgitation (AR). The types and sites of procedures are summarized in Table 3.

Changes in the Past Decade

Clinical changes during the past decade are summarized in Tables 1 and 2. Prevalences of hypertension and dyslipidemia had significantly decreased, which may be related to the differences in age between the 2 groups.

Time from onset to diagnosis was significantly shortened

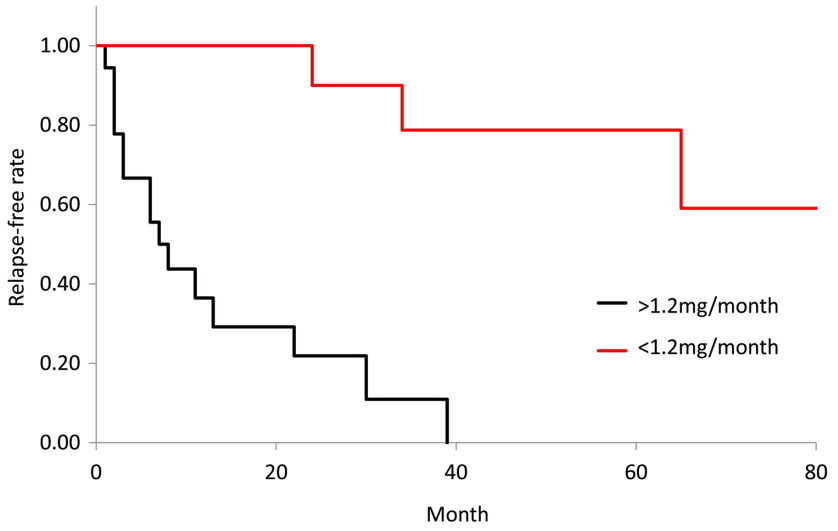

Figure 2. Kaplan-Meier curves of relapse-free patients with mean dose reduction rate of prednisolone. The relapse-free rate was significantly higher in the group with mean dose reduction rate of prednisolone <1.2mg/month (59.1% vs. 0%, P=0.0001).

Table 6. Differences in TA Patients With the HLA-B52 Allele

	HLA-B52 (–)	HLA-B52 (+)	P value
n	43	46	
Age at onset (years)	27.7±13.0	24.0±9.3	0.13
Hypertension (%)	51.2	41.3	0.40
Dyslipidemia (%)	25.6	26.1	0.96
Diabetes mellitus (%)	13.9	6.5	0.30
Angiographic classification (%)			
Type I	32.6	39.1	0.52
Type IIa	4.7	15.2	0.16
Type IIb	9.3	8.7	1.0
Type III	0	0	1.0
Type IV	4.7	0	0.23
Type V	48.8	37.0	0.26
Coronary artery lesions (%)	7.0	6.5	1.0
Pulmonary artery lesions (%)	7.3	0	0.10
Renal artery lesions (%)	25.6	21.7	0.58
Moderate or severe AR (%)	16.3	26.1	0.26
Dialysis (%)	2.3	2.2	1.0
Loss of vision (%)	0	6.5	0.24
Death (%)	0	0	1.0
Maximum dose of prednisolone (mg)*	29.8±14.6	31.5±17.3	0.69
Use of immunosuppressive agent (%)	16.3	19.6	0.65
Surgical treatments (%)	20.9	17.4	0.67

*Among patients treated with glucocorticoids.
Abbreviations see in Tables 1,2.

during the decade. Digital subtraction angiography (DSA) had been replaced with computed tomographic angiography (CTA), magnetic resonance angiography (MRA), and ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG PET). In 1 patient who did not show abnormal findings on either CTA or MRA, TA was diagnosed with ^{18}F-FDG PET/CT (Figure 1). Further, combined use of imaging tools to improve the diagnosis of TA had also increased (1.4±0.7 vs. 2.0±0.8, P=0.001). The frequency of occlusion in branches of the aortic arch and the incidence of moderate or severe AR had significantly decreased. In TA patients with onset after 2000, there were no cases of loss of vision, dialysis for chronic renal failure, or deaths. The number of patients treated with glucocorticoids and immunosuppressive agents had significantly increased, and the maximum dose of prednisolone had increased.

Differences in Patients With Late Onset TA

Among the 106 patients, there were 14 (13%) whose age at onset was more than 40 years. There were no differences in their clinical characteristics, except for significantly more coronary artery disease and hypertension, and the complication

of moderate or severe AR was significantly less (Table 4).

Activity Profiles

Among the 35 patients with TA onset after 2000, 24 (69%) showed a relapsing-remitting clinical course after glucocorticoid treatment (Table 5). The mean prednisolone dose at relapse was 13.3±7.5 mg, and the mean duration until relapse was 15.4±17.3 months. The mean dose reduction rate of prednisolone was significantly higher in the relapsing-remitting group. The area under the ROC curve of the mean dose reduction rate of prednisolone for predicting relapse was 0.86. The sensitivity, specificity, PPV, and NPV of the mean dose reduction rate values of prednisolone at the optimal cutoff level of >1.2 mg/month determined from the AUC curve for predicting relapse were: 83.3%, 75.0%, 83.3%, and 75.0%, respectively. The relapse-free rate is shown in Figure 2. In the multiple linear regression stepwise analysis, the mean dose reduction rate of prednisolone (P=0.01) was the only significant independent determinant for relapse during glucocorticoid treatment.

HLA Typing

Among the 89 patients in whom we evaluated the HLA type, 46 (52%) had the HLA-B52 allele. No differences in clinical characteristics were found between the 2 groups (Table 6).

Discussion

This study was conducted to clarify the clinical characteristics of TA in a Japanese population. In our cohort, Type V was the most frequent angiographic classification of TA, followed by Type I, and only few patients showed Type IV lesions. This is similar to the result previously reported from Japan.[7] However, the distributions of the lesions varies among countries. It is reported that Type V (54.5%) is the most frequent followed by Type II (22.3%) in Korea, Type I (40%) is the most frequent followed by Type V (30.4%) in China, and Type V (54.9%) is the most frequent followed by Type IV (28.4%) in India.[7,10,11] Although the reason for this difference is unknown, these variations in the distribution of arterial lesions in different countries indicate that ethnic and genetic factors play an important role in pathogenesis of TA.

To the best of our knowledge, this is the first study to investigate the recent changes in TA. We found that vascular involvement became less severe in patients who developed TA in the past decade, suggesting that early diagnosis and improved medical treatment can control disease activity before the development of severe vascular involvement.

We also showed that the time from onset to diagnosis was significantly shortened in the past decade, which may be related to the development of noninvasive diagnostic imaging tools such as ultrasound, CTA, MRA, and PET. DSA had traditionally been the gold standard for clinical imaging in TA, but it is invasive and cannot be used to evaluate inflammatory changes in the arterial wall.[12] Ultrasonography, CTA, and MRA can assess luminal and mural changes, as well as angiographic appearance, which could lead to an early diagnosis of TA through detection of prestenotic lesions.[12–15] Recently, ^{18}F-FDG PET was shown to be a tool for diagnosing and monitoring disease activity in patients with TA, because it can estimate the degree as well as the localization of inflammation.[16,17] ^{18}F-FDG PET may be a promising imaging tool for early diagnosis of patients with prestenotic lesion and normal CTA or MRA findings as shown in Figure 1. We also experience cases of middle-aged women with stenotic lesions in the main branches of the aorta and/or coronary arteries, without significant increase in conventional inflammatory biomarkers such as CRP and ESR. These patients could be diagnosed as having atherosclerosis, but because these patients show inflammatory changes in the arterial wall on MRA or PET, we would diagnose them as TA. The development of noninvasive diagnostic imaging tools thus decreases the incidence of misdiagnosis between TA and atherosclerosis. These imaging tools revealed that inflammation of the aorta and its main branches is more widely spread than we expected from the angiographic extent of vascular lesions. Therefore, early diagnosis and treatment could change the distribution and severity of vascular involvement.

Further, there have been remarkable developments in the medical treatments for TA in recent years. For TA patients who are resistant to glucocorticoids, immunosuppressive agents are reported to induce disease remission and prevent the development of new angiographic arterial lesions.[2,18–21] There are reports suggesting that infliximab, a human-murine chimeric monoclonal antibody against TNF-α, is an effective treatment for TA patients refractory to conventional therapies.[22,23] In this study, we showed that the maximum dose of prednisolone and the patients treated with immunosuppressive agents had increased in the past decade. The overall use of immunosuppressive agents (18.9%) was relatively low compared with other cohort studies reported from other countries such as Italy (54%),[5] US (73%),[24] and Turkey (84%).[25] From our current investigation, we think that the use of immunosuppressive agents should be encouraged, as it appears to decrease the severity of vascular involvement. Further studies are needed to investigate the clinical utility of these new agents. The use of antiplatelet agents may also be encouraged, as de Souza et al reported that they reduced ischemic events in TA patients.[26]

Although the vascular involvement has become less severe in the past decade, the number of patients who require surgical treatment has not changed, which may be related to recent technical advances in vascular surgery. However, the treatment approach has tended to shift slightly toward less invasive endovascular treatment.[27] It is reported that the restenosis rate after bypass procedures is between 5% and 31%, with a follow-up period of 0.6–6.2 years; further, percutaneous transluminal angioplasty/stenting has a much higher restenosis rate than the former (12–71.4% with a follow-up period of 0.5–5 years).[28] Moreover, the restenosis rate was reduced when surgical treatment was performed during the inactive stage of the disease, and when the patient was treated with both glucocorticoids and immunosuppressive agents.[29,30] In our cohort, surgical treatments were performed during the inactive stage of the disease in all patients, but immunosuppressive agents were prescribed in only 3 patients (12.5%). It is necessary to strictly control the disease activity before and after the surgical treatment using immunosuppressive agents to reduce the complication of the treated arteries.

The 2 large-vessel arteritis, TA and giant cell arteritis (GCA), may be indistinguishable in their histopathologic and radiographic findings. Primary differences between these 2 disorders are the age of the affected patients and distribution of affected arteries. TA typically begins before the age of 40, whereas GCA typically begins in patients older than 50 years. Some investigators describe these 2 types of arteritis belonging to the same category from a pathological viewpoint, and they propose that large-vessel arteritis should be divided according to the onset age as large-vessel arteritis of juvenile onset and that of late onset. However, we think that TA is a unique clinical entity irrespective of the onset age. From this point of view, we investigated clinical characteristics of TA according to the onset age. We found that the clinical features basically do not vary with

the onset age. Therefore, we think that it is clinically insignificant to differentiate TA from GCA based on onset age.

Among the 35 patients who developed TA after 2000, 70% of the patients experienced a relapsing-remitting clinical course. Prediction of relapse is a key clinical issue in the management of TA. It is reported that even if corticosteroid therapy is effective, 72% of cases experience multiple recurrences within 6 months after the dose of prednisolone was tapered to <10 mg daily.[24] In this study, the mean dose reduction rate of prednisolone was the only significant independent determinant for relapse during glucocorticoid treatment. The cutoff level >1.2 mg/month in the mean dose reduction rate of prednisolone for predicting relapse may provide an important clinical suggestion.

Investigation of 89 HLA-typed TA patients revealed that there was no difference in the distribution of vascular involvement between patients with and without the HLA-B52 allele. This was contrary to the result previously reported by Kitamura et al who reported that frequencies of AR, pulmonary artery lesions, and ischemic heart disease were significantly increased in patients with the HLA-B52 allele.[8] Changes in the clinical characteristics of TA in recent years may account for this conflicting result.

This study is one of the most comprehensive and large-scale clinical studies for TA conducted in the past decade. However, this study has several potential limitations. The main limitation was the small sample size, and because this was a single center and retrospective study, there may be a bias in assessment and treatment of TA. Although it could take many years, large-scale prospective studies in patients with TA are encouraged to identify the most effective assessment and treatment method.

In conclusion, the prognosis of TA patients has improved in the past decade, and this may be because of early diagnosis owing to the development of noninvasive diagnostic imaging tools and improved medical treatment.

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Disclosures

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