Clinical Manifestations and Longterm Outcome for Patients with Takayasu Arteritis in China

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ABSTRACT. ***Objective.*** To describe a large cohort of patients with Takayasu arteritis in China.

Methods. We retrospectively analyzed 566 patients hospitalized in Fuwai Hospital between 2002 and 2013. Data collected were clinical characteristics, laboratory findings, angiographic features, treatment, and longterm outcome.

Results. The female to male ratio was 3.8 to 1, and the mean age of onset was 28.9 ± 12.0 years. The most common inflammatory symptom, initial symptom, and coexisting disease were fever (52, 9.2%), dizziness (214, 37.8%), and hypertension (HTN; 392, 69.3%), respectively. Pulmonary artery, coronary artery involvement, and aortic regurgitation were found in 83 (14.7%), 66 (11.7%), and 181 (36.7%) patients, respectively. Elevation of the erythrocyte sedimentation rate was observed in 131 patients (23.1%). Treatment included drugs, interventional therapy, autologous blood vessel transplant, artificial blood vessel transplant, and aortic valve replacement. During a mean followup of 5.0 ± 0.2 years, 32 patients died, including 1 patient who died suddenly during coronary angiography. HTN, major complications, and a progressive disease course were significant prognostic markers.

Conclusion. HTN, rather than fever, is the leading reason for patients with Takayasu arteritis to see a doctor in China. HTN, major complications, and a progressive disease course are statistically significant predictors of survival. Because of cardiovascular events associated with the disease, early diagnosis and treatment are urgent to improve prognosis. (First Release Oct 1 2014; J Rheumatol 2014;41:2439–46; doi:10.3899/jrheum.140664)

Key Indexing Terms:
TAKAYASU ARTERITIS ANGIOGRAPHY RENAL ARTERY
CORONARY ARTERY PULMONARY ARTERY

Takayasu arteritis (TA), also known as "pulseless disease", is a chronic inflammatory vasculitis of unknown etiology mainly affecting large vessels, especially the aorta and its main branches, as well as coronary and pulmonary arteries. Clinical manifestations are varied because of the differences of site and severity of the involved arteries. The aim of our study was to describe the baseline characteristics, clinical features, angiographic findings, treatment, and longterm outcome of patients with TA in China.

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MATERIALS AND METHODS

We retrospectively analyzed 566 patients with TA between 2002 and 2013 who were hospitalized in Fuwai Hospital. The following data were obtained: age, sex, clinical manifestations, history, left ventricular ejection fraction (LVEF), inflammatory markers [erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), high-sensitivity CRP (hsCRP)], angiographic findings, treatment (medicine, percutaneous, or surgical), and longterm outcome. The local ethics committee approved the study protocol.

Diagnostic criteria. The diagnosis of TA was based on the following 1990 criteria of the American College of Rheumatology: (1) age at disease onset < 40 years, (2) claudication of extremities, (3) decreased brachial artery pulse, (4) blood pressure difference > 10 mmHg, (5) bruit over subclavian arteries or aorta, and (6) arteriogram abnormality. The presence of 3 or more of these 6 criteria led to a diagnosis of TA[1].

Anatomic classification. Patients were classified into 4 categories according to the involvement of arteries: (type I) involvement of the aortic arch and its branches, (type II) involvement of the descending aorta and abdominal aorta, (type III) the combined features of type I and type II, and (type IV) involvement of the pulmonary artery[2].

Disease activity. Patients who demonstrated new onset or worsening of at least 2 of the US National Institutes of Health criteria were considered to have active disease: (1) systemic features such as fever or musculoskeletal problems (no other cause identified); (2) elevated ESR; (3) features of vascular ischemia or inflammation, such as claudication, diminished or absent pulse, bruits, vascular pain (carotidynia), asymmetric blood pressure in either upper or lower limbs (or both); and (4) typical angiographic features[3].

Major complications. We used the criteria proposed by Ishikawa and

Maetani, with the presence of at least 1 of these conditions caused by TA: (1) microaneurysm formation (stage 2 retinopathy); (2) severe hypertension (HTN; a brachial pressure of ≥ 200 mmHg systolic or ≥ 110 mmHg diastolic; alternatively, a popliteal pressure of ≥ 230 mmHg systolic or ≥ 110 mmHg diastolic may be used); (3) Grade 3+ or 4+ aortic regurgitation; and (4) angiographic demonstration of an aortic or arterial aneurysm with a diameter more than twice the norm. Patients with 2 or more of these complications, including Takayasu retinopathy, HTN, aortic regurgitation, and aortic or arterial aneurysm, were also considered to have major complications, even if each of the complications did not meet the criteria listed above[4].

Progressive course of TA. A progressive course of TA was diagnosed if the past clinical course was characterized by the development of progressive severe symptoms (such as fever, dizziness, headache, blurred vision, fatigue, dyspnea, and claudication) after a period of years since onset.

Imaging. Abnormal angiographic findings were defined as stenosis ≥ 50%, occlusion or near occlusion (stenosis of ≥ 95%), and aneurysm detected by conventional, computerized tomography angiography (CTA) or magnetic resonance angiography (MRA). Arterial wall thickening and dissection were also detected using CTA and MRA.

Pulmonary arterial HTN (PAH). PAH was diagnosed using transthoracic echocardiography and was classified as mild (pulmonary arterial systolic pressure 30–50 mmHg), moderate (pulmonary arterial systolic pressure 50–70 mmHg), or severe (pulmonary arterial systolic pressure > 70 mmHg).

Statistical analysis. Statistical analysis was performed using SPSS Statistics 19.0 (IBM SPSS Statistics). Categorical data was presented as total number and percentage of cases. We used independent Student t tests or chi-square tests to examine differences between groups. The Kaplan-Meier method was used to estimate the cumulative survival rates after diagnosis. Univariate and multivariate Cox regression analysis were performed to determine the prognostic value of clinical variables, including age at disease onset, sex, clinical manifestations, laboratory findings (elevated ESR, elevated CRP, and elevated hsCRP), and history of vascular revascularization or surgery. Values of $p < 0.05$ were considered statistically significant.

RESULTS

General characteristics. Four hundred forty-eight (79.2%) of the 566 patients with TA were women, and the female to male ratio was 3.8 to 1. The average age of the patient for the first hospitalization was between 5 and 86 years (36.3 ± 13.4), and the onset age ranged from 2 to 68 years (28.9 ± 12.0). Patients with an onset age between 20 and 40 years accounted for the largest proportion (298, 52.7%), followed by those ≤ 20 years (158, 27.9%). Patients ≥ 40 years made up the smallest proportion (110, 19.4%). History of onset of the disease varied from 3 days to 50.1 years (7.6 ± 0.4 yrs; Table 1). The time lag for patients whose onset age was < 20 years was significantly shorter than for those whose onset age was ≥ 20 years (7.1 ± 9.0 yrs vs 8.9 ± 11.1 yrs, respectively, $p = 0.001$). A previous history of tuberculosis was found in 41 patients (7.2%).

Clinical classification. According to angiographic findings and clinical examinations, most patients were of the type III (214, 37.8%), followed by type I (111, 19.6%) and type II (99, 17.5%). Involvement of pulmonary arteries was detected in 83 patients (14.7%). The rest of the 59 cases (10.4%) were patients with atypical site involvement, such as the coronary artery or aortic valve.

Table 1. General characteristics of 566 patients with TA.

General Clinical Characteristics	N or Value	Proportion, %*
Female	448	79.2
Median age, yrs[a]	36.3 ± 13.4	
Disease onset age, yrs[b]	28.9 ± 12.0	
≤ 20	158	27.9
20–40	298	52.7
≥ 40	110	19.4
Time lag, yrs[c]	7.6 ± 0.4	
Inflammatory symptoms		
Fever	52	9.2
Emaciation	13	2.3
Arthralgia	10	1.8
Carotidynia	25	4.4
Amaurosis fugax	19	3.4
Cardiovascular risk factors		
Hypertension	62	11.0
Diabetes mellitus	17	3.0
Hyperlipidemia	28	4.9
Smoking	47	8.3
Vascular symptoms		
Dizziness	214	37.8
Syncope	60	10.6
Blindness or visual disturbances	58	10.2
Secondary hypertension	330	58.3
Angina pectoris	57	10.1
Myocardial infarction	9	1.6
Pulselessness	124	21.9
Stroke	28	4.9
Transient ischemic attack	58	10.2
Claudication	161	28.4
Other comorbidities or symptoms		
Renal failure	6	1.1
Congestive heart failure	151	26.7
Dyspnea	48	8.5
Hemoptysis	25	4.4
Laboratory variables		
Elevated ESR	131	23.1
Elevated CRP	119	21.0
Elevated hsCRP	165	29.2
Echocardiography		
LVEF < 50%	57	11.6
PAH, mmHg	19.2 ± 31.6	

*Representing proportion of 566 patients with TA. [a]The average age of patients for the first hospitalization. [b]The presence of the earliest particular symptom or disease that is attributed to TA. [c]The time between the occurrence of initial symptom and the diagnosis of TA. TA: Takayasu arteritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; hsCRP: high-sensitivity CRP; LVEF: left ventricular ejection fraction; PAH: pulmonary arterial pressure.

Clinical features. Clinical features of patients with TA are shown in Table 1. The most common coexisting disease was HTN (392, 69.3%). Severe HTN was observed in 81 patients (13.7%). Diabetes mellitus, hyperlipidemia, and congestive heart failure occurred in 17 (3.0%), 28 (4.9%), and 151 patients (26.7%), respectively. Congestive heart failure was associated with moderate to severe aortic regurgitation (66, 11.7%), severe renal arterial stenosis (23, 4.1%), and pulmonary artery involvement (62, 11.0%).

Stroke (28, 4.9%) and transient ischemic attack (58, 10.2%) were the most common reasons why TA was frequently misdiagnosed. One patient, whose initial symptoms were dizziness and syncope, was diagnosed to have moyamoya disease.

The common initial presenting symptoms were dizziness (214, 37.8%), amaurosis fugax (19, 3.4%), syncope (60, 10.6%), claudication (161, 28.4%), and blindness or visual disturbances (58, 10.2%), which suggested vascular ischemia. Inflammatory symptoms, such as fever (52, 9.2%), emaciation (13, 2.3%), arthralgia (10, 1.8%), and carotidynia (25, 4.4%), were much less common. A total of 368 patients (65.0%) were found to have vascular murmurs that were frequently heard over the cervical (219, 38.7%), supraclavicular (72, 12.7%), epigastrium (126, 22.3%), and umbilical regions (45, 8.0%). Abnormal artery pulses frequently occurred in the extremities, including the radial and dorsal arteries.

One hundred twenty-nine patients (22.8%) were classified as being in the active stage of the disease on their initial hospitalization, and among them there were 104 women (80.6%) and 25 men (19.4%).

Imaging findings. Angiography was performed in 88.0% (498) of the 566 patients with TA, including conventional angiography (370, 65.4%), CTA (107, 18.9%), and MRA (21, 3.7%), and 3 patients received 18F-fluorodeoxyglucose positron emission tomography (FDG-PET). The descending aorta (150, 26.5%) was the most frequently involved segment of the aorta. The most frequently involved branch was the left subclavian artery (278, 49.1%), followed by the left common carotid artery (176, 31.1%). The most common feature of the involved aortic vessels was stenosis, except for the ascending aorta and the subclavian artery, which were dilation and occlusion or near occlusion, separately. A total of 83 cases (14.7%) had pulmonary arterial involvement, including 22 patients who were diagnosed with single pulmonary artery involvement. Upper lobe pulmonary arterial branches showed abnormalities most frequently and the right pulmonary artery in the upper lobe was most often involved. Coronary artery involvement was observed in 66 patients (11.7%), and 14 patients had single coronary artery disease (Table 2). The ostia (75, 35.7%) and proximal (56, 26.7%) segments of the coronary artery were more frequently involved than the middle (49, 23.3%) and distal (30, 14.3%) segments. Ostia of the left main coronary artery (25, 11.9%) were most frequently involved, followed by ostia of the right coronary artery (23, 11.0%). Only 1 patient was detected to have a coronary aneurysm.

Among the 392 patients with HTN, lesions of the renal artery and constriction of the aorta were found in 212 (37.5%) and 118 patients (20.8%), respectively, which were confirmed using angiography and clinical features. Both the renal artery stenosis and aortic coarctation were correlated with HTN (both $p < 0.001$).

FDG-PET was performed in patients whose ESR and CRP were elevated, showing that the responses were negative.

Laboratory findings. At baseline, the mean ESR, CRP, and hsCRP were 19.1 ± 20.4 mm/h (reference value < 5 mm/h in men and < 20 mm/h in women), 10.9 ± 17.9 mg/l (reference value 0–8 mg/l), and 5.1 ± 5.7 mg/l (reference value 0–3 mg/l), respectively. Elevated ESR, CRP, and hsCRP were found in 131 (23.1%), 119 (21.0%), and 165 patients (29.2%), respectively (Table 1).

Among the 493 patients (87.1%) who underwent echocardiographic evaluation, the mean LVEF was 62.1 ± 11.3%, and LVEF was < 50% in 57 patients (11.6%). A segmental left ventricular wall motion was abnormality present in 12 patients. Aortic valve regurgitation (AR; 181, 36.7%) was more common than mitral valve regurgitation (75, 15.2%). A total of 66 patients had more than moderate regurgitation. The mean pulmonary arterial systolic pressure was 19.2 ± 31.6 mmHg. PAH was observed in 88 patients (17.8%). Mild, moderate, and severe PAH was noted in 27, 21, and 40 patients, respectively.

Therapy. Among the patients with HTN, 304 (57.6%) received antihypertensive drugs and 137 (34.9%) underwent revascularization. Pure percutaneous transluminal artery balloon dilation and stent implantation were performed in 80 patients (20.4%) and 55 patients (14.0%), respectively. Five patients received nephrectomy (including 1 who underwent autorenal transplantation simultaneously) and 2 patients had autologous blood vessel implantation. Twenty-five of the patients with moderate to severe AR had aortic valve replacement. Among the patients with coronary artery involvement, 1 died during coronary angiography. Thirty-two patients (48.5%) received revascularization, including percutaneous coronary intervention (PCI) in 16 (24.2%) and coronary artery bypass grafting (CABG) in 14 patients (21.2%).

Three hundred thirty-three patients (58.7%) were administered glucocorticoid (GC; prednisone). Those patients were either in the active stage (or with normal level of ESR, but elevation of CRP level) or had revascularization. The initial dosage was 20–40 mg per day for 4 weeks; it was gradually reduced to a maintenance dosage of 5–10 mg per day for at least 6 months. Seventy patients who were not prescribed prednisone initially were given prednisone at the 1-month followup after discharge from hospital if there were elevations of ESR or CRP levels. In total, 486 patients (85.9%) received prednisone during the whole course of disease. Eighty patients who had never been prescribed prednisone were either in the nonactive stage, used Chinese traditional herbs, or did not want to take prednisone. Immunosuppressive agents were given to 23 patients because of GC resistance, relapse during GC dose reduction, or serious side effects associated with steroid treatment. Repeated and prolonged courses of immunosuppressive

Table 2. Angiographic findings and revascularization of 566 patients with TA.

Characteristics	Stenosis	Occlusion or Near Occlusion	Dilation	Aneurysm	Thickening	Dissection	Total Lesion	PTA	Stent Implant	Autologous Blood Vessel Transplant	Artificial Blood Vessel Transplant
Ascending aorta	4	1	30	11	36	0	92	0	0	4	11
Aortic arch	24	0	15	5	45	0	74	0	0	3	5
Descending aorta	65	2	20	20	41	2	150	2	26	2	4
Abdominal aorta	85	9	11	13	23	2	143	10	14	0	0
Brachiocephalic trunk	13	15	11	1	30	0	70	6	0	1	0
Celiac artery	10	18	4	2	4	1	38	0	0	0	0
Superior mesenteric artery	16	44	2	1	2	0	65	2	2	0	0
Left common carotid artery	71	80	7	2	16	0	176	4	5	3	0
Right common carotid artery	45	44	14	1	4	0	108	9	0	2	0
Left internal carotid artery	8	2	3	0	1	0	14	0	1	0	0
Right internal carotid artery	4	4	6	0	0	0	14	0	0	0	0
Left vertebral artery	20	16	7	0	4	0	47	8	2	0	0
Right vertebral artery	17	7	6	0	1	0	31	3	3	0	0
Left subclavian artery	95	152	8	1	22	0	278	48	15	3	0
Right subclavian artery	41	84	9	8	22	0	164	28	10	3	0
Left iliac artery	10	7	0	2	3	0	22	1	1	0	0
Right iliac artery	9	6	0	2	4	1	22	3	3	0	0
Left renal artery	99	56	8	2	11	0	176	58	40	1	0
Right renal artery	93	69	6	2	7	0	177	52	23	1	0
Coronary artery	33	20	5	1	8	0	66	2	14	14	0
Pulmonary artery	19	32	29	1	2	0	83	7	2	0	0

TA: Takayasu arteritis; PTA: percutaneous transluminal angioplasty.

therapy were required in 14 patients because of the relapsing nature of their TA. Antiplatelet therapy, including aspirin, clopidogrel, and both in combination, were used by 397 patients (70.1%), 179 (31.6%), and 172 (30.4%), respectively. Warfarin (anticoagulant therapy) was prescribed for 71 patients (12.5%). Nine patients (1.6%) were treated with antiplatelet and anticoagulant therapy simultaneously. An antilipemic agent was prescribed for 82 patients (14.5%). Sildenafil was administered to 9 patients (1.6%) with PAH.

Outcomes. Three hundred thirty-two patients (58.7%) were followed for 5.0 ± 0.2 years (range 0.3–11.0 yrs). During followup, the condition of 220 patients (66.3%) had improved, 32 (9.6%) had remained unchanged, 48 (14.5%) had worsened, and 32 patients (9.6%) had died. One patient had died during coronary angiography. The total survival rate at 1, 3, 5, and 10 years after diagnosis was 99.0%, 98.0%, 94.0%, and 58.0%, respectively (Figure 1). The mean age at death was 45.0 ± 14.5 years (range 21.1–88.7 yrs). Causes of death included acute myocardial infarction in 6, heart failure in 21, cerebral hemorrhage in 4, and sudden cardiac death in 1 patient. Among those who had died, these had been performed in 2 patients each: CABG, Bentall operation, and renal artery stent implantation. Six patients had received PCI and 30 patients had received medical treatment only. As to the outcome events of patients who were alive, heart failure (32 patients) was the most common endpoint. One patient received a heart transplant because of repeated heart failure. CABG and PCI were performed in 6 patients each because of angina pectoris or acute myocardial infarction.

Univariate Cox analysis revealed statistically significant predictors of survival: age at disease onset, elevated CRP, elevated hsCRP, HTN, disease progression, and major complications. Sex, elevated ESR, and a history of vascular revascularization or surgery were not determinants of mortality. Multivariate Cox regression analysis showed that only HTN, major complications, and a progressive disease course were significantly associated with outcome (regression coefficients were 4.664, 1.959, and 1.870, respectively).

A total of 208 patients with HTN were followed for 5.3 ± 0.2 years (range 0.3–11.0 yrs). The difference in blood pressure between baseline and followup is shown in Table 3. There was a significant decrease of blood pressure at followup compared with that at baseline, and showed no relation to the stage of HTN, except for diastolic blood pressure in second-stage patients. Blood pressure dropped significantly in patients with severe HTN-related acute heart failure. The blood pressure level was statistically significantly decreased in 94 patients who received renal artery revascularization. Restenosis of the renal artery and aortic artery after angioplasty were observed in 16 and 11 patients, respectively. Revascularization of the renal artery and aortic artery during followup was performed in 16 patients each.

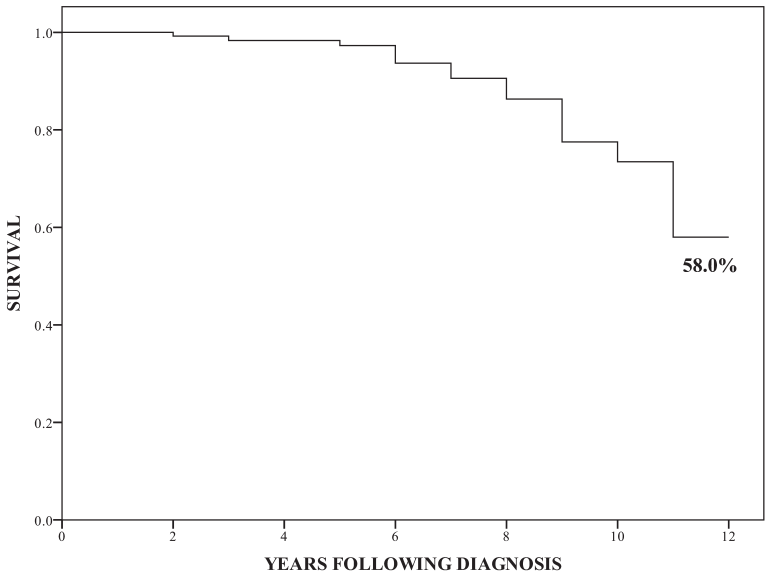

Figure 1. Overall survival curve after the diagnosis in the 332 patients. The 1-, 3-, 5-, and 10-year rates were 99.0%, 98.0%, 94.0%, and 58.0%, respectively.

Table 3. Change of blood pressure between baseline and followup.

Characteristics	n (%)	BP	BP at Baseline, mmHg	BP at Followup, mmHg	p
All HTN	392 (69.3)	SBP	147.8 ± 52.3	126.4 ± 47.1	< 0.001
		DBP	80.4 ± 32.8	73.0 ± 27.1	< 0.001
Patients received renal artery revascularization	82 (14.5)	SBP	142.8 ± 65.5	119.0 ± 53.6	< 0.001
		DBP	83.5 ± 39.7	71.6 ± 31.2	< 0.001
Severe HTN with HF	6 (1.1)	SBP	190.0 ± 19.2	148.1 ± 25.6	< 0.001
		DBP	108.7 ± 20.0	81.7 ± 11.6	< 0.001
1st stage HTN	46 (8.1)	SBP	120.1 ± 47.4	104.7 ± 53.0	0.024
		DBP	72.06 ± 31.5	67.2 ± 33.8	0.006
2nd stage HTN	50 (8.8)	SBP	156.5 ± 15.4	144.1 ± 19.0	< 0.001
		DBP	81.2 ± 18.3	85.0 ± 10.4	0.233
3rd stage HTN	66 (11.7)	SBP	171.5 ± 54.8	135.7 ± 46.9	< 0.001
		DBP	95.4 ± 26.6	75.3 ± 26.6	< 0.001

BP: blood pressure; HF: heart failure; HTN: hypertension; SBP: systolic BP; DBP: diastolic BP.

DISCUSSION

TA is a chronic autoimmune systemic vasculitis of unknown etiology that is prevalent in Asian and Middle Eastern countries. The greatest frequency of TA was reported in Japan. Beginning in 1990, there were about 5000 cases added to the list of intractable diseases over the next decade, and the number of patients increased by 200–400 every 3 years[5]. Conversely, the incidence of TA was 2.6 cases per million population annually in the United States[6], 0.3 cases per year per million inhabitants under 40 years of age in the United Kingdom[7], 1.2 cases per million per year in Sweden[8], and 1 case per million per year in Germany[9]. Patient ethnicity and differences in criteria used for diagnosis may explain the variability. TA commonly presents in women. The female to male ratio was 3.8 to 1 with the onset age ranging from 2–68 years in our study, numbers consistent with a previous study in China[10] in which the female to male ratio varied from 29:1–1.2:1[3,11]. Though the etiology of TA is unknown, previous studies have revealed that genetic components were involved in the pathogenesis of TA, and there was an association between HLA alleles and TA. Thus far, HLA-B*52:01 has been the only established common genetic factor for TA[12,13,14]. But Takamura, *et al* reported that the HLA-B67 allele could be a new and important marker for TA because of its high OR compared with HLA-B52 (OR 4.94 vs 3.35, respectively)[15].

The disease frequently presents in patients below the age of 40, and over half of the patients presented between the

ages of 20–40 in our study. The proportion with an age of onset > 40 years was low, but not uncommon. Our study suggested that the proportion was 19.4%, while the frequency was 17.5% in Italian and 32.0% in French patients[16,17]. One of the most widely used criteria for the diagnosis of TA[1] is an age at disease onset of < 40 years, that may lead to the misdiagnosis of TA in patients > 40 years. The mean age of onset was 28.9 ± 12.0 years, ranging from 2–68 years, which is further evidence that TA can be diagnosed in older people. According to our investigation, most patients in this group were women with no cardiovascular risk factors and imaging findings that confirmed the characteristics of TA. Owing to no involvement of important blood vessels, most of the patients did not have an acute stage, therefore they came to the hospital much later than at the time of disease onset.

Type III was the most common classification of TA in our study, while previous studies showed that type I was the most common. One reason for this difference was that imaging technology has developed very fast in recent years, and patients with TA usually underwent systemic vascular imaging instead of only the arteries associated with symptoms. In this way, almost all of the arteries involved can be identified. The other reason is that patients of TA came to the hospital much later after the disease had occurred, thus the arteries had been extensively involved.

Fever was not common in this cohort. Only 9.2% of patients had a history of fever. Conversely, fever was the most common symptom in other studies[18,19]. One reason for this difference may be that the medical history of this cohort took place over a long period of time, such that many patients had forgotten whether they had fever. Another reason could be that patients and doctors in this cohort made nothing of the fever and, therefore, the doctor decided against further examination. The most common reason why patients went to see a doctor was HTN. HTN presented in 69.3% of the studied patients, and 330 of them also had associated lesions of the renal artery (37.5%) or aorta (20.8%). HTN was reported to be between 4% and 72% in previous studies[2,19,20,21,22]. There were 81 patients who were admitted to our hospital with severe HTN, and 6 of them manifested as acute left heart failure. If heart failure was because of the abrupt onset of HTN, response to therapy was usually good. This response was the same as in another study in China[10]. Generally, the outcome of hypertensive patients was good because their blood pressure had dropped significantly compared to baseline.

Premature atherosclerosis has been observed in TA. Patients with TA may be associated with arterial atherosclerotic disease (AD), which may make clinical diagnosis difficult. TA and arterial AD can be identified as follows: (1) the symptom of TA usually appears at a relatively younger age than does arterial AD, and the former primarily affects women; (2) patients with TA rarely had risk factors for atherosclerosis; and (3) angiography imaging suggest that the long segmented diffused lesions of vessels are more common in the ostia or proximal site of arteries in TA, while the lesions of arterial AD are characterized by significant calcified plaque. During conventional angiography, compared to the arterial AD lesions, the pressure of balloon dilation and retraction recoil are much higher for the vascular lesions of TA. Repeated dilation is necessary and residual stenosis is much more common in patients with TA.

A total of 22.8% of patients were diagnosed as in the active stage of TA in the present study, while in previous studies, 32.0%–84.3% of total patients were in the acute phase of TA[19,23]. We used ESR as a marker of disease activity, but it was neither sensitive nor specific enough to monitor disease activity in TA[24]. A diagnosis of active stage of TA should not be ruled out in patients with normal ESR values. Conversely, we must also consider the possibility of a misdiagnosed activity phase. Previous studies reported that FDG-PET may be an important examination method for early diagnosis and for monitoring disease activity[25]. In our study, there were 3 patients with elevated ESR and CRP who had FDG-PET, and the result turned out to be negative. A validated or globally accepted set of criteria to evaluate disease activity of TA is needed.

GC are the mainstay of active disease treatment in TA. The initial dose in our study was lower than in the other studies[16,17]. The result of our study showed that most patients could have a remission of disease without immunosuppressive agents, and a dose of 0.5 mg per kg of body weight of prednisone could be effective, reduce the side effects of drugs, and improve the compliance of patients. Only for patients who could not reach remission of disease should immunosuppressive agents be added on the basis of sufficient dose of GC. During the clinical course, we found that some vascular lesions progressed even though ESR and CRP were normal. That is why some of the patients diagnosed to be in the inactive stage of TA were also prescribed GC.

Eighty-three patients (86.5%) out of 96 who had pulmonary arteriography were observed to have pulmonary artery involvement. The incidence was similar to that reported in Japan (70.0% and 86.0%)[26,27]. Conversely, pulmonary involvement was as low as 12.2% in a French study[17]. Pulmonary HTN was observed in 88 patients and was caused by pulmonary artery involvement or left ventricular filling pressure elevation. Occlusion or near occlusion was the most frequent sign suggesting pulmonary artery involvement in our study, which was different from a previous study[28]. The prognosis was worse in patients with TA with pulmonary artery involvement. Among the 31 patients with pulmonary artery involvement who were followed for 4.5 ± 3.2 years, 7 had died because of cor pulmonale, and 12 had worsened or remained unchanged.

Coronary artery involvement was found in 11.7% of the

patients with TA in our present investigation, which was slightly higher than in our previous study[29]. The difference may be because of an increased prevalence of coronary angiography. Ostia lesions of the right artery and the left main artery were the most common findings. This result was in agreement with previous studies[30]. With regard to prognosis, a total of 10 patients died during followup except for 1 who died during the angiography procedure.

A total of 181 patients (36.7%) were observed to have AR in our study, which was in line with another study from Turkey (33.0%)[21]. Over a third had more than moderate regurgitation and 30 patients received aortic valve replacement. The prognosis of patients with AR was poor; 10 died during the followup (including 1 who underwent surgery), and the condition of 18 patients worsened.

The survival rate at 5 years after diagnosis was 94.0% in our study. Previous studies reported that the rate ranged from 67%–100%[4,31]. The survival rate at 10 years after diagnosis was 58.0%. The result was much lower than in the previous studies[4,31]. First, the rate of loss to followup was higher than in the previous studies. Second, patients went to the doctor long after disease onset, and they had had multiple sites of artery involvement. Third, involvement of coronary and pulmonary arteries were much frequent in our study, which may affect the prognosis of patients with TA. The Cox proportional hazard regression model identified that HTN, major complications, and a progressive disease course were significant prognostic markers. Arnaud, *et al* reported similar results[17]. A study by Ishikawa and Maetani reported that the presence of major complications and a progressive disease course were significantly associated with outcome, and the survival rate was 58.3% versus 92.7% for patients > 35 years and ≤ 35 years of age, respectively[4]. Heart failure proved to be the main reason why patients died.

We have described the clinical features, angiographic findings, treatments, and longterm outcomes of patients with TA. There were some limitations to our study. Our study had a large sample size, but it was a single-center retrospective study. We also did not investigate the possible disease-associated alleles in the Chinese patients with TA, and the percentage of lost followup was high. In a future study, we will focus on the basic research of TA and design multicenter, cohort, or randomized controlled studies, and investigate biomarkers that can be used to evaluate the activity of TA.

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