Clinical Characteristics of Heart Involvement in Chinese Patients with Takayasu Arteritis

Jing Li, Hongchao Li, Fei Sun, Zhe Chen, Yunjiao Yang, Jiuliang Zhao, Mengtao Li, Xinping Tian, and Xiaofeng Zeng

ABSTRACT. ***Objective.*** To understand the characteristics of heart involvement in Chinese patients with Takayasu arteritis (TA).

Methods. The medical charts of 411 patients with TA (325 women, 86 men) were retrospectively reviewed. The comparison of clinical manifestations was carried out between the patients with TA with (n = 164) and without (n = 247) heart involvement.

Results. The median age at disease onset was 23.0 years (18.0–30.0) in 411 patients with TA, and 23.0 years (17.3–30.0) in 164 patients with heart involvement. The disease duration of the heart involvement group (median: 24.0 mos) was significantly longer than those patients without heart involvement (the control group, median: 16.0 mos). Hypertension (57.3% vs 46.6%; p = 0.033), renal dysfunction (17.1% vs 7.7%; p = 0.003), and bruit in the subclavian artery (45.1% vs 34.4%; p = 0.029) were more common in the heart involvement group than patients without. Valvular abnormalities were found in 134 (81.7%) patients in the heart involvement group, myocardial abnormalities in 26 (15.9%), and coronary artery abnormalities in 19 patients (11.6%). The age at onset (yrs) and disease duration (mos) of patients with myocardial, valvular, and coronary arterial abnormalities were 18.8/13.0, 23.8/23.5, and 26.8/57.0, respectively. In the heart involvement group, 22 patients (84.6%) with myocardial abnormalities, 15 (78.9%) with coronary arterial abnormalities, and 89 (66.4%) with valvular abnormalities had Numano type V vessel involvement. The level of high-sensitivity C-reactive protein was higher in the heart involvement group (median: 10.0 mg/l), and the difference was significant when compared to the control group (median: 7.0 mg/l; p = 0.017).

Conclusion. Patients with TA complicated with cardiac abnormalities are not rare, especially in patients with Numano type V vessel involvement. We suggest that echocardiogram screening may be a helpful tool to understand the whole feature of patients with TA. (First Release August 15 2017; J Rheumatol 2017;44:1867–74; doi:10.3899/jrheum.161514)

Key Indexing Terms:
TAKAYASU ARTERITIS CARDIAC ABNORMALITIES VALVULAR INVOLVEMENT

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Accepted for publication June 9, 2017.

Takayasu arteritis (TA) is an uncommon systemic vasculitis mainly involving the aorta and its major branches. The pathogenesis of TA remains unknown, and the majority of the TA population consists of women at child-bearing age[1]. The prevalence of TA is much higher in Asia and Africa than in other countries[1]. The pathological characteristic is granulomatosis inflammation in the adventitia and media of the involved arteries[2]. Fibrosis develops gradually as the disease progresses, followed by stenosis or occlusion of blood vessels, which then results in organ ischemia[3]. Sometimes the destruction of the elastica and muscularis can result in artery dilation or aneurysm[3].

Heart involvement is not infrequently found in patients with TA. Besides the coronary arteries, cardiac valves can also be involved[4]. Cardiac abnormalities are considered related to poor prognosis of TA[5], which needs to be taken into consideration when taking care of patients with TA. In our study, we retrospectively reviewed the medical records of patients with TA admitted to our hospital over the past 20 years and analyzed the clinical features of patients with TA with cardiac abnormalities.

MATERIALS AND METHODS

Patients. Medical charts of 810 patients with the diagnosis of TA who had been admitted to Peking Union Medical College Hospital, a Chinese national referral center, from 1990 to 2014 were reviewed retrospectively. Of these patients, 411 with complete angiographic evaluation and dataset were included into our study. The heart involvement group was 164 patients with evidence of heart involvement, and the other 247 patients without TA-related cardiac abnormalities were treated as the control group (Figure 1). The study protocol was approved by the Institutional Review Board of Peking Union Medical College Hospital (approval no. S-478). Written informed consent was waived because of the retrospective chart review design of this study.

Methods. A case search was performed electronically in the information systems of the hospital using The International Classification of Diseases, 10th revision (ICD-10) code for TA (M31.4). The diagnosis was reconfirmed through chart review by a senior rheumatologist according to the 1990 American College of Rheumatology criteria for TA[6]. All patients needed to have catheter angiography or computed tomography angiography (CTA) performed and the arterial involvement must meet the diagnostic criteria for TA to be included into our study. In addition, all patients had echocardiography at least once during their hospital stay. Serum active reactants of those patients included in the study were tested at least once. Patients who had ever been admitted for 2 or more hospital stays were considered as a single case. Therefore, only 411 patients were included into our study. Their first reports of echocardiogram were collected and analyzed. Both clinical and laboratory test results were collected. A database file was built by 4 junior rheumatologists entering the information with Epidata (Version 3.1), and data were exported to SPSS software for further analysis. The input data in the database were mutually checked by all 4 rheumatologists to ensure the data accuracy. One hundred sixty-four patients with evidence of TA-related heart involvement were included in the heart involvement group, and the other 247 patients without heart involvement were treated as the control group, including 2 patients with coronary atherosclerotic heart disease and 1 patient with congenital heart disease (atrial septal defect with left-to-right shunt; Figure 1).

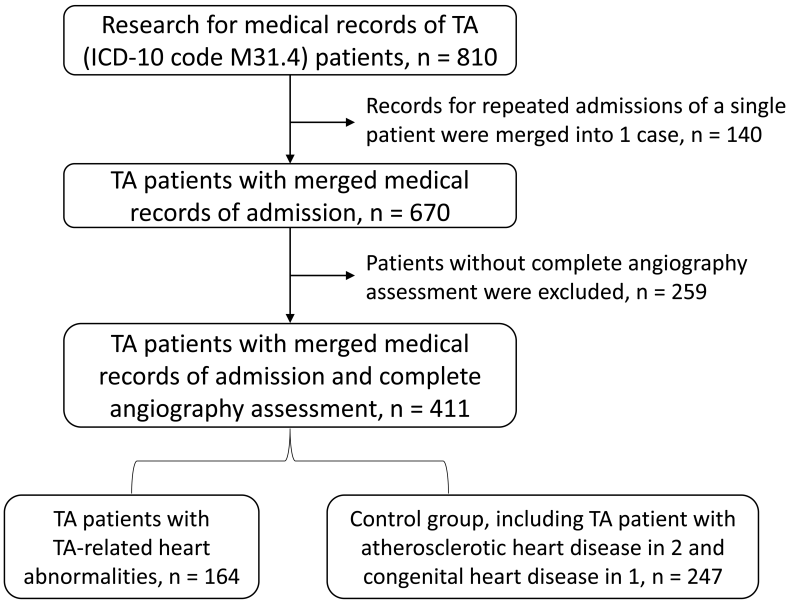

Figure 1. A case search was performed electronically in the information systems of the hospital using the ICD-10 code for TA (M31.4), and 810 medical charts of patients with the diagnosis of TA who had been admitted to the Peking Union Medical College Hospital from 1990 to 2014 were found. There were 411 patients with complete angiographic evaluation and datasets who were included in this study. Of the patients, 164 who had evidence of heart involvement were subdivided into the heart involvement group and the other 247 patients without cardiac abnormalities were treated as the control group. Two patients with coronary atherosclerotic heart disease and 1 patient with congenital heart disease (atrial septal defect with left-to-right shunt) were included in the control group. ICD-10: International Classification of Diseases, 10th ed; TA: Takayasu arteritis.

The demographic data, clinical symptoms, physical examination findings, laboratory tests, angiographic presentations, and cardiac abnormalities were collected and analyzed. The angiographic classification was based on Hata and Numano's criteria[7]. Cardiac abnormalities were evaluated by Doppler echocardiography, including valvular abnormalities, myocardial abnormalities, and pericardial effusion, and coronary artery tomography and coronary angiography to detect coronary arterial abnormalities. Coronary arterial abnormalities included mural thickening, narrowing, or occlusion of the lumen of coronary arteries. Valvular abnormalities included insufficiency, stenosis, or thickening of valves. Myocardial abnormalities included myocardial hypertrophy, ventricular dilatation, and left ventricle dysfunction, while those related to coronary abnormalities or valvular diseases were excluded. Comparisons of clinical manifestations between the heart involvement group and the control group were carried out. Renal dysfunction was defined as the estimated glomerular filtration rate < 90 ml/min/1.73 m^2. Congestive heart failure was defined as ejection fraction ≤ 40% by Doppler echocardiography or typical clinical symptoms (i.e., circulatory congestion, exertional dyspnea, orthopnea, jugular venous distension, etc.) with rales heard on physical examination, with or without pleural effusion observed on chest radiography.

Disease activity was evaluated based on the US National Institutes of Health criteria[1].

Statistical analysis. The variables of this study were not distributed in a normal pattern. We described the numerical variables as median (Q1, Q3), and the categorical variables as numbers (percentage). Comparisons between groups were made using the Mann-Whitney U test for numerical data, and the chi-square test for categorical data. Fisher's exact tests were performed when the expected frequencies were < 5. A 2-sided p value < 0.05 was considered statistically significant. Analysis was performed with the SPSS software (version 19.0, IBM SPSS statistics).

RESULTS

Demographic data. The sex ratio was 1:3.8 (86 men, 325 women), and the median age at disease onset was 23.0 years (18.0–30.0) in the 411 patients with TA. Among the 164 patients with heart involvement, the sex ratio was 1:3.4 (37 men, 127 women), and the median age at onset was 23.0 years (17.3–30.0), without significant difference compared to the control group (n = 247). There was significant difference in disease duration before admission between the heart involvement group (median 24.0 mos) and the control group (median 16.0 mos; p = 0.001). More patients had longer duration (more than 60 mos) in the heart involvement group than the control group (26.8% vs 17.0%; p = 0.016). The proportion of patients with active disease and without active disease was not different between the 2 groups (81.1% vs 79.4%; Table 1).

Clinical features. Vascular bruits were the most common clinical findings during physical examination in the heart involvement group, which were located at the carotid (66.5%), subclavian (45.1%), and abdominal (32.3%) arteries area, followed by hypertension (HTN; 57.3%). The common symptoms were malaise (31.1%), fever (27.4%), and weight loss (25.0%). Weight loss was more common in the heart involvement group (25.0% vs 16.6%; p = 0.037), while arthralgia was more common in the control group (12.1% vs 4.3%; p = 0.006). These conditions were more common in the heart involvement group: HTN (57.3% vs 46.6%; p = 0.033), renal dysfunction (17.1% vs 7.7%; p = 0.003), and bruit in the subclavian artery area (45.1% vs 34.4%; p = 0.029). There were no differences in the frequency of bruits in other areas, and stroke between the 2 groups (Table 1).

Cardiac manifestations. Coronary artery abnormalities were found in 19 patients (19/164, 11.6%) of the heart involvement group, clinically presented as angina pectoris in 14 (14/164, 8.5%) and myocardial infarction in 3 (3/164, 1.8%). Coronary arteries angiographic examination, including catheter angiography and CTA, of these 19 patients demonstrated concentric thickening of vessel wall, which resulted in stenosis and/or occlusion in 17 cases, and mural thickening without obvious stenosis in 2 cases, meanwhile combining with calcification of vessel wall in 3 cases and atherosclerosis in 3 cases. All coronary arterial abnormalities were not secondary to the expansion of aortic root, which might produce stenosis of the coronary ostia or very proximal segment of the coronary arteries (Table 2).

Valvular abnormalities were found in Doppler echocardiography of 201 patients. One hundred and thirty-four patients (134/164, 81.7%) were assessed to have pathological valvular abnormalities, including single valve involvement in 90 cases (67.2%) and 2 or more valves involvement in 44 cases (32.8%). Aortic insufficiency (84/134, 62.7%) was the most common finding, followed by mitral insufficiency (55/134, 41.0%), tricuspid insufficiency (19/134, 14.2%), thickening of aortic valve (12/134, 9.0%), anterior mitral valve leaflet prolapse (8/134, 6.0%), pulmonary insufficiency (7/134, 5.2%), and aortic stenosis combined with mitral insufficiency (1/164, 0.6%). Pulmonary valvular abnormality was found only in combined valvular abnormalities. Among valvular insufficiency, 80.6% (108/134) was mild and 41.8% (56/134) was moderate to severe, which was more common in aortic and mitral valves. Other cardiac abnormalities combined with valvular abnormalities were found by Doppler echocardiography in 30 patients (30/134, 22.4%), including dilated aortic root, and enlargement of cardiac chambers (Table 2 and Table 3).

Twenty-six patients (26/164, 15.9%) demonstrated myocardial abnormalities on Doppler echocardiography, including diffusely decreased ventricular wall motion, cardiac chambers enlargement, and decrease of contractility, while those related to coronary abnormalities or valvular diseases were excluded. Clinically evident heart failure happened in 61 patients (61/411, 14.8%), including 52 patients (52/164, 31.7%) with heart involvement and 24 patients (24/26, 92.3%) with myocardial abnormalities. In addition, 9 patients (9/61, 14.8%) presented clinical features of heart failure due to decreased diastolic function, resulting from HTN caused by stenosis of renal arteries.

Ages at onset of patients with TA were 18.8 (15.9–24.1), 23.8 (17.1–32.1), and 26.8 (21.2–40.5) years in patients with myocardial, valvular, and coronary arterial abnormalities, and duration of disease at first admission was 13.0 (6.0–36.0),

Table 1. Demographic data and clinical features of 411 patients with Takayasu arteritis. Values are n (%) unless otherwise specified.

Characteristic	Total	Heart Involved Group	Control Group	p	Chi-square
Total, n	411	164	247		
Sex					
Female	325 (79.1)	127 (77.4)	198 (80.2)	0.54	0.44
Male	86 (20.9)	37 (22.6)	49 (19.8)		
Age at onset, yrs, median (IQR)	23.0 (18.0–30.0)	23.0 (17.3–30.0)	23.0 (18.0–31.0)	0.89	
< 20	145 (35.3)	56 (34.1)	89 (36.0)		
≥ 20 to < 30	163 (39.7)	68 (41.5)	95 (38.5)		
≥ 30 to < 40	72 (17.5)	25 (15.2)	47 (19.0)		
≥ 40	31 (7.5)	15 (9.1)	16 (6.5)		
Duration of disease at admission, mos,					
median (IQR)	21.0 (6.0–60.0)	24.0 (7.3–84.0)	16.0 (4.0–48.0)	0.001*	
< 60	325 (79.1)	120 (73.2)	205 (83.0)		
≥ 60	86 (20.9)	44 (26.8)	42 (17.0)	0.016*	5.75
Disease activity while taking first echocardiogram test					
Active	329 (80.0)	133 (81.1)	196 (79.4)	0.67	0.19
Stable	82 (20.0)	31 (18.9)	51 (20.6)		
Constitutional findings					
Fever	128 (31.1)	45 (27.4)	83 (33.6)	0.19	1.75
Malaise	122 (29.7)	51 (31.1)	71 (28.7)	0.61	0.26
Weight loss	82 (20.0)	41 (25.0)	41 (16.6)	0.037*	4.36
Symptoms					
Arthralgia	37 (9.0)	7 (4.3)	30 (12.1)	0.006*	7.47
Rash	32 (7.8)	11 (6.7)	21 (8.5)	0.51	0.44
Vascular findings					
Vascular bruit					
Carotid arteries	257 (62.5)	109 (66.5)	148 (59.9)	0.18	1.80
Subclavian arteries	159 (38.7)	74 (45.1)	85 (34.4)	0.029*	4.77
Abdominal	114 (27.7)	53 (32.3)	61 (24.7)	0.09	2.86
Hypertension	209 (50.9)	94 (57.3)	115 (46.6)	0.033*	4.56
Ischemic stroke	22 (5.4)	5 (3.0)	17 (6.9)	0.09	2.86
Renal dysfunction	47 (11.4)	28 (17.1)	19 (7.7)	0.003*	8.56
Laboratory findings					
Level of ESR, mm/h, median (IQR)	26.0 (11.0–65.0)	28.0 (11.0–69.0)	26.0 (11.0–65.0)	0.83	
Level of CRP, mg/l, median (IQR)	12.8 (3.4–44.8)	16.3 (4.7–52.5)	12.3 (3.2–43.8)	0.23	
Level of hs-CRP, mg/l, median (IQR)	8.8 (2.0–12.5)	10.0 (2.9–26.0)	7.0 (1.8–10.0)	0.017*	
Level of WBC, 10^9/l, median (IQR)	8.2 (6.6–11.0)	8.5 (6.7–11.4)	8.0 (6.5–10.6)	0.21	
Numano angiographic classification					
Type I	91 (22.1)	25 (15.2)	66 (26.7)	0.006*	7.53
Type IIa	16 (3.9)	6 (3.7)	10 (4.0)	0.84	0.04
Type IIb	16 (3.9)	8 (4.9)	8 (3.2)	0.40	0.71
Type III	12 (2.9)	4 (2.4)	8 (3.2)	0.77**	0.22
Type IV	26 (6.3)	11 (6.7)	15 (6.1)	0.80	0.07
Type V	250 (60.8)	110 (67.1)	140 (56.7)	0.028*	4.82

*p < 0.05. ** Fisher's exact test. IQR: interquartile range; ESR: erythrocyte sediment rate; CRP: C-reactive protein; hs-CRP: high-sensitivity CRP; WBC: white blood cell.

23.5 (7.0–74.5), and 57.0 (22.0–120.0) months in these patients, respectively. The proportion of patients with active disease while they taking first Doppler echocardiography was 88.5%, 79.1%, and 78.9% in those 3 subgroups (Table 2).

Pericardial effusion was found in 30 patients (30/164, 18.3%) of our study. Our data on cardiac abnormalities and those reported in the literature are listed in Table 4[4,5,8,9].

Cardiac abnormalities in different angiographic patterns. In Table 1, type V vessel involvement (67.1% vs 56.7%; p = 0.028) was more common, and type I (15.2% vs 26.7%; p = 0.006) was less common in the heart involvement group than in the control group. In the heart involvement group, these patients were attributed to Numano type V vessel involvement by angiography: 15 patients (15/19, 78.9%) with coronary artery involvement, 89 patients (89/134, 66.4%) with valvular abnormalities, and 22 patients (22/26, 84.6%) with myocardial abnormalities (Table 2). Therefore, this type of vessel involvement was the most common form that tended to have heart involvement.

Laboratory test results. The erythrocyte sedimentation rate or C-reactive protein (CRP) were elevated in 164 patients with heart involvement, but the differences were not significant

Table 2. Angiographic classification and clinical features in 164 patients with Takayasu arteritis who had cardiac abnormalities. Values are n (%) unless otherwise specified.

Characteristic	Coronary Arterial Abnormalities	Valvular Abnormalities	Myocardial Abnormalities
Total, n	19	134	26
Angiographic classifications			
Type I	2 (10.5)	21 (15.7)	0
Type IIa	0	3 (2.2)	1 (3.9)
Type IIb	1 (5.3)	7 (5.2)	0
Type III	0	4 (3.0)	0
Type IV	1 (5.3)	10 (7.5)	3 (11.5)
Type V	15 (78.9)	89 (66.4)	22 (84.6)
Age at onset, yrs, median (IQR)	26.8 (21.2–40.5)	23.8 (17.1–32.1)	18.8 (15.9–24.1)
< 20	4 (21.1)	44 (32.8)	14 (53.8)
≥ 20 to < 30	6 (31.6)	53 (39.6)	11 (42.3)
≥ 30 to < 40	4 (21.1)	23 (17.2)	0
≥ 40	5 (26.3)	14 (10.4)	1 (3.8)
Duration of disease at admission, mos, median (IQR)	57.0 (22.0–120.0)	23.5 (7.0–74.5)	13.0 (6.0–36.0)
< 60	10 (52.6)	98 (73.1)	23 (88.5)
≥ 60	9 (47.4)	36 (26.9)	3 (11.5)
Disease activity while taking first echocardiogram test			
Active	15 (78.9)	106 (79.1)	23 (88.5)
Stable	4 (21.1)	28 (20.9)	3 (11.5)

IQR: interquartile range.

Table 3. Valvular abnormalities in 134 patients with Takayasu arteritis. Values are n (%) unless otherwise specified.

Variable	Total	Aortic Valves	Mitral Valves	Tricuspid Valves	Pulmonary Valves
Type of valvular abnormality					
Insufficiency	134 (100)	84 (62.7)	55 (41.0)	19 (14.2)	7 (5.2)
One valve involved	90 (67.2)	59 (44.0)	24 (17.9)	7 (5.2)	0
More than 1 valve involved	44 (32.8)	25 (18.7)	31 (23.1)	12(9.0)	7 (5.2)
Stenosis	1 (0.6)	1 (0.6)	0	0	0
Others					
Thickening of aortic valves	12 (9.0)				
Anterior mitral valve leaflet prolapse	8 (6.0)				
Degree of valvular abnormalities					
Mild insufficiency	108 (80.6)	52 (38.8)	42 (31.1)	9 (6.7)	5 (3.7)
Medium to severe insufficiency	56 (41.8)	30 (22.4)	14 (10.4)	10 (7.5)	2 (1.5)
Mild stenosis	1 (0.6)	1(0.6)	0	0	0
Combined with other cardiac abnormalities	30 (22.4)	17 (12.7)	17 (12.7)	7 (5.2)	4 (3.0)
Enlargement of left atrium	21 (15.7)	10 (7.5)	16 (11.9)	5 (3.7)	4 (3.0)
Enlargement of left ventricle	15 (11.2)	5 (3.7)	11 (8.2)	4 (3.0)	3 (2.2)
Enlargement of right atrium	9 (6.7)	3 (2.2)	7 (5.2)	6 (4.5)	2 (1.5)
Enlargement of right ventricle	6 (4.5)	0	4 (3.0)	4 (3.0)	2 (1.5)
Dilatation of aortic root	8 (6.0)	8 (6.0)	2 (1.5)	1 (0.6)	0
More than 1 abnormality	18 (13.4)	7 (5.2)	12 (9.0)	7 (5.2)	4 (3.0)

when compared with the control group. The level of high-sensitivity CRP (hs-CRP) was higher in the heart involvement group (median was 10.0 mg/l), and the difference was significant when compared with the control group (median was 7.0 mg/l; p = 0.017). Renal dysfunction was more common in the heart involvement group (28/164, 17.1%) when compared with the control group (19/247, 7.7%; p = 0.003; Table 1).

TA-related interventions and mortality. In our study, 119 operations and interventions were performed during different stages of disease, and 12 patients died, with a median age of 33.5 years (19.8–59.8) during their hospital stay. The median survival time was 102.5 months (46.0–242.5). The type of interventions and causes of death were collected and analyzed in a previous article[10].

Table 4. Review of other studies for cardiac abnormalities of Chinese patients with Takayasu arteritis. Values are % unless otherwise specified.

Variable	Yang, *et al*[5]	Zhu, *et al*[4]	Jiang, *et al*[9]	Wan, *et al*[8]	This Study
n	566	524	290	85	411
Heart involved	ND	8.6	ND	64.7	39.9
Myocardial abnormalities	ND	2.3	ND	7.1	6.3
Coronary arterial abnormalities	11.7	0.6	ND	10.6	4.6
Valvular abnormalities					
Aortic insufficiency	36.7	3.2	14.5	34.1	20.4
Aortic stenosis	ND	0.2	0.0	0.0	0.2
Mitral insufficiency	15.2	4.6	8.3	15.3	13.4
Tricuspid insufficiency	ND	4.4	4.5	14.1	4.6
Pulmonary insufficiency	ND	0.8	3.1	4.7	1.7

ND: no data.

DISCUSSION

TA is a chronic systemic vasculitis. The majority of patients with TA are women under 40 years old[1]. The median age at disease onset in our study is 23.0 years old, and the sex ratio is 1:3.8 (86 men, 325 women), numbers that are consistent with another study in Chinese patients with TA[5]. Heart involvement is not rare in TA, which may include all structures of the heart such as coronary artery, valve, myocardium, and pericardium. The reports in the literature had demonstrated that 8.6% of Chinese patients with TA might have heart involvement[4], but we found 39.9% (164/411) in our study. In patients with heart involvement in our study, the median age at disease onset was 23.0 years, and the sex ratio was 1:3.4, which were not significantly different from those patients without heart involvement. The median disease duration at first admission of the heart involvement group was longer than that of the control group, and the difference was significant (Table 1). This suggested that cardiac abnormalities might be more common in patients with TA with longer disease duration. Further, there was an upward tendency of disease duration while patients with heart involvement were subdivided into patients with myocardial abnormalities, valvular abnormalities, and coronary arterial abnormalities. Meanwhile, a downward trend of age at disease onset was found in those subgroups (Table 2). This might suggest that myocardial abnormalities might develop more rapidly in patients with younger age at onset, while coronary arterial abnormalities were to the contrary and valvular abnormalities were intermediate. This might be caused by the differences in the inflammatory process developing in these cardiac structures. Myocardial abnormalities might result from infiltration of inflammatory cells, inflammation of cardiomyocytes, and deposition of extracellular matrix[11]. Valvular abnormalities might be caused by chronic fibrosis of valves and destruction of annulus tissue. Coronary arterial abnormalities might result from migration of vascular smooth muscle cells and deposition of extracellular matrix.

Multiple cardiac abnormalities could be found in patients with type V Numano angiographic pattern, a finding consistent with other studies in Chinese patients with TA[8,12]. So it might be reasonable to have Doppler echocardiography performed in patients with type V angiographic pattern when the diagnosis of TA is established.

Coronary artery involvement in TA is common in patients with TA, and its occurrence rate varied from 10% to 30% in previous reports[13,14,15], while the prevalence ranged from 7.7% to 16.4% in Chinese patients[5,8,16,17], and 4.6% in our study. Because coronary angiography was not routinely performed in patients with TA, the rate of coronary involvement in TA might be underestimated. Because coronary arteries could be involved in the whole disease process of TA, the stenosis and occlusion were more frequently found at the bifurcation and proximal segments of coronary arteries[18], and the subsequent myocardial ischemia was one of the causes of death in TA. Therefore, early detection of coronary artery involvement, especially before occlusion, was important to reduce the mortality rate of patients with TA. In addition to classical catheter angiography examination, which is still the gold standard for diagnosis, CTA and magnetic resonance imaging of coronary arteries could also demonstrate abnormalities of vessel wall and change of vessel lumen simultaneously. When coronary artery involvement is suspected, patients should undergo coronary angiography without delay. Coronary abnormalities were usually discovered simultaneously with other vessel abnormalities consistent to TA in more than 95% patients[19]. Stenosis of coronary artery lumen could be the result of intima proliferation, thickening of media and adventitia, fibrosis, and contracture of vessel wall. Inflammation of vessel wall would accelerate the process of atherosclerosis, leading to early-onset atherosclerosis of coronary arteries[2,20]. The level of hs-CRP had been shown to be a possible independent risk factor for TA combined with coronary artery involvement[21]. Nineteen patients (19/164, 11.6%) had coronary artery involvement in our study, and the level of hs-CRP was significantly higher in the heart involvement group than that in the control group, which also suggested that elevated hs-CRP might be associated with cardiac abnormalities in Chinese patients with TA.

Valvular abnormalities in patients with TA presented mainly as insufficiency, especially aortic insufficiency, the most common finding in TA[1,9]. In our study, 134 cases (134/411, 32.6%) with valvular abnormalities had valve insufficiency, in which 84 patients (84/411, 20.4%) had aortic insufficiency, which was consistent with previous studies. The incidence rate of aortic insufficiency varied from 7.0% to 20.0% in other studies[1,22], 18.0% in a Korean report and higher in active stage of TA[23]. The incidence of aortic insufficiency reported in Chinese patients with TA ranged from 14.5% to 36.7%[5,9]. The pathogenesis of aortic regurgitation was considered to be related to thickening of aortic valves

and enlargement of aortic root[24]. We found both valve thickening and dilated aortic root in our study. Enlargement of cardiac chambers, especially the left ventricle, could be caused by aortic regurgitation. Jiang, *et al* also reported other types of valvular insufficiency, including mitral, tricuspid, and pulmonary valve insufficiency[9]. The reported incidence rate of mitral insufficiency ranged from 4.6% to 15.3%[4,5,8,9], while in our study it was 13.4% (55/411), including 17 cases with enlargement of left cardiac chambers in Doppler echocardiography. Insufficiency of tricuspid or pulmonary valves was relatively uncommon. Valvular stenosis was rare in patients with TA. Only 1 patient in our center had ever been found to have mild aortic stenosis[4].

Myocardial abnormalities were reported in 24.4% to 27.0% Chinese patients with TA, including myocarditis, enlargement of cardiac chambers, and dilated cardiomyopathy[4,11]. The incidence rate of myocardial abnormalities in our study was 6.3% (26/411). The pathogenesis of myocardial abnormalities was unclear, while Pan, *et al* speculated that similar inflammation in the vessel wall of arteries could occur in the myocardium[11]. The most common clinical feature of myocardial abnormalities in TA was heart failure, and some without evident symptoms[12]. The incidence rate of heart failure in patients with TA was 13.2% in the study by Lee, *et al*[23], and 26.7% in Chinese patients with TA reported by Yang, *et al*[5], while it was up to 65.0% in patients with TA combined with myocardial abnormalities in Pan, *et al*[11]. In our study, heart failure was found in 14.8% (61/411) of patients with TA, but this percentage was increased to 92.3% (24/26) in patients with myocardial abnormalities. The age at onset of patients with TA with myocardial abnormalities might be younger in several reports[12]. The median age at onset of our study was 18.8 years (15.9–24.1) in patients with myocardial abnormalities, which was similar to the reports in the literature, but younger than 23.0 years (17.3–30.0) in patients with cardiac abnormalities. This might suggest that myocardial abnormalities in young patients with TA might be insidious at onset and could lead to heart failure and poor prognosis.

The prognosis of TA complicated with cardiac abnormalities was generally poorer than without because cardiac complications have been known to be the common cause of death in these patients[5,18]. Treatment should focus on controlling TA disease progress. Intervention or surgical operation should be considered for severe TA-related cardiac abnormalities that might lead to heart failure. The right time of operation should be based not only on the TA disease activity, but also the severity of the abnormalities. As in patients with acute coronary syndrome, revascularization should be considered in most cases to avoid irreversible damage of myocardium, but medical treatment for TA should be initiated at the same time[14].

The major limitation of our study is that only inpatients with complete angiography evaluation are included, and no followup information is available. Therefore, the selection of the study patients is biased, and the prognosis of these patients could not be analyzed. A few patients had not taken the Doppler echocardiography test, which could increase the selection bias as well. The retrospective analysis and chart review of our study have recall bias, and compromise the power of the conclusion. The lack of a standardized protocol for treatment is another important limitation of our study. Further prospective longitudinal study is needed.

Patients with TA complicated with cardiac abnormalities are not rare, especially in patients with type V blood vessel involvement. Therefore, we suggest that echocardiography should be performed when the diagnosis of TA is established, especially in patients with Numano type V blood vessel angiography pattern. Correct diagnosis and proper treatment in early stages of TA may improve the longterm prognosis. TA with cardiac abnormalities as the initial manifestation is sometimes easily misdiagnosed, or diagnosis is delayed. When atypical myocardium, coronary arteries, or valves involvement were found, especially in young women with asymmetric blood pressure and pulsation, TA should be considered.

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