Takayasu's arteritis in Turkey – clinical and angiographic features of 248 patients

M. Bicakcigil[1], K. Aksu[2], S. Kamali[3], Z. Ozbalkan[4], A. Ates[4], O. Karadag[5], H.T.E. Ozer[6], E. Seyahi[7], S. Akar[8], F. Onen[8], A. Cefle[9], S.Z. Aydin[10], N. Yilmaz[10], A.M. Onat[11], V. Cobankara[12], E. Tunc[13], M.A. Ozturk[14], I. Fresko[7], Y. Karaaslan[4], N. Akkoc[8], A.E. Yücel[15], S. Kiraz[5], G. Keser[2], M. Inanc[3], H. Direskeneli[10]

Departments of Rheumatology at [1]Yeditepe University, Faculty of Medicine, Istanbul; [2]Ege University, Faculty of Medicine, Izmir; [3]Istanbul University, Istanbul Faculty of Medicine, Istanbul; [4]Ankara Numune Training and Research Hospital, Ankara; [5]Hacettepe University, Faculty of Medicine, Ankara; [6]Cukurova University, Faculty of Medicine, Adana; [7]Istanbul University, Cerrahpasa Faculty of Medicine, Istanbul; [8]Dokuz Eylül University, Faculty of Medicine, Dokuz Eylül University, Izmir; [9]Kocaeli University, Faculty of Medicine, Kocaeli; [10]Marmara University, Faculty of Medicine, Istanbul; [11]Gaziantep University, Faculty of Medicine, Gaziantep; [12]Pamukkale University Faculty of Medicine, Denizli; [13]Suleyman Demirel University, Faculty of Medicine, Isparta; [14]Gazi University, Faculty of Medicine, Ankara; [15]Başkent University, Faculty of Medicine, Ankara, Turkey.

Muge Bicakcigil, MD; Kenan Aksu, MD; Sevil Kamali, MD; Zeynep Ozbalkan, MD; Askin Ates, MD; Omer Karadag, MD; Huseyin T.E. Ozer, MD; Emire Seyahi, MD; Servet Akar, MD; Fotos Onen F, MD; Ayse Cefle, MD; Sibel Zehra Aydin; Neslihan Yilmaz; Ahmet Mesut Onat, MD; Veli Cobankara, MD; Ercan Tunc, MD; Mehmet Akif Ozturk, MD; Izzet Fresko, MD; Yasar Karaaslan, MD; Nurullah Akkoc, MD; Ahmet Eftal Yücel, MD; Sedat Kiraz, MD; Gokhan Keser, MD; Murat Inanc, MD; Haner Direskeneli, MD.

Please address correspondence to:
Muge Bicakcigil, MD,
Yeditepe Universitesi Hastanesi,
Devlet yolu Ankara cad. No:102/104,
34752 Kozyatağı, İstanbul, Turkey.
E-mail: mbicakcigil@yeditepe.edu.tr
or: muge.b@superonline.com

Received on January 7, 2009; accepted in revised form on April 17, 2009.

Clin Exp Rheumatol 2009: 27 (Suppl. 52): S59-S64.

Key words: Takayasu's arteritis, clinical and angiographic features, prognosis.

Competing interests: none declared.

ABSTRACT

Objective. *Takayasu's arteritis (TA) is a chronic, inflammatory vasculitis affecting the aorta and its major branches. Although it is more prevalent in Far-East Asia, the distribution of the disease is worldwide with different vascular involvement patterns and clinical manifestations. The objective of this study was to evaluate the demographic, clinical, angiographic and prognostic features of TA patients in Turkey.*

Methods. *Clinical and angiographic findings of 248 TA patients (228 female, 27 male) followed at 15 Rheumatology Centers were prospectively evaluated according to a predefined protocol.*

Results. *The mean age was 40.1 years (30.2 years at the clinical onset). Clinical manifestations included constitutional symptoms in 66%, absent or diminished pulses in 88%, bruits in 77%, extremity pain in 69%, claudication in 48%, hypertension in 43% and cerebrovascular accidents (CVA) in 18% of the patients. Renal artery stenosis, aortic regurgitation and pulmonary hypertension were present in 26%, 33% and 12%, respectively. According to the new angiographic classification, type V (50.8%) and Type I (32%) were the most frequent types of involvement. Corticosteroids were the main treatment in 93% of the patients alone (9%) or in combination with immunosuppressive agents (84%). Most frequently preferred immunosuppressive agents were methotrexate (63%), azathioprine (22%) and cyclophosphamide (13%). Remission was observed at least once in 94% of the patients and sustained remission in 71% during follow-up.*

Conclusion. *The demographical, clinical and angiographic findings of TA patients in our series were similar to those reported from Japan, Brazil and Colombia. Combination therapies with immunosuppressive agents were the preferred choice of treatment in Turkey.*

Introduction

Takayasu's arteritis (TA) is a chronic, inflammatory disease that primarily involves large vessels such as the aorta and its main branches, including the pulmonary and coronary arteries. It predominantly affects women and usually has its onset during the second or third decades of life. The early systemic phase is characterized by the presence of nonspecific inflammatory features. During the later stages, evidence of vascular involvement and insufficiency becomes clinically apparent due to dilatation, narrowing or occlusion of the proximal or distal branches of the aorta (1, 2).

The disease was initially thought to affect young female patients only from the Far-East Asia. However, over the last decades, reports from different geographical regions showed that TA can affect individuals from both genders, at any age and in all ethnic groups with a worldwide distribution. Moreover, TA shows different patterns of arterial involvement, disease expression and prognosis in different regions of the world (2-20).

The objective of this study was to evaluate the clinical, angiographic and prognostic features of a large group of TA patients followed at different Rheumatology Clinics in Turkey.

Materials and methods

In this multicenter, prospective study, we evaluated the clinical and demographic profiles of 248 patients with Takayasu's arteritis followed at the Rheumatology outpatient clinics of 15 University and State Hospitals in Turkey between 1999 and 2008. All

patients fulfilled the proposed classification criteria of the American College of Rheumatology for Takayasu's Arteritis (21). Clinical and angiographic findings were assessed according to a predefined protocol. Clinical data were reviewed with special attention to medical therapy, surgical procedures performed and any associated autoimmune or rheumatological disorders. A detailed clinical examination for asymmetry or absence of arterial pulsations, presence of a bruit over the aorta or its branches and blood pressure recording in all four limbs were carried out with also an ophthalmological examination to document the presence of hypertensive changes or Takayasu's retinopathy in a subgroup of patients (n=161). Classical ophthalmic features of the disease due to reduced ocular perfusion such as dilatation of small vessels, capillary microaneurysm formation, drop-out and arterio-venous anastomoses were accepted as Takayasu's retinopathy (22).

We defined active disease using NIH guidelines, including onset or worsening of at least 2 of the following disease features: 1-presence of systemic signs or symptoms, 2-elevation of acute-phase reactants, 3- onset of signs or symptoms of vascular insufficiency, 4-angiographic progression (15). Remission was defined as the resolution of clinical and laboratory features of active disease and the absence of new vascular lesions. Sustained remission was defined as remission for at least 6 months while on a treatment regimen that included 10 mg/day of prednisolone (18).

All patients underwent full aortography or digital subtraction angiography (DSA) except one who had a left nephrectomy operation. She was diagnosed by clinical history and Doppler ultrasonography. The angiographic findings were grouped according to the angiographic classification for Takayasu's arteritis, defined at the International Conference on Takayasu's Arteritis in Tokyo in 1994 (23). The arteriographic classification is as follows: Type I involves branches of aortic arch, Type IIa involves ascending aorta, aortic arch and its branches, Type IIb a combination of Type IIa and the involvement of thoracic descending aorta, Type III involves the thoracic descending aorta, the abdominal aorta and/or renal arteries, Type IV involves only the abdominal aorta and/or renal arteries, Type V a combination of Type IIa and Type IV. Patients were evaluated for the presence of aortic regurgitation and pulmonary hypertension by transthoracic echocardiography. The study was approved by the Research Ethics Committee of Marmara University School of Medicine and written informed consent was obtained from each patient.

Statistical analysis

All values were expressed as the mean ± standard deviation. The chi square test was used to compare clinical manifestations and arterial involvement between male and female patients. A *p*-value less than 0.05 was considered to be significant. Statistical analysis was performed using the GraphPad-InStat 3 application package.

Results

Two hundred and forty-eight TA patients (221 female and 27 male, F/M: 8.2/1) with a mean age of 40.1 years (range 19-76 years) were studied. The mean age at clinical onset and at the time of the diagnosis was 30.2 years (range 8-65 years) and 33 years (range 12-70 years), respectively. The interval between the onset of symptoms attributable to TA and the diagnosis ranged from 0 to 240 months, with a mean of 34.2 months. The mean follow-up time was 87.1 months (range 12-361 months). In 35 (14%) patients, symptoms related with TA had started after the age of 40 years. None of these patients had classical features of giant-cell arteritis (GCA) such as temporal artery or scalp tenderness, decreased or absent pulse, visual loss, and jaw claudication or new-onset headache. There was also one family with two siblings diagnosed with TA. The patients' demographic profiles were summarized in Table I.

Constitutional symptoms such as low-grade fever, weight loss, weakness and loss of appetite were present in 163 of the patients (66%) before the vascular signs and symptoms arose. The most frequently encountered symptom was weakness (56%). The systemic and specific symptoms and signs associated with TA and observed during the course of the disease were shown in Table II.

Signs and symptoms of vascular involvement were observed in 97% of the patients. The most frequent vascular signs were the decreased or absent peripheral arterial pulses (88%) and bruits (carotid: 59%, subclavian: 49%, abdominal: 22% and femoral: 9.8%). A blood pressure difference was detected in 81% of the patients and hypertension was observed in 43%. Claudication and extremity pain were encountered in 48% and 69% of the patients, respectively. Renal artery stenosis was present in 28% of patients. Twenty-seven patients (11%) were also reported to experience the Raynaud's phenomenon.

Fifty-seven percent of the study population experienced cardiac symptoms including palpitations, dyspnea and chest pain in decreasing order with 37%, 22% and 17%, respectively. A history of myocardial infarction was present in 16 patients (6.4%), whereas 33% of the study population had aortic valve regurgitation, 12% had pulmonary hypertension and 4.8% had pericarditis.

One hundred and fifty-six of TA patients (63%) had central nervous system or ocular signs or symptoms. Headache was the most prominent neurological complaint (48%), patients also experienced blurred vision (21%) and syncope (19%). Cerebrovascular accidents were observed in 18% of the patients (15% stroke and 3% transitional ischemic attack).

Ophthalmological examination of 161 patients revealed that 29% of the cases had hypertensive and 6.8% had Takayasu's retinopathy. Additionally, cataract was present in 4, glaucoma in 2, and uveitis in 4 TA patients.

Musculoskeletal symptoms were present in 42% (arthralgia: 39%, myalgia: 30%, and arthritis: 7.7%). Arthralgia and arthritis were mainly in the large joints of the lower extremities. Erythema nodosum was observed in 8.8% of the cases.

By using the 1994 angiographic classification for Takayasu's arteritis (23), type V (n=126, 51%) was the most frequent involvement pattern among the study population, followed by type I (n=79,

Table I. Demographic profiles of 248 TA patients.

	Min.	Max.	Mean ± SD
Age	19	76	40.1 ± 14
Age at clinical onset (years)	8	65	30.2 ± 14
Age at the time of diagnosis (years)	12	70	33.1 ± 12
Delay in diagnosis (months)	0	240	34.2 ± 44
Follow-up time (months)	12	361	87.1 ± 56

32%) involvement. The other involvements in descending order were as follows: Type IIa in 17 (6.9%), type IV in 9 (3.7%), type IIb and type III in 8 patients each (Table III). Although pulmonary and coronary angiographies were not routinely performed, coronary and pulmonary involvements were detected in 22 (8.9%) and in 17 cases (6.9%), respectively. Two patients had fistula formation between bronchial artery and coronary artery resulting in coronary steal syndrome. When we compared clinical and angiographic features, no significant difference was observed between male and female patients.

Table II. Systemic and specific symptoms and signs of 248 TA patients.

Clinical manifestations	n.	(%)
Systemic symptoms	163	(66%)
Fatigue/malaise	139	(56%)
Fever	68	(27%)
Significant weight loss	62	(25%)
Loss of apatite	84	(34%)
Vascular	240	(97%)
Absent pulses or diminished pulses	218	(88%)
Asymmetric or absence of blood pressure	201	(81%)
Extremity pain	171	(69%)
Claudication	119	(48%)
Bruits	190	(77%)
Carotid	146	(59%)
Subclavian	121	(49%)
Abdominal	55	(22%)
Femoral	24	(9.6%)
Hypertension	106	(43%)
Pain over artery	32	(13%)
Raynaud's phenomenon	27	(11%)
Renal artery stenosis	69	(28%)
Ocular	57	(36%)
Hypertensive retinopathy	46/161	(29%)
Takayasu's retinopathy	11/161	(6.8%)
Central nervous system	156	(63%)
Syncope	47	(19%)
Headache	119	(48%)
Dizziness	59	(24%)
Visual disturbances	53	(21%)
Stroke	37	(15%)
Transient ischemic attack	7	(3%)
Cardiac	141	(57%)
Exertional dyspnea	54	(22%)
Palpitation	91	(37%)
Angina pectoris	41	(17%)
Pericarditis	12	(4.8%)
Aortic regurgitation	61/184	(33%)
Pulmonary hypertension	22/184	(12%)
Musculoskeletal	104/248	(42%)
Arthralgia	97	(39%)
Myalgia	74	(30%)
Synovitis	19	(7.7%)

In the angiographic evaluations, most frequently involved arteries were subclavian (76%), carotid (52%) and renal arteries (28%). The types of lesions were stenosis (78%), occlusion (46%), dilatation (18%), and irregularity of the vascular walls (17%). The distribution of arterial involvement was given in detail in Table IV.

Of the 106 hypertensive patients, 65% had renal artery involvement. Carotid (51%) and abdominal aorta (42%) involvements were the most prominent features at the remaining 37 hypertensive patients. A carotid and/or vertebral artery involvement was present in 78% of patients who had suffered cerebrovascular accidents.

Six of the study group had Hashimato tyroiditis. Ankylosing spondylitis (n=5), psoriasis (n=4) and inflammatory bowel disease (n=2) were among the other systemic inflammatory disorders. Two patients had sensorineural hearing loss. Amyloidosis, vitiligo, leucocytoclastic vasculitis, familial Mediterranean fever and systemic sclerosis were diagnosed in one patient each.

With respect to treatment, all patients were treated with anti-platelet or anticoagulant medications. Only seventeen (7%) patients who were in the late nonactive phase of the disease, were followed without any immunosuppressive (IS) medication. Two hundred thirty one patients (93%) with active disease were treated with corticosteroids (CS) alone (9%) or in combination with IS agents with a mean of 77 months duration. Corticosteroids were started at a dose of 0.5-1 mg/kg/day for 1 month and tapered to a maintenance dose of 5-10 mg/day by approximately 6 to 12 months. Immunosuppressive drugs were added to CS therapy in the great majority of patients (84%) to achieve and maintain disease remission and also used as a steroid-sparing agent. These included methotrexate in 63%, azathioprine in 22%, cyclophosphamide in 13%, leflunomide in 6% and mycophenolate mofetil in 3% of cases. Three resistant cases were treated with tumor necrosis factor inhibitors (Table V). As 25 patients were lost in follow-up, medical

Table III. Angiographic findings of 247 TA patients.

Lesion type	n. (%)
Type I	79 (32%)
Type IIa	17 (6.9%)
Type IIb	8 (3.2%)
Type III	8 (3.2%)
Type IV	9 (3.7%)
Type V	126 (51%)

treatment outcomes and prognosis were evaluated in 223 patients. After the initiation of the treatment, in 205 patients remission was observed in 94% at least once and first remission was achieved at a mean of 13.2 months (2 - 102 months). Sustained remission was observed in 71% of the patients during follow-up. In 12 patients, TA continued actively throughout the follow-up period. Twelve patients died during the follow-up and 16% of the patients were still active at the last visit.

Surgical procedures and percutaneous transluminal angioplasty (PTCA) were performed in 64 patients (26%), 30 patients had an angioplasty (12 renal, 10 subclavian, 5 iliac, 2 femoral, 2 axillary, 2 coronary artery and 1 abdominal aorta), 26 patients had a by-pass or a graft operation (3 abdominal aorta, 6 carotid, 8 subclavian, 4 coronary, 3 axillary, 3 femoral artery), three patients were operated because of aortic coarctation while another four were operated for aortic aneurysms. Three patients also had aortic valve replacement operation.

Discussion

In this study, clinical features, angiographic findings and prognosis of 248 patients diagnosed with Takayasu's arteritis from Turkey were evaluated. One of the characteristic epidemiologic features of TA is the preponderance of the disease in young women and its onset during the second or third decades of life. The female to male ratio among patients with TA varies from 9.4:1 to 1.6:1 in different series (2-20). The predominance of TA in females observed in our study is similar to Japan (6), Korea (7), USA (15) and Mexico (10), although such female predominance was not observed in India (9), Thailand (4), Israel (3), Colombia (13) and China (8).

Table IV. Arterial involvement and type of detected lesions in 247 patents with TA.

Vascular involvement	(%)	Stenosis (%)	Occlusion (%)	Dilatation (%)	Irregularity (%)
1. *Aorta*					
Ascending aorta	10	20		60	27
Aortic arch	10	16		33	58
Thoracic aorta	11	50		37	43
Abdominal aorta	22	71	9	35	12
2. *Aortic arch branches*					
Subclavian	76	63	57	6	8
Carotid	52	82	26	3	12
Vertebral	19	54	46	19	7
Axillary	11	56	43	7	
3. *Visceral branches*					
Celiac	11	62	37	6	11
Superior mesenteric	12	47	51	18	13
Inferior mesenteric	1	1			
4. *Renal artery*	26	85	13	8	17
5. I*liac artery*	13	72	32	6	
Total lesions		78	46	18	17

The average age of the patients at presentation in our study was 32.2 years and was similar to series from Asian and other countries (2, 3, 16).

Takayasu's arteritis and GCA share many clinical and pathological features. The most discriminatory feature between the two diseases is the age of onset (24). Thirty-five patients (14%) in our series had disease onset at age >40. In all these late-onset TA patients the presence of possible GCA-associated abnormalities were excluded. Recently other series from Korea (23%), Italy (17%), USA (13%) and Mexico (9%) also reported late-onset TA patients (20, 14, 15, 19). However, it was noted that a variant of GCA also exists in which involvement of the large arteries of upper extremities dominates the clinical presentation and often occurs without involvement of the cranial arteries (25).

Table V. Treatment modalities of 248 TA patients.

Treatment modalities	n. (%)
Only anti-aggregant	17 (7%)
Only steroid	22 (9%)
Steroid+immunosuppressive	209 (84%)
Methotrexate	156 (63%)
Azathioprine	55 (22%)
Cyclophosphamide	32 (13%)
Leflunomide	14 (6%)
Mycophenolate mofetil	9 (4%)
Anti-TNF	3 (1.2%)

Another approach suggested by Maksimowicz-McKinnon *et al*. may be to describe these late-onset patients as a "large-vessel vasculitis" group with TA and GCA in a single spectrum (26).

Diagnosis of TA is often delayed due to a lack of specific laboratory parameters and nonspecific clinical features in its acute stage (1). The interval from the initial symptoms until the time of the diagnosis was 34 months in our series, whereas American series reported only 10 months of delay with an overall excellent prognosis (15).

The early systemic phase is characterized by the presence of nonspecific inflammatory features (1). In our series 66% of patients had constitutional symptoms at disease initiation. While this finding shows a similarity with the Mexican (2), American (15) and Italian (14) series, systemic symptoms were encountered approximately in only one third of the patients in some other series (11, 12) and in Indian series systemic features of disease activity were reported infrequently (9).

Correlating with other series reported by Lupi-Herrera *et al*. (2) and Hall *et al*. (5), vascular ischemic signs such as vascular bruits and extremity pain were observed as the main findings of the disease in the majority of our patients. However, in series from India, hypertension had been a predominant feature and vascular ischemic findings were reported

infrequently (9, 6). When hypertension was compared with the results from India (9) where renal artery was involved indispensably and hypertension was observed in 77%, only 43% of Turkish patients had hypertension and renal artery stenosis was determined in only 65% of this group. Abdominal aorta and carotid artery were the other frequently involved arteries in hypertensive patients. Abnormal vascular compliance of aorta and dysfunctional aortic and carotid sinus baroreceptors might be alternative mechanisms in hypertensive cases without renal artery stenosis (9, 27).

In TA central nervous system disease is an important consequence of vascular injury and more than half of the patients may develop neurological manifestations (28). Serious cerebrovascular disease can occur either due to uncontrolled hypertension or as a result of carotid or brachiocephalic obstruction (29). Similar to findings reported by Kerr *et al*. from USA (15), carotid, vertebral artery or involvement of both were present in 78% of the patients with CVAs. In order to prevent these serious complications, an aggressive medical and surgical approach should be considered at early stages (30).

Pulmonary artery involvement, reported to range from 14% to 86% in various series (31, 32), was detected with a low frequency in 17 patients (6.9%). Pulmonary angiography is not recommended routinely for TA patients without clinical symptoms. Sharma *et al*. and Lupi *et al*. reported no pulmonary symptoms in their series of 44 and 22 patients respectively (31, 32). However, Lupi *et al*. (32) detected pulmonary involvement in 50% of their patients suggesting that despite a high frequency of pulmonary involvement, the presence of pulmonary symptoms in TA was unusual.

The frequency of ocular changes in aortitis syndrome has been reported in 10-60% of patients (2, 33). We determined findings compliant with Takayasu's retinopathy in only 6.8% of the patients who had a fundus examination. In patients with TA, routine fluorescein angiography may reveal further subtle changes (34). Four of our patients had uveitis. Kerr *et al*. reported uveitis in two patients who had associated sarcoidosis (15). However, no association with another systemic disorder was present in our patients with uveitis.

Turkoglu *et al*. and Ureten *et al*. reported their TA series consisting of 14 and 45 patients respectively from Turkey (35, 36). Although there was an insufficient number of patients in these series to compare, Turkoglu *et al*. (35) reported a F/M ratio of 3:7, whereas Ureten *et al*. (36) gave a similar gender ratio as in our series. Ureten *et al*. also reported a higher abdominal aorta involvement which might explain the higher frequency of hypertension observed in their series. Moreover, they described lower frequency of bruits, aortic valvular insufficiency and CVAs compared to our series.

The etiology of TA has not been clarified yet, but is thought to be autoimmune and an association with various autoimmune and inflammatory disorders has been reported in occasional case reports (15, 37-39). Ohta *et al*. observed that 11 out of 36 patients had at least one other chronic or subacute inflammatory disease (39). Similarly 24 patients (10%) had another autoimmune/inflammatory disease in our series. Although the association of various diseases with TA is of interest, there is no hypothesis at presence to propose a common immunological mechanism for the pathogenesis of TA and the associated diseases. Otherwise coexistence of these autoimmune/inflammatory diseases with TA may be coincidental. We also detected sensorineural hearing loss in two patients who were responsive to high-dose corticosteroids. There are previously reported cases of TA with sensorineural hearing loss which are also reported to show good-responses to CS therapy. Vasculitis of the arteries in the inner ear has been speculated as the etiopathogenetic mechanism in these cases (40).

Different patterns of vascular involvement in TA result in various clinical outcomes in different populations. Our patients had involvement of aortic arch and its main branches (type I, IIa, IIb) as frequently as observed in Japanese (17), Brazilian (11) and Colombian (12) patients. In contrast, abdominal aorta and renal artery involvement (type IV) was more frequently observed in India (28%) (17) and Thailand (19%) (4), where hypertension was the most prominent feature, while similar to Japan (1.3%) (17) type IV vascular involvement was present infrequently in our series (Table VI).

Sharma *et al*. reported that Indian male patients with TA had a higher frequency of abdominal aorta and renal artery involvement resulting in more frequent hypertension, whereas female patients were characterized by the involvement of aortic arch and its branches similar to Japanese patients. They pointed to a possible role of gender on the distribution of vascular lesions in TA (41). In our series hypertension was observed in 37% of male and 43% of female patients and renal artery was involved in 26% and 28%, respectively. Although we have limited number of male patients, our results did not support the observations made by Sharma *et al*.

Corticosteroids are accepted as the most effective therapy in controlling clinical manifestations and inducing remission of the disease. Corticosteroid therapy has been used in 93% of our patients similar to series from USA and Brazil (15, 11). In India, where most of the patients present in the chronic phase, only 15% were treated with CSs (9). It has been suggested that at least half of the patients with TA may be unresponsive to CSs or may have a relapsing disease (42). Moreover, chronic high-dose CS therapy results with serious complications. Various immunosuppressive agents are being employed frequently (84%) as steroid-sparing agents in Turkey. This IS usage seem to be higher compared to most other series (15-73%) from USA (18), India (9) and Mexico (19) and might have a favorable result on disease outcome and mortality. However, there are only a few, uncontrolled studies investigating the effect of various IS agents (43, 44) in TA, and multicenter, prospective, randomized-controlled studies aiming to explore the role of cytotoxic therapy on angiographic progression are required.

We can conclude that the aortic arch and its branches are involved with a high frequency as in series from Japan (6, 17), Brazil (11) and Colombia (12), leading to a high frequency of vascular ischemic findings in the majority of patients in

Table VI. Angiographic findings of TA patients in different geographic regions according to angiographic classification (19).

Country	Type I (%)	Type IIa (%)	Type IIb (%)	Type III (%)	Type IV (%)	TypeV (%)
Japan (n=80) (17)	24	11	10	0	1.3	54
India (n=102) (17)	7	1	6	3	28	55
Thailand (n=63) (4)	0	0	11	3	19	67
Brazil (n=32) (11)	21	4	0	4	14	57
Colombia (n=35) (12)	34	11	6	0	20	29
Turkey (n=248)	32	6.9	3.2	3.2	3.7	51

Turkey. In contrast to series from India (17) and Thailand (4), a female predominance was observed and hypertension and its complications were detected with a lesser extent due to a less frequent involvement of abdominal aorta and renal arteries. The unique demographic, clinical and angiographic findings in Turkish TA patients support the previous observations that ethnicity and geographic distribution may play an important role on the disease phenotype in TA.

References

1. NUMANO F: Takayasu arteritis - beyond pulselessness. *Intern Med* 1999; 38: 226-32.
2. LUPI-HERRERA E, SANCHEZ-TORRES G, MARCUSHAMER J, MISPIRETA J, HORWITZ S, VELA JE: Takayasu's arteritis. Clinical study of 107 cases. *Am Heart J* 1977; 93: 94-103.
3. ROSENTHAL T, MORAG B, RUBINSTEIN Z, ITZCHAK Y: Takayasu arteritis in Israel-update. *Int J Cardiol* 1996; 54 (Suppl.): 137-40.
4. SUWANWELA N, PIYACHON C: Takayasu arteritis in Thailand; clinical and imaging features. *Int J Cardiol* 1996; 54 (Suppl.): 117-34.
5. HALL S, BARR W, LIE JT, STANSON AW, KAZMIER FJ, HUNDER GG: Takayasu's arteritis: A study of 32 North American patients. *Medicine* (Baltimore) 1985; 64: 89-99.
6. KOIDE K: Takayasu arteritis in Japan. *Heart vessels* 1992; 7 (Suppl.): 48-54.
7. PARK YB, HONG SK, CHOI KJ *et al*.: Takayasu arteritis in Korea: clinical and angiographic features. *Heart Vessels* 1992; 7 (Suppl.): 55-9.
8. ZHENG D, FAN D, LIU L: Takayasu arteritis in China: a report of 530 cases. *Heart Vessels* 1992; 7 (Suppl.): 32-6.
9. JAIN S, KUMARI S, GANGULY NK, SHARMA BK: Current status of Takayasu arteritis in India. *Int J Cardiol* 1996; 54 (Suppl.): 111-6.
10. DABAGUE J, REYES PA: Takayasu arteritis in Mexico: a 38 year clinical perspective through literature review. *Int J Cardiol* 1996; 54 (Suppl.): 103-9.
11. SATO EL, HATTA FS, LEVY-NETO M, FERNANDES S: Demographic, clinical and angiographic data of patients with Takayasu arteritis in Brazil. *Int J Cardiol* 1998; 66 (Suppl.): 67-70.
12. CANAS CA, JIMENEZ CA, RAMIREZ LA *et al*.: Takayasu arteritis in Colombia. *Int J Cardiol* 1998; 66 (Suppl.): 73-9.
13. TEOH PC, TAN LK, CHIA BL, CHAO TC, TAMBYAH JA, FENG PH: Non-specific aorto-arteritis in Singapore with special reference to hypertension. *Am Heart J* 1978; 95: 683-90.
14. VANOLI M, DAINA E, SALVARANI C *et al*. for THE ITAKA STUDY GROUP: Takayasu arteritis: a study of 104 Italian patients. *Arthritis Rheum* 2005; 53: 100-7.
15. KERR GS, HALLAHAN CW, GIORDANO J *et al*.: Takayasu arteritis. *Ann Intern Med* 1994; 120: 919-29.
16. SHARMA BK, SAGAR S, SINGH AP, SURI: Takayasu Arteritis in India. *Heart Vessels* 1992; 7 (Suppl.): 37-43.
17. MORIWAKI R, NODA M, YAJIMA M, SHARMA BK, NUMANO F: Clinical manifestations of Takayasu Arteritis in İndia and Japan-new classification of angiografic findings. *Angiology*, 1997; 48: 369-79.
18. MAKSIMOWICZ-MCKINNON K, CLARCK TM, HOFFMAN GS: Limitations of therapy and a guarded prognosis in an American cohort of Takayasu's arteritis patients. *Arthritis Rheum* 2007; 56: 1000-9.
19. SOTO ME, ESPINOLA N, FLORES-SUAREZ LF, REYES PA: Takayasu's arteritis: clinical features in 110 Mexican Mestizo patients and cardiovascular impact on survival and prognosis. *Clin Exp Rheumatol* 2008; 26 (Suppl. 49): 9-15.
20. PARK MC, LEE SW, PARK YB, CHUNG NS, LEE SK: Clinical characteristics and outcomes of Takayasu's arteritis: analysis of 108 patients using standardized criteria for diagnosis, activity assessment, and angiographic classification. *Scand J Rheumatol* 2005; 34: 284-92.
21. AREND WP, MICHEL BA, BLOCH DA *et al*.: The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. *Arthritis Rheum* 1990; 33: 1129-34.
22. UYAMA M, ASAYAMA K: Retinal vascular changes in Takayasu disease (pulseless disease), occurrence and evaluation of the lesion. *Doc Ophthalmol Proc Ser* 1976; 9: 549-54.
23. HATA A, NODA M, MORIWAKI R, NUMANO F: Angiographic findings of Takayasu arteritis: new classification. Int J Cardiol 1996; 54 (Suppl.): 155-63.
24. MICHEL BA, AREND WP, HUNTER GG: Clinical differentiation between giant cell (temporal) arteritis and Takayasu's arteritis. *J Rheumatol* 1996; 23: 106-11.
25. BRACK A, MARTINEZ-TABOADA V, STANSON A, GORONZY JJ, WEYOND CM: Disease pattern in cranial and large-vessel giant cell arteritis. *Arthritis Rheum* 1992; 4; 311-7.
26. MAKSIMOWICZ-MCKINNON K, HOFFMAN GS: Large vessel vasculitis. *Clin Exp Rheumatol* 2007; 25: 58-9.
27. ASK-UPMARK E: On the pathogenesis of the hypertension in Takayasu's syndrome. *Acta Med Scand* 1961; 169: 467-77.
28. CANTU C, PINEDA C, BARINAGARREMENTERIA F *et al*.: Noninvasive cerebrovascular assesment of Takayasu arteritis. *Stroke* 2000; 31: 2197-202.
29. SHARMA BK, JAIN S, SAGAR S: Systemic manifestations of Takayasu arteritis: the expanding spectrum. *Int J Cardiol* 1996; 54 (Suppl.): 149-54.
30. GIORDANO JM, LEAVITT RY, HOFFMAN G, FAUCI AS: Experience with surgical treatment for Takayasu's disease. *Surgery* 1991; 109: 252-58.
31. SHARMA S, KAMALAKAR T, RAJANI M, TALWAR KK, SHRIVASTAVA S: The incidence and patterns of pulmonary artery involvement in Takayasu's arteritis. *Clin Radiol* 1990; 42: 177-81.
32. LUPI E, SÁNCHEZ G, HORWITZ S, GUTIERREZ E: Pulmonary artery involvement in Takayasu's arteritis. *Chest* 1975; 67: 69-74.
33. SAGAR S, KAR S, GUPTA A, SHARMA BK: Ocular changes in Takayasu arteritis in India. *Jpn Ophthalmol* 1994; 38: 87-102.
34. CHUN YS, PARK SJ, PARK IK, CHUNG H, LEE J: The clinical and ocular manifestations of Takayasu arteritis. *Retina* 2001; 21: 132-40.
35. TURKOGLU C, MEMIS A, PAYZIN S *et al*.: Takayasu arteritis in Turkey. *Int J Cardiol* 1996; 54 (Suppl.): 135-8.
36. URETEN K, OZTURK MA, ONAT AM *et al*.: Takayasu's arteritis: results of a university hospital of 45 patients in Turkey. *Int J Cardiol* 2004; 96: 259-64.
37. LENHOFF SJ, MEE AS: Crohn disease of colon with Takayasu's arteritis. *Post grad Med J* 1982; 58: 386-9.
38. NAKAYAMA H, SHIMAO S, HAMAMOTO T, MUNEMURA C, NAKAI A: Neutrophilic dermatosis of the face associated with aortitis syndrome and Hashimoto's thyroiditis. *Acta Derm Venereol* 1993; 73: 380-1.
39 OHTA Y, OHYA Y, FUJII K, TSUCHIHASHI T, SATO K, ABE I, LIDA M: Inflammatory diseases associated with Takayasu's arteritis. *Angiology* 2003; 54: 339-44.
40. KANZAKI J: Immune mediated sensorineural hearing loss. *Acta Otolaryngol* (Suppl.) 1994; 514: 70-2.
41. SHARMA BK, JAIN S: A possible role of sex determining distribution of lesions in Takayasu arteritis. *Int J Cardiol* 1998; 66 (Suppl.): 81-4.
42. SHELHAMER JH, VOLKMAN DJ, PARRILLO JE, LAWLEY TJ, JOHNSTON MR, FAUCI AS: Takayasu's arteritis and therapy. *Ann Inter Med* 1985; 103: 121-6.
43. HOFFMAN GS, LEAVITT RY, KERR GS, ROTTEM M, SNELLEN MC, FAUCI AS: Treatment of glucocorticoid-resistant or relapsing Takayasu arteritis with methotrexate. *Arthritis Rheum* 1994; 37: 578-82.
44. DAINA E, SCHIEPPATI A, REMUZZI G: Mycophenolate mofetil for the treatment of Takayasu arteritis: report of three cases. *Ann Intern Med* 1999; 130: 422-26.