THE AMERICAN COLLEGE OF RHEUMATOLOGY 1990 CRITERIA FOR THE CLASSIFICATION OF TAKAYASU ARTERITIS

WILLIAM P. AREND, BEAT A. MICHEL, DANIEL A. BLOCH, GENE G. HUNDER, LEONARD H. CALABRESE, STEVEN M. EDWORTHY, ANTHONY S. FAUCI, RANDI Y. LEAVITT, J. T. LIE, ROBERT W. LIGHTFOOT, JR., ALFONSE T. MASI, DENNIS J. McSHANE, JOHN A. MILLS, MARY BETTY STEVENS, STANLEY L. WALLACE, and NATHAN J. ZVAIFLER

Criteria for the classification of Takayasu arteritis were developed by comparing 63 patients who had this disease with 744 control patients with other forms of vasculitis. Six criteria were selected for the *traditional format classification*: onset at age ≤40 years, claudication of an extremity, decreased brachial artery pulse, >10 mm Hg difference in systolic blood pressure between arms, a bruit over the subclavian arteries or the aorta, and arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities. The presence of 3 or more of these 6 criteria demonstrated a sensitivity of 90.5% and a specificity of 97.8%. A *classification tree* also was constructed with 5 of these 6 criteria, omitting claudication of an extremity. The classification tree demonstrated a sensitivity of 92.1% and a specificity of 97.0%.

Takayasu arteritis (TA) is a chronic inflammatory disease of unknown etiology that primarily involves the aorta and its major branches. A review of the history of TA indicates early descriptions of patients in 1856, 1872, and 1908, but a full discussion of "pulseless disease" was not published until 1948. Two large series of patients from the Far East were described in 1967 (1) and 1978 (2). A recent review of American patients established the incidence of Takayasu arteritis in Olmsted County, Minnesota, as 2.6 cases per million persons per year (3). The 32 North American cases of TA described by investigators at the Mayo Clinic comprised 26 females and 23 Caucasians with a median age at diagnosis of 31 years (3).

The diagnosis of Takayasu arteritis often is delayed for months to years because many patients manifest nonspecific symptoms of fever, myalgias, arthralgias, weight loss, and anemia. The pathology in the aorta and branches during this early stage consists of granulomatous changes in the media and adventitia (3). This disease process progresses, at variable rates, to a sclerotic stage, with intimal hyperplasia, medial degeneration, and adventitial fibrosis. The aorta and involved arteries develop segmental narrowings, which lead to clinical manifestations of ischemia. However, the inflammatory and pulseless stages of Takayasu arteritis may overlap, and the course between the onset of symptoms and the establishment of

From the American College of Rheumatology Subcommittee on Classification of Vasculitis (Diagnostic and Therapeutic Criteria Committee of the Council on Research).

Supported in part by NIH grant AM-21393 to ARAMIS.

William P. Arend, MD: University of Colorado Health Science Center, Denver, CO; Beat A. Michel, MD: Rheumaklinik Universitätsspital, Zurich, Switzerland; Daniel A. Bloch, PhD: Stanford University, Stanford, CA; Gene G. Hunder, MD: Mayo Clinic, Rochester, MN, and Chair, Subcommittee on Classification of Vasculitis; Leonard H. Calabrese, DO: Cleveland Clinic Foundation, Cleveland, OH; Steven M. Edworthy, MD: University of Calgary, Calgary, Alberta, Canada; Anthony S. Fauci, MD: NIAID, NIH, Bethesda, MD; Randi Y. Leavitt, MD, PhD: NIAID, NIH, Bethesda, MD; J. T. Lie, MD: Mayo Clinic, Rochester, MN; Robert W. Lightfoot, Jr., MD: University of Kentucky, Lexington, KY; Alfonse T. Masi, MD, DrPH: University of Illinois College of Medicine, Peoria, IL; Dennis J. McShane, MD: Stanford University, Stanford, CA; John A. Mills, MD: Massachusetts General Hospital, Boston, MA; Mary Betty Stevens, MD: Johns Hopkins University, Baltimore, MD; Stanley L. Wallace, MD: SUNY Downstate Medical Center, Brooklyn, NY (Dr. Wallace is deceased); Nathan J. Zvaifler, MD: University of California, San Diego, San Diego, CA.

Address reprint requests to the American College of Rheumatology, 17 Executive Park Drive NE, Atlanta, GA 30329.

Submitted for publication October 2, 1989; accepted in revised form April 3, 1990.

Table 1. Age at clinical onset of disease in 63 patients with Takayasu arteritis

Age (years)	No. of patients
1–10	1
11–20	17
21–30	21
31–40	19
>40	4
Unspecified	1

the diagnosis may be highly variable (4,5). Retrospective reviews have emphasized the clinical and radiologic features of this disease (1–7). Based upon data from 96 Japanese patients with TA, criteria for the diagnosis have recently been proposed (8).

Corticosteroids in high doses are the primary treatment recommended for Takayasu arteritis. The erythrocyte sedimentation rate (ESR) is often an accurate guide for directing therapy. Unlike giant cell (temporal) arteritis, it has been emphasized that patients with Takayasu arteritis may require treatment with low doses of corticosteroids for extended periods of time (3). The efficacy of cytotoxic or immunosuppressive agents in Takayasu arteritis has not been established.

The present study, based upon prospectively

Table 2. Comparison of the sensitivity and specificity of potential criteria variables for Takayasu arteritis*

Criterion	No. of patients (n = 63)	No. of controls (n = 744)	Sensitivity (%)	Specificity (%)
History				
1. Arm claudication	62	733	45.2	97.4
2. Leg claudication	61	733	26.2	94.5
3. Arm or leg claudication†‡	62	732	51.6	93.3
4. Age at disease onset ≤40 years†‡§	62	739	95.2	68.1
5. Age at disease onset ≤25 years	62	739	50.0	81.5
6. Localized headache	62	742	35.5	69.9
Physical				
7. BP difference >10 mm Hg†‡§	43	482	72.1	95.6
8. Bruit over right or left subclavian arteries	53	541	58.5	97.6
9. Bruit over abdominal aorta	54	592	59.3	97.5
10. Subclavian or aortic bruit†‡§	57	519	80.7	95.2
11. Decreased subclavian artery pulse	46	515	50.0	98.4
12. Decreased brachial artery pulse†‡§	58	625	74.1	95.7
13. Decreased radial artery pulse	62	676	45.2	96.0
14. Aortic valve murmur†	62	735	32.3	96.1
Laboratory and radiologic				
15. ESR ≥50 mm/hour (Westergren)	59	662	57.6	37.5
16. Arteriographic narrowing of aorta or its primary branches	62	149	85.5	81.2
17. Arteriographic aneurysm of aorta or its primary branches	59	146	20.3	95.9
18. Arteriographic occlusion of aorta or its primary branches	62	144	51.6	86.1
19. Arteriographic narrowing of renal or abdominal arteries	49	179	75.5	74.9
20. Arteriographic narrowing of aorta or extracranial arteries	61	116	98.4	62.1
21. Arteriographic narrowing of aorta or branches, renal or abdominal arteries, or extracranial arteries	62	149	100.0	43.6
22. Arteriographic narrowing or occlusion of entire aorta, its primary branches or large arteries in the proximal upper or lower extremities†‡§	62	144	96.8	78.5

* Values are the number of cases or controls with the variable described or tested. The sensitivity is the proportion of cases positive for the variable tested or described. The specificity is the proportion of controls negative for the variable tested or described. BP = blood pressure (systolic; difference between arms); ESR = erythrocyte sedimentation rate.
† Criterion is one of the final "short list" of variables (n = 7) (see text).
‡ Criterion is used for the traditional format classification.
§ Criterion is used for the tree classification.

Table 3. 1990 criteria for the classification of Takayasu arteritis (traditional format)*

Criterion	Definition
Age at disease onset ≤40 years	Development of symptoms or findings related to Takayasu arteritis at age ≤40 years
Claudication of extremities	Development and worsening of fatigue and discomfort in muscles of 1 or more extremity while in use, especially the upper extremities
Decreased brachial artery pulse	Decreased pulsation of 1 or both brachial arteries
BP difference >10 mm Hg	Difference of >10 mm Hg in systolic blood pressure between arms
Bruit over subclavian arteries or aorta	Bruit audible on auscultation over 1 or both subclavian arteries or abdominal aorta
Arteriogram abnormality	Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not due to arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental

* For purposes of classification, a patient shall be said to have Takayasu arteritis if at least 3 of these 6 criteria are present. The presence of any 3 or more criteria yields a sensitivity of 90.5% and a specificity of 97.8%. BP = blood pressure (systolic; difference between arms).

gathered data, provides criteria that best classify patients with Takayasu arteritis in comparison with a control group of patients with other forms of vasculitis.

For a description of the patient selection and evaluation methods, see the articles by Hunder et al (9) and Bloch et al (10), which appear elsewhere in this issue of *Arthritis and Rheumatism*.

RESULTS

Patient population. Sixty-three patients with Takayasu arteritis were prospectively enrolled in the vasculitis criteria study, using the data collection form described by Hunder et al (9). In 62 patients, the diagnosis was supported by the presence of arteriographic abnormalities in the aorta and its primary branches. The comparison group consisted of 744 control patients with other forms of vasculitis.

Summary statistics of age, sex, and race of the 63 patients with TA and the 744 control patients with other forms of vasculitis are shown in the introductory paper by Hunder et al (9). There was a higher percentage of females (85.7%) and younger age (mean 26.4 years) in the TA patients compared with the control group. The ages at disease onset in the TA patients are shown in Table 1. Fifty-eight of the 63 patients were age 40 or younger at the onset of symptoms; age was not specified in 1 patient.

Table 2 lists the single variables and combinations that were chosen for further evaluation as possible criteria for TA. The initial univariate analyses indicated that these items might be possible discriminators of TA from other forms of vasculitis. Table 2 includes, for each variable or combination, the numbers of cases and controls, the sensitivity, and the specificity. The 7 "short-list" variables that, in the judgment of committee members, best identified Takayasu arteritis are also shown in Table 2.

Traditional format classification. Six of the 7 most discriminatory criteria (the "short list") were chosen for the classification of Takayasu arteritis using a traditional format rule (see ref. 10). One criterion, aortic murmur, had poor sensitivity (32.3%) despite its good specificity (96.1%), and it was not utilized in our further analyses.

Table 3 presents the definitions for the 6 criteria selected. Age ≤40 years was the sole demographic criterion; claudication of the arms or legs was the only historical criterion. Three of the criteria were findings from the physical examination: decreased brachial artery pulse, systolic blood pressure difference of >10 mm Hg (between arms), and the presence of a bruit over the subclavian arteries or aorta. The sixth criterion included focal or segmental abnormalities of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, as determined by arteriography.

Classification by the presence of 3 or more of these 6 criteria yielded a sensitivity of 90.5% and a specificity of 97.8%. With this traditional format rule, 6 (9.5%) of the 63 patients with TA did not meet the required 3 or more criteria for classification as having TA. These 6 patients met a total of 12 criteria, including age ≤40 at disease onset in all 6 and an abnormal arteriogram in 4 of them.

Using the traditional format rule, 16 (2.2%) of the 744 control patients were misclassified as having Takayasu arteritis. These 16 control patients met a total of 55 criteria, including decreased brachial artery pulse in 15, extremity claudication in 14, an abnormal arteriogram in 10, and a bruit over the aorta or subclavian arteries in 9. The diagnosis in 11 of these 16 misclassified control patients was giant cell arteritis. Other diagnoses included central nervous system vasculitis in 2, periarteritis nodosa in 2, and unspecified leukocytoclastic vasculitis in 1.

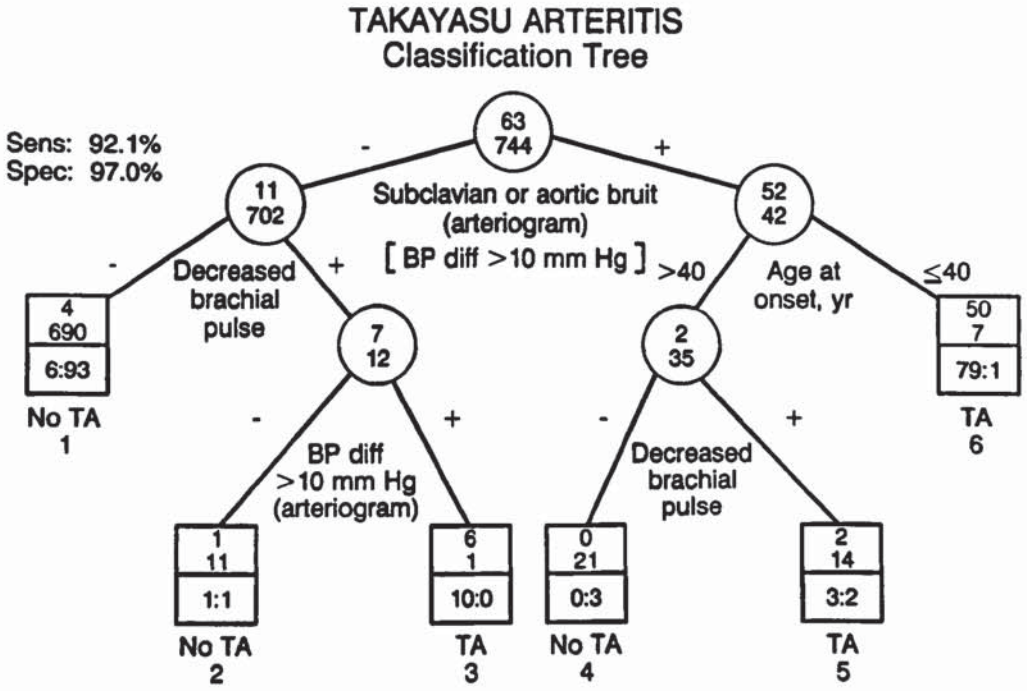

Figure 1. Classification tree for Takayasu arteritis (TA). The circles and boxes contain the number of patients with TA (top number) and the number of control patients with other forms of vasculitis (bottom number). The bottom half of the boxes shows the percentage of patients with TA (out of all TA cases) (left number) and the percentage of controls (out of all controls) (right number). Boxes specify whether patients are classified as having TA or not having TA (No TA); the numbers under these specifications are the subset numbers (see Table 3 for definitions of criteria and Table 4 for explanations of subsets.) Parentheses and brackets indicate the first and second surrogate variables, respectively, that are to be used when the dividing criterion is not defined. BP diff = difference (between arms) in systolic blood pressure.

Tree classification. The second method of classification was by classification tree (Figure 1). All 7 criteria in the "short list," as shown in Table 2, were considered as potential discriminators. The resulting 5 criteria, including an abnormal arteriogram as a surrogate (see ref. 10), were the same as those listed for the traditional format in Table 3, except for claudication of the extremities.

The primary variable separating the majority of the TA patients (right branch) from most of the control patients (left branch) was the presence of a bruit over the subclavian arteries or aorta. If this criterion was not defined, the first and second surrogate variables were arteriography and blood pressure difference of >10 mm Hg between arms, respectively. The variables utilized to further subdivide these groups are indicated in Figure 1 and in Table 4. The classification tree formed 6 subsets; 3 included subjects classified as having TA, and 3 included subjects classified as controls (non-TA). Most of the Takayasu arteritis patients (79%) were correctly classified by the presence of the 2 criteria listed under subset 6 in Table 4. An additional 8 Takayasu arteritis patients were correctly classified by the presence of criteria yielding subsets 3 and 5.

These results indicate that the most helpful criteria in classifying patients with Takayasu arteritis are a subclavian or aortic bruit, age ≤40 years at disease onset, decreased brachial artery pulse, and a blood pressure difference of >10 mm Hg between arms. Absence of 3 of these 4 criteria excludes the classification of TA.

Using the tree method of classification, 5 TA patients and 22 control patients were misclassified, giving a sensitivity of 92.1% and a specificity of 97.0%. Of the 5 patients misclassified as not having TA, none had a bruit over the subclavian or aortic artery, or, if this criterion was undefined, the surrogate criterion was negative, all were age 40 or younger, and 4 had positive arteriograms. Of the 22 misclassified control patients, 15 had giant cell arteritis. All of these 15 patients were over 40 years old, and 11 had positive

Table 4. 1990 classification tree for Takayasu arteritis (TA)*

TA subsets	No. of patients TA/non-TA	% correctly classified	% TA patients in subset	Non-TA subsets	No. of patients TA/non-TA	% correctly classified	% non-TA patients in subset
6. Subclavian or aortic bruit and age ≤40 at disease onset	50/7	88	79	1. Absence of subclavian or aortic bruit and normal brachial artery pulse	4/690	99	93
3. Decreased brachial artery pulse and BP difference >10 mm Hg (between arms)	6/1	86	10	2. Absence of subclavian or aortic bruit and BP difference <10 mm Hg (between arms)	1/11	92	1
5. Subclavian or aortic bruit and decreased brachial artery pulse	2/14	13	3	4. Subclavian or aortic bruit, age >40 at disease onset, and normal brachial artery pulses	0/21	100	3

* The subset numbers also appear below the subset boxes in Figure 1. Missing data rules: If the information on subclavian or aortic bruit is not available, substitute arteriogram; if the arteriogram data are not available, substitute blood pressure (BP) difference (systolic; between arms), or as listed. The classification tree yields a sensitivity of 92.1% and a specificity of 97.0%. See Table 3 for definitions of criteria.

arteriograms. The remaining 7 misclassified controls had 6 different diagnoses; all were 40 years old or younger, and only 1 had a positive arteriogram. Thus, the presence of giant cell arteritis and of an abnormal arteriogram may falsely lead to the classification of a patient as having Takayasu arteritis.

DISCUSSION

The classification of Takayasu arteritis includes 6 criteria for the traditional format and 5 criteria for the tree classification method. It should be emphasized that the 63 patients with TA were compared with a control group of 744 patients who had another form of vasculitis. Within this population of patients with vasculitis, it was possible to identify criteria for both the traditional and tree formats that had high degrees of sensitivity and specificity. These results indicate a basic clinical similarity of cases of Takayasu arteritis, namely, involvement of the aorta, its primary branches, or large proximal extremity arteries in a younger person.

The tree method of classification resulted in the formation of 3 subsets that contained 58 subjects classified as having Takayasu arteritis (Table 4). Subset 6, with 50 cases, was defined by the presence of a bruit over the aorta or subclavian arteries (or a surrogate variable) and age ≤40 at onset of the disease. Subset 3, with 6 cases, was defined by the presence of a decreased brachial pulse and a blood pressure difference of >10 mm Hg between arms (or an abnormal arteriogram as a surrogate). Subset 5, with 2 cases, was defined by the presence of a subclavian or aortic bruit (or a surrogate variable) and a decreased brachial artery pulse. The only other form of vasculitis in which these findings might be present would be giant cell arteritis; this diagnosis usually would be excluded by the age criterion.

These criteria sets should be easy to use in clinical studies. Arteriography is the only invasive test and should be performed in all patients suspected of having TA. However, a positive arteriogram can also be seen in patients with giant cell arteritis, and clinical criteria are necessary to differentiate giant cell arteritis from Takayasu arteritis. The remaining criteria can be obtained by taking the patient's history and performing a careful physical examination.

The criteria for classification of Takayasu arteritis established by this study can be compared with predominant disease characteristics emphasized in previous reviews. Based upon 96 Japanese patients with TA, one obligatory criterion of ≤40 years of age was recommended for diagnostic purposes (8). This mandatory requirement would prevent misclassification of older patients with giant cell arteritis. This same study suggested 2 major diagnostic criteria: arteriographic evidence of left and right midsubclavian artery stenosis or occlusion (8). This was followed by 9 minor diagnostic criteria including a high ESR of unknown cause, carotid artery tenderness, hyperten-

sion, aortic regurgitation, or arteriographic evidence of lesions in the pulmonary artery, left mid–common carotid artery, distal brachiocephalic artery, or thoracic or abdominal aorta (8).

In addition to the obligatory criterion of age ≤40, the presence of 2 major criteria, or 1 major and 2 minor criteria, or 4 or more minor criteria were said to suggest a diagnosis of Takayasu arteritis with a sensitivity of 84% (8). However, those 96 Japanese patients with TA were compared with only 12 patients with another disease of the aorta and not with a control group with other forms of vasculitis. The criteria recommended by the Japanese study demonstrated a greater sensitivity for patients with active disease than for those with inactive disease (8). Furthermore, these were recommended diagnostic criteria and not classification criteria as determined by our study.

An obligatory criterion of age ≤40 years at disease onset would have excluded 4 of our 63 patients, possibly because of a later onset of disease or because TA was not diagnosed in some patients until vascular ischemia had developed, at a later stage in the disease process. A high ESR, carotid artery tenderness, and/or hypertension are present in many patients with Takayasu arteritis. However, the present study indicates that these features lack high enough sensitivity and specificity to differentiate patients with TA from patients with other forms of vasculitis.

The nature of this study on classification of disease precludes an emphasis on some of the other aspects of diagnosis and treatment of Takayasu arteritis. These have been emphasized in recent retrospective reviews (1–8). Features of TA that are not recognized by these classification criteria but may be invoked in diagnosis include fever, postural dizziness, arthralgias, myalgias, weight loss, headache, and hypertension probably secondary to renal artery stenosis (3). The laboratory features of elevated ESR, anemia, or hypergammaglobulinemia are important supporting evidence, even though they may not be of value in a classification scheme. For purposes of diagnosis, all patients with suspected Takayasu arteritis should undergo a complete arteriographic study of the aorta and its major branches because multiple sites of segmental involvement are commonly found (3).

REFERENCES

1. Nakao K, Ikeda M, Kimata S-I, Niitani H, Miyahara M, Ishimi Z-I, Hashiba K, Takeda Y, Ozawa T, Matsushita S, Kuramochi M: Takayasu's arteritis: clinical report of eighty-four cases and immunological studies of seven cases. Circulation 35:1141–1155, 1967
2. Ishikawa K: Natural history and classification of occlusive thromboaortopathy (Takayasu's disease). Circulation 57:27–35, 1978
3. Hall S, Barr W, Lie JT, Stanson AW, Kazmier FJ, Hunder GG: Takayasu arteritis: a study of 32 North American patients. Medicine (Baltimore) 64:89–99, 1985
4. Shelhamer JH, Volkman DJ, Parrillo JE, Lawley TJ, Johnston MR, Fauci AS: Takayasu's arteritis and its therapy. Ann Intern Med 103:121–126, 1985
5. Ishikawa K: Patterns of symptoms and prognosis in occlusive thromboaortopathy (Takayasu's disease). J Am Coll Cardiol 8:1041–1046, 1986
6. Yamato M, Lecky JW, Hiramatsu K, Kohda E: Takayasu arteritis: radiographic and angiographic findings in 59 patients. Radiology 161:329–334, 1986
7. Perniciaro CV, Winkelmann RK, Hunder GG: Cutaneous manifestations of Takayasu's arteritis: a clinicopathologic correlation. J Am Acad Dermatol 17:998–1005, 1987
8. Ishikawa K: Diagnostic approach and proposed criteria for the clinical diagnosis of Takayasu's arteriopathy. J Am Coll Cardiol 12:964–972, 1988
9. Hunder GG, Arend WP, Bloch DA, Calabrese LH, Fauci AS, Fries JF, Leavitt RY, Lie JT, Lightfoot RW Jr, Masi AT, McShane DJ, Michel BA, Mills JA, Stevens MB, Wallace SL, Zvaifler NJ: The American College of Rheumatology 1990 criteria for the classification of vasculitis: introduction. Arthritis Rheum 33: 1065–1067, 1990
10. Bloch DA, Michel BA, Hunder GG, McShane DJ, Arend WP, Calabrese LH, Edworthy SM, Fauci AS, Fries JF, Leavitt RY, Lie JT, Lightfoot RW Jr, Masi AT, Mills JA, Stevens MB, Wallace SL, Zvaifler NJ: The American College of Rheumatology 1990 criteria for the classification of vasculitis: patients and methods. Arthritis Rheum 33:1068–1073, 1990