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Comparison of the 2022 ACR/EULAR classification criteria with the 1990 ACR classification criteria for Takayasu arteritis

Duygu Tecer, Mehmet Nur Kaya, Özlem Kılıç, Sedat Yılmaz
Gülhane Training and Research Hospital, Rheumatology Department, Ankara, Turkey

Abstract. *Background and aim:* Takayasu arteritis (TAK) mostly affects the aorta and its major branches and has an unclear origin. This study aimed to compare the 1990 American College of Rheumatology (ACR) classification criteria with the 2022 ACR/European League Against Rheumatism (EULAR) classification criteria for TAK on the basis of clinical data analysis of patients with TAK and other major vascular diseases. *Methods:* This retrospective study was conducted in a single-center. The results included 34 TAK patients routinely followed at a tertiary rheumatology center from October 2017 to February 2024. The accuracy, sensitivity, specificity, positive predictive values (PPV), negative predictive values (NPV), and area under the receiver operating characteristic (ROC) curve (AUC) of the classification criteria were compared. *Results:* The sensitivity (91.2%), specificity (90.9%), PPV (93.9%), NPV (86.9%), accuracy (94.4%) and AUC (0.983 (0.957-0.998)) of the 2022 ACR/EULAR classification criteria for TAK were higher than those of the 1990 ACR classification criteria for TAK (76.4%, 86.3%, 88.9%, 64.2% and 0.75, respectively), and the difference in AUC was statistically significant (0.860 (0.757-0.963), $p < 0.001$). *Conclusions:* The study concluded that the 2022 ACR/EULAR classification criteria were more appropriate for the patient population under investigation and exhibited superior classification performance in comparison to those in 1990. These findings are supported by clinical experience. It is evident that the findings of this study require further validation through the implementation of prospective multicentre studies with increased patient numbers.

Key words: Takayasu arteritis, classification, sensitivity, specificity

Introduction

Since Takayasu Arteritis (TAK) mainly affects the aorta and its major branches, it is categorized as a large vessel vasculitis. Nonetheless, there are some histological and clinical similarities with another large vessel vasculitis called giant cell (temporal) arteritis (GCA) (1). It is more prevalent in Asia, between 80% and 90% of cases are in women, and the age at onset is typically between 10 and 40 years. Due to the typically subacute start of symptoms in TAK, there is frequently a month to year-long delay in diagnosis, during which vascular disease may become evident and ischemic symptoms may occur (2, 3). TAK is characterized by abnormal cell-mediated immune responses, particularly involving cytotoxic lymphocytes such as natural killer cells and CD8+ T cells. These cells infiltrate the aortic tissue and contribute to vessel wall inflammation and damage (4). The repercussions of vascular disease are frequently identified as the initial sign of TAK. As narrowing, occlusion, or aneurysmal dilation of the arteries progresses, ischemic pain in the arms or legs and/or cyanosis, dizziness or reduced blood flow, arterial pain and tenderness, or nonspecific constitutional

Received: 23 April 2025
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Correspondence: Duygu Tecer, M.D.
Gülhane Training and Research Hospital, Rheumatology, Ankara, Turkey
E-mail: duygu-tecer@hotmail.com
ORCID: 0000-0002-8816-6181

symptoms occur (4, 5). Early symptoms of TAK are atypical, clinical manifestations vary greatly among individuals, and specific serological indicators are lacking, so the diagnosis remains challenging. Until today, the ACR's 1990 criteria are the most often used criteria in clinical trials for the classification of patients as TAK. These criteria consist of 6 items, and a patient meeting 3 or more of the 6 criteria can be classified as having TAK (6). Nevertheless, they have significant drawbacks, including the exclusion of individuals older than 40 and the scarcity of imaging techniques at the time (7). Updated classification criteria for TAK, the 2022 American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR), have been published. Scientists from different nations proposed several classification criteria for TAK after the first idea, and it was challenging to come to an agreement on all of them. Patients with a score of ≥ 5 points can be classified under these new classification criteria, which have a 99% specificity and 94% sensitivity (8). However, it should keep in mind that the incidence and clinical manifestations of TAK may vary by region due to the variability of environmental and ethnic differences. In order to verify the functionality of the 2022 ACR/EULAR classification criteria for TAK and to compare it with the 1990 ACR classification criteria in Turkish patients, this study analyze clinical data from patients with TAK and other major vascular illnesses.

Patients and Methods

Study subjects

This study was designed as a retrospective study conducted in a single tertiary rheumatology center. Diagnosis of two independent rheumatologists with a minimum of ten years of experience was used as gold standard. Thirty-seven patients with TAK who were initially diagnosed and regularly followed up were evaluated for inclusion in this study, and three patients were excluded due to insufficient data. A total of 34 patients who were regularly followed between October 2017 and February 2024 were included in the final analyses. Eighteen patients with atherosclerotic stenosis and four patients with GCA were included in the control group. Demographic data, clinical symptoms and imaging findings indicating vascular involvement were retracted from patient's electronical medical records. The 1990 ACR classification criteria and the 2022 ACR/EULAR updated classification criteria for TAK were used to re-score and classify of all patients. This study was approved by the local ethics committee in accordance with the tenets of the Declaration of Helsinki (date: 05.12.2024 and decision number: 2024/90).

Statistical analysis

Statistical analyses were performed using the MAC-compatible SPSS program, version 28. The Kolmogorov-Smirnov test was used to assess whether the variables were not normally distributed. Normally distributed variables were expressed as mean ± standard deviation (SD), non-normally distributed parametric variables as median (interquartile range - IQR), and categorical variables as number (n) and percentage (%). The chi-square test for categorical variables and Fisher's exact test (when the assumptions of the chi-square test were not valid) were used to compare demographic characteristics, clinical data, laboratory parameters, and imaging findings. When the data were normally distributed between the two groups, the independent samples T test was used, and when the data were not normally distributed, the Mann-Whitney test was used. Using the clinical diagnosis of rheumatologists as the gold standard, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy and area under the receiver operating characteristic (ROC) curve (AUC) of the classification criteria were compared.

Results

A total of 56 patients were included in the study. Thirty-four of these patients were diagnosed with TAK, and the remaining 22 patients diagnosed with other diseases with major vascular involvement were evaluated as the control group. The number of TAK patients diagnosed at the age of ≤60 years was 33 (97.1%), while 15 (68.1%) of the patients in the control group were diagnosed, and there was a significant difference between the two groups (p=0.031). Thirty-three (97.1%) of the TAK patients were female, and 8 (36.3%) of the patients in the control group were female, and there was a significant difference between the two groups (p < 0.001). The number of patients with reduced pulse in the upper extremity

was 30 (88.2%) in the patients diagnosed with TAK compared to 1 (4.5%) in the control group (p<0.001). Other information regarding demographic, clinical and imaging findings between both groups is shown in Table 1.

The sensitivity (91.2%), specificity (90.9%), PPV (93.9%), NPV (86.9%), accuracy (94.4%) and AUC (0.983 (0.957-0.998)) of the 2022 ACR/EULAR classification criteria for TAK were higher than those of the 1990 ACR classification criteria for TAK (76.4%, 86.3%, 88.9%, 64.2% and 0.75, respectively), and the difference in AUC was statistically significant (0.860 (0.757-0.963), p < 0.001) (Table 2; Figures 1, 2).

Discussion

Takayasu's arteritis is a vasculitis that has long been known to be a cause of stenosis as well as dilation or aneurysm formation of affected arteries (9). Although the pathophysiology of TAK is not fully known, immune cell types that play an important role in regulating genetic risk are thought to be important. The majority of invading cells in the aortic tissue were cytotoxic lymphocytes, particularly gamma-delta T lymphocytes, according to immunohistopathological analysis (10). Although the left middle or proximal subclavian artery is the most common initial vascular lesion, other branches of the aorta may be involved as the disease progresses. The pulmonary arteries and abdominal aorta are involved in about half of patients (11). A wide range of symptoms might result from the vessel's inflammatory process, which can cause the relevant artery segments to constrict, block, or enlarge. Takayasu arteritis is an uncommon disease that has recently gained more attention. However, due to the insidious nature of its course and the heterogeneity of its clinical manifestations, diagnosis and classification of TAK remain challenging (12). According to the ACR (1990), the classification criteria for TAK comprise six elements that are presently widely utilized in clinical practice. In the American population, the sensitivity and specificity of these criteria are 90.5% and 97.8%, respectively (6). In a large Chinese cohort, the 2022 criteria achieved a sensitivity of 92.6% and an AUC of 0.981, compared to 45.7% sensitivity and an AUC of 0.874 for the 1990 criteria, with similar improvements in positive and negative predictive values and overall accuracy (13, 14). The classification criteria for TAK were developed on the basis of a study that involved 63 patients with the disease and 744 patients with other forms of vasculitis who served as controls. The control

Table 1. Comparison of general status and clinical features between Takayasu arteritis and control groups

Variables	Takayasu arteritis (n=34)	Control group (n=22)	p
Age ≤ 60 years at time of diagnosis, n (%)	33 (97.1)	15 (68.1)	0.031
Clinical Criteria, n (%)			
Female	33 (97.1)	8 (36.3)	p<0.001
Angina or ischemic cardiac pain	7 (20.6)	10 (45.5)	0.048
Arm or leg claudication	9 (26.4)	6 (27.2)	0.952
Vascular bruit	18 (52.9)	4 (18.2)	0.009
Reduced pulse in upper extremity	30 (88.2)	1 (4.5)	p<0.001
Carotid artery abnormality	17 (50)	3 (13.6)	p<0.001
Imaging Criteria, n (%)			
Number of affected arterial territories (select one)			
One arterial territory	12 (35.3)	10 (45.5)	0.447
Two arterial territories	11 (32.3)	8 (36.4)	0.757
Three or more arterial territory	11 (32.3)	9 (40.9)	0.514
Symmetric involvement of paired arteries	5 (14.7)	6 (27.2)	0.565
Abdominal aorta involvement with renal or mesenteric involvement	6 (17.7)	6 (27.2)	0.391

Table 2. Comparison of evaluation indices of different diagnostic/classification criteria

Classification criteria	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)	AUC (95%)
1990 ACR	76.4	86.3	88.9	64.2	75.0	0.860 (0.757-0.963)
2022 ACR/EULAR	91.2	90.9	93.9	86.9	94.4	0.983 (0.957-0.998)

Abbreviations: AUC, receiver operating characteristic curve; ACR, American College of Rheumatology; EULAR, European Alliance of Associations for Rheumatology.

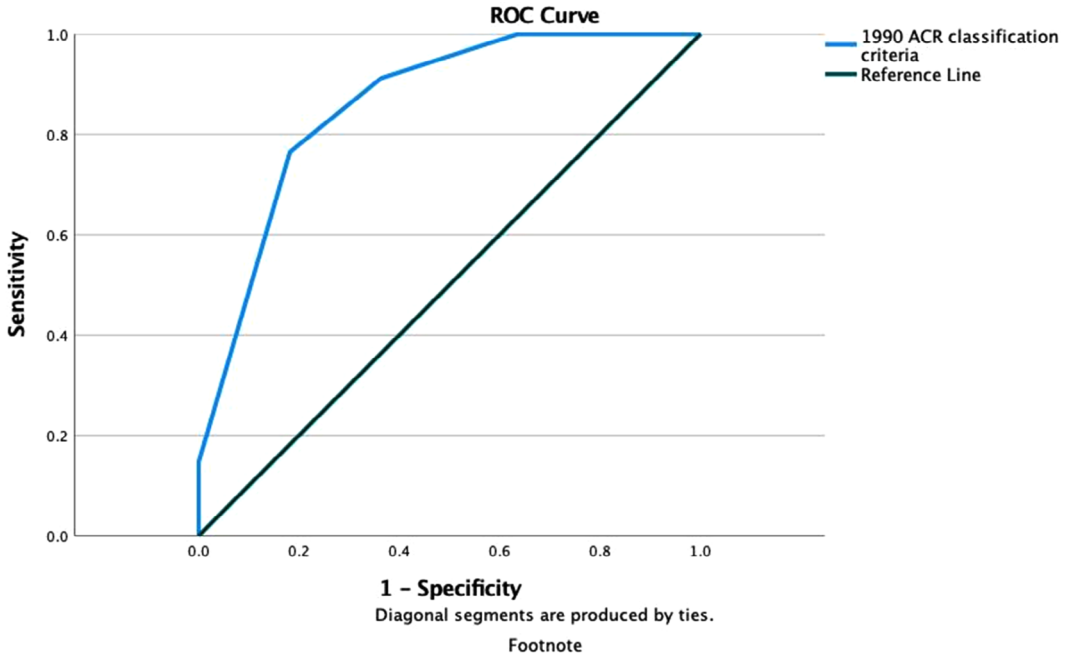

Figure 1. Comparison of the 1990 ACR classification criteria with the ROC curve.

group, which primarily comprised cases of small vessel vasculitis, did not include the following conditions: atherosclerosis, congenital aortic disease, viral vasculitis, and other macrovascular disorders (6). The 2022 ACR/EULAR classification criteria for TAK represent a significant advancement over the 1990 ACR criteria, particularly in terms of sensitivity and the incorporation of modern imaging techniques. The new criteria demonstrate improved sensitivity (95% vs. 82%) and negative predictive value, which suggests a higher likelihood of correctly identifying patients with TAK (15). This improvement is crucial for early and accurate diagnosis, which can lead to better patient management and outcomes. However, the 2022 criteria had lower specificity than the 1990 criteria in the validation study (63% vs. 90%), suggesting a higher rate of false-positive results. This reduction in specificity could lead to over-diagnosis, particularly in populations with conditions that mimic TAK, such as GCA (14). The specificity issues are partly addressed by adjusting the cut-off points, which improves the balance between sensitivity and specificity (15). The inclusion of advanced imaging modalities in the 2022 criteria, such as computed tomography angiography and positron emission tomography, enhances diagnostic accuracy by providing detailed visualization of vascular involvement (17). These modalities have been shown to improve the concordance rate between the two sets of criteria, particularly in patients under 60 years of age (17). The criteria's performance varies across different demographics and settings. For instance, the 2022

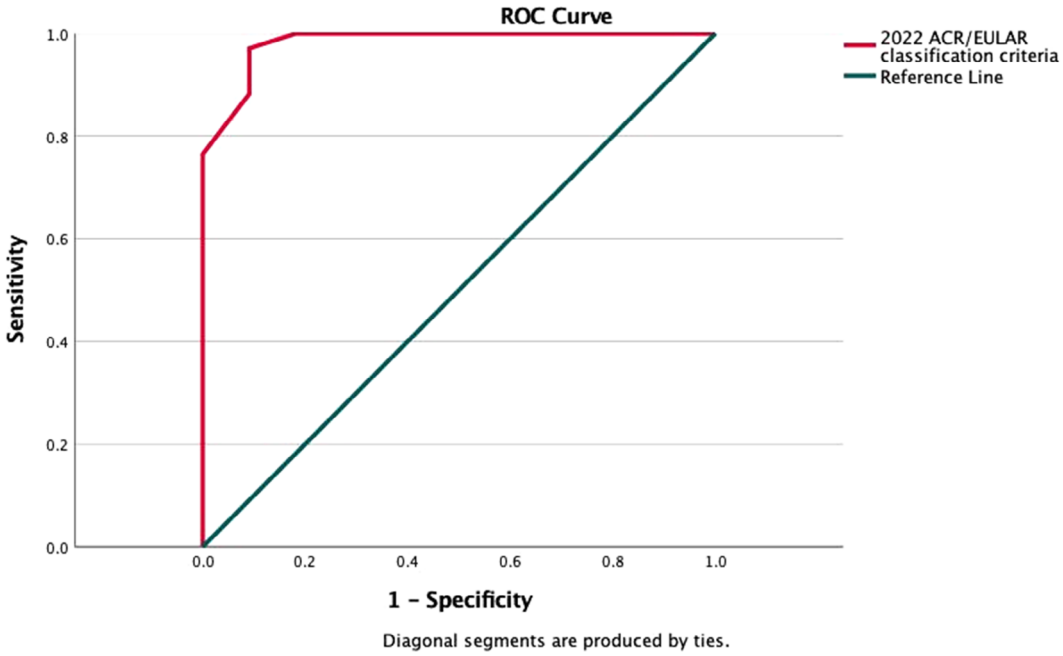

Figure 2. Comparison of the 2022 ACR/EULAR classification criteria with the ROC curve.

criteria show greater specificity in males compared to females and perform differently across age groups, with higher specificity observed in older patients. This variability suggests that while the new criteria are generally more effective, they may require further refinement to ensure consistent performance across diverse populations. There are several restrictions on this research. First, biases were unavoidably introduced by the retrospective nature of this study and the fact that the patients' disease trajectories varied. Second, there was insufficient diversity in the disorders that were part of the control group. Lastly, because this study was limited to a single facility and a small sample size, it may be argued that it does not accurately represent the circumstances in our nation as a whole.

Conclusion

In conclusion, the 2022 ACR/EULAR criteria for TAK offer a major advance in sensitivity and diagnostic accuracy, especially with modern imaging, but require careful application and possible adjustment to balance specificity in diverse clinical settings. Ongoing validation in larger, multi-center studies is needed to optimize their use in practice.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article. The authors declare no competing financial interests in relation to the work described.

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References

1. Pugh D, Karabayas M, Basu N, et al. Large-vessel vasculitis. Nat Rev Dis Primers 2022;7:93. doi: 10.1038/s41572-021-00327-5
2. Dabague J, Reyes PA. Takayasu arteritis in Mexico: a 38-year clinical perspective through literature review. Int J Cardiol 1996; 54(Suppl):S103–S109. doi: 10.1016/S0167-5273(96)88779-1
3. Hall S, Barr W, Lie JT, et al. Takayasu arteritis. A study of 32 North American patients. Medicine (Baltimore) 1985;64:89–99.
4. Mason JC. Takayasu arteritis—advances in diagnosis and management. Nat Rev Rheumatol 2010;6:406–415. doi: 10.1038/nrrheum.2010.82
5. Serra R, Butrico L, Fugetto F, et al. Updates in pathophysiology, diagnosis and management of Takayasu arteritis. Ann Vasc Surg 2016; 35:210–225. doi: 10.1016/j.avsg.2016.02.011

6. Arend WP, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum 1990;33:1129–1134. doi: 10.1002/art.1780330811
7. Seeliger B, Sznajd J, Robson JC, et al. Are the 1990 American College of Rheumatology vasculitis classification criteria still valid? Rheumatology (Oxford) 2017;56:1154–1161. doi: 10.1093/rheumatology/kex075
8. Grayson PC, Ponte C, Suppiah R, et al. 2022 American College of Rheumatology/EULAR classification criteria for Takayasu arteritis. Ann Rheum Dis 2022;81:1654–1660. doi: 10.1136/ard-2022-223482
9. Alibaz-Öner F, Aydın SZ, Direskeneli H. Recent advances in Takayasu's arteritis. Eur J Rheumatol 2015;2:24–30. doi: 10.5152/eurjrheumatol.2015.0060
10. Inder S. Immunophenotypic analysis of the aortic wall in Takayasu's arteritis: involvement of lymphocytes, dendritic cells and granulocytes in immuno-inflammatory reactions. Cardiovasc Surg 2000;8:141–148. doi: 10.1016/S0967-2109(99)00100-3
11. Svensson C, Eriksson P, Zachrisson H. Vascular ultrasound for monitoring of inflammatory activity in Takayasu arteritis. Clin Physiol Funct Imaging 2020;40:37–45. doi: 10.1111/cpf.12601
12. Oura K, Yamaguchi Oura M, Itabashi R, Maeda T. Vascular imaging techniques to diagnose and monitor patients with Takayasu arteritis: a review of the literature. Diagnostics (Basel) 2021;11:1993. doi: 10.3390/diagnostics11111993
13. Cao R, Yao Z, Lin Z, Jiao P, Cui L. The performance of the 2022 ACR/EULAR classification criteria for Takayasu's arteritis as compared to the 1990 ACR classification criteria in a Chinese population. Clin Exp Med 2023;23(8):5291–5297. doi: 10.1007/s10238-023-01140-y
14. Cao RJ, Yao ZQ, Jiao PQ, Cui LG. [Article in Chinese]. Beijing Da Xue Xue Bao Yi Xue Ban 2022;54:1128–1133. doi: 10.19723/j.issn.1671-167X.2022.06.012
15. Tomelleri A, Padoan R, Kavadichanda CG, et al. Validation of the 2022 American College of Rheumatology/EULAR classification criteria for Takayasu arteritis. Rheumatology (Oxford) 2023;62:3427–3432. doi: 10.1093/rheumatology/kead161
16. Betrains A, Moreel L, Blockmans D. The 2022 American College of Rheumatology/EULAR classification criteria for giant cell arteritis and Takayasu arteritis: comment on the articles by Ponte et al. and Grayson et al. Arthritis Rheumatol 2023;75:1074–1074. doi: 10.1002/art.42444
17. Ha JW, Pyo JY, Ahn SS, et al. Application of the 2022 ACR/EULAR criteria for Takayasu arteritis to previously diagnosed patients based on the 1990 ACR criteria. Mod Rheumatol 2024;34:1006–1012. doi: 10.1093/mr/road105