


Evaluating the diagnostic accuracy of the 2022 ACR/EULAR classification criteria for giant cell arteritis in routine clinical practice

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ABSTRACT

Aims: The 2022 American College of Rheumatology (ACR)/European Alliance of Associations for Rheumatology (EULAR) classification criteria for giant cell arteritis (GCA) were developed to enhance diagnostic accuracy by incorporating advanced imaging modalities and addressing large vessel involvement. This study evaluates the performance of these criteria in routine clinical care.

Methods: This study was retrospective and single-center. The results included 25 GCA patients routinely followed at a tertiary rheumatology center from March 2017 to January 2024. The accuracy, sensitivity, specificity, positive and negative predictive values, and area under the receiver operating characteristic (ROC) curve (AUC) of the classification criteria were compared.

Results: The sensitivity (92.0%), specificity (92.9%), positive predictive value (92.0%), negative predictive value (92.9%), accuracy (92.4%) and AUC (0.979 (0.925-0.998)) of the 2022 ACR/EULAR classification criteria for GCA were higher than those of the 1990 ACR classification criteria for GCA (88.0%, 85.7%, 84.6%, 88.9% and 86.8%, respectively), and the difference in AUC was statistically significant (0.871 (0.770-0.973), $p < 0.001$).

Conclusion: These findings indicate that the 2022 ACR/EULAR criteria significantly improve the sensitivity and maintain adequate specificity compared to the 1990 criteria, making them a valuable tool for diagnosing GCA in clinical practice. The new classification criteria will help to select the right patients and will reduce clinical errors.

Keywords: Giant cell arteritis, vasculitis, classification criteria

INTRODUCTION

Giant cell arteritis (GCA), a systemic inflammatory rheumatic disease, is one of the most common forms of systemic vasculitis. The pathogenesis of GCA is not fully understood. Clinical studies provide evidence for the importance of specific pathways in the pathogenesis of vascular inflammation. Immune system research shows inflammation of the arteries, primarily involving CD4⁺ T lymphocytes and macrophages, generally leading to a granulomatous reaction with the presence of giant cells. As a result of the inflammation, intimal hyperplasia and lumen occlusion can be seen in the arteries.¹ The disease is rarely seen in individuals under the age of 50; however, its incidence increases with age, most commonly affecting individuals in their seventh decade.² GCA is more common in people of Northern European descent and in women.³ The first classification criteria for GCA were published by the American College of Rheumatology (ACR) in 1990.⁴ These criteria are not intended to diagnose patients but rather to be used as classification criteria for

clinical trials. Their low sensitivity in clinical studies has limited their use for diagnostic purposes in daily practice.⁵ In the 1990s, due to the inadequacy of imaging techniques, attempts were made to establish classification criteria using clinical features, laboratory findings and invasive methods. With a better understanding of disease pathophysiology and the growing diagnostic value of imaging, techniques such as ultrasound (US), fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT), and magnetic resonance imaging (MRI) have been incorporated in double-blind, randomized controlled trials of newly developed drugs for the treatment of GCA.^{6,7} The development of new classification criteria became essential due to the limited sensitivity and specificity of previous criteria and the emergence of advanced imaging modalities. In clinical practice, it is valuable in terms of differentiating it from other diseases included in the differential diagnosis with modern imaging methods, and it can also be considered

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to reduce the need for temporal artery biopsy, which is an invasive procedure.

In 2022, the European Alliance of Associations for Rheumatology (EULAR) and the ACR published newly classification criteria for GCA.⁸ These new criteria include new clinical criteria that were not included in the previous criteria and modern imaging techniques that are increasingly used in routine practice.⁴ Although the high sensitivity of the new classification criteria meets the need, concerns regarding potential limitations in specificity, as reported in some studies, may affect their broader applicability. Additionally, as with many autoimmune diseases, geographic variations in incidence and clinical presentation may influence the sensitivity and specificity of the criteria, which may affect the specificity and sensitivity results. Epidemiologic studies have reported that being Northern European ancestry is important predisposing factor for GCA. Female predominance in the GCA has been reported in many different cohorts, and this gender difference is more pronounced in the northern part of Europe.⁹ Given these factors, we aimed to evaluate the classification performance of the 2022 ACR/EULAR criteria in a Turkish GCA cohort and to compare them with the 1990 ACR classification criteria.

METHODS

The study was conducted with the permission of the Non-Intervention Scientific Research Ethics Committee of the University of Health Sciences Gülhane Training and Research Hospital (Date: 05.12.2024, Decision No: 2024/89). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was designed as a retrospective study and carried out in a tertiary center. Medical records of patients diagnosed with GCA between March 2017 and January 2024 were reviewed. Clinical diagnoses were confirmed by two independent rheumatologists with a minimum of five years of experience. All valid medical records were manually reviewed before confirming the diagnosis. GCA was diagnosed based on clinical findings, imaging results, and temporal artery biopsy if available, in accordance with the 1990 ACR protocols. Twenty-eight patients over the age of 50 with elevated acute phase reactants and constitutional symptoms were included as the control group. The control group consisted of patients diagnosed with infections, malignancy, polymyalgia rheumatica, nonspecific headache, and fever of unknown origin.

All data specified in the 2022 ACR/EULAR GCA classification criteria were retrospectively collected from the hospital registry system and included: Demographic characteristics, clinical findings, laboratory parameters including C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), imaging modalities, temporal artery biopsy with evidence of vasculitis if present. Patients whose clinical, laboratory, or imaging data were unavailable in the hospital records were excluded from the study. During the diagnostic phase, imaging is requested from patients based on clinical suspicion. PET/CT was not routinely requested due to the duration of the procedure and radiation exposure risks. A patient was classified as having

GCA if the total score from the imaging and clinical findings is six or more, after meeting the requirements of the GCA 2022 ACR/EULAR classification criteria.⁸ To be classified as having GCA, a patient must meet three or more of the five criteria listed in the 1990 ACR classification criteria.⁴ The clinical diagnosis was accepted as the reference standard for all patients. To investigate the performance of the new GCA criteria, all patients were classified according to the 1990 ACR classification criteria and the updated 2022 ACR/EULAR classification criteria for GCA. The features of the machines used in imaging methods are as follows. For large-vessel evaluation, US machines with 6–15 MHz transducers were used. The scan began with gray-scale US, followed by color doppler mode. All PET images were interpreted by experienced nuclear medicine physicians using the Discovery 690-GE Healthcare PET/CT scanner.

Statistical Analysis

The data analysis was conducted using SPSS version 28, which is compatible with Mac. The distribution of variables was tested with the Shapiro-Wilk test. Parametric variables that were not regularly distributed were presented as median interquartile range (IQR), normally distributed variables as mean±standard deviation (SD), and categorical variables as number (n) and percentage (%). The independent samples t-test was conducted for comparison of normally distributed data, and the Mann-Whitney test was used to test whether there was a difference between two groups when the data were non-normally distributed. The area under the curve (AUC) of the receiver operating characteristic (ROC) was calculated. Also, sensitivity, specificity, accuracy, positive predictive values, and negative predictive values were evaluated.

RESULTS

A total of 27 patients with GCA were identified, and two patients were excluded due to the incomplete data. Also, after exclusion of patients with incomplete data, 28 patients were included as a control group. Nineteen (67.9%) of the patients in the control group were female and the mean age was 66.4±3.7 years. Of the patients diagnosed with GCA, 17 (68%) were female and the mean age was 71.5±7.3 years. There was a statistically significant difference between the two groups in the comparison of clinical criteria ($p<0.001$). In the comparison of acute phase values, a statistically significant difference was found between the two groups ($p<0.001$). Temporal artery US comparison showed a statistically significant difference between the two groups ($p<0.001$). When evaluating the imaging findings between the two groups, temporal artery and bilateral axillary US were found to be statistically significant, but no significance was found for FDG-PET uptake in the aorta. Further details of the demographic, clinical and imaging results of the two groups are shown in [Table 1](#).

The 2022 ACR/EULAR classification criteria for GCA had higher sensitivity (92.0%), specificity (92.9%), positive predictive value (92.0%), negative predictive value (92.9%), accuracy (92.4%), and AUC (0.979 (0.925-0.998)) compared to the 1990 ACR classification criteria for GCA (88.0%, 85.7%, 84.6%, 88.9%, and 0.86.8%, respectively). The difference in

Table 1. Comparison of general status and clinical features between giant cell arteritis and control groups			
Variables	Giant cell arteritis (n=25)	Control group (n=28)	p
Age ≥50 years at time of diagnosis, n (%)	25 (100.0)	28 (100.0)	0.119
Clinical criteria, n (%)			
Morning stiffness in shoulders/neck	23 (92.0)	7 (25)	<0.001
Sudden visual loss	2 (8.0)	0 (0)	<0.001
Jaw or tongue claudication	12 (48)	0 (0)	<0.001
New temporal headache	22 (88)	1 (3.6)	<0.001
Scalp tenderness	16 (64)	1 (3.6)	<0.001
Abnormal examination of the temporal artery	20 (80)	0 (0)	<0.001
Laboratory, imaging, and biopsy criteria, n (%)			
Maximum ESR ≥50 mm/hour or maximum CRP ≥10 mg/liter	25 (100.0)	26 (92.8)	0.621
Positive temporal artery biopsy or halo sign on temporal artery ultrasound	13 (52.0)	0 (0)	<0.001
Bilateral axillary involvement	2 (8.0)	1 (3.6)	<0.001
FDG-PET activity throughout aorta	2 (8.0)	3 (10.7)	0.471

ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein; FDG-PET: Fluorodeoxyglucose positron emission tomography

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	88.0	85.7	84.6	88.9	86.8	0.871 (0.770-0.973)
2022 ACR/EULAR	92.0	92.9	92.0	92.9	92.4	0.979 (0.925-0.998)

AUC: Area under the curve, ACR: American College of Rheumatology, EULAR: European Alliance of Associations for Rheumatology

AUC was statistically significant (0.871 (0.770-0.973), $p<0.001$) (Table 2, Figure 1, 2).

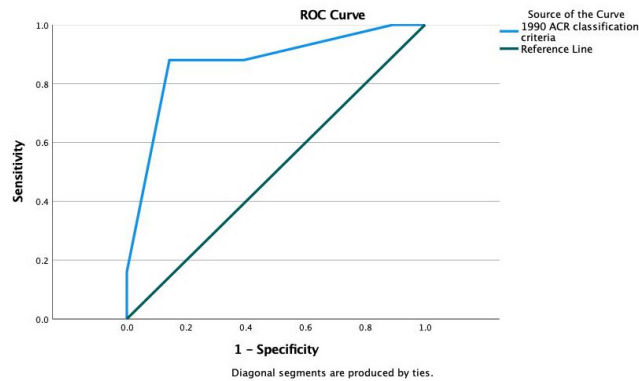


Figure 1. ROC curve according to 1990 ACR classification criteria
ROC: Receiver operating characteristic, ACR: American College of Rheumatology

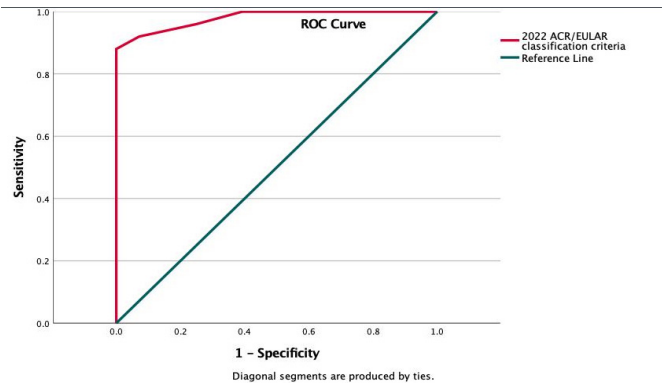


Figure 2. ROC curve according to 2022 ACR/EULAR classification criteria
ROC: Receiver operating characteristic, ACR: American College of Rheumatology, EULAR: European Alliance of Associations for Rheumatology

DISCUSSION

The 2022 ACR/EULAR criteria have shown comparable specificity and a significant increase in sensitivity in the diagnosis of GCA. The findings of the present study demonstrated a high level of diagnostic accuracy, as evidenced by an AUC value of 0.979, sensitivity of 92.0%, and specificity of 92.9%. In the study, AUC was shown to be 0.928, sensitivity was 92.6% and specificity was 71.8%.¹⁰ Similar results were found in another study where the sensitivity was 87.3% and the specificity was 70.3%.¹¹ The new criteria demonstrate a significant improvement in sensitivity, with studies reporting values ranging from 87.0% to 98.0%. Specificity, however, varies more widely, with reported values between 57.5% and 94.8%.^{10,12,15} The reasons for this difference in sensitivity and specificity between studies may be due to the different societies in which the criteria were applied, the differences in the diseases in the control group, and the differences in the imaging methods used. This information led to similar results in several patient subgroups, such as those with biopsy-proven GCA and isolated large-vessel GCA, where sensitivity was close to 100%.¹¹ The 1990 ACR criteria did not perform as well as the 2022 ACR/EULAR criteria. In our study, the AUC was 0.871, with sensitivity at 88.0% and specificity at 85.7%. In the study conducted by Molina-Collada et al.¹⁰, the overall sensitivity of the 1990 ACR criteria was found to be 53.2% and the specificity was found to be 80.2%. Another study found a sensitivity of 66.1% and a specificity of 85.1%.¹² The significant contribution of advanced imaging modalities such as FDG-PET and US, which have improved the detection of GCA, particularly in individuals without traditional cranial symptoms, is responsible for this increase in diagnostic accuracy.^{13,14} The inclusion of imaging modalities in the 2022

criteria allows for the identification of a broader range of GCA phenotypes, including cranial and extracranial large-vessel involvement.⁸ This is particularly important for patients who may not exhibit classic cranial symptoms but have significant extracranial vasculitis, which can now be more accurately classified and treated.¹¹ The criteria's ability to classify patients with mixed GCA phenotypes further supports their utility in diverse clinical settings. Studies have shown that the use of US and FDG-PET significantly increases the likelihood of identifying GCA. FDG-PET activity in the aorta and its branches or the presence of a halo sign on US are important markers of GCA in research.^{16,17} In the diagnosis of large-vessel GCA, where cranial symptoms are typically rare, this is an important consideration.¹¹ Once the 2022 criteria are routinely used, it will be possible to diagnose GCA more accurately and earlier than with the previous criteria. This is crucial for starting treatment early and avoiding consequences such as vision loss. However, the new standards have some drawbacks. For example, the weighting of abrupt vision loss and the inclusion of polymyalgia rheumatica (PMR) symptoms may lead to false-positive results in people with non-vasculitic ophthalmic disorders and PMR.¹¹ Although they provide significant improvements over the 1990 criteria, clinicians should consider the possibility of false-positive results and consider all clinical findings when making a diagnosis of GCA.

Limitations

The study has some limitations. The main limitation is that it is retrospective, which may lead to biases regarding patient selection and data collection. A fixed cut-off score of ≥ 6 for classification criteria may not be optimal for all patient populations. Although imaging techniques are useful for identifying large vessel involvement, they may not be interpreted in the same way in different medical settings. This can affect how accurate the results are and whether they can be used in the same way, especially in places with limited access to advanced imaging equipment. The number of patients is limited in terms of generalizability of the data to the population, but it should not be forgotten that this disease is also rare in the population.

To improve specificity and avoid false positives, future studies should focus on improving the criteria. This could include the inclusion of more diagnostic indicators or the inclusion and weighting of additional symptoms or imaging results in the criteria. To ensure accurate and reliable diagnosis, agreement on efficient imaging techniques and uniformity of clinical results are needed.¹⁰

CONCLUSION

The 2022 ACR/EULAR classification criteria for GCA represent a significant advancement in the field of rheumatology, offering healthcare professionals a more sophisticated instrument with which to diagnose GCA in routine clinical practice. Their integration of imaging techniques aligns with current clinical practices and enhances the ability to diagnose and manage various GCA phenotypes effectively. However, ongoing evaluation and potential adjustments are necessary

to address the remaining challenges in specificity and atypical presentations. Further research is needed to improve the criteria and reduce false-positive results.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Non-Intervention Scientific Researches Ethics Committee of the University of Health Sciences Gülhane Training and Research Hospital (Date: 05.12.2024, Decision No: 2024/89).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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