

# Advanced Imaging Techniques Use in Giant Cell Arteritis Diagnosis: The Experience at Walter Reed National Military Medical Center

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**Background:** If not diagnosed in a timely manner, giant cell arteritis (GCA) can lead to significant morbidity. The 1990 American College of Rheumatology criteria for GCA do not include screening technologies, though proposed criteria do.

**Methods:** This study evaluated current clinical practices in diagnosing GCA and the use of screening technologies such as ultrasound, magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET). A retrospective chart review was conducted of patients who underwent diagnostic testing for GCA from 2016 through 2022 at Walter Reed National Military Medical Center.

**Results:** Seventy-eight charts were reviewed; 42 patients (54%) had a GCA diagnosis and 36 patients (46%) were GCA

negative. Temporal artery biopsy was positive for 19 (45%) patients. Most patients did not undergo bilateral temporal artery biopsies despite recommendations. Among those diagnosed with GCA, 29 (69%) underwent biopsy, and 25 (60%) received diagnostic imaging.

**Conclusions:** Evidence supports the use of additional screening tools beyond clinical and laboratory data to improve the diagnostic yield of temporal artery biopsy. Initial screening with ultrasound is a cost-effective and widely available modality that may reduce the risk of false-negative biopsy results. Other tests include vascular MRI/CT and PET. The target goal is to increase the diagnostic yield of temporal artery biopsies to  $\geq 70\%$ .

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Giant cell arteritis (GCA), the most commonly diagnosed systemic vasculitis, is a large- and medium-vessel vasculitis that can lead to significant morbidity due to aneurysm formation or vascular occlusion if not diagnosed in a timely manner.<sup>1,2</sup> Diagnosis is typically based on clinical history and inflammatory markers. Laboratory inflammatory markers may be normal in the early stages of GCA but can be abnormal due to other unrelated reasons leading to a false positive diagnosis.<sup>3</sup> Delayed treatment may lead to visual loss, jaw or limb claudication, or ischemic stroke.<sup>2</sup> Initial treatment typically includes high-dose steroids that can lead to significant adverse reactions such as hypothalamic-pituitary-adrenal axis dysfunction, metabolic syndrome, premature atherosclerosis, and increased risk of infection.<sup>4-6</sup>

The 1990 American College of Rheumatology (ACR) criteria for GCA are widely recognized (Table 1).<sup>7</sup> The criteria focuses on clinical manifestations, including new onset headache, temporal artery tenderness, age  $\geq 50$  years, erythrocyte sedimentation rate (ESR)  $\geq 50$  mm/hr, and temporal artery biopsy with positive anatomical findings.<sup>8</sup> When 3 of the 5 1990 ACR criteria are present, the sensitivity and specificity is estimated to be  $> 90\%$  for GCA vs alternative vasculitides.<sup>7</sup>

Although the 1990 ACR criteria do not include imaging, modalities such as ultrasound, computed tomography angiography (CTA), 18F-FDG positron emission tomography (PET), and magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA) may be used in GCA diagnosis.<sup>8-10</sup> These imaging modalities have been added to the proposed ACR classification criteria for GCA.<sup>11</sup> For this updated point system standard, age  $\geq 50$  years is a requirement and includes a positive temporal artery biopsy or temporal artery halo sign on ultrasound (+5 points), an ESR  $\geq 50$  mm/h or C-reactive protein (CRP)  $\geq 10$  mg/L (+3 points), or sudden visual loss (+3 points). Scalp tenderness, jaw or tongue claudication, new temporal headache, morning stiffness in shoulders or neck, temporal artery abnormality on vascular examination, bilateral axillary vessel involvement on imaging, and 18F-FDG PET activity throughout the aorta are scored +2 points each. With these new criteria, a cumulative score  $\geq 6$  is classified as GCA. Diagnostic accuracy is further improved with imaging: ultrasonography (sensitivity 55% and specificity 95%) and 18F-FDG PET (sensitivity 69% and specificity 92%), CTA (sensitivity 71% and specificity 86%), and MRI/MRA (sensitivity 73% and specificity 88%).<sup>12-15</sup>

In recent years, clinicians have reported increased glucose uptake in arteries observed on PET imaging that suggests GCA.<sup>9,10,16-20</sup> 18F-FDG accumulates in cells with high metabolic activity rates, such as areas of inflammation. In assessing temporal arteries or other involved vasculature (eg, axillary or great vessels) for GCA, this modality indicates increased glucose uptake in the lining of vessel walls. The inflammation of vessel walls can then be visualized with PET. 18F-FDG PET presents a noninvasive imaging technique for evaluating GCA but its use has been limited in the United States due to its high cost.

METHODS

Approval for a retrospective chart review of patients evaluated for suspected GCA was obtained from the Walter Reed National Military Medical Center (WRNMMC) Institutional Review Board. The review included patients who underwent diagnostic procedures such as ultrasound, MRI, CT angiogram, and PET studies from 2016 through 2022. *International Classification of Diseases* codes used for case identification included: M31.6, M31.5, I77.6, I77.8, I77.89, I67.7, and I68.2. The *Current Procedural Terminology* code used for temporal artery biopsy is 37609.

RESULTS

Seventy-eight charts were reviewed and 42 patients (54%) were diagnosed with GCA (Table 2). This study sample had a much higher proportion of African American subjects (31%) when compared with the civilian population, likely reflecting the higher representation of African Americans in the armed forces. Twenty-eight females (67%) were GCA positive. The most common presenting symptoms included 27 patients (64%) with headache, 17 (40%) with scalp tenderness, and 14 (33%) with jaw pain. The mean 1990 ACR score was 3.8 (range, 2-5). With respect to the score criteria: 41 patients (98%) were aged ≥ 50 years, 31 (74%) had new onset headache, and 31 (74%) had elevated ESR (Table 3). Acute ischemic optic neuropathy was documented in 4 patients (10%) with confirmed GCA. The mean ESR and CRP values at diagnosis were 66.2 mm/h (range, 7-122 mm/h) and

TABLE 1. ACR Criteria for Classification of GCA

Criterion	Definition
Age	Symptoms or findings beginning at age 50 y
New headache	New onset of or new type of localized pain in the head
Temporal artery abnormality	Temporal artery tenderness to palpation or decreased pulsation, unrelated to atherosclerosis of cervical arteries
Elevated ESR	≥ 50 mm/h by the Westergren method
Biopsy	Specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells

Abbreviations: ACR, American College of Rheumatology; ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis.

TABLE 2. Demographic Profile

Characteristic	GCA positive	GCA negative
Patients, No.	42	36
Age, y		
Median (range)	62 (31-93)	62.5 (31-90)
Mean (SD)	76 (10)	61 (16.5)
Sex, No. (%)		
Female	28 (67)	17 (47)
Male	14 (33)	19 (53)
Race and ethnicity, No. (%)		
African American	9 (21)	15 (42)
Asian	2 (5)	2 (6)
White	21 (50)	14 (39)
Hispanic	1 (2)	0 (0)
Mixed/other	7 (17)	3 (8)
Unknown	2 (5)	2 (6)
Shingles vaccine, No. (%)		
Yes	36 (86)	15 (42)
No	6 (14)	9 (25)
Unknown	0 (0)	12 (33)
Military status, No. (%)		
Active-duty	11 (26)	8 (22)
Active-duty dependent	31 (74)	28 (78)
Autoimmune disease, No. (%) <sup>a</sup>		
Yes	21 (50)	11 (31)
No	17 (40)	20 (56)
Unknown	4 (10)	5 (14)
Polymyalgia rheumatica	14 (33)	2 (6)
Thyroid disease <sup>b</sup>	6 (14)	1 (3)
Rheumatoid arthritis	3 (7)	1 (3)
Systemic lupus erythematosus	1 (2)	1 (3)

Abbreviation: GCA, giant cell arteritis

<sup>a</sup>Patients may have ≥ 1 disease.

<sup>b</sup>Hashimoto thyroiditis and hypothyroidism.

8.711 µg/mL (range, 0.054 – 92.690 µg/mL), respectively. Twenty-seven patients (64%) underwent biopsy: 24 (89%) were unilateral and 3 (11%) were bilateral (Table 4). Four patients with GCA (10%) were missing biopsy data. Nineteen patients with GCA

**TABLE 3.** Clinical Features and Adverse Outcomes

Criteria	GCA positive, No. (%) (n = 42)	GCA negative, No. (%) (n = 36)
Baseline symptoms		
Headache	27 (64)	17 (47)
Visual disturbance	11 (26)	5 (14)
Jaw pain	14 (33)	8 (22)
Scalp tenderness	17 (40)	8 (22)
Orbital pain	4 (10)	3 (8)
Cranial nerve III involvement	1 (2)	1 (3)
Fever	7 (17)	0 (0)
Chills	2 (5)	0 (0)
Fatigue	8 (19)	1 (3)
Myalgias	6 (14)	0 (0)
Baseline pain rating		
0-3	9 (21)	12 (33)
4-7	13 (31)	6 (17)
8-10	5 (12)	1 (3)
Unknown	15 (36)	17 (47)
Change in vision at diagnosis	10 (24)	0 (0)
Improved with treatment		
Yes	8 (80)	NA
No	2 (20)	NA
No change in vision at diagnosis	12 (29)	1 (3)
Incomplete data on vision	20 (48)	35 (97)
Acute ischemic optic neuropathy		
Yes	4 (10)	1 (3)
No	33 (79)	16 (44)
Unknown	5 (12)	19 (53)
No. of 1990 ACR criteria		
1	1 (2)	1 (3)
2	4 (10)	8 (22)
3	8 (19)	12 (33)
4	15 (36)	0 (0)
5	7 (17)	0 (0)
Unknown	7 (17)	15 (42)
Temporal artery abnormality	19 (45)	4 (11)
Elevated ESR	31 (74)	18 (50)
Abnormal biopsy	19 (45)	0 (0)
New onset headache	31 (74)	18 (50)
Age ≥ 50 y	41 (98)	28 (78)

Abbreviations: ACR, American College of Rheumatology; ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis; NA, not applicable.

(70%) had biopsies with pathologic findings consistent with GCA.

Twenty-five patients with GCA (60%) received ≥ 1 imaging modality. The most common imaging modality was MRI, which was used for 18 (43%) patients. Fourteen patients (33%) had 18F-FDG PET, 12 patients (29%) had MRA, and 11 patients (26%) had CTA. The small number of patients who underwent point-of-care ultrasound (POCUS), brain MRI, or dark blood

MRI were negative for disease. Five patients who underwent 18F-FDG PET had findings consistent with GCA. One patient with GCA had CTA of the head and neck with radiographic findings supportive of GCA.

## DISCUSSION

The available evidence supports the use of additional screening tests to increase the temporal artery biopsy yield for GCA. Inflammatory laboratory markers demonstrate some sensitivity but are nonspecific for GCA. In this study, only 60% of patients with GCA underwent diagnostic imaging as part of the workup. There are multiple factors that may contribute to the underutilization of advanced imaging in the diagnosis of GCA, including outdated standardized diagnostic criteria, limited resources (direct access to modalities), and lack of clinician awareness of diagnostic testing options. In this retrospective review, 30 patients (71%) were diagnosed with GCA with a 1990 ACR GCA score ≤ 3. Of these 30 patients, 19 underwent confirmatory biopsy followed by prolonged courses of steroid therapy. In addition, only 25 patients underwent advanced imaging to increase diagnostic accuracy of the suspected syndrome.

A large meta-analysis demonstrated a sensitivity of 77.3% (95% CI, 71.8-81.9%) for temporal artery biopsy.<sup>21</sup> The overall yield was 40% in the meta-analysis. Advanced noninvasive imaging represents an appropriate method of evaluating GCA.<sup>8-20</sup> In our study, 18F-FDG PET demonstrated the highest sensitivity (36%) for the diagnosis of GCA. Ultrasonography is recommended as an initial screening tool to identify the noncompressible halo sign (a hypoechoic circumferential wall thickening due to edema) as a cost-effective and widely available technology.<sup>22</sup> Other research has corroborated the beneficial use of ultrasonography in improving diagnostic accuracy by detecting the noncompressible halo sign in temporal arteries.<sup>22,23</sup> GCA diagnostic performance has been significantly improved with the use of B-mode probes ≥ 15 MHz as well as proposals to incorporate a compression sign or interrogating the axillary vessels, showing a sensitivity of 54% to 77%.<sup>23,24</sup>

**TABLE 4.** Laboratory Tests and Imaging Modalities

Criteria	GCA positive (n = 42)	GCA negative (n = 36)
ESR, mean (SD) [range], mm/h	66.0 (35.8) [5 to 120]	52.3 (31.3) [1 to > 120]
C-reactive protein, mean (SD) [range], µg/mL	10.9 (25.0) [0.1 to 120.0]	4.2 (7.1) [.055 to 29.0]
Biopsy confirmed, No. (%)		
Yes	19 (45)	1 (3)
No	8 (19)	20 (56)
Unknown	4 (10)	15 (42)
Not biopsied	11 (26)	0 (0)
Biopsy performed, No. (%)		
Yes	27 (64)	22 (61)
No	11 (26)	0 (0)
Unknown	4 (10)	14 (39)
Biopsy attempts, No. (%)		
0	11 (26)	0 (0)
1	24 (57)	22 (61)
2	3 (7)	0 (0)
Unknown	4 (10)	14 (39)
Time on steroids prior to biopsy, mean (SD) [range], d	9 (12) [0 to 38]	4 (5) [0 to 16]
Biopsy site, No. (%)		
Unilateral temporal artery	28 (67)	20 (56)
Bilateral temporal artery	1 (2)	0 (0)
Unknown	13 (31)	16 (44)
Most common biopsy findings, No.		
Intimal thickening	3	4
Elastic lamina infiltrate	11	0
Giant cells only	3	0
Targeted vascular ultrasound, No. (%)		
Positive	6	2
Negative	0 (0)	0 (0)
Negative	6 (100)	2 (100)
Computed tomography angiography, No. (%)		
Positive	11	3
Negative	1 (9%)	0 (0)
Negative	10 (91%)	3 (100)
Magnetic resonance angiography, No. (%)		
Positive	12	5
Negative	1 (8)	0 (0)
Negative	11 (92)	5 (100)
Magnetic resonance imaging, No. (%)		
Positive	18	9
Negative	0 (0)	2 (22)
Negative	18 (100)	7 (78)
Magnetic resonance imaging dark blood, No. (%)		
Positive	6	0
Negative	0 (0)	0 (0)
Negative	6 (100)	0 (0)
Positron emission tomography, No. (%)		
Positive	14	1
Negative	5 (36)	0 (0)
Negative	9 (64)	1 (100)

Abbreviations: ESR, erythrocyte sedimentation rate; GCA, giant cell arteritis.

POCUS may reduce the risk of a false-negative biopsy and improve yield with more frequent utilization. However, ultrasonography may be limited by operator skills and visualization of the great vessels. The accuracy of ultrasonography is dependent on the experience and adeptness of the operator. Additional studies are needed to establish a

systematic standard for POCUS training to ensure accurate interpretation and uniform interrogation procedure.<sup>24</sup> Artificial intelligence (AI) may aid in interpreting results of POCUS and bridging the operator skill gap among operators.<sup>25,26</sup> AI and machine learning techniques can assist in detecting the noncompressible halo sign and

compression sign in temporal arteries and other affected vessels.

In comparing the WRNMMC patient population with other US civilian GCA cohorts, there are some differences and similarities. There was a high representation of African American patients in the study, which may reflect a greater severity of autoimmune disease expression in this population.<sup>27</sup> We also observed a higher number of females and an association with polymyalgia rheumatica in the data, consistent with previous reports.<sup>28,29</sup> The females in this study were primarily civilians and therefore more similar to the general population of individuals with GCA. In contrast, male patients were more likely to be active-duty service members or have prior service experience with increased exposure to novel environmental factors linked to increased risk of autoimmune disease. This includes an increased risk of Guillain-Barré syndrome and Graves disease among Vietnam veterans exposed to Agent Orange.<sup>30,31</sup> Other studies have found that veterans with posttraumatic stress disorder are at increased risk for severe autoimmune diseases.<sup>32,33</sup> As more women join the active-duty military, the impact of autoimmune disease in the military service population is expected to grow, requiring further research.

## CONCLUSIONS

Early diagnosis and treatment of GCA are critical to preventing serious outcomes, such as visual loss, jaw or limb claudication, or ischemic stroke. The incidence of autoimmune disease is expected to rise in the armed forces and veteran populations due to exposure to novel environmental factors and the increasing representation of women in the military. The use of additional screening tools can aid in earlier diagnosis of GCA. The 2022 ACR classification criteria for GCA represent significant updates to the 1990 criteria, incorporating ancillary tests such as the temporal artery halo sign on ultrasound, bilateral axillary vessel screening on imaging, and 18F-FDG PET activity throughout the aorta. The updated criteria require further validation and supports the adoption of a multidisciplinary approach that includes ultrasonography, vascular MRI/CT, and 18F-FDG PET. Furthermore, AI may play a future key role in ultrasound interpretation and

study interrogation procedure. Ultimately, ultrasonography is a noninvasive and promising technique for the early diagnosis of GCA. A target goal is to increase the yield of positive temporal artery biopsies to  $\geq 70\%$ .

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## Ethics and consent

This research was determined to be exempt from review by the Walter Reed National Military Medical Center Department of Research Programs Institutional Review Board.

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