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Validation of a multimodal algorithm for diagnosing giant cell arteritis with imaging

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ABSTRACT

Purpose: The purpose of this study was to identify which combination of imaging modalities should be used to obtain the best diagnostic performance for the non-invasive diagnosis of giant cell arteritis (GCA).
Materials and methods: This IRB-approved prospective single-center study enrolled participants presenting with a suspected diagnosis of GCA from December 2014 to October 2017. Participants underwent high-resolution 3T magnetic resonance imaging (MRI), temporal and extra-cranial arteries ultrasound and retinal angiography (RA), prior to temporal artery biopsy (TAB). Diagnostic accuracy of each imaging modality alone, then a combination of several imaging modalities, was evaluated. Several algorithms were constructed to test optimal combinations using McNemar test.
Results: Forty-five participants (24 women, 21 men) with mean age of 75.4 ± 16 (SD) years (range: 59–94 years) were enrolled; of these 43/45 (96%) had ophthalmological symptoms. Diagnosis of GCA was confirmed in 25/45 (56%) patients. Sensitivity and specificity of MRI, ultrasound and RA alone were 100% (25/25; 95% CI: 86–100) and 86% (19/22; 95% CI: 65–97), 88% (22/25; 95% CI: 69–97) and 84% (16/19; 95% CI: 60–97), 94% (15/16; 95% CI: 70–100) and 74% (14/19; 95% CI: 49–91), respectively. Sensitivity, specificity, positive predictive and negative predictive values ranged from 95 to 100% (95% CI: 77–100), 67 to 100% (95% CI: 38–100), 81 to 100% (95% CI: 61–100) and 91 to 100% (95% CI: 59–100) when combining several imaging tests, respectively. The diagnostic algorithm with the overall best diagnostic performance was the one starting with MRI, followed either by ultrasound or RA, yielding 100% sensitivity (22/22; 95% CI: 85–100%) 100% (15/15; 95% CI: 78–100) and 100% accuracy (37/37; 95% CI: 91–100).
Conclusion: The use of MRI as the first imaging examination followed by either ultrasound or RA reaches high degrees of performance for the diagnosis of GCA and is recommended in daily practice.

1. Introduction

Giant cell arteritis (GCA) is a segmental and focal inflammatory arteritis, affecting the large and medium caliber arteries. Its incidence is estimated at 17.8 / 100,000 in subjects over 50 years of age and 46 / 100,000 over 70 years of age [1,2]. Early and accurate diagnosis of GCA is crucial to prevent the most serious complications that are ophtalmological and neurological ischemias. Management is considered an emergency intervention, and only an early steroid therapy may prevent complications [2].

Diagnostic confirmation of GCA remains challenging. There is a wide spectrum of clinical features in GCA, sometimes with nonspecific clinical or biological signs. Although debated, temporal artery biopsy (TAB) remains widely performed for the diagnosis of GCA despite its lack of sensitivity, estimated at approximately 75%, its invasiveness and the risks related to the intervention [3]. Several diagnostic tools have recently been tested for diagnosing GCA, such as magnetic resonance imaging (MRI) [4–15], ultrasound [15–24] or retinal angiography (RA) [25,26]. This strategy is supported by the

Abbreviations: ACR, American College of Rheumatology; CI, Confidence interval; ICG, Indocyanine green angiography; EULAR, European Alliance of Associations for Rheumatology; Fa, Fluorescein angiography; GCA, Giant cell arteritis; MRI, Magnetic resonance imaging; NPV, Negative predictive value; PET-CT, Positron emission tomography computed tomography; PPV, Positive predictive value; RA, Retinal angiography; SD, Standard deviation; STARD, Standards for Reporting of Diagnostic Accuracy Studies; TAB, Temporal artery biopsy

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most recent European Alliance of Associations for Rheumatology (EULAR) guidelines, which state that a suspected diagnosis of GCA should be confirmed by imaging (ultrasound or MRI for temporal or other cranial arteries), ultrasound, CT, positron emission tomography computed tomography (PET-CT) or MRI for the aorta/extracranial arteries or histopathological analysis with TAB [27,28]. EULAR guidelines suggest performing a second test if the first one is negative, but the clinical suspicion of GCA persists [28]. To date, few studies have tried to combine diagnostic imaging modalities, such as ultrasound and PET-CT, to diagnose GCA, instead of assessing each tool separately for diagnostic utility [29,30].

The purpose of this study was to identify which combination of imaging modalities should be used to obtain the best diagnostic performance for the non-invasive diagnosis of GCA.

2. Material and methods

2.1. Study population and design

A prospective single center study was conducted in a tertiary referral hospital specialized in ophthalmological and neurological diseases (A.Rothschild Foundation Hospital). This study was approved by an institutional review board (ID RCB: 2014-A01553 −44). Signed informed consent was obtained from all subjects. This study follows the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines. Patients were enrolled from December 2014 to October 2017. All patients older than 50 years referred to our center for a suspected diagnosis of GCA were prospectively included in this study. For each patient, clinical, biological, paraclinical and imaging data were performed prior to a TAB. Patients with a TAB prior to MRI, ultrasound or RA were not included. Selection of patients is shown in Fig. 1. All imaging examinations were performed within seven days following the onset of symptoms, before TAB and before or within the five days following initiation of treatment.

2.2. Clinical, biological and paraclinical data

Systemic and cranial symptoms (weight loss, anorexia, fever, headache, jaw claudication, scalp tenderness, temporal artery tenderness, facial pain, tongue claudication, polymyalgia rheumatic related symptoms) and ophthalmological findings (visual acuity loss such as amaurosis fugax, blindness, diplopia, blurred vision) were noted at admission. Fundus photos were acquired. Urgent laboratory testing included screening for inflammatory biologic syndrome (*i.e.*, erythrocyte sedimentation rate, C-reactive protein level).

2.3. Ultrasound of the temporal and extra-cranial arteries

All patients had a conventional ultrasound including B-mode and color-doppler flow imaging, performed with a high frequency broad band (8−18 MHz) linear probe using the same scanner (Logic E9, General Electric Healthcare). Ultrasound examination was performed by three skilled radiologists, specialized in extra-cranial artery imaging (A. L., F. C. and J.-C. S. with 10-, 15- and 30 years of experience, respectively). The basic examination was performed in B-mode with all variables (gain, focus and depth) set to obtain an optimal-quality image. Color-doppler flow imaging of the temporal and extra-cranial arteries was subsequently performed. A positive diagnosis of GCA was defined by the presence of a halo sign or a thickened arterial wall of the temporal arteries.

2.4. Retinal angiography

When GCA was suspected in patients presenting with ophthalmic manifestations, two RA techniques were performed: fluorescein angiography (FA) was obtained when there was no history of allergy and indocyanine green angiography (ICG) was obtained regardless of history of allergy. RA (Spectralis HRA II) was performed to detect early stages of retinal and/or choroidal ischemia defined by delay in choroidal vessels filling on fluorescein angiography or the presence of non-vascularized choroidal areas on ICG. Early phases of RA were obtained to detect delay in choroidal vessel filling. Pictures of both eyes were obtained for comparison. Patchy choroidal vessels filling persisting until FA retinal venous phase was considered pathological. In ICG, early phase imaging made for better visualization of choriocapillaris lobules. Late phase imaging at 40 min was obtained to detect abnormalities in retinal pigment epithelium that occur in severe choroidal ischemia. FA was also used to confirm optic disk edema when

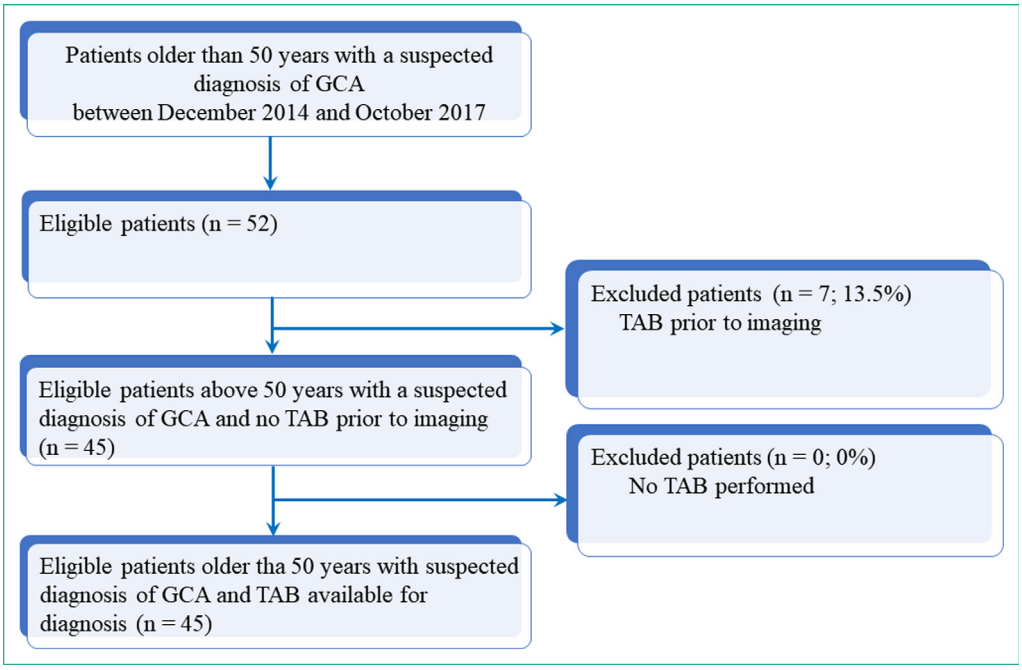

Fig. 1. Study flowchart. GCA: giant cell arteritis; TAB: temporal artery biopsy.

there was suspicion for arteritic ischemic optic neuropathy, and to study retinal vessel filling in patients with suspected retinal arterial occlusion.

2.5. MRI

2.5.1. MRI protocol

All MRI examinations were performed on the same 3 Tesla Ingenia® (Philips Medical Systems) device with a 32-channel head coil. The MRI protocol included pre- and post-contrast three-dimensional fat-saturated turbo spin echo high resolution vessel-wall imaging dedicated for visualizing the extracranial artery wall (Table 4) [13,14]. Post-contrast imaging was performed after intravenous administration of a single bolus (0.1 mmol/kg) of Gadobutrol (Gadovist®; Bayer HealthCare).

2.5.2. MR image analysis

Two senior neuroradiologists specialized in GCA (A. L., F. C. with 10- and 15 years of experience respectively) blinded to all data, independently read in a random fashion anonymized MRI examinations. All reading sessions were completed on a dedicated workstation with the Carestream Vue PACS software (Carestream Health). A consensus reading was performed six weeks after to resolve discrepancies and to serve for statistical analyses.

The presence of GCA-related inflammatory changes on extracranial arteries was based on the evaluation of wall thickening and mural enhancement of the following six extra-cranial arterial segments: left and right frontal and parietal branches of the superficial temporal artery and of the occipital artery, using a 4-point scale (Score 0: no wall thickening (< 0.6 mm) and no mural enhancement; Score 1: no wall thickening (< 0.6 mm) and slight mural enhancement; Score 2: wall thickening (> 0.6 mm) and substantial mural enhancement; Score 3: marked wall thickening (> 0.7 mm) and strong mural enhancement with perivascular inflammatory infiltration [8,12]. Scores of 0 and 1 were considered negative for GCA, whereas scores of 2 and 3 were considered positive. At least one positive segment out of the six analyzed was required to establish a positive diagnosis of GCA with MRI. A negative diagnosis of GCA with MRI was made when all arteries were considered readable and were assigned a score of 0 or 1. The MRI was considered inconclusive for GCA when at least one arterial segment was considered unreadable.

2.6. Reference standard

TAB was performed to establish the presence of GCA for every patient. Length of the TAB should be at least of 1.5–2.0 cm. Final diagnosis of GCA was made in patients with positive TAB. In patients with a negative TAB, a review of the clinical and biological chart including response to corticosteroid therapy (but excluding imaging findings) was performed by an interdisciplinary panel of rheumatologists, internists and ophthalmologists not involved in the management of the patient. A final diagnosis of GCA based on American College of Rheumatology (ACR) criteria was determined by consensus [31].

2.7. Statistical analysis

Quantitative variables were expressed as means ± standard deviations (SD) and ranges or medians, interquartile ranges and ranges, whereas qualitative variables were expressed as raw numbers, proportions and percentages. Differences between GCA positive and GCA negative patients were searched using Chi-square (χ^2) test or Fisher exact test for categorical data and Student *t*-test or Mann-Whitney U test for continuous data. Accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each imaging modality (MRI, ultrasound and FA) alone or for a combination of several imaging modalities and reported with their 95% confidence intervals (CI). Several algorithms were constructed to test optimal combinations using McNemar test. Inter and intra-observer agreement for MRI reading was assessed using non-weighted Cohen's kappa statistics and interpreted as follows: 0.0–0.2: poor correlation; 0.21–0.4: fair correlation; 0.41–0.6: moderate correlation; 0.61–0.8: good correlation; 0.81–1: almost perfect correlation [32]. A *P* value < 0.05 was considered significant. All analyses were performed using R software (version 3.4.3).

3. Results

3.1. Patient characteristics

Forty-five patients (24 women and 21 men) with a mean age of 75.4 ± 16 years (range: 59–94 years) were included. Among them, 25/45 patients (55%) had a final diagnosis of GCA (GCA positive group). TAB was positive in 19/45 patients (42%). Mean age was greater in patients with GCA (79.4 ± 8.3 [SD] years) than in those without GCA (71.3 ± 8 [SD] years) (*P* = 0.002). Jaw claudication was found in 16/25 patients (64%) with GCA and in 0/20 patients (0%) without GCA (*P* < 0.001). Scalp tenderness was more frequently found in patients with GCA (12/25; 48%) than in those without GCA (3/20; 15%) (*P* = 0.03). Median erythrocyte sedimentation rate and C-reactive protein serum level were significantly greater in patients with GCA (67.1 and 64.9) respectively as compared to those without GCA (40.8 and 13.2, respectively) (*P* = 0.02 and *P* < 0.001, respectively). There were no other clinical or biological differences observed between the two groups. Clinical and biological characteristics are reported in Table 1.

3.2. Diagnostic performance of MRI, ultrasound and ra alone or in combination

Sensitivities of MRI, ultrasound and RA alone were 100% (25/25; 95% CI: 86–100), 86% (19/22; 95% CI: 65–97) and 88% (22/25; 95% CI: 69–97), respectively and specificities were 84% (16/19; 95% CI 60–97), 94% (15/16; 95% CI: 70–100) and 74% (14/19; 95% CI: 49–91),

Table 1
Clinical and biological characteristics of patients with (GCA +) or without (GCA -) giant cell arteritis.

	GCA+ (*n* = 25)	GCA– (*n* = 20)	*P*
Age	79.4 ± 8.3 [59–94]	71.3 ± 8.0 [60–89]	0.002
Sex			0.10
Male	9 (36%)	12 (60%)	
Female	16 (64%)	8 (40%)	
Weight loss	2 (8%)	0 (0%)	0.50
Anorexia	1 (4%)	1 (5%)	> 0.99
Fever	0 (0%)	0 (0%)	N.A.
Headache	18 (72%)	10 (50%)	0.20
Jaw claudication	16 (64%)	0 (0%)	< **0.001**
Scalp tenderness	12 (48%)	3 (15%)	**0.03**
Artery tenderness	13 (52%)	6 (30%)	0.20
Swallowing problem	1 (4%)	0 (0%)	> 0.99
Facial pain	3 (12%)	2 (10%)	> 0.99
Tongue claudication	0 (0%)	0 (0%)	NA
Polymyalgia rheumatica	2 (8%)	0 (0%)	0.50
Ophthalmological symptoms	25 (100%)	18 (90%)	0.20
Amaurosis fugax	3 (12%)	5 (25%)	0.40
ESR* (mm/hour)	67.1 (42.8, 95) [15–114]	40.8 (15, 62.8) [3–100]	**0.02**
CRP* (mg/L)	64.9 (35.8, 94) [9–179]	13.2 (3, 19.3) [1–36]	< **0.001**

ESR: erythrocyte sedimentation rate. CRP: C-reactive protein. N.A. not applicable. Numbers in brackets are ranges. Bold indicates significant *P* value.
* Indicates expressed as means, interquartile ranges and ranges. Bold indicates significant *P* value after appropriate statistical correction.

Table 2
Diagnostic performance of magnetic resonance imaging (MRI), ultrasound and retinal angiography for diagnosing giant cell arteritis.

	MRI	Ultrasound	Retinal angiography	TAB
Sensitivity (%)	100 (25/25) [86–100]	86 (19/22) [65–97]	88 (22/25) [69–97]	62 (19/25) [30–85]
Specificity (%)	84 (16/19) [60–97]	94 (15/16) [70–100]	74 (14/19) [49–91]	100 (18/18) [85–100]
Positive predictive value (%)	89 (25/28) [72–98]	95 (19/20) [75–100]	81 (22/27) [62–94]	100 (19/19) [85–100]
Negative predictive value (%)	100 (16/16) [79–100]	83 (15/18) [59–96]	82 (14/17) [57–96]	58 (18/24) [30–81]
Accuracy (%)	93 (41/44) [81–99]	89 (34/38) [75–97]	82 (36/44) [67–92]	86 (37/43) [72–95]

Numbers in parentheses are proportions; numbers in brackets are 95% confidence interval.
TAB: Temporal artery biopsy.

respectively (Table 2). When combining several imaging tests, sensitivities, specificities, PPVs and NPVs ranged from 95 to100% (95% CI: 77–100), 30 to 100% (95% CI: 38–100), 81 to 100% (95% CI: 61–100) and 91 to 100% (95% CI: 59–100) respectively (Table 3 and Fig. 2).

Sensitivities, specificities, PPVs and NPVs of the two diagnostic algorithms starting with MRI (MRI + ultrasound and MRI + RA) were all 100% (Table 3). Specificities were significantly greater for algorithms starting with MRI than those starting with RA or with ultrasound. Fig. 3 shows the algorithm that yielded best performance for diagnosing GCA. Fig. 4 shows imaging examinations in a patient with GCA.

3.3. Inter-reader agreement

Inter-reader agreement was almost perfect (kappa = 0.85; 95% CI: 0.58–1) when assessing the presence of GCA-related inflammatory changes on extracranial arteries:

4. Discussion

Our prospective study showed that a combination of several diagnostic imaging examinations, namely MRI, ultrasound and RA yielded higher diagnostic performance as compared to using each modality alone. All combinations of imaging modalities yielded greater sensitivities than that of the TAB. To our knowledge, our study is the first prospective one combining several imaging tests for diagnosing GCA instead of simply comparing them individually. As a result, several algorithms which could be used in clinical practice were tested and validated.

Our results support the EULAR recommendations which recommend MRI and ultrasound as first-line investigations for patients with suspected GCA [28]. We showed that MRI and ultrasound alone had a greater sensitivity than TAB. Moreover, we showed that MRI and ultrasound or MRI and RA when combined had sensitivities, specificities and accuracies of 100%, supporting the EULAR recommendations to combine more than one test if the first one is negative [28].

The results of this are in line with those of previous studies evaluating diagnostic performance of MRI, ultrasound and RA [4–11,15,19–24,30,33–43]. A recent meta-analysis evaluating the diagnostic value of imaging techniques in the diagnosis of cranial GCA, including 17 studies evaluating ultrasound and 8 MRI examination, showed substantial differences in sensitivity among them. Pooled sensitivity and specificity were 77% and 96% for ultrasound and 73% and 88% for MRI [44].

All three imaging techniques have specific advantages and limitations. Ultrasound remains a first-line imaging modality because of its availability, low cost, and lack of ionizing radiation. Good diagnostic performance is linked to expertise, but this is also valid for all the other imaging tests. One of the advantages of MRI is a higher standardization of data acquisition, though it has known limitations around the need for high resolution dedicated to vessel-wall imaging techniques, higher costs, and possible side effects of contrast agents [45–48]. RA is used more often performed when patients have ophthalmological symptoms. It can induce allergic reaction, and it is not available in every center.

According to EULAR recommendations for the use of imaging in large vessel vasculitis, ultrasound should be considered a first-line imaging modality to perform in patients with suspected predominantly cranial GCA [27]. Our results support these recommendations, showing that ultrasound is accurate when diagnosing GCA, as reported by two recent studies [30,43]. We showed that the best algorithms (*i.e.*, the one with the overall better diagnostic performance) were systematically the ones starting with an MRI, with 100% accuracy, sensitivity and specificity. Dedicated high resolution vessel wall imaging should be set up in all referral centers for GCA and radiologists should be trained to interpretate this imaging. However, the algorithms starting with ultrasound provided excellent sensitivities and specificities as well, almost similar to those starting with MRI. Using ultrasound as a first diagnostic exam would be more practical in terms of the cost-effectiveness and accessibility to resources. This strategy appears to be efficient and might be recommended in most centers where ultrasound is easily accessible. Ultrasound should be performed in combination with MRI or RA if ultrasound is inconclusive.

Prompt diagnosis and treatment is essential to avoid irreversible ischemic complications in patients with GCA [49]. It is also relevant

Table 3
Diagnostic performance of various combinations of imaging modalities for diagnosing giant cell arteritis.

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
ultrasound + MRI	100 (22/22) [85–100]	93 (14/15) [68–100]	96 (22/23) [78–100]	100 (14/14) [77–100]	97 (36/37) [86–100]
ultrasound + RA	95 (21/22) [77–100]	67 (10/15) [38–88]	81 (21/26) [61–93]	91 (10/11) [59–100]	84 (31/37) [68–94]
RA + ultrasound	95 (21/22) [77–100]	67 (10/15) [38–88]	81 (21/26) [61–93]	91 (10/11) [59–100]	84 (31/37) [68–94]
RA + MRI	100 (22/22) [85–100]	30 (11/15) [45–92]	85 (22/26) [65–96]	100 (11/11) [72–100]	89 (33/37) [75–97]
MRI + ultrasound	100 (22/22) [85–100]	100 (15/15) [78–100]	100 (22/22) [85–100]	100 (15/15) [78–100]	100 (37/37) [91–100]
MRI + RA	100 (22/22) [85–100]	100 (15/15) [78–100]	100 (22/22) [85–100]	100 (15/15) [78–100]	100 (37/37) [91–100]
TAB	62 (19/25) [30–85]	100 (18/18) [85–100]	100 (19/19) [85–100]	58 –18/24) [30–81]	86 (37/43) [72–95]

Numbers in parentheses are proportions; numbers in brackets are 95% confidence interval. MRI: Magnetic resonance imaging; RA: retinal angiography; TAB: Temporal artery biopsy.

Table 4
MRI sequence parameters.

Scanning technique	Pre-contrast 3D fat-saturated TSE HR-VWI	3D FLAIR T2-WI	3D DWI	3D supra-aortic vessel MRA	2D SWI	Post- contrast 3D fat-saturated TSE HR-VWI
Repetition time (ms)	1000	8000	9411	8.9	29	1000
Echo time (ms)	30	340	82	2.9	7.2	30
Inversion time (ms)	NA	2400	NA	NA	NA	NA
Number of excitations	1	1	2	1	1	1
Field of view (mm^3)	221 × 221 × 59	240 × 240 × 183	230 × 263 × 120	280 × 240 × 168	230 × 189	221 × 221 × 59
Bandwith (kHz)	754	947	45.5	283	255	754
Acquisition matrix	404 × 402 × 108	240 × 240 × 183	116 × 129 × 60	700 × 600 × 420	384 × 316	404 × 402 × 108
Acquired voxel size (mm^3)	0.55 × 0.55 × 0.55	1 × 1 × 1	2 × 2 × 2	0.4 × 0.4 × 0.4	0.6 × 0.6 × 3	0.55 × 0.55 × 0.55
Reconstructed voxel size (mm^3)	0.5 × 0.5 × 0.55	1 × 1 × 1	0.8 × x0.8 × 2	0.3 × 0.3 × 0.4	0.3 × 0.3 × 1.5	0.5 × 0.5 × 0.55
Acquisition duration	4 min 45 s	5 min 4 s	3 min 18 s	4 min 11 s	2 min 15 s	4 min 45 s

2D: Two-dimensional; 3D: Three-dimensional; R-VWI: High-resolution vessel-wall imaging; TSE: Turbo spin-echo; FLAIR: Fluid attenuation inversion recovery; WI: Weighted-imaging; DWI: Diffusion weighted-imaging; MRA: Magnetic resonance angiography; SWI: Susceptibility weighted-imaging; NA: Not applicable.

to rule out GCA quickly to avoid treatment using steroids, especially in elderly patients. Based on our findings, it would be appropriate for patients with a suspicion of GCA to be placed on fast-track clinics or in specialized tertiary centers that offer rapid access to imaging techniques. This strategy would improve the performance of rapid diagnosis and treatment of GCA. This approach is recommended by the 2018 EULAR guidelines, which state that all patients presenting with signs and symptoms of GCA should be urgently referred to a specialized team for further multidisciplinary diagnostic work-up and management [27,28]. During the course of the study, most of the enrolled patients underwent MRI, ultrasound and RA the same day or a few days after their admission for suspected diagnosis of GCA, with immediate results, as compared to several days of delay before obtaining the results of the TAB. Based on the results of our study, our center has set up a fast-track multidisciplinary clinic for diagnostic work-up and management of patients with suspected GCA, allowing our patients to undergo at least two imaging examinations within 24 to 48 hours after the onset of symptoms [50].

Our study has some limitations. First, the overall number of patients remains low in a single center. Second, this study was performed in a tertiary center specializing in ophthalmological and neurological diseases. A majority of our patients presented with visual symptoms, which is greater than the rate of 7–60% of patients with GCA reported in the literature [51]. This might limit the generalization of our results to all patients with GCA, especially those with large-vessel GCA. Third, imaging examinations were performed no later than seven days after the onset of symptoms and before treatment or within five days after the beginning of steroid therapy, which are optimal conditions to detect inflammatory changes of the arteries. The high accuracy of our results may be lower in patients with delayed examinations or in those who are under treatment, thus our algorithm might not work under sub-optimal conditions. Fourth, further studies comparing the capabilities of artificial intelligence and our algorithm should be warranted [52,53]. Fifth, we did not evaluate PET-CT, thus we could not integrate it into our study. Therefore, we could not compare our results with those of Imfeld et al. who showed

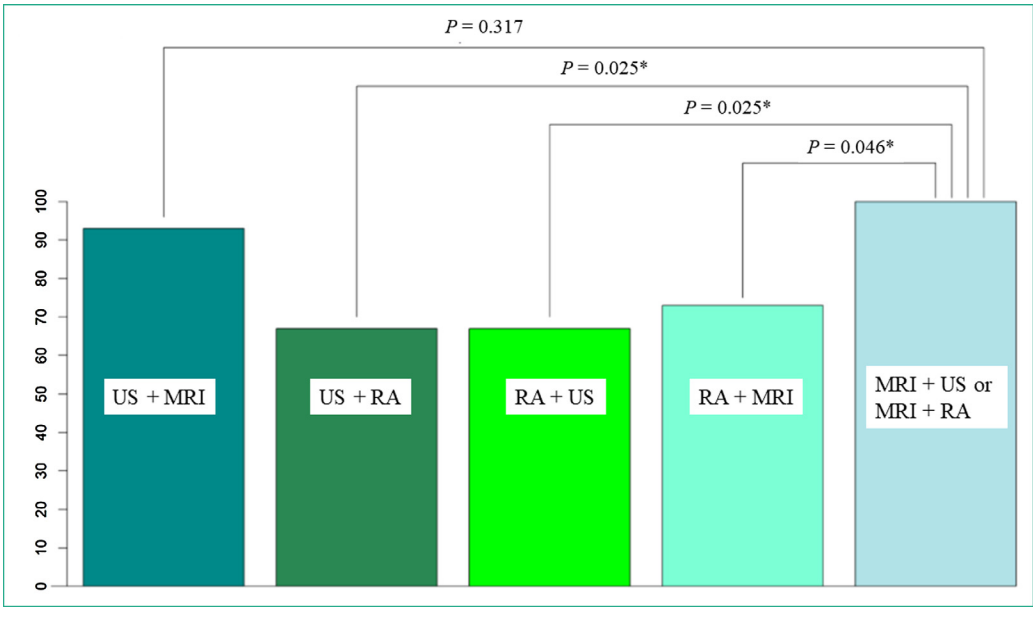

Fig. 2. Graph shows bar plots comparing the specificity of several combinations of imaging modalities. The asterisks * indicate significant differences after appropriate statistical correction. MRI: Magnetic resonance imaging; RA: Retinal angiography; US: Ultrasound. Y-axis represent percentages.

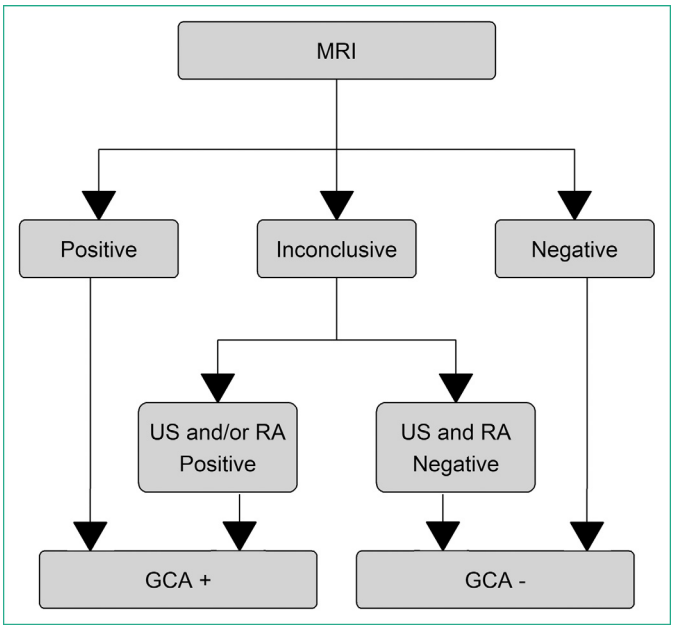

Fig. 3. Algorithm showing the best performance for diagnosing giant cell arteritis (GCA) using a combination of several imaging modalities. MRI: Magnetic resonance imaging; RA: Retinal angiography; US: Ultrasound.

that a combination of ultrasound and PET-CT increases the diagnostic yield by 16–20% [29]. Finally, we used state-of-the-art diagnostic examinations on high-end devices, performed and read by trained readers, which may not be reproducible in all centers worldwide [54]. Further studies including multicenter studies are needed to evaluate our algorithm in various conditions.

In conclusion, in this prospective study, we developed a new multimodal algorithm for the diagnosis of giant cell arteritis. The use of MRI as the first imaging examination followed by either ultrasound or RA reaches high degrees of performance for the diagnosis of GCA and surpasses each examination used alone for the diagnosis of GCA. This approach based on multimodal imaging techniques could be used in daily practice.

Human rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patients.

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Credit author statement

All authors have made substantial contributions to all the categories established by the ICMJE:

"Conception and design, or acquisition of data, or analysis and interpretation of data,"

"Drafting the article or revising it critically for important intellectual content,"

"Final approval of the version to be published,"

"Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved."

A. Lecler, G. Clavel: Conceptualization, - Data curation, - Formal analysis, - Funding acquisition, - Investigation, - Methodology, - Project administration, - Resources, - Software, - Supervision, - Validation, - Visualization, - Writing - original draft, - Writing - review & editing.

J. Savatovsky: Conceptualization, - Data curation, - Formal analysis, - Funding acquisition, - Investigation, - Methodology, - Software, - Supervision, - Validation, - Visualization, - Writing - review & editing.

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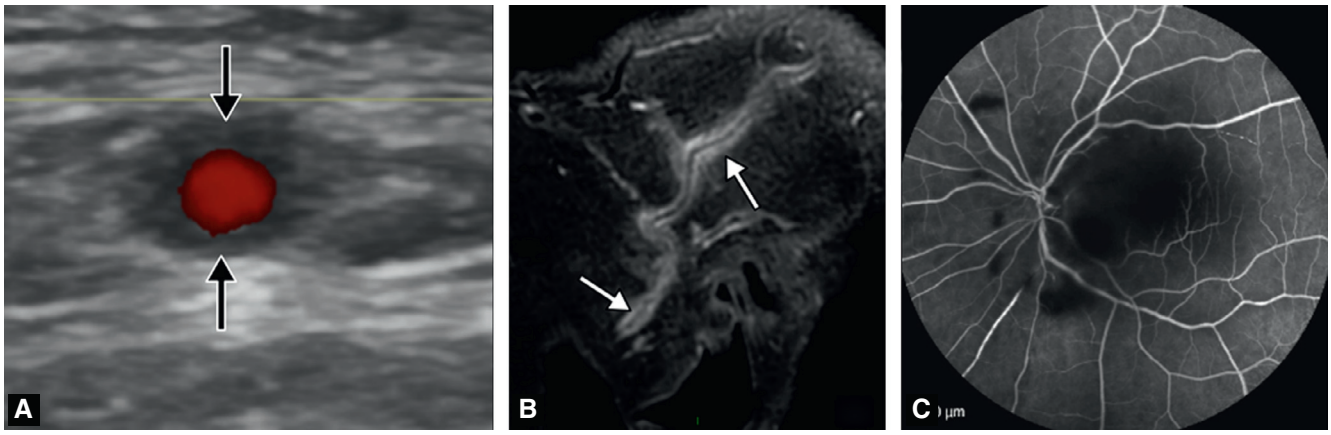

Fig. 4. 96-year-old man with a positive diagnosis of GCA. Ultrasound image (a) shows a halo sign and a thickened arterial wall of the right temporal artery (black arrows). High-resolution vessel-wall MRI (b) shows grade 3 inflammatory changes of the right temporal artery (white arrows). Retinal angiography (c) shows choroidal delay in the territory of the short medial posterior ciliary artery.

Ethical statement

This study was approved by an institutional review board (ID RCB: 2014-A01553−44). Signed informed consent was obtained from all subjects. This study follows the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines.

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