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Clinical science

PET/CT of cranial arteries for a sensitive diagnosis of giant cell arteritis

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Abstract

Objectives: To investigate the performance of cranial PET/CT for the diagnosis of GCA.

Methods: All patients with a suspected diagnosis of GCA were prospectively enrolled in this study and had a digital PET/CT with evaluation of cranial arteries if they had not started glucocorticoids >72 h previously. The diagnosis of GCA was retained after at least 6 months of follow-up if no other diagnosis was considered by the clinician and the patient went into remission after at least 6 consecutive months of treatment. Cranial PET/CT was considered positive if at least one arterial segment showed hypermetabolism similar to or greater than liver uptake.

Results: For cranial PET/CT, sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were 73.3%, 97.2%, 91.7% and 89.7%, respectively. For extracranial PET/CT, diagnostic performance was lower (Se = 66.7%, Sp = 80.6%, PPV = 58.8%, NPV = 85.3%). The combination of cranial and extracranial PET/CT improved overall sensitivity (Se = 80%) and NPV (NPV = 90.3%) while decreasing overall specificity (Sp = 77.8%) and PPV (PPV = 60%).

Conclusion: Cranial PET/CT can be easily combined with extracranial PET/CT with a limited increase in examination time. Combined cranial and extracranial PET/CT showed very high diagnostic accuracy for the diagnosis of GCA.

Trial registration: ClinicalTrials.gov, https://clinicaltrials.gov, NCT05246540.

Keywords: GCA, PET CT, diagnosis

Rheumatology key messages

- Cranial PET/CT can be easily combined with extracranial PET/CT.
- Cranial PET/CT allows the study of main cervical arteries (temporal, occipital, maxillar and vertebral).
- Combined (cranial and extracranial) PET/CT has excellent performance for excluding GCA (NPV = 90%).

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Introduction

Temporal artery biopsy (TAB) remains the gold standard for the diagnosis of giant cell arteritis (GCA) [1], especially in cases of cranial GCA [2]. However, TAB is an invasive procedure and [3] lacks sensitivity [4], so that other complementary exams are often needed to definitely confirm the diagnosis of GCA.

Vascular imaging techniques have acquired an increasingly important role for the diagnosis of GCA. Doppler ultrasound is an accessible technique that is mainly used to evaluate the temporal and axillary arteries to show hypoechogenic thickening of the arterial wall, which is known as the 'halo sign'. However, Doppler ultrasound is limited by its dependence on the operator and by its lack of sensitivity and specificity, estimated at 68 and 81%, respectively [5]. Angio-MRI can also detect temporal arteritis with a high sensitivity (93%) and relatively high specificity (75–78%), but temporal artery abnormalities disappear after one week of GC treatment, and it is difficult to access the exam early enough in most centres [6]. Angio-CT has primarily been studied to detect inflammation in the extracranial arteries, mainly the aorta and its main branches [7], but its usefulness for the assessment of the temporal arteries is still limited [8].

[18F]-fluorodeoxyglucose (FDG) PET/CT is increasingly used for the diagnosis of GCA because of its high sensitivity for the detection of large-vessel vasculitis. However, PET/CT has to be performed in the 72 h after starting glucocorticoids (GC) because the hypermetabolism signal significantly decreases afterward [9]. PET/CT was first used to detect large-vessel vasculitis, but recent papers have demonstrated that new generation PET/CT can be used to study cranial arteries including the temporal, occipital and maxillary arteries, thus increasing its diagnostic value in GCA. In a retrospective study evaluating PET/CT for the diagnosis of GCA, the detection of significant hypermetabolism in the cranial arteries had variable sensitivity (64–82%) according to the number of arteries that were studied, and high specificity (100%) [10]. In another study, which prospectively enrolled 58 patients with a suspicion of GCA, 12 of whom had positive TAB, a negative PET/CT of cranial arteries had excellent predictive value to exclude the diagnosis of GCA (87%) [11].

We therefore designed this prospective study to investigate the diagnostic performance of cranial and extracranial PET/CT for the diagnosis of GCA in a population of patients with a suspected diagnosis of GCA.

Patients and methods

Population

Between November 2018 and June 2020, all patients who underwent a digital PET/CT in the context of a suspicion of GCA in the nuclear medicine department (CRLCC Georges Francois Leclerc Centre) and that were subsequently followed-up at the Dijon University Hospital were considered for inclusion. Patients under 50 years old, those who had received GC for >72 h [9], those who were followed for previously diagnosed GCA and those who had capillary glycaemia >7 mmol/l just before the PET/CT were excluded.

Definition and data collection

Clinical, biological and paraclinical data were prospectively collected in a standardized case report form (details in the supplementary materials available at *Rheumatology* online).

The diagnosis of GCA was retained if the clinician had not considered any other diagnosis after at least 6 months of follow-up, and if the patient went into remission following GCA treatment administered for at least 6 consecutive months. The clinicians in charge of the patients had access to cranial PET/CT images but not to the 0–3 scoring system. Patients with GCA were classified into three groups: cranial GCA (C-GCA), large-vessel GCA (LV-GCA) and the combination of both (definitions in the supplementary methods available at *Rheumatology* online).

PET/CT procedure

The exam was performed prior to biopsy. The procedure is detailed in supplementary methods available at *Rheumatology* online.

PET/CT analysis

Each PET/CT was reviewed by two nuclear medicine physicians (B.D-B. and J-L.A.) with extensive experience reading PET/CT in GCA and who were blinded to clinical and paraclinical data. They used a workstation with triangulation tools for 3D vision (AW Server workstation; General Electric Healthcare, Waukesha, WI, USA). Eight cranial artery segments (vertebral, occipital, temporal and maxillary) and 12 other large arteries (thoracic aorta, abdominal aorta, axillary, carotid, subclavian, femoral and iliac) were analysed (representative analyses in Supplementary Figs S1 and S2, available at *Rheumatology* online).

Visual assessment

A standardized visual assessment system on a 0- to 3-point scale based on established criteria [9], comparing arterial hypermetabolism with liver uptake, was used to determine the level of hypermetabolism in each arterial segment as follows: 0 = no FDG uptake (lower than the mediastinal blood pool); 1 = low-grade uptake (less than liver uptake); 2 = intermediate-grade uptake (similar to liver uptake), 3 = high-grade uptake (higher than liver uptake) (Supplementary Fig. S2, available at *Rheumatology* online). For the primary end point of this study, PET/CT was considered positive if at least one arterial segment had a ≥ grade 2 hypermetabolism. In case of disagreement between the two readers on any segment, the final result was established by a consensus reading following the interpretation of the images by a third nuclear physician (C.D.).

Semiquantitative assessment

SUVmax (maximum standard uptake value) was measured for each arterial segment defined as a target by drawing a manually delineated volume of interest (VOI) that included each whole vascular segment and avoided areas of atherosclerosis.

Cranial SUVmax was defined for each patient as the maximum SUVmax value for the eight cranial artery segments. Similarly, vertebral, occipital, temporal and maxillary SUVmax were defined for each patient as the maximum SUV of each pair of arteries.

Target-to-liver or blood pool ratios were used to account for the possible overlap of SUVmax between GCA patients and non-GCA patients [12], and the potential loss of specificity when SUVmax is analysed alone [13]. Liver SUVmax and blood-pool SUVmax were recorded by drawing a 3-cm VOI in the right lobe of the liver (to calculate a target-to-liver ratio)

and by drawing a VOI in the centre of the superior vena cava (to calculate a target-to-blood pool ratio), respectively [9].

Statistical analyses

The primary outcome was the sensitivity and the specificity of cranial PET/CT compared with the gold-standard clinical diagnosis. Sensitivity and specificity of extracranial PET/CT were calculated using the clinical diagnosis of GCA as the gold-standard reference. ROC curves were constructed for target to-liver ratios and target-to-blood pool ratio. The analyses were also repeated using positive TAB as a reference for the diagnosis of GCA.

Continuous variables are expressed as medians (interquartile range) and categorical variables as numbers (%). Mann–Whitney tests were used to compare continuous variables and Fisher's exact tests were used to compare qualitative variables. Statistical significance was set at $P < 0.05$ (two tailed). Statistical analyses were performed using R (version 4.1.1) and SAS (version 9.4) software.

Ethics

Included patients underwent a PET/CT as part of their management because GCA was suspected. After receiving written consent, they did not object to the use of their data for this study, as required by French legislation. This study was approved by the Institutional Review Board and the Ethics Committee of Dijon University Hospital and registered with ClinicalTrials.gov, number NCT05246540.

Results

Studied population

Digital cranial and extracranial PET/CT was performed in 111 patients, of whom 60 were finally excluded. Therefore, 51 patients were included in the final analysis, and 15 (29.4%) of these patients had a final diagnosis of GCA (Fig. 1).

Patient characteristics are summarized in Table 1. All 15 GCA patients fulfilled at least 3/5 of the ACR criteria and 12 (80%) met the GiACTA criteria [1]. Seven had C-GCA, two had LV-GCA and six had a combination of both. By contrast, none of the 36 patients without a final diagnosis of GCA met the GiACTA criteria while three (8.3%) fulfilled ≥3 of the ACR criteria. The diagnoses retained for the 36 non-GCA patients are reported in Supplementary Table S1, available at *Rheumatology* online. Results of TAB were available for 32/51 (62.7%) patients including 14/15 (93.3%) GCA patients and 18/36 (50%) non-GCA patients. One TAB performed in a GCA patient was not available because the sample did not contain an analysable artery. TAB showed arterial lesions consistent with GCA in 10/14 GCA patients (71.4%) and 0/18 in non-GCA patients (0%). Results of the Doppler ultrasound were available in 15/15 (100%) GCA patients and 22/36 (61.1%) non-GCA patients. Doppler ultrasound showed at least one sign of GCA in 10/15 (66.7%) GCA patients, including seven bilateral halo signs, two unilateral halo sign and one bilateral temporal artery occlusion. In non-GCA patients, Doppler ultrasound was abnormal in 3/22 (13.6%) of cases, including one discrete bilateral halo and two unilateral halo signs (Table 1).

PET/CT descriptions

Visual qualitative assessment

PET/CT results were available in 51/51 (100%) patients. A total of 11/15 GCA patients had at least one cranial artery with ≥ grade 2 uptake, *vs* only 1/36 in non-GCA patients. Ten of the 15 GCA patients had also at least one extra-cranial segment with a grade ≥ 2 uptake whereas it was the case in 7/36 non-GCA patients. When combining cranial and extracranial PET/CT, 12/15 GCA patients and 8/36 non GCA patients had at least one cranial or extra-cranial segment with a grade ≥ 2 uptake. Results are summarized in Table 2.

Cranial PET/CT was considered positive in one non-GCA patient because both maxillary arteries had a grade 3 uptake. This patient had been hospitalized for left hemispheric ischaemic stroke secondary to a dissection of the M1 portion of the left middle cerebral artery. He had no cranial signs of GCA or polymyalgia rheumatica, TAB was not performed and no GC therapy was started, so the diagnosis of GCA was not retained. In 18 months of follow-up, he never developed signs of GCA. Among the seven non-GCA patients who had a positive extracranial PET/CT, only one had at least one segment with a grade 3 uptake (thoracic and abdominal aorta). The diagnosis of GCA was not retained in this patient because of the absence of clinical signs of GCA or polymyalgia rheumatica, the absence of acute phase reaction and negative TAB. The patient did not receive GC and remained symptom-free with normal C-reactive protein during one year of follow-up. For the 6/7 remaining non-GCA patients with positive extracranial PET/CT results, the grade 2 uptake was explained by alternative diagnoses: type B thoracic and abdominal aortic dissection ($n = 1$); mycotic aneurysm of the iliac arteries ($n = 1$); atheroma of the femoral arteries ($n = 1$), abdominal aorta ($n = 1$) or axillary artery ($n = 1$); or polyaneurysmal dystrophy of the iliac artery ($n = 1$). The analyses of each arterial segment showed that hypermetabolism of the cranial arteries was very rare in non-GCA patients, whereas hypermetabolism was more frequent in other arterial territories prone to atheromatous lesions, such as the aorta or iliac arteries (Table 2).

Semiquantitative assessment

Target-to-blood pool ratios of SUVmax in GCA patients and non-GCA patients are presented in Supplementary Fig. S3 and target-to-liver ratios in Supplementary Fig. S4, both available at *Rheumatology* online. The SUVmax ratios of all cranial arteries were significantly higher in GCA patients than in non-GCA patients. In GCA patients, the highest SUVmax ratios were observed in the maxillary arteries, followed by the vertebral and temporal arteries, while FDG uptake was lower in the occipital arteries.

Diagnostic accuracy

The sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) results for PET/CT defined according to the gold standard (clinical diagnosis) of GCA are reported in Table 3. For cranial PET/CT, Se, Sp, PPV and NPV were 73.3% (95% CI: 51.0%, 95.7%), 97.2% (95% CI: 91.9%, 102.6%), 91.7% (95% CI: 76.0%, 107.3%) and 89.7% (95% CI: 80.2%, 99.3%), respectively. For extracranial PET/CT, diagnostic performance was lower (Se = 66.7%, Sp = 80.6%, PPV = 58.8%, NPV = 85.3%). The combination of cranial and extracranial PET/CT improved overall sensitivity

Table 1 Comparison of GCA patients and non-GCA patients

	GCA patients ($n = 15$)	Non-GCA patients ($n = 36$)	*P*-value
≥3/5 ACR criteria, *n* (%)	15 (100%)	3 (8,3%)	
GIACTA criteria fulfilled, *n* (%)	12 (80%)	0 (0%)	
Sex, F/H	11/4	21/15	0.3
Age (years), median (IQR)	79 (74–79)	71 (62–84)	0.2
Cardiovascular risk factors, *n* (%)			
Active or past smoking	4 (27%)	13 (36%)	0.5
Diabetes	0 (0%)	6 (17%)	0.2
Arterial hypertension	9 (60%)	24 (67%)	0.6
Dyslipidaemia	2 (13%)	15 (42%)	0.050
Cardiovascular medical past history, *n* (%)			
Ischaemic cardiopathy	1 (6,7%)	7 (19 %)	0.4
Myocardial infarction	1 (6,7%)	4 (11 %)	> 0.9
Stroke	1 (6,7%)	1 (2,8%)	0.5
Peripheral arterial disease	1 (6,7%)	2 (5,6%)	> 0.9
Constitutional symptoms			
Fever	2 (13%)	7 (19 %)	0.7
Weight loss	8 (53%)	11 (31 %)	0.4
Cephalic signs			
Headache	10 (67%)	11 (31 %)	0.017
Scalp tenderness	4 (27%)	11 (31 %)	> 0.9
Jaw claudication	9 (60%)	4 (11 %)	< 0.001
Temporal artery tenderness or induration	11 (73,3%)	2 (5,6%)	< 0.001
Stroke	0 (0%)	3 (8,3%)	0.5
Visual signs	6 (40%)	6 (17%)	0.14
Blurring	0 (0%)	3 (8.3%)	0.5
Transient visual loss	1 (6.7%)	1 (2.8%)	0.5
Hallucinations	0 (0%)	1 (2.8%)	> 0.9
Diplopia	5 (33%)	1 (2.8%)	0.006
AAION	1 (6.7%)	2 (5.6%)	> 0.9
PION	0 (0%)	1 (2.8%)	> 0.9
CRAO	0 (0%)	0 (0%)	—
Polymyalgia rheumatica	4 (27%)	8 (22%)	0.7
Biology			
Hb (g/dL), available data	15/15	36/36	
Median (IQR)	11.4 (10.85–11.95)	12.3 (11.67–13.12)	0.024
CRP (mg/l), available data	15/15	35/36	
Median (IQR)	78 (48, 111)	23 (5–109)	0.043
ESR (mm), available data	9/15	11/36	
Median (IQR)	84 (60–86)	32 (21–80)	0.018
Temporal artery ultrasonography			
Available data	15/15	22/36	
Positive	10/15	3/22	
Temporal artery biopsy			
Available data	14/15	18/36	
Positive[a]	10/14	0/18	
Treatment with GC the day of PET/CT	6/15[b]	2/36[b]	
If yes, duration (days), median (range)	1 (0–3)	0.50 (0–1)	

[a] TAB was considered positive if it shows transmural granulomatous inflammation or at least involving the media.
[b] None of these patients received high-dose IV corticosteroids.
AAION: acute anterior ischaemic optical neuropathy; CRAO: central retinal artery occlusion; GC: glucocorticoids; Hb: hemoglobinemia; PION: posterior ischemic optical neuropathy.

(Se = 80%) and NPV (NPV = 90.3%), while decreasing the overall specificity (Sp = 77.8%) and PPV (PPV = 60%).

Value of cranial SUVmax ratios for the diagnosis of GCA

Analyses of ROC curves computing target-to-blood pool ratios and target-to-liver ratios for cranial SUVmax resulted in an area under the curve (AUC) of 94.4% (95% CI: 88.5%, 100%) and 95.2% (95% CI: 89.6%, 100%), respectively (Fig. 2A, B). In comparison, AUC of the ROC curves of the extracranial SUVmax to blood pool ratio or liver ratio were lower: 70.7% (95% CI: 55.9%, 85.4%) and 74.1% (95% CI: 59.1%, 89.1%), respectively.

The analysis of different target-to-blood pool ratio thresholds for cranial SUVmax are shown in Fig. 2C and of different target-to-liver ratio thresholds for cranial SUVmax in Fig. 2D. All GCA patients had a target-to-blood pool ratio higher than 1.16 and a target-to-liver ratio higher than 0.71 (100% sensitivity and 80.6% specificity for both). The vast majority of non-GCA patients (35/36) had a target-to-blood pool ratio under 1.60 (66.7% sensitivity and 97.2% specificity) and a target-to-liver ratio under 0.82 (80% sensitivity and 97.2% specificity). The best compromises between sensitivity and specificity were found for thresholds at 1.20 (86.7% sensitivity and 86.1% specificity) for target-to-blood pool ratio, and 0.78 (86.7% sensitivity and 88.9% specificity) for target-to-liver ratio.

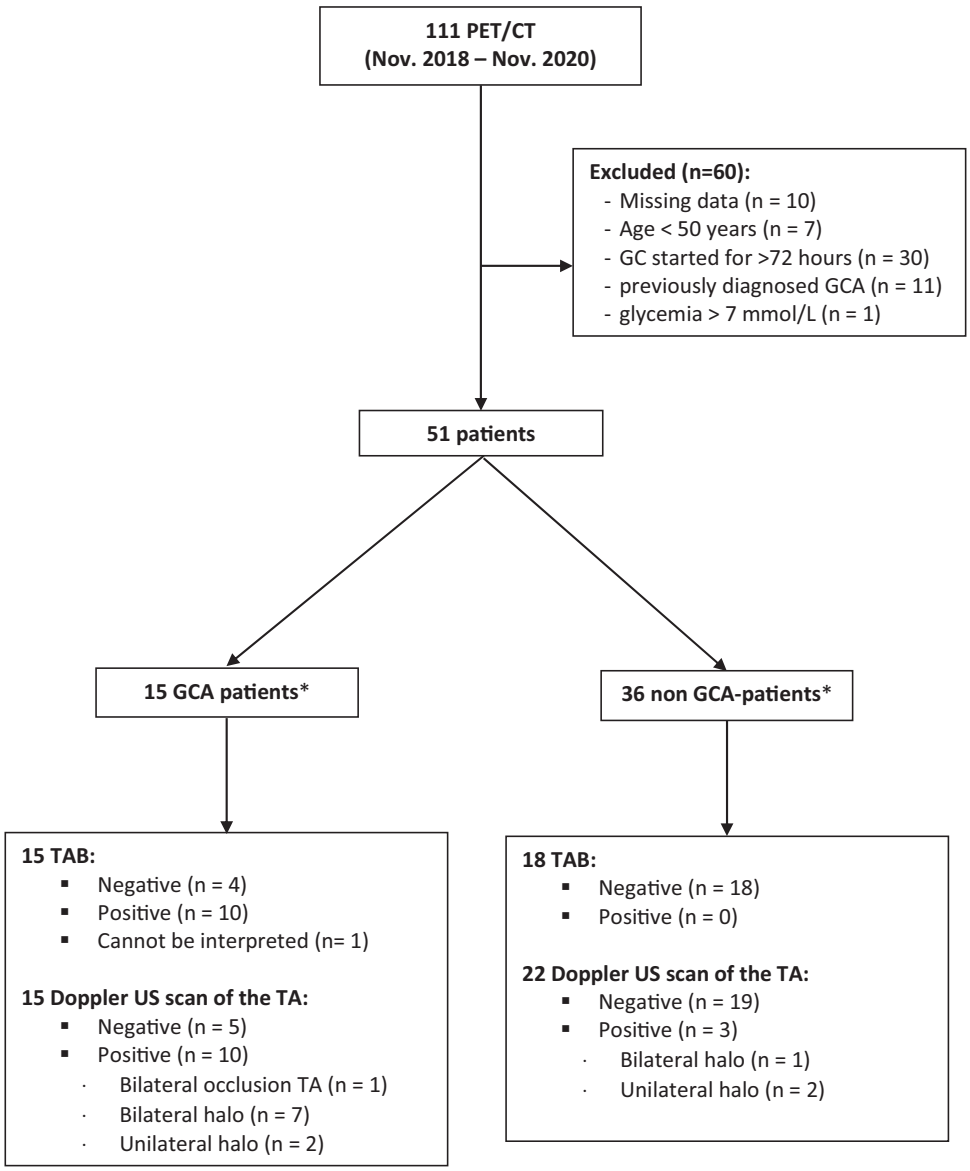


Figure 1. Flow chart of the study

*According to the reference clinical diagnosis. GC: glucocorticoids; TA: temporal artery; TAB: temporal artery biopsy

ROC curves and AUC results for target-to-blood pool ratios and target-to-liver ratios of SUVmax of each cranial artery are shown in Fig. 2E and F. The best AUCs were found for the vertebral (93.2% and 93%) and maxillary arteries (89.6% and 90.7%). The AUC results for the temporal arteries were around 84% (83.3% and 84.3%, precisely). The occipital arteries had the lowest AUC results (70.2% and 75.7%).

Comparison with TAB results

TAB results were available for 32/51 patients (14/15 GCA patients). Considering TAB as the reference for the diagnosis of GCA, cranial PET/CT gave the following results: Se = 70.0% (95% CI: 41.6%, 98.4%), Sp = 86.4% (95% CI: 72.0%, 100.7%), PPV = 70.0% (95% CI: 41.6%, 98.4%) and NPV = 86.4% (95% CI: 72.0%, 100%). ROC curves and the description of temporal SUVmax by TAB results for all patients and for GCA patients only are presented in Supplementary Fig. S5, available at *Rheumatology* online. The temporal/blood-pool SUVmax ratios and the temporal/liver SUVmax ratios were significantly higher in patients with positive TAB than in patients with negative TAB ($P < 0.01$). By contrast, the difference was not statistically different when the same analysis was done in the subgroup of GCA patients ($P = 0.7$; Supplementary Fig. S5, available at *Rheumatology* online).

Discussion

PET/CT is not currently recommended for the study of cranial arteries by any guidelines, and these arteries are still more commonly studied by Doppler ultrasound [14]. In the last few years, cranial PET/CT has become more widely available following the development of new generation PET/CT scans, making it more suitable for use in the diagnosis of GCA. One prospective study [11] and two case-control studies [10, 15] have already suggested promising results using FDG-PET/CT for the diagnosis GCA. The present study aimed to evaluate the diagnostic performance of cranial PET/CT in addition to extracranial PET/CT.

Table 2 Comparison of PET/CT between GCA patients and non GCA patients

	GCA patients ($n = 15$)	Non GCA patients ($n = 36$)	*P*-value*
Cranial PET/CT			
At least one segment ≥ 2 (%)[a]	11 (73.3%)	1 (2.8%)	<0.001
Cranial SUVmax—median (IQR)	3.83 (2.90, 5.03)	1.91 (1.65, 2.23)	<0.001
Extra-cranial PET/CT			
At least one segment ≥2 (%)	10 (66.7%)	7 (19.4%)	0.001
Extra-cranial SUVmax—median (IQR)	3.35 (2.84, 3.89)	2.66 (2.42, 3.00)	0.007
Cranial and extra-cranial PET/CT combination			
At least one segment ≥ 2 (%)	12 (80%)	8 (22.2%)	<0.001
Global SUVmax—median (IQR)	4.34 (3.13, 5.12)	2.66 (2.42, 3.04)	<0.001
Liver SUV—median (IQR)	3.36 (2.92, 3.62)	3.26 (2.82, 3.64)	>0.9
Blood pool SUV– median (IQR)	1.98 (1.65, 2.20)	1.96 (1.68, 2.15)	0.9
Visual grade 2–3 (%)			
Left occipital artery	5 (33%)	0 (0%)	0.001
Right occipital artery	5 (33%)	0 (0%)	0.001
Left temporal artery	7 (47%)	0 (0%)	<0.001
Right temporal artery	8 (53%)	0 (0%)	<0.001
Left maxillary artery	8 (53%)	1 (2.8%)	<0.001
Right maxillary artery	7 (47%)	1 (2.8%)	<0.001
Left vertebral artery	8 (53%)	0 (0%)	<0.001
Right vertebral artery	8 (53%)	0 (0%)	<0.001
Thoracic aorta	6 (40%)	2 (5.6%)	0.005
Abdominal aorta	5 (33%)	3 (8.3%)	0.039
Left carotid artery	4 (27%)	1 (2.8%)	0.022
Right carotid artery	2 (13%)	0 (0%)	0.082
Left subclavian artery	6 (40%)	1 (2.8%)	0.002
Right subclavian artery	5 (33%)	1 (2.8%)	0.006
Left axillary artery	4 (27%)	1 (2.8%)	0.02
Right axillary artery	3 (20%)	1 (2.8%)	0.071
Left iliac artery	3 (20%)	3 (8.3%)	0.3
Right iliac artery	5 (33%)	2 (5.6%)	0.018
Left femoral artery	6 (40%)	1 (2.8%)	0.002
Right femoral artery	5 (33%)	1 (2.8%)	0.006

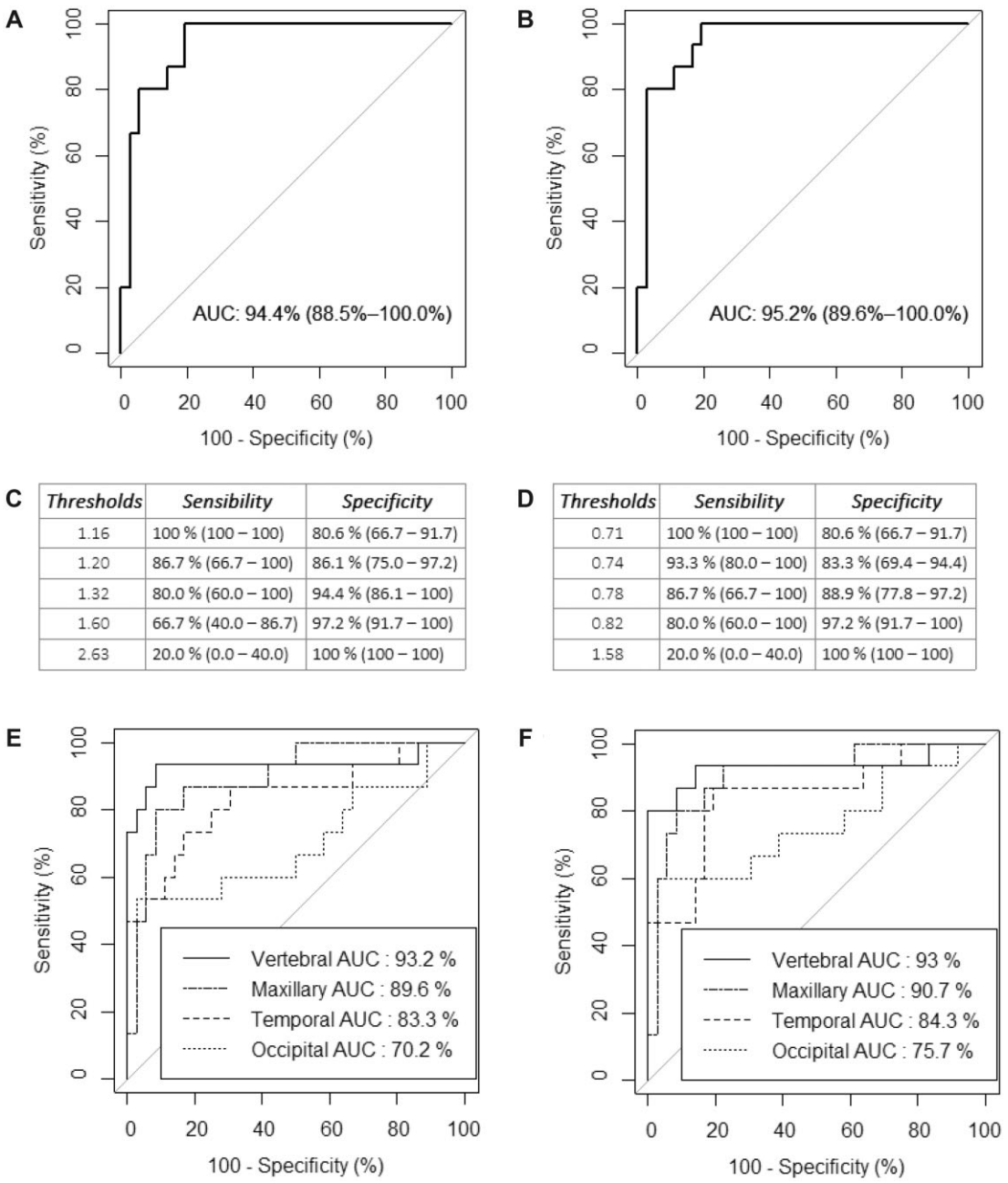
[a] 100% of cases had at least one symmetrical artery involved.
* Mann–Whitney test was used to compare continuous variables and Fisher's exact test was used to compare qualitative variables.

Table 3 Diagnostic accuracy of PET/CT

Grade ≥ 2	Cranial PET/CT Grade ≥ 2	Extra-cranial PET/CT Grade ≥ 2	Combination of cranial and extra-cranial PET/CT
Sensitivity [95% CI]	73,3% [51,0, 95,7]	66,7% [42,8, 90,5]	80,0% [59,8, 100,2]
Specificity [95% CI]	97,2% [91,9, 102,6]	80,6% [67,6, 93,5]	77,8% [64,2, 91,4]
Predictive positive value [95% CI]	91,7% [76,0, 107,3]	58,8% [35,4, 82,2]	60,0% [38,5, 81,5]
Predictive negative value [95% CI]	89,7% [80,2, 99,3]	85,3% [73,4, 97,2]	90,3% [79,9, 100,7]
Positive likelihood ratio	26,2	3,44	3,6
Negative likelihood ratio	0,27	0,41	0,26

In daily practice, clinicians retain a diagnosis of GCA when there are unequivocal clinical signs of GCA and evidence of vasculitis. This is why we chose to evaluate the diagnostic performance of PET/CT *vs* the typical diagnostic approach based on the absence of an alternative diagnosis and a favourable clinical course with GC treatment for at least 6 months. When compared with the clinical diagnosis of GCA, the present study showed that cranial PET/CT had a sensitivity of 73.3% and a specificity of 97.2%. Comparison with previous studies is challenging, especially considering the different criteria used for PET/CT positivity and the definition of GCA. The prospective study by Sammel *et al.* [11] reported a sensitivity of 71% and a specificity of 91% compared with a gold standard similar to ours. Nienhuis *et al.* [15] and Nielsen *et al.* [10] published two case-control studies involving melanoma patients as controls. Nienhuis *et al.* included cases of GCA confirmed by positive TAB, and they reported a sensitivity of 83% and a specificity of 75%. Nielssen *et al.* included cases of GCA fulfilling the ACR criteria, confirmed after 6 months of follow-up, and reported a sensitivity of 82% and a specificity of 100%. One advantage of our work is that we evaluated the performance of PET/CT in a population suspected of GCA rather than controls in whom this diagnosis would not have been suspected in real-life conditions.

An additional strength of our study is the association of extracranial large-vessel PET/CT with cranial PET/CT in a single procedure. When comparing these two PET/CT separately, the performance of cranial PET/CT was found to be better than that of extracranial large-vessel PET/CT. However, this result should be analysed with caution because it probably depends on the included GCA population. It can be assumed that higher proportions of cranial-GCA patients



C

Thresholds	*Sensibility*	*Specificity*
1.16	100 % (100 – 100)	80.6 % (66.7 – 91.7)
1.20	86.7 % (66.7 – 100)	86.1 % (75.0 – 97.2)
1.32	80.0 % (60.0 – 100)	94.4 % (86.1 – 100)
1.60	66.7 % (40.0 – 86.7)	97.2 % (91.7 – 100)
2.63	20.0 % (0.0 – 40.0)	100 % (100 – 100)

D

Thresholds	*Sensibility*	*Specificity*
0.71	100 % (100 – 100)	80.6 % (66.7 – 91.7)
0.74	93.3 % (80.0 – 100)	83.3 % (69.4 – 94.4)
0.78	86.7 % (66.7 – 100)	88.9 % (77.8 – 97.2)
0.82	80.0 % (60.0 – 100)	97.2 % (91.7 – 100)
1.58	20.0 % (0.0 – 40.0)	100 % (100 – 100)

Figure 2. Study of the sensitivity and specificity PET CT of cranial arteries for the diagnosis of GCA

(**A**, **B**) ROC curves assessing the sensitivity and specificity for the diagnosis of GCA of the cranial SUVmax target-to-blood pool ratio (**A**, positivity thresholds in **C**), the cranial SUVmax target-to-liver ratio (**B**, positivity thresholds in **D**), and for each pair of cranial artery (target-to-blood pool ratios in **E**, target-to-liver ratios in **F**).

would result in better performance of cranial PET/CT, and vice versa. In our study, there were finally few GCA patients with isolated large-vessel involvement. By contrast, it is interesting to note that the combination of cranial and extracranial PET/CT in a single procedure improved overall sensitivity, which was 80% in our study, which is higher than the sensitivity of each of the exams used alone.

The main limit of our study relies on the fact that clinicians in charge of the patients had access to cranial PET/CT images. However, they had no access to the 0–3 grading score system. In addition, among the 15 patients in whom the diagnosis of GCA was retained, only one had no evidence of vasculitis with usual complementary exams (i.e. TAB, temporal artery Doppler or extracranial PET/CT) but this 77-year-old man fulfilled ACR criteria for the diagnosis of GCA. Thus, clinicians' access to images probably did not influence their final diagnosis and decision to initiate treatment. If this were the case, it would have been quite marginal and could have contributed to a moderate overestimation of PET/CT performance in our study. The positivity of PET/CT in our study relied on a standardized visual 0-to-3 grading system. Current guidelines for extracranial PET/CT state that this score should be interpreted with caution due to frequent false positives related to atherosclerotic vascular uptake, particularly in the iliac and femoral arteries. Thus, a score of 3 should be considered positive for active large-vessel vasculitis (LVV)

and a score of 2 indicative of possible LVV [9]. To date, there is no recommended threshold for positive cranial PET/CT. In our study, the high level of specificity observed for cranial PET/CT suggests that, compared with extracranial PET/CT, concerns about possible false positives due to atherosclerosis may not be relevant for cranial PET/CT. However, this hypothesis remains to be confirmed in a larger study.

In order to better determine the threshold of positivity of cranial PET/CT, we measured the SUV of each arterial segment and computed target-to-liver ratios and target-to-blood pool ratios. Analyses of the ROC curves plotted with these ratios confirmed that cranial PET/CT had excellent discriminating power for the diagnosis of GCA. Our comparison of ROC curves according to arterial territories showed that the involvement of the vertebral and maxillary arteries had the highest value for the diagnosis of GCA, the temporal arteries had an intermediate value, and the occipital arteries had the lowest value. These results are consistent with those of Nienhuis *et al.* [15].

In conclusion, the current study confirmed that cranial PET/CT is a very sensitive diagnostic test for GCA. The main advantage of this technique is that it can be combined with extracranial PET/CT to increase performance while prolonging the examination time only minimally and without exposing the patient to higher levels of radioactivity. However, PET/CT remains an expensive examination that is sometimes difficult to access, and the performance of the test decreases after the initiation of GC treatment [9], which may limit its use in daily practice.

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Data availability statement

Full data are available on request to T.T. or M.S.

Supplementary data

Supplementary data are available at *Rheumatology* online.

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