Early diagnosis and follow-up of aortitis with [18F]FDG PET and MRI

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Abstract. The aim of this prospective study was to compare fluorine-18 fluorodeoxyglucose ([18F]FDG) positron emission tomography (PET) with magnetic resonance imaging (MRI) in patients with early aortitis, at the time of initial diagnosis and during immunosuppressive therapy. The study population consisted of 15 patients (nine females and six males; median age 62 years, range 26–76 years) who presented with fever of unknown origin or an elevated erythrocyte sedimentation rate or elevated C-reactive protein and who showed pathological aortic [18F]FDG uptake. Fourteen of these patients had features of early giant cell arteritis (GCA), while one had features of early Takayasu arteritis. During follow-up, seven PET scans were performed in six patients with GCA 4–30 months (median 19 months) after starting immunosuppressive medication. The results of [18F]FDG imaging were compared with the results of MRI at initial evaluation and during follow-up and with the clinical findings. At baseline, abnormal [18F]FDG uptake was present in 59/104 (56%) of the vascular regions studied in 15 patients. Seven follow-up PET studies were performed in six patients. Of 30 regions with initial pathological uptake in these patients, 24 (80%) showed normalisation of uptake during follow-up. Normalisation of [18F]FDG uptake correlated with clinical improvement and with normalisation of the laboratory findings. All except one of the patients with positive aortic [18F]FDG uptake were investigated with MRI and MRA. Thirteen of these 14 patients showed inflammation in at least one vascular region. Of 76 vascular regions studied, 41 (53%) showed vasculitis on MRI. Of 76 vascular regions studied with both PET and MRI, 47 were concordantly positive or negative on both modalities, 11 were positive on MRI only and 18 were positive on PET only. MRI was performed during follow-up in six patients: of 17 regions with inflammatory changes, 15 regions remained unchanged and two showed improvement. Whole-body [18F]FDG PET is valuable in the primary diagnosis of early aortitis. The results of [18F]FDG PET and MRI in the diagnosis of aortitis in this study were comparable, but FDG imaging identified more vascular regions involved in the inflammatory process than did MRI. In a limited number of patients [18F]FDG PET was more reliable than MRI in monitoring disease activity during immunosuppressive therapy.

Keywords: [18F]FDG PET – Hybrid camera – MRI – MRA – Aortitis

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Introduction

Aortitis is defined as an inflammatory process that involves one or more layers of the aortic wall and can be caused by multiple mechanisms, including several systemic rheumatic or connective tissue diseases, giant cell arteritis (GCA) and Takayasu arteritis. GCA is a systemic, inflammatory, giant cell vasculitis that predominantly affects the cranial arteries. The most common presenting manifestations are headache, jaw claudication, polymyalgia rheumatica and visual symptoms [1]. GCA may also involve large vessels, especially the aorta and the subclavian and axillary arteries. In this localisation GCA is the basis for aneurysms, dissections and stenotic lesions [2]. Takayasu arteritis is a chronic, giant cell vasculitis of unknown aetiology, which primarily involves the aorta, its main branches and the coronary and pulmonary arteries.

This work is dedicated to the memory of Professor Wolfgang Becker.

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Early stages of the disease show panarteritis and inflammatory arterial wall thickening, while advanced (fibrotic) stages comprise arterial stenosis and aneurysmal transformation [3]. Overlapping clinical, radiological and pathological features are relatively common in GCA and Takayasu arteritis. Thus, the clinical classification of aortitides is rather difficult and often misleading [4].

Traditional approaches in the diagnosis of aortitis are mainly based on the characteristic angiographic and clinical features of rather advanced cases [5]. On angiography, patients with aortitis show irregular vessel walls, arterial stenosis, poststenotic dilatation, aneurysmal transformation or even occlusion. It is now clear that these diagnostic criteria are not suited to the diagnosis of early aortic involvement by GCA and Takayasu arteritis. During this stage, angiography will be completely normal but magnetic resonance imaging (MRI) already shows subtle inflammatory wall thickening of the aorta [6].

The aim of this study was to perform a detailed prospective comparison of fluorine-18 fluorodeoxyglucose positron emission tomography ([^{18}F]FDG PET), MRI and the corresponding clinical findings in a series of patients with early aortitis in order to assess the value of PET in the primary diagnosis of aortitis and in monitoring the response to immunosuppressive therapy.

Materials and methods

Patients

Inclusion criteria for this prospective study were the presence of pathological [^{18}F]FDG uptake in the aorta in patients with fever of unknown origin (FUO) or an elevated erythrocyte sedimentation rate or elevated C-reactive protein. All patients except one were subsequently investigated by MRI. The study was approved by the local ethics committee.

Fifteen patients with pathological [^{18}F]FDG uptake in the aorta were identified ([^{18}F]FDG dedicated PET: *n*=7; [^{18}F]FDG hybrid PET: *n*=8; nine females and six males; median age 62 years, range 26–76 years). Fourteen of these patients had features of GCA according to the ACR criteria [7] and one patient had features of Takayasu arteritis [6, 8]. The clinical findings of these cases were more indicative of early than of advanced vasculitis. Seven follow-up PET studies were performed in six patients (patients 1, 2, 3, 6, 7 and 8) 4–30 months (median 19 months) after starting immunosuppressive medication.

MRI was performed in 14/15 of our patients at initial evaluation and in six patients (patients 1, 2, 3, 6, 7 and 8) with GCA 4–34 months (median 19 months) after starting immunosuppressive medication.

The results of [^{18}F]FDG imaging were subsequently correlated with the results of MRI scanning and the clinical and laboratory findings.

Reference group 1

In order to determine normal values for vascular uptake on [^{18}F]FDG hybrid PET (hPET), a reference group of 38 patients (14 females, 24 males; median age 54 years, range 48–75 years) with malignancy who underwent [^{18}F]FDG hPET of the trunk were visually scored (see below).

Reference group 2

In order to determine normal values for vascular uptake on [^{18}F]FDG dedicated PET (dPET), a reference group of 40 patients (19 females, 21 males; median age 56 years, range 43–77 years) with malignancy or chronic osteomyelitis who underwent [^{18}F]FDG dPET of the trunk were visually scored (see below).

[18F]FDG hPET and [18F]FDG dPET

Hardware for [18F]FDG hPET. [^{18}F]FDG hPET was performed with a double-head coincidence camera (DHCC, Prism 2000 XP, Marconi Medical Systems, Espelkamp, Germany). The intrinsic resolution of the system before reconstruction is 5 mm transaxially. The axial field of view is 35 cm.

Hardware for [18F]FDG dPET. An ECAT Exact HRplus PET scanner (Siemens, CTI Co., Knoxville, Tenn., USA) with 32 rings and an axial field of view of 15.5 cm was used for data acquisition. The intrinsic resolution of the system before reconstruction is 4 mm transaxially. In contrast to hPET, correction for scatter and random coincidences and attenuation correction using a transmission scan are routinely performed.

Patient preparation and PET acquisition. Imaging was performed after an overnight fast. The serum glucose level was measured in all patients and was below 100 mg/dl (range 73–98 mg/dl). Acquisition was started 1 h after injection of 296 MBq [^{18}F]FDG for hPET and 1 h after injection of 370 MBq [^{18}F]FDG for dPET. The acquisition for whole-body hPET involved the rotation of each detector over 180° with 30 stops and an acquisition time of 70 s for the first angle, and comprised four contiguous bed positions. For whole-body imaging with dPET, we used 2-D acquisition and six to eight contiguous bed positions (12 min/bed position; transmission with ^{68}Ga/^{68}Ge rod sources for attenuation correction: 25% of time; emission: 75% of time).

Reconstruction of hPET raw data. After rebinning the raw data, transaxial tomographic images were generated using an iterative (ISA) algorithm. Attenuation correction is part of this algorithm and is performed under the assumption of homogeneous attenuation [9].

Reconstruction of dPET raw data. After rebinning the list mode raw data and attenuation correction, iterative reconstruction of the transaxial slices into a 256×256 matrix was performed using the ordered subset-expectation maximisation (OS-EM) algorithm (two iterations, eight subsets) [10].

Evaluation and scoring of data. Transaxial tomograms of the patients and the reference groups were evaluated and scored by two independent readers blinded to the results of MRI scanning using four scores: 0, no uptake present; 1+, low-grade uptake (uptake present but lower than liver uptake); 2+, intermediate-grade uptake (similar to liver uptake); 3+, high-grade uptake (between liver uptake and cerebral uptake or similar to the uptake in the cerebral cortex).

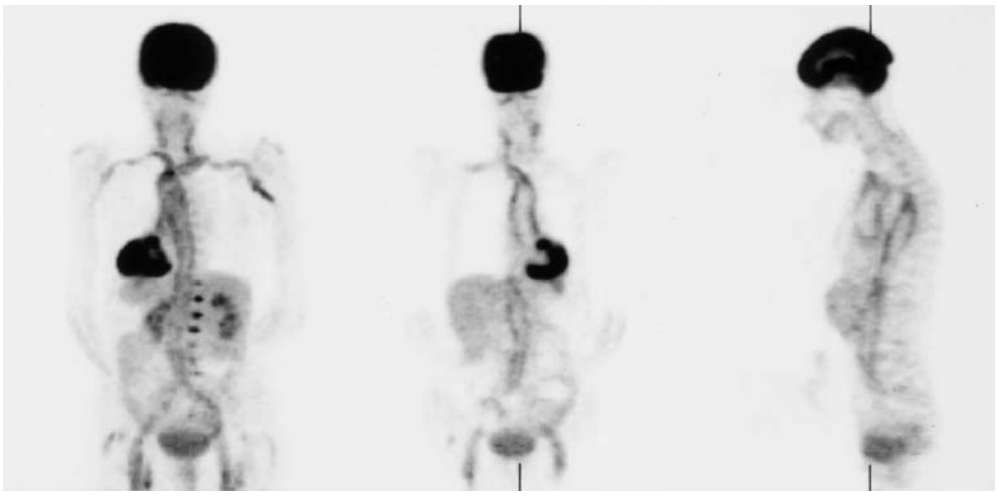

Fig. 1. FDG PET of the aorta and large/medium-sized vessels with grade 3+ uptake (patient 9; 3-D reconstruction dorsal projection, coronal and sagittal views)

Magnetic resonance imaging

Hardware. MR examinations were performed on 1.5-T MR imaging systems (Magnetom Vision and Symphony/Quantum, Siemens, Erlangen, Germany) with a maximum gradient strength of 25 or 30 mT/m by using a four-channel body phased-array coil. Non-enhanced ECG-triggered T1-weighted spin-echo sequences and HASTE sequences were used in the evaluation of the abdominal and the thoracic aorta. For MRA, non-enhanced and contrast-enhanced (CE) examinations were performed using a 3D FLASH sequence. Gadopentetate dimeglumine (Magnevist, Schering, Berlin, Germany) with a concentration of 0.15 mmol per kilogram body weight was injected in an antecubital vein by using an MR-compatible power injector. In addition, post-contrast fat-suppressed T1-weighted spin-echo images were used for the evaluation of wall disease.

Post-processing of data. The post-processing of CE-MRA included subtraction of data sets, multiplanar reformats (MPR) and use of a maximum intensity projection (MIP) algorithm. Coronal and sagittal projection angiograms of the abdominal and thoracic vessels were calculated using the subtracted images.

Evaluation and scoring of data. MRI data sets were evaluated and scored by two independent readers as follows: thickening (2 mm) and contrast enhancement of the vessel wall on transverse MR images were considered indicative of early Takayasu arteritis, and detection of stenoses or aneurysmal enlargement using CE-MRA was considered indicative of advanced Takayasu arteritis. On the follow-up scans, wall thickness was re-evaluated by two independent readers.

Results

Reference group 1 (hPET)

No visible [^{18}F]FDG uptake was present in the aorta. Grade 1+ uptake in at least one large aortic branch was seen in 8/38 (22%) patients and grade 2+ uptake in 1/38 patients (2.6%). Grade 3+ uptake was not noted in our patients. These findings indicate that any visible [^{18}F]FDG uptake in the aorta and 2+/3+ uptake in large aortic branches should be considered as pathological.

Reference group 2 (dPET)

Grade 1+ or 2+ [^{18}F]FDG uptake in the (proximal) ascending aorta was present in 35/40 (87%) patients. Grade 1+ uptake in the aortic arch was present in 4/40 (10%) patients. No patient showed visible uptake in the descending aorta or the abdominal aorta. Grade 1+ uptake in at least one large aortic branch was seen in 32/40 (80%) patients and grade 2+ uptake in 14/40 (35%) patients. Grade 3+ uptake was not noted. These findings indicate that grade 3+ uptake in the ascending aorta, grade 2+/3+ uptake in the aortic arch, any visible uptake in the descending or abdominal aorta and grade 3+ uptake in a large aortic branch should be considered as pathological.

Baseline [^{18}F]FDG PET

Eight patients were imaged with hPET and seven with dPET. All showed pathological [^{18}F]FDG uptake in at least one region of the aorta (Figs. 1, 2, 3a). Abnormal [^{18}F]FDG uptake was present in 59/104 (56%) vascular regions studied. Table 1 shows the semiquantitative results of [^{18}F]FDG baseline imaging in the 15 patients.

[^{18}F]FDG PET during follow-up

To date we have performed seven follow-up scans (hPET: n= 1; dPET: n=6) in six patients with immunosuppressive medication. Of 30 regions with initial pathological uptake, 24 (80%) showed normalisation of uptake during follow-up (Fig. 3b). Normalisation of [^{18}F]FDG uptake correlated with clinical improvement and normalisation of the laboratory findings in all patients. Semiquantitative results of [^{18}F]FDG follow-up-imaging are displayed in Table 2.

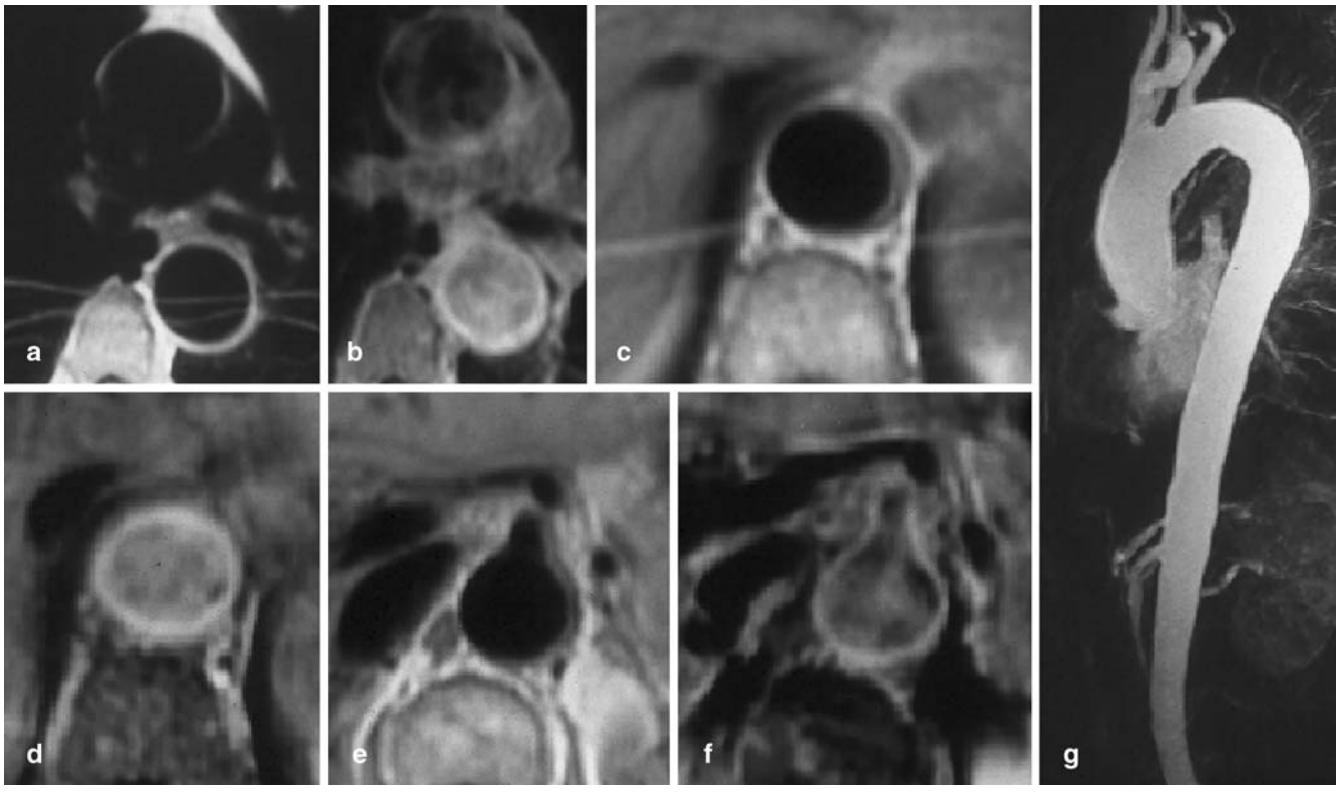

Fig. 2. MRI and MRA of the same patient (patient 9). Native and contrast-enhanced transverse T1-weighted SE-image shows thickened aortic wall and significant enhancement of the thoracic (**a** native, **b** contrast enhanced) and abdominal aorta (**c** native, **d** contrast enhanced) and the truncus coeliacus (**e** native, **f** contrast enhanced). MRA (**g**) shows no abnormalities

Table 1. Semiquantitative results of baseline [^{18}F]FDG PET (n=15)[a]

Patient	Imaging	Localisation						
		A. asc	Arch	A. desc	A abd	A. subcl	A. carot	Aa. Iliofem
1	hPET	3+	3+	3+	3+	0	3+	3+
2	hPET	3+	3+	3+	3+	3+	3+	3+
3	hPET	3+	0	3+	0	0	0	2+
4	hPET	3+	2+	2+	2+	2+	2+	n.d.
5	hPET	2+	0	0	0	2+	2+	3+
6	hPET	0	0	0	0	2+	2+	3+
7	hPET	3+	3+	3+	3+	3+	3+	3+
8	dPET	3+	3+	3+	0	2+	3+	1+
9	dPET	3+	3+	3+	3+	3+	3+	3+
10	dPET	1	0	1	0	1	0	0
11	dPET	3+	3+	0	0	3+	3+	0
12	dPET	1	2+	2+	0	1	0	0
13	hPET	2+	0	0	3+	1	0	1
14	dPET	1	1	2+	1+	1	0	1
15	dPET	1	0	2+	2+	0	0	1

A. asc, Ascending aorta; Arch, aortic arch; A. desc, descending aorta; A abd, abdominal aorta; A. subcl, subclavian artery; A. carot, common carotid artery; Aa. Iliofem, iliofemoral arteries, n.d., not done

0, No uptake present; 1+, low-grade uptake (uptake present but lower than liver uptake); 2+, intermediate-grade uptake (similar to liver uptake); 3+, high-grade uptake (between liver uptake and cerebral uptake or similar to the uptake in the cerebral cortex)

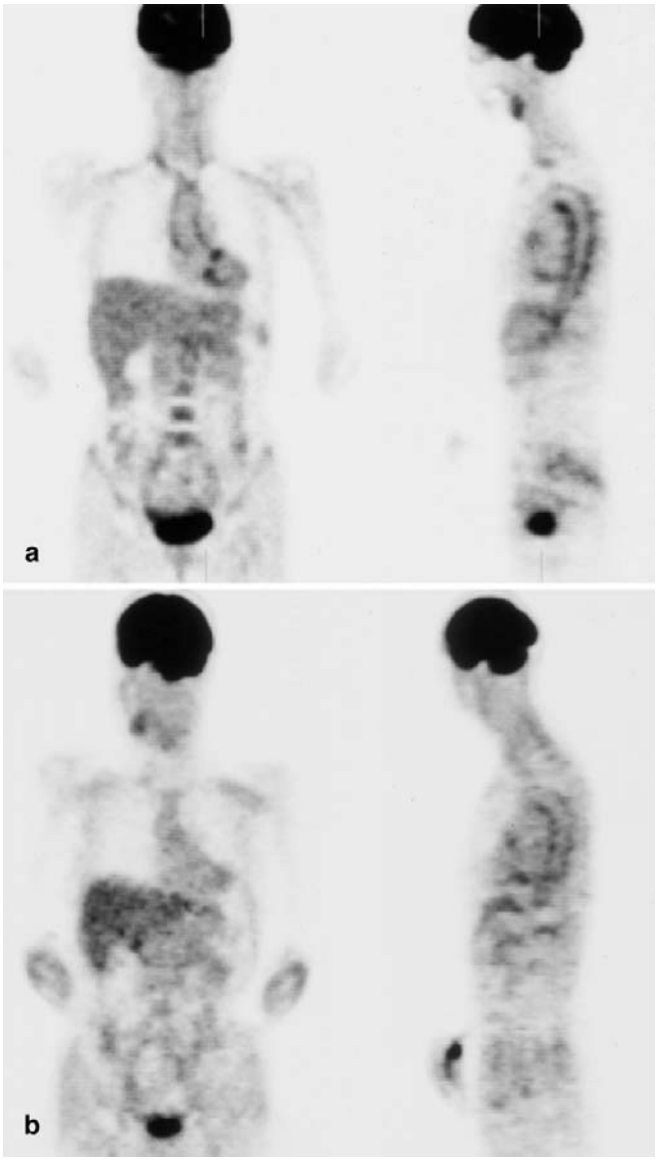

Fig. 3a, b. FDG PET focussed on the thoracic aorta in patient 7. **a** Initial investigation: grade 3+ uptake in the thoracic aorta (coronal and sagittal views). **b** Follow-up: normalisation in the ascending aorta, declining uptake in the descending aorta (coronal and sagittal views)

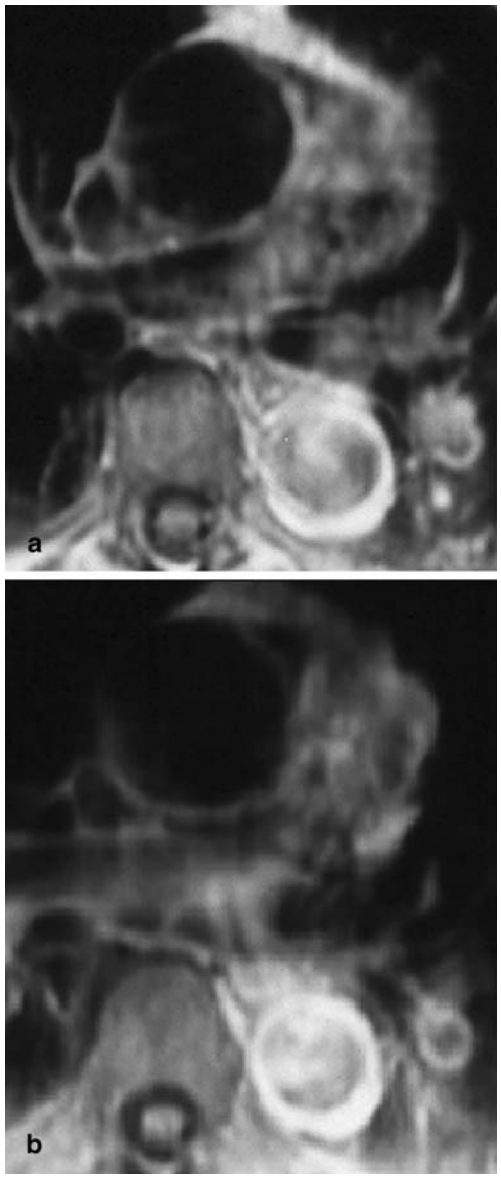

Fig. 4. MRI and of the same patient (patient 7). Contrast-enhanced transverse T1-weighted SE-image shows wall thickening and significant enhancement of the thoracic aorta (**a**) with no improvement during follow-up (**b**)

Baseline MRI/MRA

With one exception (patient 15), all patients with positive aortic [^{18}F]FDG uptake were investigated with MRI and MRA. Thirteen of these 14 patients showed wall thickening and contrast enhancement in at least one vascular region (Fig. 4). One patient who was positive on [^{18}F]FDG PET (patient 13) was negative on MRI, but the abdominal aorta, which showed maximum uptake on the PET scan, was not investigated by MRI. Of 76 vascular regions studied, 41 (53%) showed vasculitis on MRI. Of 76 vascular regions studied with both PET and MRI, 47 were concordantly positive or negative on both modalities, 11 were positive on MRI only and 18 were positive on PET only. MRA was negative in all patients. The results of initial MRI are displayed in Table 3.

MRI during follow-up

To date we have performed follow-up scans in six patients. Of 17 regions with vessel wall thickening, 15 remained unchanged (Fig. 5) and two improved. The results of follow-up MRI are displayed in Table 4

Table 2. Semiquantitative results of [^{18}F]FDG PET during follow-up (n=6)[a]

Patient	Imaging	Localisation						
		A. asc	Arch	A. desc	A abd	A. subcl	A. carot	Aa. Iliofem
1	hPET	2+	0	0	0	0	0	0
	dPET	1+	1+	1+	1+	1+	1+	1+
2	dPET	2+	2+	0	0	0	0	0
3	dPET	1+	2+	2+	1+	1+	1+	1+
6	dPET	1+	0	0	2+	2+	2+	2+
7	dPET	2+	2+	2+	0	0	0	0
8	dPET	1+	1+	1+	0	1+	1+	1+

hPET, hybrid PET; dPET, dedicated PET; other abbreviations and scoring are as defined in Table 1

Table 3. Results of baseline MRI (n=14)

Patient	Localisation						
	A. asc	Arch	A. desc	A abd	A. subcl	A. carot	Aa. Iliofem
1	Normal	Normal	Aortitis	n.d.	Normal	Normal	n.d.
2	Normal	Normal	Aortitis	Aortitis	Vasculitis	Vasculitis	n.d.
3	Normal	Aortitis	Aortitis	n.d.	Normal	Normal	n.d.
4	Aortitis	Normal	Normal	n.d.	Normal	Normal	n.d.
5	Normal	Normal	Normal	Normal	Normal	Normal	Vasculitis
6	Normal	Normal	n.d.	n.d.	Normal	Vasculitis	n.d
7	Normal	Aortitis	Aortitis	n.d.	Vasculitis	Vasculitis	n.d.
8	Aortitis	Aortitis	Aortitis	n.d.	Vasculitis	Vasculitis	n.d.
9	Aortitis	Aortitis	Aortitis	n.d.	Vasculitis	Vasculitis	n.d.
10	Aortitis	Aortitis	Aortitis	Aortitis	Vasculitis	Vasculitis	n.d.
11	Aortitis	Aortitis	Normal	Normal	Normal	Normal	n.d.
12	Aortitis	Aortitis	Aortitis	Normal	Normal	Normal	n.d.
13	Normal	Normal	Normal	n.d.	Normal	Normal	n.d.
14	Aortitis	Aortitis	Aortitis	Aortitis	Vasculitis	Vasculitis	n.d.

Abbreviations are as defined in Table 1

Table 4. MRI during follow-up (n=6)

Patient	Localisation						
	A. asc	Arch	A. desc	A abd	A. subcl	A. carot	Aa. Iliofem
1	Normal	Normal	Improved	n.d.	Normal	Normal	n.d.
2	Normal	Normal	Unchanged	Unchanged	Unchanged	Unchanged	n.d.
3	Normal	Unchanged	Unchanged	n.d.	Normal	Normal	n.d.
6	Normal	n.d.	n.d.	n.d.	Normal	Improved	n.d.
7	Normal	Unchanged	Unchanged	n.d.	Unchanged	Unchanged	n.d.
8	Unchanged	Unchanged	Unchanged	n.d.	Unchanged	Constant	n.d.

Abbreviations are as defined in Table 1

Discussion

Our findings indicate that [^{18}F]FDG PET performed with either a hybrid or a dedicated system is highly effective in the identification of patients with untreated early aortitis.

None of the patients showed late complications of vasculitis such as stenosis, aneurysmal transformation or occlusive disease on MRA. Had a traditional angiographic approach been used in the diagnosis of aortitis, the correct diagnosis would have been missed in all of these cases. The frequency of aortic involvement in

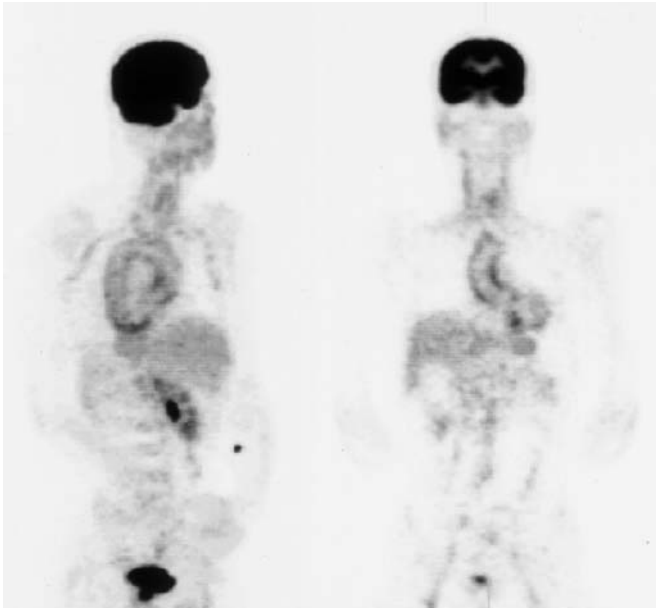

Fig. 5a, b. FDG-PET focussed on the thoracic aorta in patient 8 (3-D projection and coronal view): 3+ uptake in the thoracic aorta

GCA patients, based on clinical and angiographic data, has been reported to be between 3% and 15% [2]. Our data suggest that the real incidence may be even higher, as revealed by techniques like MRI and PET. Early recognition of aortitis may be of importance because large-vessel GCA may require a different approach to treatment to prevent the life-threatening complications [1].

Increased aortic [^{18}F]FDG uptake has previously been described in a limited number of patients with GCA [11], polymyalgia rheumatica [12] and Takayasu arteritis [8, 13, 14]. However, there have been no previously reported comparisons of [^{18}F]FDG PET, MRI and clinical findings in larger series of patients with early aortitis, at the time of initial diagnosis and during immunosuppressive therapy.

In our patients the results of MRI and [^{18}F]FDG PET were broadly comparable, but [^{18}F]FDG PET identified more vascular regions involved in the inflammatory process. This indicates that whole-body [^{18}F]FDG PET should be used as the first-line investigation of choice if vasculitis of the large and medium-sized arteries is suspected, because the chance of a positive finding may be higher than with MRI.

In a limited number of patients, [^{18}F]FDG PET was more reliable than MRI in monitoring disease activity during immunosuppressive therapy. Normalisation of [^{18}F]FDG uptake during follow-up clearly correlated with clinical improvement and normalisation of the laboratory findings. Interestingly, MRI of the same patients performed at similar time points showed improvement in only 2 of 17 regions with initial vessel wall thickening. These preliminary data may indicate a more rapid response of [^{18}F]FDG uptake to successful therapy compared with the more delayed changes of morphology that are visualised by MRI.

In conclusion, our preliminary data indicate that whole-body [^{18}F]FDG PET is valuable as a first-line investigation in the primary diagnosis of early aortitis, especially in cases with uncharacteristic symptoms such as FUO.

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