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Research paper

# Imaging giant cell arteritis and Aortitis in contrast enhanced 18F-FDG PET/CT: Which imaging score correlates best with laboratory inflammation markers?

Susann-Cathrin Olthof[a,*], Patrick Krumm[a], Jörg Henes[b], Konstantin Nikolaou[a], Christian la Fougère[c], Christina Pfannenberg[a], Nina Schwenzer[a]

[a] Department of Diagnostic and Interventional Radiology, University Hospital of Tuebingen, Hoppe-Seyler-Straße 3, 72076 Tuebingen, Germany
[b] Department of Internal Medicine II, University Hospital of Tuebingen, Otfried-Mueller Straße 10, 72076, Tuebingen, Germany
[c] Department of Nuclear Medicine, University Hospital of Tuebingen, Otfried-Mueller-Straße 14, 72076 Tuebingen, Germany

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ABSTRACT

*Purpose:* To define the most appropriate imaging parameters in combined Fluorodeoxyglucose (FDG) PET/CT reflecting the inflammatory burden in large vessel vasculitis.

*Methods:* Two readers retrospectively graded disease extent and activity in 17 LVV patients using visual and quantitative scores in FDG PET and contrast enhanced CT. Visual PET scores were assessed corresponding to FDG-uptake vs. liver uptake (score 0–3). CT visual scoring referred to the affected vessel extent (score 1–5). Quantitative PET scores relied on normalized SUV ratios. For quantitative CT evaluation vessel wall thickness was correlated with FDG- uptake. Imaging scores were correlated with Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP). Intraclass correlation coefficients (ICC) were measured for interreader reliability.

*Results:* Visual PET scores showed stronger correlation with CRP (ρ 0.640, 0.541 for reader I and II, respectively) than with ESR levels (ρ 0.477, 0.447). Quantitative PET showed strongest correlation with CRP using liver as reference tissue.

Visual CT scores did neither correlate with ESR nor with CRP levels (ESR: ρ 0.085, 0.294 with p 0.743, 0.252; CRP: ρ 0.322, 0.395 with p 0.208, 0.116). Quantitative CT evaluation correlated with ESR levels in one reader (ρ 0.505, −0.026), however no correlation between quantitative CT measures and quantitative PET scores was found. Best ICC between readers was 0.994 for highest $SUV_{avg}$ vessel/highest $SUV_{avg}$ liver.

*Conclusions:* Visual and quantitative PET scores were superior to CT scores with best ICC and strongest correlations between quantitative PET score and inflammation markers especially when using vessel to liver ratios.

## 1. Introduction

Large vessel vasculitis (LVV) is a common disease mainly in elderly people, encompassing Takayasu Arteritis (TA), Giant cell arteritis (GCA) as well as Aortitis [1], which is thought to be a precursor stage of GCA [2]. All LVV subtypes affect the aortic branches; however, only giant cell arteritis additionally attaints the temporal arteries [3]. Diagnosis of LVV is still based on clinical criteria of the American College of Rheumatology (ACR) [4,5]. Consequently, three of the five following criteria are mandatory for diagnosis of GCA: age ≥50 years, headache, ESR ≥ 50 mm/h, thickening of the temporal arteries and pathologic arterial biopsy. Although suggested as gold standard for diagnosis of GCA by the ACR [5] temporal artery biopsy (TAB) suffers from a high rate of false negative results (15–70%) [6].

18F-FDG PET as a non-invasive diagnostic imaging tool offers high diagnostic sensitivities of 87%–90% and specificities of 73–98% for disease assessment of LVV [7]. However, the diagnostic performance of 18F-FDG-PET in LVV is limited by additional pathologic changes due to arteriosclerosis, distributed often in the iliofemoral arteries [6]. Therefore, 18F-FDG PET/CT is superior to 18F-FDG PET alone in

*Abbreviations:* ACR, American College of Rheumatology; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; 18F-FDG PET/CT, 18 fluorine fluorodeoxyglucose positron-emission tomography; FOV, field of view; GCA, giant cell arteritis; i.v., intravenous; mBq, mega Becquerel; mg/dl, milligram/decilitre; ROI, region of interest; $SUV_{avg}$, standard-uptake value average; $SUV_{max}$, standard-uptake value maximum; TA, Takayasu-Arteriitis; VJI, internal jugular vein

* Corresponding author at: Department of Diagnostic and Interventional Radiology, University Hospital of Tuebingen, Hoppe−Seyler−Str. 3, 72076 Tuebingen, Germany.
*E-mail addresses:* susann-cathrin.olthof@med.uni-tuebingen.de (S.-C. Olthof), patrick.krumm@med.uni-tuebingen.de (P. Krumm), joerg.henes@med.uni-tuebingen.de (J. Henes), konstantin.nikolaou@med.uni-tuebingen.de (K. Nikolaou), christian.lafougere@med.uni-tuebingen.de (C. la Fougère), christina.pfannenberg@med.uni-tuebingen.de (C. Pfannenberg), nina.schwenzer@uni-tuebingen.de (N. Schwenzer).

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identification and differentiation of arteriosclerotic plaques due to the CT component. Furthermore, contrast-enhanced CT is useful to identify significant stenoses and aneurysms which represent well-known complication of LVV. It was also reported that the inflammatory processes in the vessel wall identified by 18F-FDG PET/CT correlate with the vessel wall thickening in contrast-enhanced CT [8].

So far, there is no agreement regarding the examination protocols (e.g. the use of contrast enhanced CT) and systematic analysis of 18F-FDG PET/CT scans in imaging of vasculitis [9]. Furthermore, there is no consensus regarding PET and CT imaging scores impairing the comparability between different 18F-FDG PET/CT reports [10].

Therefore, we applied standardized visual and quantitative imaging scores for 18F-FDG PET and CT on untreated LVV patients and analysed the reliability of measurements between the two readers and the correlation with inflammatory markers to define the most appropriate imaging parameters reflecting the inflammatory burden in large vessel vasculitis.

## 2. Material and methods

### 2.1. Patients

Between 03/2012 and 03/2015, all patients with suspected LVV who received an 18F-FDG PET/CT examination for confirmation of disease or evaluation of disease extent were retrospectively evaluated (n = 161). Inclusion criteria were clinical findings according to the criteria of the American College of Rheumatology (ACR), medical history and the results of clinical examination. Exclusion criteria were 18F-FDG PET/CT without intravenous contrast agent (n = 15), already initiated systemic immunosuppressive treatment (n = 37), unavailability of ESR and CRP levels, or ESR and CRP levels more than two weeks apart from the PET/CT exam, final diagnoses other than vasculitis (n = 89), or diagnosed small vessel vasculitis (n = 3). Finally, our study group consisted of 17 patients with proven LVV (13 female and 4 male) with a mean age of 65 years ( ± 11.7 years), suffering from giant cell vasculitis (n = 10) or aortitis (n = 7) according to ACR criteria [5] (Fig. 1). The study was approved by the institutional ethics committee.

### 2.2. Laboratory results

Inflammatory markers ESR (mm/h) and CRP (mg/dl) were acquired prior to therapy. Mean ESR values were 66.94 mm/h ( ± 31.72 mm/h) and CRP values were 6.92 mg/dl ( ± 5.29 mg/dl). Mean blood sugar level was 113 mg/dl before PET/CT examination ( ± 20.6 mg/dl).

### 2.3. PET/CT scanning protocol

All PET/CT scans were acquired with the same PET/CT scanner and our standard examination protocol (Biograph mCT Siemens Healthineers, Knoxville TN). After at least six hours of fasting patients were administered a mean dose of 338 MBq (Mega Becquerel; ± 19 MBq) of 18F-FDG. i.v. The uptake time was 60 min. Contrast-enhanced CT examination encompassed a field of view from skull base to mid thigh in venous phase including an additional chest CT in inspiration (Ultravist 370 Bayer Healthcare Pharmaceuticals Berlin, Germany, volume adapted to body weight with 120 ml as default, flow rate 2.5 ml/s; rotation time 0.3 s, 120 kV, tube current 250 mAs, 0.6 mm collimation, table feed 30.7 mm; reconstructed image slice thickness 3–5 mm, image resolution in-plane 0.8 × 0.8 mm). We used our standard CT protocol in *early* venous phase for optimal contrast enhancement of the vessel wall along with the vessel lumen. Afterwards, PET acquisition was performed under free breathing for about 30 min depending on patients' height (PET axial FoV 21.8 cm and transaxial FoV 70 cm, 6–9 bed positions, time per bed position 2 min, 3D OSEM algorithm with 2 iterations, 21 subsets, 2 mm Gaussian filter, 400 × 400 image matrix). CT data was used for attenuation correction. Reading was performed using the commercially availabe TrueD software package (Siemens Healthineers).

### 2.4. Image analysis

All images were separately analysed by two radiologists experienced in PET/CT (S.C.O., 4 years of experience, N.S., 10 years of experience) and blinded to clinical data. Analysis of arterial involvement included seven cervico-thoraco-abdominal regions: the carotid, subclavian and axillary arteries, thoracic and abdominal aorta (supra- and infrarenal) as well as iliac and femoral arteries. Arteries were evaluated symmetrically on both sides. In case of artefacts e.g. in one subclavian artery measurements were confined to the one value of the contralateral side.

The evaluation of PET and CT examinations included both visual and quantitative analyses in the affected vessel segments. Each reading session was performed at least 4 weeks apart from each other.

### 2.5. Visual and quantitative PET analysis

For visual PET assessment we applied the four-score system according to Meller et al. [11]: no FDG-uptake (0), FDG-uptake lower than the physiological liver uptake (1), FDG-uptake as high as liver uptake (2) and higher FDG uptake than the liver uptake (3). The maximum score for seven arterial regions was 21. In case of differing scores between the symmetrical arteries, the higher score was applied.

In the case of elevated FDG-uptake in the vessel wall we measured both $SUV_{max}$ and $SUV_{mean}$ for quantitative analysis per vessel and computed a ratio between the mean of three regions of interest (ROI) in liver, bloodpool und jugular veins (SUV/liver, SUV/bloodpool, SUV/internal jugular veins) as reference tissue according to Besson et al. [10]. As further suggested by Besson et al. an additional ratio between the three highest values of $SUV_{max/avg}$ of all measured vessel ROIs per patient and three equally shaped $SUV_{max/avg}$ values in liver ROI, bloodpool and internal jugular veins [10] was calculated. Thus, the quantitative analysis encompassed four scores for vessel-to-liver analysis (see Table 1).

For vessel analysis, all ROIs were placed manually with a 60% isocontour volume (spherical) including the lumen and vessel wall. Care was taken to spare arteriosclerotic vessel sections. For reference regions circular 2D ROIs were placed: three ROIs with a diameter of 3 cm in the liver and one ROI each for the jugular vein and blood pool with varying size depending on the respective lumen. All ROIs were placed in axial images and verified on coronal and sagittal images.

### 2.6. Visual and quantitative CT analysis

For visual analysis of CT the angiographic scores according to Hata et al. [12] was used describing the number of affected vessels and aortic branches ranging from 1 (branches of the aortic arch affected) to 5 (thoracic aorta and its branches as well as abdominal aorta with or without renal arteries affected; see also Table 2).

For quantitative CT analysis we measured the wall-thickness of each vessel at two, six and ten o' clock on axial slices of the five symmetrically arteries of the carotids, axillary, subclavian, iliac and femoral arteries as well as thoracic and abdominal aorta according to Muto et al. [13] (see also Fig. 2A). For the subclavian and axillary artery wall where no circular diameter was available two values were assessed (see Fig. 2B). Thus we calculated a mean wall-thickness of all vessels per patient as well as a ratio of $W_{mean}/R$ where W indicates the vessel wall thickness and R the vessel diameter (in%), as suggested by Muto et al. [13].

### 2.7. Statistical analysis

All statistical analyses were performed using Med Calc (version 12.6 Software bvba, Ostend Belgium). Normality of the data was tested using