Original Article

Semiquantitative Interpretation Criteria for Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography in Large-Vessel Vasculitis: Pattern Recognition and Correlation with Polymyalgia Rheumatica

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Abstract

Background: Fluorine-18-fluorodeoxyglucose (^{18}F-FDG)-positron emission tomography/computed tomography (PET/CT) is emerging as a useful imaging modality in suspected large-vessel vasculitis (LVV), owing to its ability to accumulate at the sites of inflammation within the arterial walls. However, there remains scope for standardization of reporting criteria to ensure reproducibility. Recently, a semiquantitative scoring system called "total vascular score" (TVS) has been suggested as a method to standardize and harmonize FDG PET/CT evaluation in LVV patients. The purpose of this study was to assess the clinical utility of the proposed semiquantitative grading scale in LVV patients. **Materials and Methods:** Patients presenting with clinical symptoms of vasculitis, who had undergone a baseline FDG-PET/CT were evaluated. ^{18}F-FDG uptake in the major vessels was quantified with standardized uptake values ($SUVs_{max}$) using four-point scale by three independent nuclear physicians. TVS was calculated based on the calculation of the vascular uptake values with respect to mediastinal blood pool and liver uptake and the number of vessels involved. **Results:** A total of 106 PET-positive patients (74 males and 32 females) were evaluated. The most frequently involved vessels were thoracic aorta >abdominal aorta >subclavian arteries with mean SUV_{max} values of 4.05, 3.12, and 2.70, respectively. Mean TVS was 13.18 ± 3.4 (range 03–19) among 276 involved vessels. TVS showed significant positive correlation with erythrocyte sedimentation rate ($r = 0.82$; $P < 0.005$). 18 patients showed periarticular FDG uptake, with shoulder joint being the most commonly involved joint. **Conclusion:** The simplified visual and semiquantitative grading scale for interpretation and reporting classification provides better objectivity in diagnosis, communication with referring clinicians, and planning in patients of LVV.

Keywords: *Fluorodeoxyglucose-positron emission tomography/computed tomography, large-vessel vasculitis, polymyalgia rheumatica, total vascular score*

Introduction

Vasculitis is a disease affecting multiple organs in the body and is characterized by inflammation of the blood vessels with associated infiltration of leukocytes. The incidence of large-vessel vasculitis (LVV) is reported to be around 0.02% of the total population.[1] It constitutes ~10% of all cases of pyrexia of unknown origin.[2] LVV is a disease group affecting the large arteries, with two major variants: Takayasu's arteritis (TA) and giant cell arteritis (GCA).[3] GCA and polymyalgia rheumatica (PMR) may often coexist in a patient, since both belong to the same disease spectrum. Diagnosis of GCA and the assessment of its activity and extent are quite challenging. The mainstay in the diagnostic workup of GCA is temporal artery biopsy; however, it is an invasive investigation that can result in a substantial number of false-negative cases, and it does not delineate and elaborate the extracranial component of the disease.[4,5]

Imaging diagnostic procedures, e.g., computed tomography (CT) angiography, ultrasound, and magnetic resonance angiography (MRA) are operator-dependent or document only morphological changes, such as stenosis, occlusion, and aneurysmal transformation, which may occur late in the course of the disease.[6,7] Fluorine-18-fluorodeoxyglucose (^{18}F-FDG)-positron emission tomography (PET) is an operator-independent, noninvasive metabolic imaging modality which has a

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propensity to accumulate in areas of increased metabolic demand associated with inflammation and infection, and the high glycolytic activity of the inflamed arterial walls and synovia/bursa.[8] Cells involved in inflammation are able to express high levels of insulin-independent glucose transporters, especially glucose transporter (GLUT) 1 and GLUT 3, thus leading to increased ^{18}F-FDG uptake. In LVV, especially TA and GCA, there is diffuse perivascular ^{18}F-FDG uptake in the involved vascular segments with varying patterns of distribution.[9] Furthermore, whole-body ^{18}F-FDG-PET/CT provides overall detailed distribution of vessels involved. The semiquantitative values provided by the ^{18}F-FDG-PET/CT correlates well with disease severity, extent, and clinical parameters.[10] The strength of ^{18}F-FDG-PET/CT lies in its ability to accurately identify the metabolically active and inactive sites of the disease. This proves useful in assessing the treatment response, and if required, in changing the course of management. In addition, in cases with associated PMR, FDG-PET/CT whole-body scan assists in evaluating the affected joints which often coexist in nearly 50% of patients with GCA.[11] However, LVV and PMR are both separate and distinct disease entities, requiring specific management, and treatment approach.

The interpretation of ^{18}F-FDG-PET images for LVV is challenging, and there is currently no consensus on how to interpret the images in these clinical settings. There is, therefore, a need for standardization of PET readings to harmonize interpretation, especially in borderline cases in the setting of LVV. A number of heterogeneous interpretation criteria have been used in multiple clinical trials by different cooperative groups, based on semiquantitative data with variable standardized uptake values (SUV_{max}) cutoff values, on visual assessment alone or in combination, thus preventing data reproducibility.[11-17] Recently, joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group, and endorsed by the American Society of Nuclear Cardiology has been released for FDG-PET/CT imaging in LVV and PMR for standardization and harmonization of the FDG-PET imaging and reporting in LVV.[18] This includes the visual interpretation of images to quantify FDG uptake using the four points scale with respect to the liver and calculating the total vascular score (TVS) at total seven different vascular regions. The aim of this study was to assess the feasibility of joint procedural recommendation proposed by Slart *et al*. in the routine clinical application in a larger LVV patient population, and to ascertain its reproducibility by assessing interobserver agreement.

Materials and Methods

A retrospective analysis of patients, who had been referred with suspicion of LVV for ^{18}F-FDG-PET/CT, was done. The study group included cases of pyrexia of unknown origin, unexplained raised inflammatory markers, and any suspicious clinical signs and symptoms that would suggest LVV as the differential. The presence or absence of LVV was supported by clinical and biochemical follow-up, including serial measurements of the inflammatory markers (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]); other imaging modalities such as Doppler sonography, magnetic resonance imaging, CT, or conventional angiography; and histopathology. Although histopathology is the confirmatory gold standard, vascular biopsy is a cumbersome and invasive procedure, the clinician's decision after the investigations and positive response to specific treatment (corticosteroid) were considered confirmatory for the diagnosis of vasculitis. A minimum of 6 months of clinical follow-up after ^{18}F-FDG-PET/CT scan was considered adequate to establish or exclude such a diagnosis. The patients who had insufficient data for reaching a clinical decision or those lost to follow-up were excluded from further analysis.

To analyze the association between ^{18}F-FDG-PET/CT imaging results, the disease activity and extent parameters, inflammatory marker levels (CRP, ESR), and whole blood counts were recorded if they were obtained within 1 week of ^{18}F-FDG-PET/CT imaging. Spearman/Pearson correlation was determined between the TVS and inflammatory markers. The clinical improvement in each patient was assessed based on improvement in the clinical symptoms, such as features of polymyalgia, cranial ischemic manifestations, constitutional symptoms, or on follow-up scan which demonstrated reduced FDG uptake in the involved arteries following therapy. Approval for the study was taken by the Institutional Ethics Committee and informed consent was obtained from all the patients. Three experienced nuclear medicine physicians independently reviewed the scans according to the new joint procedural recommendation for each patient.

Fluorine-18-fluorodeoxyglucose-positron emission tomography/computed tomography scan

The patients fasted for at least 6 h prior to the ^{18}F-FDG injection and serum glucose level was ensured to be <160 mg/dL in all patients. Patients were given intravenous injection of 296–370 MBq (8–10 mCi) of ^{18}F-FDG. Thereafter, patients were asked to rest in an isolated quiet room for 45–60 min. The scan images were acquired on a dedicated PET-CT scanner (GE Discovery STE PET/CT with 16 slice CT). A contrast-enhanced CT transmission scan was performed first (120 KvP, 200 mAs, 0.8 s/CT rotation) with additional breathhold high-resolution CT for evaluation of lung fields. After transmission scanning, three-dimensional PET images were acquired immediately for 2 min per bed position without changing the patient position. CT-based attenuation correction of the emission images was employed. CT acquisition data were used for attenuation correction of the PET emission data and fusion of attenuation-corrected PET

images with the corresponding CT images. PET images were reconstructed by using ordered-subset expectation maximization algorithm, CT attenuation correction, dead time correction, and decay correction to beginning of each scan.

Image analysis

All the images thus acquired were reviewed by three different nuclear medicine physicians, who were blinded to the clinical and laboratory data and the final clinical diagnosis. Semiquantitative indices (SUV_{max}) of the uptake of ^{18}F-FDG were calculated for each vascular segment. The SUV was defined as the highest activity concentration every injected dose (per body weight) after radioactive decay correction. The sites of lesion with maximal SUV were recorded. Using CT images from the FDG-PET/CT, the maximal SUV was collected by drawing a 1 cm diameter circle of region of interest (ROI) over different foci. SUV_{max} for the liver and mediastinal blood pool was also calculated using the same ROI. ^{18}F-FDG vascular uptake values were recorded for each patient in seven arterial compartments: thoracic aorta, abdominal aorta, subclavian arteries, axillary arteries, carotid arteries, iliac arteries, and femoral arteries. FDG uptake in these major vessels was quantified with SUVmax using a four-point scale. FDG uptake in the joints, when involved, was also documented and graded. Follow-up FDG-PET scans were analyzed for response assessment.

LVV grading was done using the following criteria [GCA and TA; Figure 1].

- Grade 0 – No vascular uptake (≤mediastinum)
- Grade 1 – Vascular uptake < liver uptake
- Grade 2 – Vascular uptake = liver uptake, maybe PET positive
- Grade 3 – Vascular uptake > liver uptake, considered PET positive.

Grades 2 and 3 were considered PET positive. The TVS was calculated depending on the number of vessels involved. In accordance with the joint procedural statement,[12] a score was assigned to each arterial segment using a four-point scale. ^{18}F-FDG vascular uptake scores 2 (equal to or higher than liver uptake) were considered "positive" for vasculitis and scores of 0 and 1 (less than liver uptake) were considered "negative" for the diagnosis of LVV.

Statistics

All analyses were performed using the SPSS (SPSS for Windows 22.0 IBM, SPSS corporation, Chicago, Ill. USA.) software package. Continuous variables were presented as mean ± standard deviation. Categorical variables were presented as the percentage. Chi-square test, Fisher exact test, and continuity correction were used for categorical variables and unpaired *t*-test was used for continuous variables, if appropriate. Pearson's and Spearmen correlation

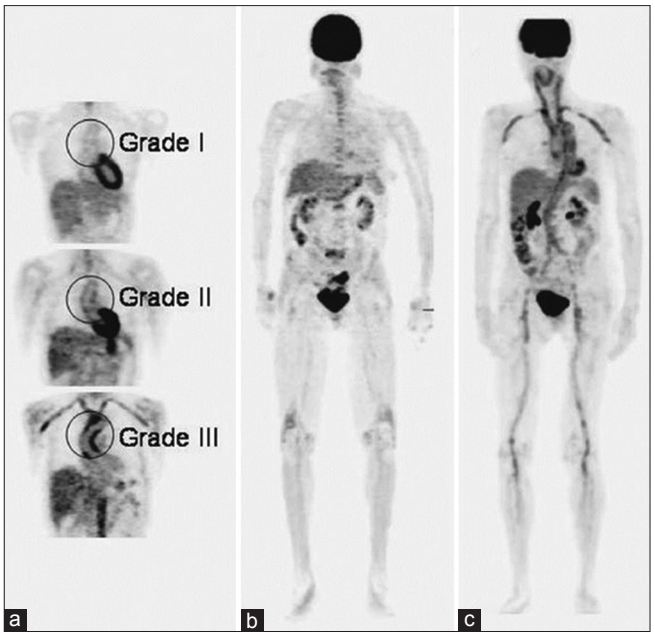

Figure 1: Figure showing examples of visual grading of fluorine-18-fluorodeoxyglucose-positron emission tomography uptake (a), nonpathological whole-body fluorine-18-fluorodeoxyglucose-positron emission tomography scan (b), whole-body fluorine-18-fluorodeoxyglucose-positron emission tomography scan showing extensive large-vessel vasculitis (c)

exponents were used to assess the relationship between continuous variables. A value of $P < 0.05$ was considered statistically significant. The method used for interobserver variability included the percentage of agreement among the reviewers and the Krippendorff's alpha. This coefficient is 0 in the case of random coincidence and below 0 in case of concordance lower than random coincidence (limits: −1; +1). Finally, the concordance among all the reviewers in terms of positivity or negativity of the FDG-PET/CT scan was tested.

Results

This study included 106 consecutive patients (74 males and 32 females) with LVV, who were evaluated by ^{18}F-FDG-PET/CT scan and who showed abnormal ^{18}F-FDG uptake. Mean age of the patients was 62 ± 09 years with male predominance (74 males and 32 females). Thoracic aorta > abdominal aorta > subclavian arteries were the most frequently involved vessels with mean SUV_{max} 4.05, 3.12, and 2.70, respectively [Table 1]. A total number of 276 vessels were found to be FDG positive (i.e., SUV_{max} value more than liver uptake) with average of 2.6 vessels involved per patient. Eighteen patients (17%) had additional finding of increased FDG uptake in the large joints, suggestive of associated PMR, the shoulder joint (13 patients) is the most commonly involved joint (average SUV_{max}–4.7). The pattern of FDG uptake was periarticular in all involved joints [Figure 2]. TVS was calculated in each patient from the involved vessels. There were 42 patients with TVS in the range of 11–15, while 14 patients had TVS more than

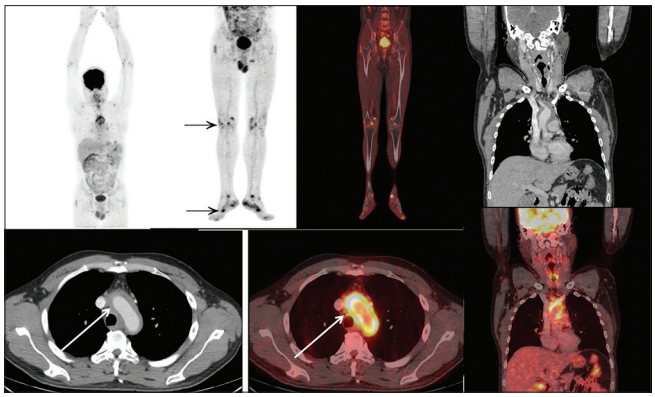

Figure 2: A 40 year-old-male with clinical diagnosis of pyrexia of unknown origin, referred to the whole-body fluorodeoxyglucose-positron emission tomography/computed tomography scan to find the cause of fever. Whole-body positron emission tomography/computed tomography scan acquired from head to toe revealed intense Grade III fluorodeoxyglucose uptake in the thoracic aorta (white arrow) and other major blood vessels with total vascular score of 17. In addition, focal intense fluorodeoxyglucose uptake was also noted in the periarticular surface of the bilateral knee and ankle joint (black arrow) suggestive of associated polymyalgia rheumatica

Table 1: The mean maximum standardized uptake value of various involved vessels

Vessel	Mean SUV_{max}
Thoracic aorta	4.05
Abdominal aorta	3.12
Subclavian	2.70
Axillary	1.54
Carotid	2.67
Iliac	2.51
Femoral	2.25

SUV_{max}: Maximum standardized uptake value

15 [Figure 3]. Mean TVS was 13.18 ± 3.4 (range 03–19) among 276 involved vessels. SUV_{max} showed significant positive correlation with the TVS (r = 0.68; P < 0.05). On laboratory parameters, elevated ESR was observed in 94 patients. On statistical analysis, a significant positive correlation (r = 0.82; P < 0.001) was observed between the TVS and elevated ESR [Figure 4]. Follow-up scans were available in 26 patients which showed favorable response to the therapy. In 19 patients, the TVS reduce to zero suggestive of complete metabolic response to therapy [Figure 5] and treatment was discontinued, while seven patients show significant reduction in TVS suggestive of partial metabolic response in which further treatment was continued till normalization of clinical parameters. Krippendorff's alpha method was performed for agreement analysis. The interobserver agreement was superior to 75% for all the criteria points of grading scale, reaching 100% in the thoracic aorta involvement.

Discussion

Patients with LVV often present with nonspecific symptoms and laboratory findings, which makes their diagnosis, management, and follow-up challenges. The role

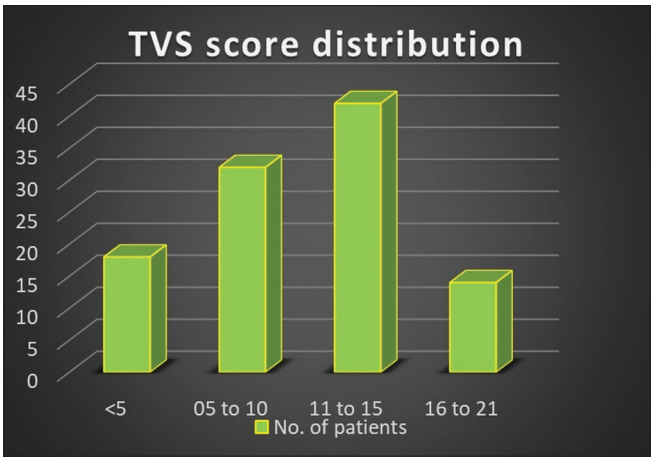

Figure 3: Bar diagram showing the distribution of the total vascular score among 106 patients

of ^{18}F-FDG-PET/CT scan in the early diagnosis of LVV including cases presenting as an isolated or in association with PMR,[19] evaluation of the extent of the disease[20,21] and also in the treatment response evaluation of these patients[12] have previously been established. However, standardization in the interpretation of the acquired PET/CT data is still an unmet need. In the present study, joint procedural recommendation proved highly reproducible and suitable for the routine reporting of FDG-PET/CT in day-to-day clinical practice. In the present study, ^{18}F-FDG-PET/CT correctly identified active disease in untreated patients of large-vessel vasculitis. A pattern of high-grade, equal to or higher than liver activity, mural ^{18}F-FDG uptake in the thoracic aorta and/or its major branches was consistently observed in all the patients. TVS was calculated using proposed standardized interpretation criteria by Rhja *et al*., which correlated well with the clinical parameters and the inflammatory markers.

Walter *et al*.[21] used a four-category visual grading to evaluate ^{18}F-FDG-uptake in a total of thirty PET-scans in patients with clinically confirmed GCA or TA. ESR (P = 0.007) and CRP levels (P = 0.005) in these patients were found to positively correlate with the scores of these patients assigned on the visual grading scale used for quantifying active inflammation. High ESR/CRP levels were also associated with a higher sensitivity of the PET scan for the presence of large-vessel vasculitis, as compared to nonelevated ESR/CR*P* values (up to a maximum of 96% sensitivity at a CRP level of 130). Blockmans *et al*.[11] conducted a similar study to evaluate the use of ^{18}F-FDG-PET in GCA and PMR. In a study conducted on a cohort of a total of 25 patients with clinical symptoms associated with GCA or PMR, PET-scan was performed and FDG uptake in the of the thoracic, femoral, and tibial arteries was assessed using a four-category scoring system similar to the system used by Walter *et al*.[21] Vascular uptake in the thoracic arteries was more frequently observed (P < 0.0001) in the patients with GCA.

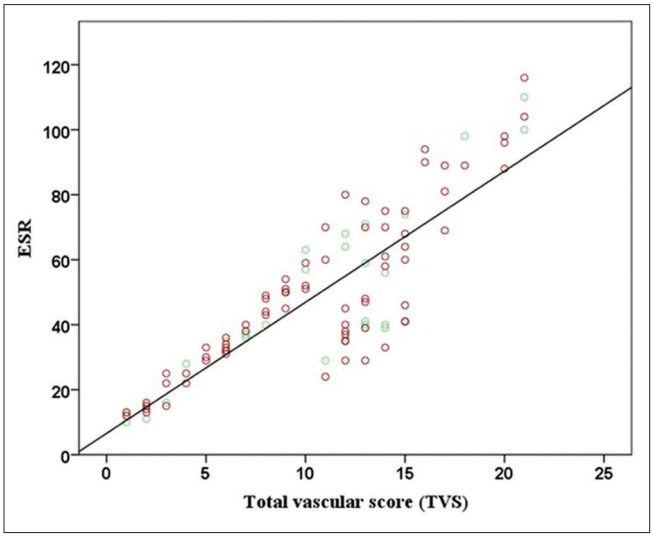

Figure 4: Scatter dot diagram showing statistical significant correlation ($r = 0.82$; $P < 0.001$) between total vascular score and erythrocyte sedimentation rate. Red dot represents male patients, while female patients are represented by green dots

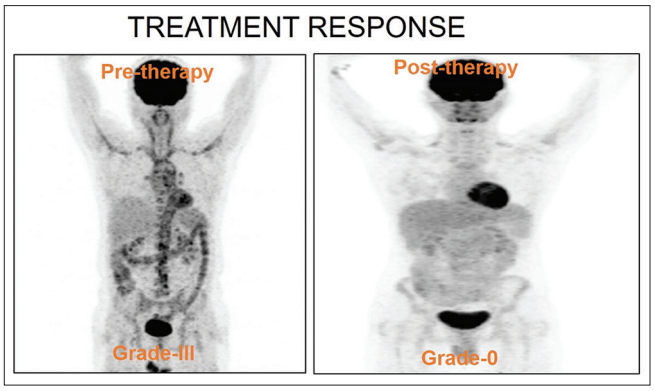

Figure 5: Whole-body fluorodeoxyglucose-positron emission tomography/computed tomography scan showing response evaluation in case of large-vessel vasculitis. After 6 weeks of steroid therapy, the total vascular score falls from 12 to 0 suggestive of complete disease remission and favorable response to therapy. Patient's clinical parameters also come to normal level

For the diagnosis of GCA or PMR, the FDG uptake in the thoracic arteries was associated with a sensitivity of 56% and a specificity of 98%. The vascular mural FDG uptake in the lower limb vessels displayed a sensitivity of 64%, but a specificity of 77%. The authors speculate that this might be explained by the fact that arteriosclerosis is more frequently observed in the lower limb vessels. By evaluating the intensity and distribution pattern of the vascular FDG uptake, we can differentiate active vasculitis from atherosclerotic lesions. Relatively linear and increased mural ^{18}F-FDG uptake was observed in the thoracic aorta and its larger branches, the carotid and subclavian arteries, in cases of untreated active vasculitis. In atherosclerosis, vascular uptake has been described as "patchy": nonlinear and less intense (less than or, rarely, equal to liver activity). Prieto-González *et al*.[22] determined sensitivity and specificity cutoff values for vascular inflammation as seen on PET/CT. A total of 32 patients were included, of whom 17 had used corticosteroids for a maximum of 3 days prior to scanning. The control group comprised twenty patients undergoing PET-scans for oncologic reasons. The optimal cutoff value (1.89) provided a sensitivity of 80% and specificity of 79%. In this study, the patients with cranial symptoms presented significantly higher values of maximal and mean SUV_{max} than patients lacking cranial manifestations.

In our study, visualization of the temporal arteries remained very difficult because of the high uptake of ^{18}F-FDG in the brain and the relatively smaller caliber and size of the cranial vessels.[23,24] This limitation was also found by Brodmann *et al*.,[23] who found that PET was unable to detect temporal inflammation but flawlessly identified extracranial involvement. Hooisma *et al*.[25] found that an elevated ESR was a statistically significant positive predictor for a positive ^{18}F-FDG-PET scan in cases of confirmed LVV. The results of the present study support that ^{18}F-FDG-PET/CT scan may also be useful for assessing the treatment response and monitoring the vascular, perivascular, and periarticular inflammatory activity in patients with LVV and PMR. Although the controversy on the routine monitoring and follow-up assessment of the patients on ^{18}F-FDG-PET/CT, remains as discussed by Blockmans *et al*.,[26] who proposed that ^{18}F-FDG-PET/CT offers no additional advantage over the conventional follow-up, based on the clinical and laboratory monitoring of patients. Nevertheless, our results indicate that ^{18}F-FDG-PET/CT scan is a useful modality for the overall management of these patients. In a single examination, it provides a precise evaluation of the extent of the disease in the entire body in comparison to the structural imaging techniques and helps not only in early diagnosis of LVV and joint involvement but also it helps in more accurate monitoring of the posttreatment inflammatory activity. Conventionally, visual interpretation and calculation of SUV_{max} of the FDG uptake in the involved vessels along with thickening seen on corresponding CT images were being used for image interpretation. There were no objective parameters to assess the overall severity and extent of the disease. The use of a standardized scoring system provides the required objectivity and reproducibility for data collection, interpretation, and comparison.

Limitations

The main limitation of our study is its retrospective nature, which precluded a valid comparison of ^{18}F-FDG-PET/CT scan with other structural imaging modalities within an acceptable time frame. FDG-PET/CT has limited resolution in evaluating the temporal arteries, owing to intense physiological FDG uptake in the brain; however, it can delineate the extracranial distribution of GCA, mainly in the thoracic aorta and its branches and the carotid and the subclavian arteries. The individuals with positive

^{18}F-FDG-PET/CT scan results and symptomatology suggestive of PMR warrant further stratification and classification to differentiate isolated PMR from GCA, which is clinically significant since GCA patients with aortic involvement are very prone to aneurysm formation and should be monitored carefully. Another limitation of our study is the advanced average age of our patients with attendant age-related inflammatory arthritic changes, giving rise to falsely increased number of total joints involved.

Conclusion

The use of whole-body scanning with ^{18}F-FDG-PET/CT is a sensitive imaging modality resulting in shorter diagnostic workup time and is also a valuable tool in monitoring treatment response in patients of LVV. Semiquantitative grading scale was validated as representing the extent and severity of inflammation. Its use is simple and provides high specificity, while maintaining high sensitivity achieved by FDG-PET scanning during the active inflammatory phase. ^{18}F-FDG-PET/CT demonstrates the overall topography of large-vessel involvement, as it can visually represent the entire body in a single image as compared to regional MRA/ultrasound/CT angiography. Whole-body structural imaging would be impractical, time-consuming, and costly, and also in the case of CT, would result in more overall radiation burden. Furthermore, the structural changes may often persist, even in the absence of active disease, thus may result in prolongation of treatment. The metabolic information obtained from the PET/CT image is a measure of the disease activity and absence of FDG uptake in follow-up studies helps to assess the response to treatment and guide end of treatment strategies. PET-CT may also help in picking up coexisting lymphadenopathy and visceral and joint involvement. Grading on the semiquantitative scale provides objectivity in diagnosis, response assessment, and in follow-up of patients with medium to LVV. Thus, the use of a standard vascular quantitative scoring system overcomes the bias associated with visual interpretation of presence or absence of disease. It provides objectivity to day-to-day reporting, and the reproducibility of the data helps in comparative studies for response assessment, follow-up, and relapse.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Koster MJ, Matteson EL, Warrington KJ. Large-vessel giant cell arteritis: Diagnosis, monitoring and management. Rheumatology (Oxford) 2018;57:ii32-42.
2. Efstathiou SP, Pefanis AV, Tsiakou AG, Skeva II, Tsioulos DI, Achimastos AD, *et al.* Fever of unknown origin: Discrimination between infectious and non-infectious causes. Eur J Intern Med 2010;21:137-43.
3. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, *et al.* 2012 revised international chapel hill consensus conference nomenclature of vasculitides. Arthritis Rheum 2013;65:1-1.
4. Salvarani C, Cantini F, Hunder GG. Polymyalgia rheumatica and giant-cell arteritis. Lancet 2008;372:234-45.
5. Chong EW, Robertson AJ. Is temporal artery biopsy a worthwhile procedure? ANZ J Surg 2005;75:388-91.
6. Einspieler I, Thürmel K, Pyka T, Eiber M, Wolfram S, Moog P, *et al.* Imaging large vessel vasculitis with fully integrated PET/MRI: A pilot study. Eur J Nucl Med Mol Imaging 2015;42:1012-24.
7. Löffler C, Hoffend J, Benck U, Krämer BK, Bergner R. The value of ultrasound in diagnosing extracranial large-vessel vasculitis compared to FDG-PET/CT: A retrospective study. Clin Rheumatol 2017;36:2079-86.
8. Kubota R, Yamada S, Kubota K, Ishiwata K, Tamahashi N, Ido T. Intratumoral distribution of fluorine-18-fluorodeoxyglucose *in vivo*: High accumulation in macrophages and granulation tissues studied by microautoradiography. J Nucl Med 1992;33:1972-80.
9. Jamar F, Buscombe J, Chiti A, Christian PE, Delbeke D, Donohoe KJ, *et al.* EANM/SNMMI guideline for 18F-FDG use in inflammation and infection. J Nucl Med 2013;54:647-58.
10. Martínez-Rodríguez I, Jiménez-Alonso M, Quirce R, Jiménez-Bonilla J, Martínez-Amador N, De Arcocha-Torres M, *et al.* 18F-FDG PET/CT in the follow-up of large-vessel vasculitis: A study of 37 consecutive patients. Semin Arthritis Rheum 2018;47:530-7.
11. Blockmans D, Stroobants S, Maes A, Mortelmans L. Positron emission tomography in giant cell arteritis and polymyalgia rheumatica: Evidence for inflammation of the aortic arch. Am J Med 2000;108:246-9.
12. Lehmann P, Buchtala S, Achajew N, Haerle P, Ehrenstein B, Lighvani H, *et al.* 18F-FDG PET as a diagnostic procedure in large vessel vasculitis-a controlled, blinded re-examination of routine PET scans. Clin Rheumatol 2011;30:37-42.
13. Fuchs M, Briel M, Daikeler T, Walker UA, Rasch H, Berg S, *et al.* The impact of 18F-FDG PET on the management of patients with suspected large vessel vasculitis. Eur J Nucl Med Mol Imaging 2012;39:344-53.
14. Blockmans D, De Ceuninck L, Vanderschueren S, Knockaert D, Mortelmans L, Bobbaers H. Repetitive 18-fluorodeoxyglucose positron emission tomography in isolated polymyalgia rheumatica: A prospective study in 35 patients. Rheumatology (Oxford) 2007;46:672-7.
15. Besson FL, de Boysson H, Parienti JJ, Bouvard G, Bienvenu B, Agostini D. Towards an optimal semiquantitative approach in giant cell arteritis: An (18) F-FDG PET/CT case-control study. Eur J Nucl Med Mol Imaging 2014;41:155-66.
16. Tezuka D, Haraguchi G, Ishihara T, Ohigashi H, Inagaki H, Suzuki J, *et al.* Role of FDG PET-CT in takayasu arteritis:

Sensitive detection of recurrences. JACC Cardiovasc Imaging 2012;5:422-9.

17. Alibaz-Oner F, Dede F, Ones T, Turoglu HT, Direskeneli H. Patients with takayasu's arteritis having persistent acute-phase response usually have an increased major vessel uptake by 18F-FDG-PET/CT. Mod Rheumatol 2015;25:752-5.
18. Slart RH; Writing group, Reviewer group, Members of EANM Cardiovascular, Members of EANM Infection and Inflammation, Members of Committees, SNMMI Cardiovascular. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: Joint procedural recommendation of the EANM, SNMMI, and the PET interest group (PIG), and endorsed by the ASNC. Eur J Nucl Med Mol Imaging 2018;45:1250-69.
19. Lavado-Pérez C, Martínez-Rodríguez I, Martínez-Amador N, Banzo I, Quirce R, Jiménez-Bonilla J, *et al.* (18) F-FDG PET/CT for the detection of large vessel vasculitis in patients with polymyalgia rheumatica. Rev Esp Med Nucl Imagen Mol 2015;34:275-81.
20. Blockmans D. The use of (18F) fluoro-deoxyglucose positron emission tomography in the assessment of large vessel vasculitis. Clin Exp Rheumatol 2003;21:S15-22.
21. Walter MA, Melzer RA, Schindler C, Müller-Brand J, Tyndall A, Nitzsche EU, *et al.* The value of [18F] FDG-PET in the diagnosis of large-vessel vasculitis and the assessment of activity and extent of disease. Eur J Nucl Med Mol Imaging 2005;32:674-81.
22. Prieto-González S, Depetris M, García-Martínez A, Espígol-Frigolé G, Tavera-Bahillo I, Corbera-Bellata M, *et al.* Positron emission tomography assessment of large vessel inflammation in patients with newly diagnosed, biopsy-proven giant cell arteritis: A prospective, case-control study. Ann Rheum Dis 2014;73:1388-92.
23. Brodmann M, Lipp RW, Passath A, Seinost G, Pabst E, Pilger E, *et al.* The role of 2-18F-fluoro-2-deoxy-D-glucose positron emission tomography in the diagnosis of giant cell arteritis of the temporal arteries. Rheumatology (Oxford) 2004;43:241-2.
24. Belhocine T, Blockmans D, Hustinx R, Vandevivere J, Mortelmans L. Imaging of large vessel vasculitis with (18) FDG PET: Illusion or reality? A critical review of the literature data. Eur J Nucl Med Mol Imaging 2003;30:1305-13.
25. Hooisma GA, Balink H, Houtman PM, Slart RH, Lensen KD. Parameters related to a positive test result for FDG PET(/CT) for large vessel vasculitis: A multicenter retrospective study. Clin Rheumatol 2012;31:861-71.
26. Blockmans D, de Ceuninck L, Vanderschueren S, Knockaert D, Mortelmans L, Bobbaers H, *et al.* Repetitive 18F-fluorodeoxyglucose positron emission tomography in giant cell arteritis: A prospective study of 35 patients. Arthritis Rheum 2006;55:131-7.