Potential clinical utility of quantitative ^{18}F-FDG PET/CT parameters in evaluating vascular inflammation in giant cell arteritis

C. Ricordi[1,2], R. Durmo[3], P. Giorgi Rossi[4], C. Salvarani[1,2], A. Versari[3], A. Filice[3], G.G. Hunder[5], F. Muratore[1,2], C. Marvisi[1,2]

[1]Rheumatology Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Italy; [2]University of Modena and Reggio Emilia, Modena, Italy; [3]Nuclear Medicine Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Italy; [4]Epidemiology Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Italy; [5]Division of Rheumatology, Mayo Clinic, Rochester, MN, USA.

Abstract

Objective

We aim to evaluate the utility of two novel quantitative PET/CT-derived parameters, Total Inflammatory Vascular Volume (TIVV) and Total Inflammatory Glycolysis Volume (TIGV), in assessing disease activity, treatment response, and predicting relapse in patients with large-vessel giant cell arteritis (LV-GCA).

Methods

Three LV-GCA patients underwent baseline and serial follow-up 18F-FDG PET/CT scans. Disease activity was assessed using conventional visual methods (Meller's scale and PETVAS) and the novel quantitative parameters TIVV and TIGV, calculated using a semiautomated method based on FDG uptake thresholds relative to liver SUV_{mean}.

Results

In Case 1, treatment initially deemed ineffective by visual criteria showed the greatest reduction in inflammatory burden using TIVV/TIGV. In this patient, the application of quantitative parameters could have prevented multiple ineffective treatment changes.

In Case 2, increasing TIVV and TIGV values preceded clinical relapse, which was undetected by visual assessment.

In Case 3, declining quantitative values, despite persistent visual hypermetabolism, supported our decision to continue therapy and aligned with clinical remission.

Conclusion

In all cases, TIVV and TIGV provided an earlier and more accurate assessment of vascular inflammation than traditional methods. Therefore, TIVV and TIGV may offer more accurate and standardized measures for evaluating disease activity and guiding treatment in LV-GCA. These metrics could address limitations of current visual and semiquantitative approaches but warrant validation in large studies.

Key words

giant cell arteritis, FDG PET/CT, inflammation

*Caterina Ricordi, MD**
*Rexhep Durmo, MD, PhD**
Paolo Giorgi Rossi, PhD
Carlo Salvarani, MD
Annibale Versari, MD
Angelina Filice, MD
Gene G. Hunder, MD
*Francesco Muratore, MD***
*Chiara Marvisi, MD***

**Contributed equally as first authors.*
***Contributed equally as last authors.*

Please address correspondence to:
Carlo Salvarani
U.O. di Reumatologia,
Azienda Unità Sanitaria Locale-
IRCCS di Reggio Emilia,
Viale Risorgimento 80,
42123 Reggio Emilia, Italy.
E-mail: carlo.salvarani@ausl.re.it

Received on September 1, 2025; accepted in revised form on October 7, 2025.

Competing interests: The institution of P. Giorgi Rossi' received external support for independent, publicly funded studies by iCAD (software) and GE (loan of a machine). He has conducted negotiations with Roche, Hologic and Becton Dickinson to obtain reagents at a reduced price or for free for an independent study funded by the Italian Ministry of Health. A. Filice has received honoraria from Novartis, GE Healthcare and Bayer. The other authors have declared no competing interests.

Introduction

Giant cell arteritis (GCA) is an inflammatory disease affecting large- and medium-sized arteries, most commonly involving the aorta and its main branches (1).

Despite advances in imaging, reliable quantitative tools to assess disease activity, monitor treatment response, and predict long-term outcomes are lacking. Among available modalities, 18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) plays an established role in the diagnosis of large-vessel vasculitis (LVV), but its utility for monitoring disease activity over time remains debated (2). Currently, PET/CT assessment of vascular inflammation relies on qualitative and semiquantitative approaches (3, 4). However, regional uptake data from individual vascular lesions may not accurately reflect the overall inflammatory burden. To overcome this limitation, composite disease activity scores incorporating qualitative PET/CT parameters, such as the Total Vascular Score (TVS) and the PET Vascular Activity Score (PETVAS), have been developed but are not widely used in clinical practice (5, 6).

We previously reported the diagnostic and prognostic potential of two novel quantitative PET-derived metrics, Total Inflammatory Vascular Volume (TIVV) and Total Inflammatory Glycolysis Volume (TIGV), in LV-GCA (7). Adapted from oncologic imaging, these metrics quantify volumetric inflammatory burden, providing a more comprehensive assessment of vascular inflammation than conventional parameters (8).

Here, we aim to demonstrate the potential clinical utility and superiority of these novel PET-derived metrics, compared to conventional PET parameters, by illustrating their application in the routine clinical management of three selected patients with LV-GCA.

Materials and methods

Three patients with LV-GCA were selected for their representativeness in illustrating the added clinical value of the proposed novel quantitative PET-derived metrics in LVV.

Two of these patients (Cases 1 and 2) were enrolled in the TOPAZIO study (Treatment Of giant cell arteritis Patients with ultra-short glucocorticoids And tociliZumab: the role of Imaging in a prospective Observational study) and its extension (9, 10), and were also included in our recent exploratory study (7). The third patient (Case 3) was evaluated for a disease flare shortly after the first two but was neither enrolled in the TOPAZIO study nor included in the exploratory analysis assessing TIVV and TIGV as diagnostic and prognostic biomarkers in GCA. Each included patient underwent a PET/CT examination at baseline, at TOPAZIO study entry for the first two patients, and at diagnosis for the third, and had at least two follow-up PET/CT scans. For the first two patients, quantitative assessment was conducted retrospectively for research purposes. Instead, for the third patient, quantitative parameters were available at the time of the follow-up PET interpretation and directly influenced the treatment decision.

All PET/CT scans were analysed by a single experienced nuclear medicine physician (AV) blinded to clinical data. TIVV and TIGV were calculated for all PET scans using the open-source Beth Israel PET/CT Viewer plugin for FIJI (http://petctviewer.org). Areas with physiologically high FDG uptake, including the brain, bladder, myocardium, and thymus, were manually excluded.

TIVV was defined as the vascular SUV_{max} threshold relative to liver SUV_{mean}: grade 1, < -10% liver SUV_{mean}; grade 2, -10% to +10% liver SUV_{mean}; grade 3, > + 10% liver SUV_{mean}. TIGV was calculated as TIVV x SUV_{mean}. As scans with grade ≥ 2 in at least one vascular district according to Meller scale were considered indicative of active disease, only grade 2 and grade 3 were included for the final calculation of TIVV and TIGV. However, in our centre, the final interpretation of disease activity and treatment response is ultimately guided by the clinical judgement of the specialist, who integrates clinical, laboratory, and imaging findings.

Fig. 1. Changes in treatment (**A**), TIVV (**B**), TIGV (**C**), and PETVAS (**D**) in three patients with large-vessel giant cell arteritis.
BARI: baricitinib; GCs: glucocorticoid; PETVAS: positron emission tomography vascular activity score; SEK: secukinumab; TCZ: tocilizumab; TIVV: total inflammatory vascular volume; TIGV: total inflammatory glycolysis volume; tx: therapy.

Results

Case 1

An adult patient diagnosed with LV-GCA with pure extra-cranial involvement in 2014, was treated with glucocorticoids (GCs) and various conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) due to relapsing disease. In August 2019, PET/CT imaging showed a relapse showing grade 3 vascular uptake per Meller's scale. The patient was enrolled in the TOPAZIO protocol, which included three intravenous GC pulses, followed by weekly subcutaneous tocilizumab (TCZ) monotherapy. TCZ effectively controlled the disease activity and was continued beyond the study period.

Despite clinical remission, a PET/CT scan in June 2023 revealed persistent vascular hypermetabolism, with a modest increase in PETVAS. TCZ was subsequently discontinued and replaced with secukinumab, which failed to control the disease both clinically and on imaging. The patient continued to report constitutional and polymyalgic symptoms, with persistently elevated inflammatory markers. Repeated PET/CT revealed widespread grade 3 according to Meller's scale uptake at the aortic level, with further increase in PETVAS. Consequently, in January 2024, treatment was changed to the target synthetic DMARD baricitinib.

However, another relapse occurred in April 2024. At that time, treatment with TCZ and a medium dose of prednisone (0.5 mg/kg/day) was resumed. A retrospective review of all prior PET/CT scans using TIVV and TIGV confirmed that TCZ had previously achieved the greatest reduction in overall inflammatory burden, further supported by a decreasing trend in overall inflammatory volumes at the last follow up (Fig. 1, Table I, Case 1).

Case 2

Another patient diagnosed with LV-GCA in July 2019 received the same treatment protocol of patient 1. PET/CT scans from June 2020, February 2021, and December 2021 progressively showed a reduction in vascular hypermetabolism on visual assessment. Due to sustained remission, TCZ was discontinued in the summer of 2021.

In December 2021, the patient was under low-dose GCs because of vague musculoskeletal symptoms reappeared after TCZ discontinuation and the PET/CT was comparable to previous exams, with only a modest increase in PETVAS. The disease was considered inactive, and treatment was not resumed. However, the patient experienced a clinical relapse shortly thereafter, characterised by constitutional manifestations and features of polymyalgia rheumatica.

Retrospective evaluation using TIVV and TIGV revealed increased vascular metabolic activity on the December 2021 scan, suggesting subclinical activity missed by conventional visual analysis (Fig. 1, Table I, Case 2).

Table I. PETVAS, TIVV, and TIGV values, with clinical disease activity assessment at each PET/CT timepoint in three patients with large-vessel giant cell arteritis.

	PET/CT date	PETVAS	TIVV	TIGV	Clinical status
Case 1	01/08/19	18	427	986	active
	01/02/20	11	152	309	inactive
	01/10/20	18	186	416	active
	01/03/22	10	68	145	inactive
	01/06/23	11	62	189	inactive
	01/01/24	18	104	287	active
	01/02/25	9	22	57	inactive
Case 2	01/07/19	27	256	659	active
	01/06/20	9	80	178	inactive
	01/02/21	9	98	221	inactive
	01/12/21	14	367	779	inactive
Case 3	01/09/20	16	94	281	active
	01/07/21	10	64	201	inactive
	01/06/22	9	169	373	inactive
	01/03/23	24	732	1738	active
	01/10/23	24	555	1253	inactive
	01/01/24	18	203	553	inactive
	01/08/24	9	198	379	inactive

PETVAS: positron emission tomography vascular activity score; TIVV: total inflammatory vascular volume; TIGV: total inflammatory glycolysis volume.

Case 3

An adult patient was diagnosed with both cranial and extra-cranial GCA in September 2020. Due to significant cardiovascular comorbidities, a 26-week tapering regimen of GCs alongside TCZ was started from disease onset. TCZ was discontinued after approximately 18 months of treatment due to sustained remission.

A clinical and imaging relapse occurred in March 2023, prompting reinitiation of TCZ monotherapy. The patient refused GC therapy due to previously experienced side effects, including uncontrolled diabetes, hypertension, weight gain, and insomnia. Follow-up PET/CT scans in October 2023 and January 2024 showed persistent grade 3 vascular uptake despite the patient being in clinical remission, with only modest reduction in PETVAS. However, TIVV and TIGV demonstrated a marked reduction in inflammatory burden, supporting the decision to continue the current treatment strategy (Fig. 2). Clinical remission was achieved and maintained through the last follow- up (Fig. 1, Table I, Case 3).

Discussion

In this case series, we introduce the application of novel semi-automated PET/CT parameters adapted from oncology to measure the metabolic burden of vascular inflammation in LVV-GCA patients (8).

We presented three illustrative cases in which TIVV and TIGV proved more accurate in assessing disease activity and predicting disease flare than conventional qualitative and semiquantitative PET/CT parameters. In the first two cases, their use could have influenced the clinical assessment and guided therapeutic decisions, while in the third, quantitative parameters directly impacted the treatment approach.

Case 1 highlights the clinical relevance of these metrics: treatment with TCZ was considered ineffective and discontinued based on visually interpreted PET/CT findings. However, retrospective analysis using quantitative metrics revealed that TCZ had been the most effective therapy in reducing the overall inflammatory burden. In this patient, the application of quantitative parameters could have prevented multiple ineffective treatment changes.

In the second case, conventional visual PET assessment did not detect subclinical disease activity preceding the relapse, which was retrospectively evident using TIVV and TIGV metrics.

In the third case, persistently high visual scores were discordant with decreasing

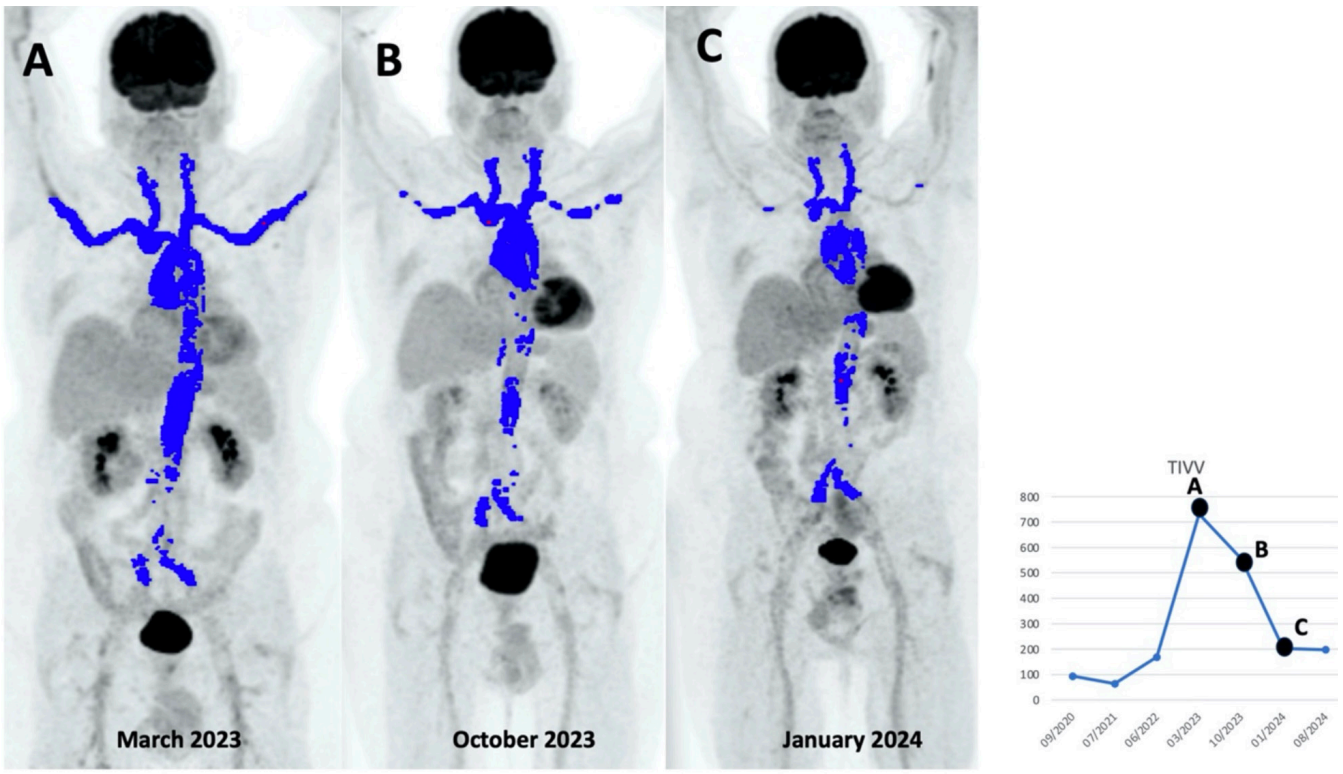

Fig. 2. Changes in total inflammatory vascular volume occurring in Case 3 at different timepoints (A, B, C). TIVV: total inflammatory vascular volume.

quantitative parameters, which showed a clear trend toward reduced vascular inflammation. Although these volumetric metrics are not yet validated for routine clinical decision-making, their consistent downward trend supported the interpretation of treatment response and reinforced the multidisciplinary decision to continue TCZ therapy.

Several studies have evaluated the accuracy of qualitative and semi-quantitative FDG PET metrics in distinguishing active from inactive LVV and in predicting relapse risk (11, 12). However, as demonstrated in our case series, these conventional approaches show limited reliability in assessing disease activity, monitoring treatment response, and, crucially, predicting relapses.

Visual grading systems such as Meller's scale are widely used for their simplicity but are hampered by significant inter-observer variability and low sensitivity to changes. Other semi-quantitative methods, such as SUV_{max} and SUV_{mean}, are more reproducible than visual assessment but are not routinely used in clinical practice due to their time-consuming nature. Furthermore, they may not accurately capture global vascular activity, as focal areas of hypermetabolism can overestimate vasculitic activity, while diffuse areas of milder hypermetabolism may be underrepresented. In our recent study, we showed that TIVV and TIGV were strongly associated with active disease, whereas SUV-based metrics (SUVmax, SUVmean) had only weak and imprecise associations. Therefore, we considered visual scores as a more appropriate comparator. Nonetheless, PETVAS provided only minor additional clinical information over the visual score in all three cases.

Although Figure 1 shows some overlap in the temporal trends among PETVAS, TIVV, and TIGV, the quantitative volumetric metrics provided a more nuanced assessment of disease burden, by more precisely capturing both the extent and intensity of inflammation. This underscores the limitations of an ordinal scale like PETVAS, which may fail to capture clinically relevant variability due to ceiling effects in widespread inflammation and underestimation in intense but segmental disease. In such scenarios, quantitative methods such as TIVV and TIGV, calculated semi-automatically and expressed on a cardinal scale, may provide a more comprehensive and standardised assessment of overall disease activity.

This case series is limited by its small sample size and the lack of long-term prospective validation of these volumetric parameters. Moreover, although the semi-automated methodology is based on open-source software, it still involves manual steps (*e.g.* exclusion of non-vascular FDG uptake), which may introduce variability and necessitate user training. Although no internal reproducibility assessment was performed in our study, the reproducibility of this technique has been previously established and validated in oncological studies (13).

In conclusion, TIVV and TIGV are promising PET/CT-derived metrics for assessing disease activity and treatment response in LV-GCA. These quantitative tools may facilitate earlier detection of disease relapses, support personalised treatment strategies, and address the limitations of visual and conventional semi-quantitative assessments.

References

1. SALVARANI C, CANTINI F, BOIARDI L, HUNDER GG: Polymyalgia rheumatica and giant-cell arteritis. *N Engl J Med* 2002; 347(4): 261-71. https://doi.org/10.1056/nejmra011913
2. GALLI E, PIPITONE N, SALVARANI C: The role of PET/CT in disease activity assessment in patients with large vessel vasculitis. *Curr Opin Rheumatol* 2023; 35(3): 194-200. https://doi.org/10.1097/bor.0000000000000931
3. SLART RHJA, GLAUDEMANS AWJM, CHAREONTHAITAWEE P *et al*.: 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(7): 1250-69. https://doi.org/10.1007/s00259-018-3973-8
4. MELLER J, STRUTZ F, SIEFKER U *et al*.: Early diagnosis and follow-up of aortitis with [18F]FDG PET and MRI. *Eur J Nucl Med Mol Imaging* 2003; 30(5): 730-36. https://doi.org/10.1007/s00259-003-1144-y
5. GRAYSON PC, ALEHASHEMI S, BAGHERI AA *et al*.: Positron emission tomography as an imaging biomarker in a prospective, longitudinal cohort of patients with large vessel vasculitis. *Arthritis Rheumatol* 2018; 70(3): 439-49. https://doi.org/10.1002/art.40379
6. 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(4): 672-77. https://doi.org/10.1093/rheumatology/kel376
7. DURMO R, MURATORE F, MARVISI C *et al*.: Exploring total inflammatory vascular volume as a diagnostic and prognostic biomarkers in giant cell arteritis. *Rheumatology* (Oxford) 202; 64(11): 5863-71. https://doi.org/10.1093/rheumatology/keaf381
8. CHAUVIE S, CASTELLINO A, BERGESIO F, DE MAGGI A, DURMO R: Lymphoma: the added value of radiomics, volumes and global disease assessment. *PET Clin* 2024; 19(4): 561-68. https://doi.org/10.1016/j.cpet.2024.05.009
9. MURATORE F, MARVISI C, CASSONE G *et al*.: Treatment of giant cell arteritis with ultra-short glucocorticoids and tocilizumab: the role of imaging in a prospective observational study. *Rheumatology* (Oxford) 2024; 63(1): 64-71. https://doi.org/10.1093/rheumatology/kead215
10. MURATORE F, MARVISI C, CASSONE G *et al*.: Treatment of giant cell arteritis with ultra-short glucocorticoids and tocilizumab: results from the extension of the TOPAZIO study. *Rheumatology* (Oxford) 2025; 64(5): 3057-62. https://doi.org/10.1093/rheumatology/keae400
11. QUINN KA, DASHORA H, NOVAKOVICH E, AHLMAN MA, GRAYSON PC: Use of 18F-fluorodeoxyglucose positron emission tomography to monitor tocilizumab effect on vascular inflammation in giant cell arteritis. *Rheumatology* (Oxford) 2021; 60(9): 4384-89. https://doi.org/10.1093/rheumatology/keaa894
12. GALLI E, MURATORE F, MANCUSO P *et al*.: The role of PET/CT in disease activity assessment in patients with large vessel vasculitis. *Rheumatology* (Oxford) 2022; 61(12): 4809-16. https://doi.org/10.1093/rheumatology/keac125
13. BOELLAARD R, BUVAT I, NIOCHE C *et al*.: International benchmark for total metabolic tumor volume measurement in baseline 18f-fdg pet/ct of lymphoma patients: a milestone toward clinical implementation. *J Nucl Med* 2024; 65(9): 1343-48. https://doi.org/10.2967/jnumed.124.267789