Editorial

PET-CT in the diagnosis and management of polymyalgia rheumatica: pros and cons

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Diagnosis

Polymyalgia rheumatica (PMR) is an inflammatory condition that typically affects individuals over the age of 50. It is characterised by severe pain and stiffness in the shoulders, hips, neck, and upper arms on both sides (1, 2). In most cases, PMR is associated with elevated levels of acute-phase reactants (1, 2).

While the diagnosis is usually straightforward when its characteristic symptoms are present (3), imaging techniques have proven valuable in both the diagnosis and management of PMR. These tools provide insight into the underlying inflammation and help distinguish PMR from other conditions. In this context, the 2012 EULAR/ACR preliminary classification criteria for PMR emphasised the role of ultrasonography (US) as a useful diagnostic tool when available (4). They highlighted the importance of US findings, particularly bilateral subacromial/subdeltoid bursitis and trochanteric bursitis, in confirming the diagnosis of PMR (1,4). The inclusion of US findings significantly enhanced the specificity of the 2012 EULAR/ACR criteria (5).

Positron emission tomography-computed tomography (PET-CT) has been found to be a valuable diagnostic tool for PMR due to its ability to visualise inflammation in periarticular structures, which are commonly affected in PMR (6, 7). Using the radioactive tracer fluorodeoxyglucose (18F-FDG), PET-CT highlights areas of increased glucose metabolism, typically seen in inflamed tissues such as bursae, synovial joints, and tendons. This technique detects inflammation at a cellular level, identifying increased activity in neutrophils, lymphocytes, monocytes, and macrophages (8, 9). Unlike conventional imaging methods like x-rays or magnetic resonance imaging (MRI), PET-CT can reveal inflammatory changes before structural damage occurs, enabling earlier diagnosis and timely treatment to manage symptoms effectively (10-12). In PMR, this imaging technique often shows increased FDG uptake in the shoulders, hips, and periarticular soft tissues. PET-CT may also reveal inflammation in areas not typically assessed through physical examination, like the spine and interspinous bursae (1).

The pros and cons of using PET-CT in the diagnosis and management of PMR are summarised in Table I and discussed in depth below.

What reasons do we have to ask for PET-CT in patients with suspected PMR?

Requesting a PET-CT scan in patients with suspected PMR can be justified for several key reasons:

- *Early detection of inflammation*: PET-CT identifies metabolic activity in inflamed tissues, such as bursae, synovial joints, and tendons, before structural changes are visible on X-ray or MRI. This early detection is essential for prompt diagnosis and treatment. In this regard, a systematic review on the diagnostic value of 18F-FDG-PET-CT in PMR confirmed a high prevalence of 18F-FDG uptake in several regions, including the interspinous bursae, hips, ischial tuberosities, shoulders, and sternoclavicular joints (13). The likelihood ratios for positive uptake in these areas were statistically significant, demonstrating their diagnostic importance. The interspinous bursae exhibited the highest positive likelihood ratio, followed by the hips, ischial tuberosities, and shoulders (13).

Table I. Pros and cons of using PET-CT in the diagnosis and management of polymyalgia rheumatica.

Pros	Cons
Early detection of inflammation	High cost and low accessibility
Differentiation from other conditions such as late-onset RA, other inflammatory arthritides (*e.g.* atypical SpA), infectious diseases, or neoplastic conditions	Radiation exposure
Detection of large-vessel vasculitis	Lack of specificity in some cases
Assessment of atypical PMR presentations Evaluation of non-responders to treatment Useful as a minimally invasive and comprehensive image technique Assessment of disease activity	Effect of glucocorticoids on FDG-PET-CT sensitivity

PET-CT: positron emission tomography-computed tomography; RA: rheumatoid arthritis; SpA: spondyloarthritis; FDG: fluorodeoxyglucose.

- Differentiation from other conditions

In some cases, late-onset rheumatoid arthritis (RA) can be challenging to differentiate from PMR. To address this, Ikuma *et al*. conducted a study to identify key sites that could help distinguish PMR from RA using 18F-FDG-PET-CT. The study included 35 patients with PMR and 46 with RA. The results showed that FDG uptake in areas such as the shoulder joints, lumbar vertebrae spinous processes, pubic symphysis, sternoclavicular joints, ischial tuberosities, greater trochanters, and hip joints was useful for differentiating PMR from RA. Notably, FDG uptake in at least one of the ischial tuberosities provided the highest diagnostic value in distinguishing the two conditions (14).

PMR can mimic other inflammatory rheumatic diseases, as well as infectious or neoplastic conditions (1, 15, 16). However, PET-CT imaging provides distinctive uptake patterns that differentiate PMR from atypical spondyloarthritis (17). Additionally, PET-CT is valuable for distinguishing PMR from malignancies and infections that may present with similar features (18).

- Detection of large-vessel vasculitis

Giant cell arteritis (GCA) is a large-vessel vasculitis that, like PMR, is more common in individuals aged 50 years and older (19). PMR is often associated with GCA (19), and PET-CT can detect inflammation in large vessels, even in the absence of overt GCA symptoms (1, 20). GCA and PMR are often overlapping conditions (19). Thus, PMR may serve as a warning sign for the potential presence of an underlying large-vessel vasculitis.

A systematic review and meta-analysis on the prevalence of subclinical GCA in patients with new-onset PMR, which included studies in which different techniques had been used for the detection of GCA, revealed a higher prevalence of subclinical GCA with PET-CT (29%) than with temporal artery biopsy (20%) or US (15%) (21).

Persistence of PMR symptoms is a common indication for performing a PET-CT scan (22). Bilateral diffuse lower limb pain, pelvic girdle pain, and inflammatory low back pain in the context of PMR are strong predictors of an underlying large-vessel vasculitis (22).

- Assessment of atypical presentations of PMR

PMR can present with only mild elevations in inflammatory markers such as C-reactive protein or erythrocyte sedimentation rate (23). In cases where laboratory findings or clinical symptoms are inconclusive, PET-CT can offer diagnostic clarity by identifying characteristic patterns of inflammation in periarticular structures (18).

- Evaluation of non-responders to treatment

For patients with PMR features who do not respond as expected to glucocorticoids, PET-CT can help reassess the diagnosis, identify persistent inflammation, or uncover alternative conditions contributing to symptoms (18).

- Useful as a minimally invasive and comprehensive image technique

PET-CT provides a whole-body view of inflammation, offering a more comprehensive assessment compared to localised imaging modalities like US or MRI (18).

- Assessment of disease activity

PET-CT can be used to monitor the extent of inflammation in patients with PMR. This can be particularly helpful in evaluating disease activity and response to therapy, especially in patients who do not respond as expected to glucocorticoid treatment (18).

What are the limitations for the use of PET-CT in patients with PMR?

- Cost and accessibility

PET-CT is expensive and not widely available, making it less practical for routine use in diagnosing PMR.

- Radiation exposure

It involves exposure to ionising radiation, which is a consideration when opting for its use. This is a crucial consideration for patients who require multiple scans over time (18).

- Lack of specificity in some case

While PET-CT can reveal inflammation, increased uptake can occur in various inflammatory, infectious, or malignant conditions (18).

- Effect of glucocorticoids on FDG-PET-CT sensitivity

Another limitation is the use of glucocorticoids before performing FDG-PET-CT. In this regard, the use of glucocorticoids can reduce the sensitivity of this image technique (24, 25). With respect to this, it has been found that within 3 days of high dose glucocorticoid treatment, FDG-PET-CT can diagnose GCA of large vessels with high sensitivity (26). However, the 18-FDG absorption is reduced in patients with GCA of large vessels after 72 hours of treatment with high doses of glucocorticoids and the results can be falsely negative if the PET-CT is performed ten days after the start of glucocorticoids (12).

For isolated PMR, some experts suggest suspending glucocorticoids to im-

prove the accuracy of FDG-PET-CT for diagnostic purposes (27). Others argue that the typical initial dose of 15 mg/day of prednisone or prednisolone, which is commonly used in isolated PMR, may reduce FDG uptake but does not significantly affect the characteristic distribution pattern seen in PET-CT scans of untreated PMR patients (12, 18).

Can PET-CT be used for the diagnosis and management of PMR?

Nielsen *et al*. have recently evaluated whether the diagnostic accuracy for PMR could be enhanced by combining FDG-PET-CT findings with the clinical baseline diagnosis or the 2012 ACR/EULAR clinical classification criteria for PMR (28). For this purpose, they assessed an investigation and a validation cohort from two countries, encompassing 66/27 and 36/21 PMR/non-PMR patients, respectively. The study demonstrated that FDG-PET/CT significantly improved the precision of diagnosing PMR by visualising inflammation that is not detectable through conventional methods. FDG-PET-CT showed better alignment with clinical diagnosis and the 2012 ACR/EULAR criteria, providing a valuable supplementary diagnostic tool. This imaging technique was particularly effective in cases with diagnostic uncertainty or overlapping with conditions like large-vessel vasculitis. According to these findings, incorporating FDG-PET-CT into diagnostic pathways for PMR could refine the accuracy of diagnoses, especially in challenging cases, although its routine use warrants further research and cost-effectiveness evaluations (28).

By visualising inflammation, PET-CT can help assess whether current treatment regimens are effective or if adjustments to therapy are necessary. Therefore, PET-CT could be used as a tool to guide the treatment of PMR. However, the use of this technique for managing PMR remains a matter of debate (18).

There are inconclusive results regarding the correlation between PET-CT findings and the risk of relapses or response to treatment in PMR. Changes in FDG uptake have been observed following glucocorticoid treatment, highlighting challenges in its usefulness for long-term management. Studies involving PET-CT scans performed on patients with isolated PMR before initiating glucocorticoid therapy, and then repeated at 3 and 6 months, indicate that FDG-PET findings in PMR patients do not correlate with their risk of relapse (29). In addition, current guidelines do not universally recommend the use of PET-CT for all PMR patients, particularly in the absence of atypical symptoms or refractory disease, due to the factors mentioned above. Further research is needed to establish clear guidelines for its use in PMR patients.

Conclusions

PET-CT is particularly valuable in cases of diagnostic uncertainty, atypical presentations (18), and when PMR is accompanied by symptoms suggestive of large-vessel vasculitis (30,31). Its capacity to identify early inflammatory changes and distinguish PMR from other conditions enhances its role in the diagnostic process.

EULAR experts recommend FDG-PET and MRI as effective diagnostic tools for detecting large-vessel involvement in patients presenting with PMR and systemic symptoms where GCA is a potential diagnosis (32). However, further research is needed to determine whether PET-CT should be routinely used in patients with isolated ("pure") PMR.

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