Imaging indications in polymyalgia rheumatica

With the recent improvement in technology, various imaging modalities are increasingly being used in the diagnosis and monitoring of musculoskeletal diseases. Although polymyalgia rheumatica (PMR) is traditionally considered a 'clinical diagnosis' the utility of imaging for diagnosis, assessment of disease severity and treatment response in PMR is increasingly recognized. Imaging not only adds to the diagnosis by detecting PMR-specific features, but also helps to make alternative diagnoses. Recently published classification criteria emphasize the importance of ultrasonography, an easily available imaging modality in the diagnosis of PMR. Herein we discuss the role and limitations of ultrasonography, MRI and fludeoxyglucose-PET scanning in the management of PMR, particularly in the diagnosis, and distinguishing it from its numerous mimics.

KEYWORDS: FDG-PET | imaging | MRI | polymyalgia rheumatica | ultrasonograpgy

The diagnosis of polymyalgia rheumatica (PMR), characterized by proximal pain and stiffness, is often uncertain owing to PMR mimics, such as rheumatoid arthritis (RA), spondyloarthritides, inflammatory myopathies connective tissue diseases and vasculitis - all of which can present with the polymyalgic syndrome in the elderly. Inflammatory markers are often discordant with disease activity and imaging techniques show promise in diagnosis and disease monitoring, improving our understanding of PMR and its overlap with inflammatory arthritis and large vessel vasculitis (LVV). In this article, we discuss imaging techniques, primarily ultrasonography (US), but also MRI and fludeoxyglucose (FDG)-PET, in the assessment of PMR. Current guidelines recommend a stepwise approach to PMR and we add the imaging requirements to facilitate the various diagnostic steps (Figure 1).

Imaging adds to PMR diagnosis by either identifying abnormalities associated with alternative diagnoses or detecting PMR-specific features. MRI studies have shown synovitis and periarticular inflammation in PMR and confirm that there is no actual muscle inflammation [1], while FDG-PET scans show vascular inflammation, synovitis, bursitis and enthesitis in a significant portion of PMR patients [1]. Recently published PMR classification criteria recognize PMR-associated ultrasound lesions in the shoulders and hips as criteria items for the scoring algorithm for the classification as PMR [2]. We review the current understanding of the role of ultrasound, MRI and PET-CT and imaging

in the diagnosis of PMR and distinguishing it from its mimics. In light of the classification criteria, we also report validation findings from a shoulder ultrasound study of consecutive patients referred from general practice for evaluation of suspected PMR. Synovitis, effusion, tenosynovitis and erosions referred in this paper are defined according to the Outcome Measures in Rheumatology (OMERACT) definitions for musculoskeletal (MSK) ultrasound [3].

Diagnostic challenges in PMR

The polymyalgic syndrome of proximal pain and stiffness, with or without elevation of inflammatory markers, is shared by several medical conditions affecting older people. Inflammatory arthritides frequently present with pain and morning stiffness. Elderly-onset RA involves large joints (most notably the shoulders) in 40% of patients [4]. In a cohort study of 116 patients with raised erythrocyte sedimentation rate (ESR) referred for shoulder girdle pain and followed-up for 12 months by Caporali et al., 35% eventually received the diagnosis of RA and 56% retained a firm diagnosis of PMR at 1 year [5]. Peripheral arthritis was present in nearly 80% of patients with RA but also in 26% of patients with PMR, indicating poor positive predictive value of this sign [5]. Similarly, Pease et al. reported that 23% of patients with PMR also have peripheral synovitis [6]. However, it is clear that persistent synovitis in multiple joints and the need for a prolonged high-dose corticosteroid therapy should prompt reconsideration of the diagnosis of PMR.

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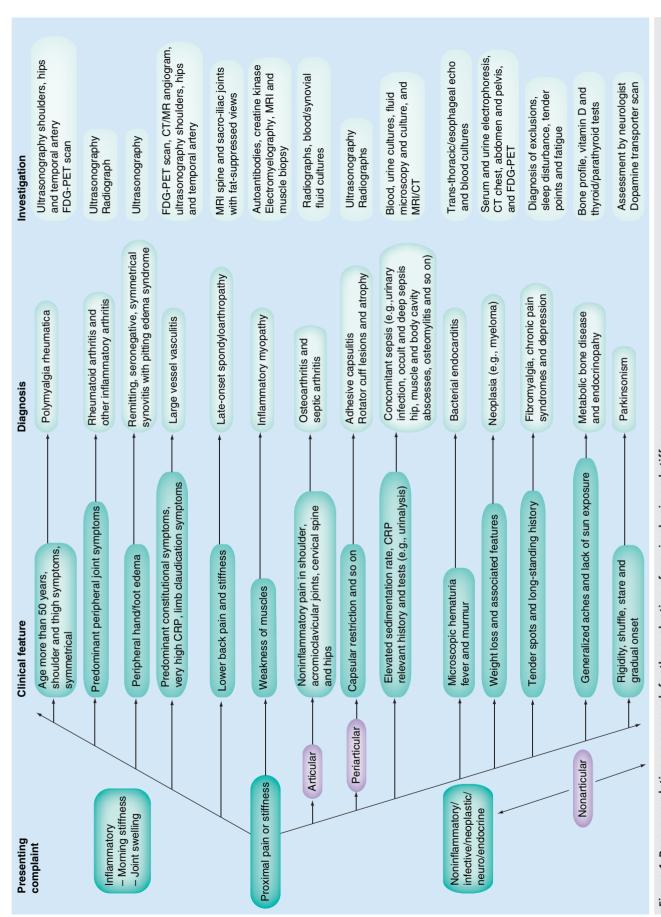


Figure 1. Recommendation on approach for the evaluation of proximal pain and stiffness. CRP: Greactive protein; CT: Computed tomograpy: FDG: Fludeoxyglucose; MR: Magnetic resonance. Reproduced with permission from [34].

Late-onset spondyloarthropathy with its features of oligoarthritis, constitutional symptoms and high ESR may easily mimic PMR [7].

The presentation of PMR can be atypical and varied. Patients with dominant constitutional symptoms (such as anemia, weight loss and low grade fever) may mimic infection or neoplasia but also systemic inflammation such as LVV. Due to overlapping clinical features, the distinction between isolated PMR and giant cell arteritis (GCA)-associated polymyalgia can be difficult. GCA can present with polymyalgia in 40-50% of patients and studies have shown that patients initially diagnosed with isolated PMR have US and histological features of GCA [8]. Evidence, however, is still lacking to support the use of temporal artery US in every PMR patient, as we do not know whether this subclinical vascular inflammation has any long-term consequences. Presentation of PMR with predominant constitutional symptoms could also represent a paraneoplastic phenomenon [9].

As no gold standard test has been established for the diagnosis of PMR, clinicians rely heavily on inflammatory markers in confirming clinical diagnosis of PMR. However, the presence of PMR with normal inflammatory markers is well described in the literature [10–13].

In addition, the notion of 'test of treatment' with a trial of steroids is a popular medical practice. However, there is no evidence that steroid responsiveness is indeed a specific PMR feature. It can vary within PMR patients and the classification criteria study failed to find it useful to distinguish PMR cases from comparators [14].

The diagnostic uncertainty also has implications for trials of novel therapies in PMR. This has driven the international initiative leading to the 2012 provisional European League Against Rheumatism (EULAR) ACR classification criteria and validated patient reported outcomes in PMR [2,14].

Imaging in PMR

■ US in PMR

US is increasingly being used as an extension to physical examination for the initial assessment of many MSK inflammatory conditions. The widespread use of US is owing to the recent improvement in technology coupled with the portability and relatively low cost of this technology. US technology offers several inherent advantages. Being noninvasive, with a quick scan time and without radiation makes US well accepted by patients [15]. There are several advantages from the clinician's point of view. It

allows contralateral examination and does not pose limitations due to metal artifacts, which can be problematic in MRI.

Ultrasound has been used in the diagnosis of PMR patients, especially in patients with the typical symptoms with normal ESR [11]. Typical findings on ultrasound include subdeltoid bursitis (FIGURE 2) and tenosynovitis of long head of biceps tendon (FIGURES 3 & 4) at the shoulders [16,17] and, less frequently, synovitis of the glenohumoral joint. In the hips, ultrasound often reveals synovitis (FIGURE 5) and trochanteric bursitis [18,19]. Interspinous bursitis can also be found on PET scanning in PMR [20].

In a series by Lange *et al.*, these ultrasound findings were found in 40.9% of PMR patients and 65.5% of elderly-onset rheumatoid arthritis (EORA) patients. The latter being characterized by more severe inflammation on ultrasound [21]. Bursitis and long head biceps tenosynovitis are more frequently bilateral in PMR patients [17]. In a series of 24 patients studied by Cantini *et al.*, US bilateral bursitis had 92.9% sensitivity, 99.1% specificity and 98.1% positive predictive value for PMR [17].

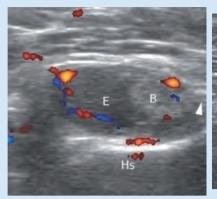
With regards to hip symptoms, Cantini et al. found in their series of 20 patients that US showed 100% sensitivity and specificity in detection of trochanteric bursitis [18]. In this study, US-detected trochanteric bursitis was seen in 100% of PMR patients and it was bilateral in 90% [18]. Inflammation of iliopsoas and ischio-gluteal bursa as seen in this study again emphasizes the extensive extra-capsular involvement in PMR.

The EULAR ACR classification criteria study evaluated consensus-generated candidate



Figure 2. Oblique image of the rotator cuff depicting acute subacromial-subdeltoid bursitis (arrows).

B: Bursitis; Del: Deltoid; GT: Greater tuberosity of humerus; SupraS: Supraspinatus.



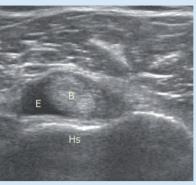


Figure 3. Transverse view reveals the sheath of biceps tendon distended by fluid. Mesotendon (arrowhead) connecting the visceral and parietal layers of the synovial envelope.

B: Biceps tendon; E: Fluid; Hs: Humeral shaft.

criteria (clinical, laboratory and ultrasound) in a 6-month prospective cohort study of 125 patients with new-onset PMR and 169 non-PMR comparison subjects with mimicking conditions. A scoring algorithm (Table 1) was developed based on morning stiffness >45 min (2 points), hip pain/limited range of motion (1 point), absence of rheumatoid factor and/or anti-citrullinated protein antibody (2 points), and absence of peripheral joint pain (1 point). The scoring scale is 0-6 (without ultrasound) and 0-8 (with ultrasound).

A score >4 has 68% sensitivity and 78% specificity for discriminating all comparison subjects from PMR. The specificity is higher (88%) for discriminating shoulder conditions from PMR and lower (65%) for discriminating RA from PMR. Adding ultrasound, a score of 5 or greater had 66% sensitivity and 81%

Figure 4. Right longitudinal view of extra-articular long head of biceps tendon showing large amount of sheath effusion (asterisk).

BT: Biceps tendon; H: Humerus.

specificity for discriminating all comparison subjects from PMR. The specificity was higher (89%) for discriminating shoulder conditions from PMR and lower (70%) for discriminating RA from PMR [14]. These criteria should be applied to patients aged 50 years or older presenting with new-onset (>12 weeks) bilateral shoulder pain and raised inflammatory markers.

Peripheral synovitis as well as other findings, such as enthesitis, carpal tunnel syndrome and pitting hand edema (RS3PE), have been described in association with PMR. All these features can be evaluated by US and illustrate the overlap with inflammatory arthritis and difficulties with the diagnosis of PMR. Salvarani et al. have postulated that the presence of peripheral synovitis in PMR could represent a high-risk subgroup with more severe disease [22].

We evaluated the scoring algorithm (with US) in a case series of 15 consecutive patients (11 female, mean age 69 years) referred from general practice for the evaluation of suspected PMR over a 6-month period. None had received prednisolone therapy prior to ultrasound. Patients underwent assessment for symptoms and signs of PMR, exclusion of competing diagnoses and shoulder US. US lesions characterized as indicative of polymyalgia were bicipital tenosynovitis, subdeltoid bursitis and glenohumeral synovitis. Eight were given the diagnosis of PMR based on British Society for Rheumatology PMR guidelines specified inclusion and exclusion criteria. Two were diagnosed with inflammatory osteoarthritis, three with RA (one seronegative), three with spondyloarthropathy and one with supraspinatus

Seven out of eight patients diagnosed with PMR had abnormalities on shoulder US. Five had bicipital tenosynovitis and three had subdeltoid bursitis, with one patient having both. One patient with clinical PMR had a normal shoulder ultrasound. None of our patients exhibited glenohumeral synovitis. In the PMR group, the median score was 7.

In the non-PMR group five had normal ultrasound, one had rotator cuff lesions with co-existent glenohumeral osteoarthritis and one had a calcified supraspinatus tendon. None had the typical PMR US features. In this group, the median value of the scoring algorithm was 3. The scoring algorithm with US appears to be quite useful in the clinic.

We acknowledge that this is a small study and larger studies are required to validate the 2012 PMR provisional classification criteria.

■ Differentiation from EORA

As already stated, although subacromial and subdeltoid bursitis are the hallmark of PMR, they are also frequently found in EORA [21]. US can help to make this differentiation by multiregional assessment like peripheral joints ultrasound Doppler study. Table 2 lists some of the characteristics that help in the differentiation.

■ Reliability of US examination

US is considered to be an operator-dependent technology with poor repeatability. However, it is reassuring to see that recent studies on MSK US have established moderate-to-good interobserver reliability [23,24]. The reliability exercise for the Polymyalgia Rheumatica Classification Criteria Study showed moderate-to-good interobserver reliability [16].

One case—control study compared US with MRI to identify hip involvement in ten patients with active PMR [18]. Trochanteric bursitis was the most frequent hip synovial inflammatory lesion of PMR identified in this study. The sensitivity/specificity of US in the detection of trochanteric bursitis was equal to MRI scan. However, US was less sensitive than MRI for the detection of hip synovitis (53 vs 63%).

■ Role of US in disease monitoring

Few studies report use of US to evaluate response to treatment in PMR. The classification criteria study showed that, prior to steroid treatment, 84% had shoulder findings and 32% had both shoulder and hip findings on US. Response to corticosteroid treatment occurred in 73% of patients by week 4 and presence of ultrasound findings at baseline predicted response to corticosteroids [14].

We feel US can be a very useful monitoring tool in patients with PMR. It is particularly helpful in patients with an unclear response to treatment, clinical relapse and patients with normal inflammatory markers. Studies have shown that inflammation on ultrasound can regress with both steroid therapy and anti-TNF [25,26]. However, the abnormalities follow a different time course for resolution compared with clinical features and inflammatory markers [17]. Macchioni *et al.* found no association between the persistence of inflammation at US and relapses/recurrences. By contrast, a positive PD signal at diagnosis was significantly associated with increased chance of relapse at follow-up [27].

■ MRI

MRI has established a very important place in the field of MSK imaging. The lack of radiation



Figure 5. A 70-year-old lady presented to the acute medical unit with profound fatigue, night sweats and fevers. Diagnosis of polymyalgia rheumatica was confirmed when ultrasound revealed bilateral synovitis (double arrowhead) and effusion of the hips (asterisk), as well as bilateral bicepital tenosynovitis and subdeltoid bursitis.

and ability to visualize deeper structures makes it ideally suited for the evaluation of PMR patients. Bilateral subacromial and subdeltoid bursitis has been shown as the hallmark of PMR on MRI [11,28]. In addition, MRI can demonstrate synovitis, tenosynovitis and extra-capsular changes [29]. MRI of the sacroiliac joints and lumbar spine with short TI inversion recovery views is useful for excluding competing diagnoses such as spondyloarthritis

Table 1. 2012 provisional The European League Against Rheumatism ACR classification criteria.

Characteristics	Points without US (0-6)	Points with US (0–8)
Morning stiffness >45 min	2 points	2 points
Hip pain/limited range of motion	1 point	1 point
Absence of rheumatoid factor and/or anti-citrullinated protein antibody	2 points	2 points
Absence of peripheral joint pain	1 point	1 point
At least one shoulder with: • Subdeltoid bursitis • And/or biceps tenosynovitis • And/or glenohumeral synovitis (either posterior or axillary) And at least one hip with synovitis and/or trochanteric bursitis	NA	1 point
Both shoulders with subdeltoid bursitis, biceps tenosynovitis or glenohumeral synovitis	NA	1 point
A scare of 4 or more is categorized as polymyaldia rhoums	atica in the algorithm	without LIC and a

A score of 4 or more is categorized as polymyalgia rheumatica in the algorithm without US and a score of 5 or more is categorized as polymyalgia rheumatica in the algorithm with US. NA: Not applicable; US: Ultrasound.

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Table 2. Ultrasound features of polymyalgia rheumatica and elderly-onset rheumatoid arthritis.			
PMR	EORA		
Shoulder			
Low-grade hypervascularity of glenohumeral joint	Marked hypervascularity of glenohumeral joint		
Subacromial/subdeltoid bursitis frequent	Subacromial/subdeltoid Bursitis less frequent (~30%)		
Bursitis bilateral	Relatively less common		
Hypervascularity asymmetrical or unilateral	Usually symmetrical		
Small effusion biceps tendon sheath	Massive effusion biceps tendon sheath		
Minimal intra-articular effusion of shoulder joint	Large intra-articular effusion of shoulder joint		
Hip			
Bilateral trochanteric bursitis is common	Trochanteric bursitis uncommon		
Hip hypervascularity common	Hip hypervascularity is uncommon		
lliopsoas and ischiogluteal Bursitis frequently seen	Relatively less frequent		
Peripheral joints			
Lower frequency of effusion/ hypervascularity	Higher frequency of effusion/hypervascularity		
Relatively less vascularity with PDUS	Marked hypervascularity at PDUS		
Nonerosive arthritis	Erosive		
EORA: Elderly-onset rheumatoid arthritis; PDUS: Power Doppler	EORA: Elderly-onset rheumatoid arthritis; PDUS: Power Doppler ultrasound; PMR: Polymyalgia rheumatica.		

in atypical situations with non-PMR clues, such as younger patients, male gender and spinal symptoms.

Figure 6. Pathological changes in polymyalgia rheumatica. Fludeoxyglucose-PET-computed tomography demonstrating symmetrical capsulitis, enthesitis of (A) the left shoulder and both hips, (B) ischial (arrow) and (C) trochanteric bursitis (closed arrowhead) and interspinous ligament inflammation at the lumbar level.

Neck pain is frequently reported by PMR patients. Salvarani et al. investigated cause of neck pain in 12 PMR patients with MRI scan [30]. All of the PMR patients had evidence of interspinous cervical bursitis at the C5-C7 level. In this study, cervical bursitis occurred significantly more frequently in patients with PMR than in control patients.

There have been attempts to differentiate PMR from RA on the basis of MRI. Marzo-Ortega et al. compared MRI scans of the hands of ten patients with new-onset PMR with another ten patients with early RA by using dynamic contrast-enhanced MRI and conventional MRI. While no significant differences were seen in the volume of synovitis and tenosynovitis, the extra-capsular changes were significantly more prominent in the PMR-related hand disease [29]. In this study, the soft tissue edema and enhancement were counted as 'extra-capsular' where the changes were apparent outside the synovial cavity adjacent to the joint capsule. MRI evidence of extra-capsular involvement in association with peripheral arthritis in PMR has also been described by Mori et al. [31].

There are limited data on the use of MRI in monitoring PMR treatment response. Salvarani et al. have previously described normalization of PMR inflammation on MRI after local

corticosteroid treatment [32]. Widespread use of MRI scan in this context may be limited, however, as it is time consuming and not cost effective.

■ FDG-PET

FDG-PET scanning has contributed significantly to the understanding of pathogenesis by detecting specific pathological changes seen in PMR (FIGURE 6). Lesions in the spinous processes are more frequently detected with FDG-PET/ CT than with MRI. In a study of 14 untreated patients with active PMR, 71% patients showed increased FDG uptake in the vertebral spinous processes while MRI detected only 20% of the corresponding lesions [20]. FDG-PET scan can help significantly in diagnosing PMR by identifying hallmark features such as bursitis in the interspinous, trochanteric or ischial regions. Another advantage of a PET scan is that it can show vascular involvement. Increased uptake of FDG in large arteries of isolated PMR patients has been reported in several studies [20,33]. This has not only helped in the early detection of LVV, but has also strengthened the argument of vasculitic nature of PMR. However, it is not clear whether asymptomatic vasculitis identified on a PET scan runs the same risk of complications as seen in symptomatic patients. There is not enough evidence to recommend aggressive treatment in this type of scenario. FDG-PET scanning should certainly be considered in the assessment of steroid-resistant PMR.

We undertook an audit of the utility of FDG-PET CT scanning and outcomes of therapeutic decisions subsequently made in 52 difficult-to-treat cases. These patients had FDG-PET CT because either there was difficulty in reducing prednisolone doses to less than 10 mg owing to active disease or inflammatory markers remained elevated

despite being on adequate treatment. Of the 52, 23 patients had PMR, 20 had GCA (12 biopsy positive) and nine had an unexplained systemic illness. In total, 63% of the PMR and GCA patients were on steroids. Fifteen had avid FDG uptake in the aorta and subclavian and axillary arteries, suggesting the presence of LVV. Of the 15 patients with LVV, four had PMR, five GCA, two patients had both GCA and PMR and the remaining four had unexplained systemic illness. All patients with LVV had successful clinical response to escalation of immunosuppression with significant reduction in inflammatory markers. Two patients had uptake in sternoclavicular and sacroiliac joints suggestive of seronegative spondyloarthropathy. One patient with connective tissue disease overlap had symmetrical uptake in the shoulders consistent with inflammatory arthritis. In two patients with atypical clinical presentation, the diagnosis of PMR was confirmed with bursal and entheseal uptake in the shoulders and hips. In three cases FDG-PET revealed cancer (pancreas in two cases and metastatic breast in one). The average dose of prednisolone prior to PET scan was 6 mg daily in PET positives compared with 21 mg daily in PET-negative patients. Our experience suggests that LVV is a common finding in both PMR and GCA exhibiting lack of steroid response, constitutional symptoms and raised inflammatory markers. Scan interpretation is influenced by dose of steroid intake and we suggest prednisolone no higher than 7.5-10 mg daily a week prior to the scan. FDG-PET can also reveal occult malignancies or confirm the PMR diagnosis.

The use of FDG-PET scanning for monitoring purposes, however, is restricted by its limited availability, high cost as well as significant radiation exposure.

Table 3. Indications for imaging.		
Imaging modality	Indication in PMR	
Ultrasonography	All patients with proximal pain and stiffness (polymyalgia presentation) – US shoulders/hips, peripheral joints (if they have peripheral symptoms), US temporal/axillary arteries (if GCA/LVV suspected)	
MRI	MRI sacro-iliac joints and lumbar spine with STIR views for excluding competing diagnoses such as spondyloarthritis in atypical situations with non-PMR clues such as the younger patient, male gender and spinal symptoms	
FDG-PET CT	PMR patients with persistently raised inflammatory markers and constitutional symptoms despite adequate steroid/adjunctive therapies as well as patients with claudication symptoms or features of aortitis	
	graphy; FDG: Fludeoxyglucose; GCA: Giant cell arteritis; LVV: Large vessel vasculitis; PMR: Polymyalgia ort Tl inversion recovery; US: Ultrasound.	

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Conclusion

Imaging provides important information on the assessment of the heterogeneous and multifactorial nature of inflammation observed in PMR. We now know PMR patients may exhibit synovitis, tenosynovitis, bursitis and vasculitis - emphasizing its overlap with both inflammatory arthritis as well as LVV. The condition has a wide differential and can be difficult to distinguish from elderly-onset inflammatory conditions and degenerative disease of the shoulder. Imaging with US, MRI and FDG-PET may help to identify alternate diagnoses including serious pathology such as cancer and infection (TABLE 3). Ultrasound findings in hips and shoulders may help to differentiate PMR from other mimics although the overlap with elderly-onset RA needs further understanding. US may help in monitoring response and obtaining tissue and bursal fluid for further assessment. FDG-PET scans in steroid unresponsive refractory patients may help to identify LVV for more intensive therapies. The full potential of imaging is yet to be explored, and further research is required.

Future perspective

There is still considerable uncertainty related to the diagnosis and outcomes of patients with PMR. The importance of imaging in establishing the correct diagnosis of PMR is recognized by the international initiative leading to the development of 2012 provisional EULAR ACR classification criteria. However, the potential of noninvasive imaging modality such as US still remains under-utilized in PMR. Widespread use of imaging may help us in establishing the true spectrum of polymyalgia rheumatica.

The challenge of subclinical inflammation (e.g., low-grade asymptomatic bursitis/ tenosynovitis) found on imaging remains and highlights the need for caution in overtreating these patients, as we do not know the long-term effect of this subclinical inflammation. There is a need for continued advances in imaging techniques. Similarly, FDG-PET scanning has raised important questions by finding lowgrade vascular uptake in isolated PMR patients. Further research is required to find out whether treatment can be recommended for such patients.

Although with the help of US, MRI and PET scans it is now well established that inflammation in PMR is extracapsular, the target for therapies remains elusive owing to the diffuse process of inflammatory involvement. The future needs to include advances in imaging technology so that subsequent response to treatment can be predicted too.

Microbubble contrast-enhanced ultrasound is an emerging imaging modality that can quantitatively assess inflammation by staying in the circulation and highlighting areas of blood flow. A future study aims to image inflamed

Executive summary

Diagnostic challenges in polymyalgic syndrome

- The polymyalgic syndrome (PMR) of proximal pain and stiffness is shared by several medical conditions affecting older people. Differentiation from elderly-onset rheumatoid arthritis is very challenging and often the diagnosis of elderly-onset rheumatoid arthritis only becomes apparent in the follow-up.
- Imaging adds to PMR diagnosis by either detecting PMR-specific features or identifying abnormalities associated with alternative diagnoses.

Role of ultrasound in polymyalgic syndrome

- Ultrasound has recently been used in the diagnosis of PMR patients. Typical findings on ultrasound include subdeltoid bursitis, tenosynovitis of long head of biceps tendon at the shoulders and hip synovitis/effusion.
- Ultrasound is particularly helpful in patients with an unclear response to treatment, clinical relapse and patients with normal inflammatory markers.

MRI

 MRI can demonstrate synovitis, tenosynovitis and extra-capsular changes. MRI is also useful for excluding competing diagnoses such as spondyloarthritis in atypical situations with non-PMR clues such as younger age of the patient, male gender and spinal symptoms.

FDG-PET scanning

FDG-PET scanning has contributed significantly to the understanding of pathogenesis by detecting specific pathological changes seen in PMR. In addition, it can reveal underlying occult neoplastic disorders or vascular uptake.

Conclusion

Imaging provides important information on the assessment of the heterogeneous and multifactorial nature of inflammation observed in PMR. Imaging with ultrasound, MRI and FDG-PET may not only help to establish the diagnosis of PMR, but also to identify alternate diagnoses.

shoulder bursae with contrast-enhanced ultrasound and obtain tissue by ultrasound-directed portal-assisted biopsy prior to steroid therapy for new PMR. Tissue and bursal fluid will be studied for biochemical, histological, immunohistochemical and cytokine characteristics. Microbubble appearances and synovial fluid and biopsy findings will be compared with subsequent clinical course and response to therapy.

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