Polymyalgia rheumatica (PMR) is the most common inflammatory rheumatic disease in the elderly and is characterized by headache, bilateral pain and stiffness in the neck, shoulders and pelvic girdle [1, 2]. PMR occurs isolated or concomitantly with giant-cell arteritis (GCA), a chronic vasculitis of large- and medium-sized vessels that is associated with severe complications including blindness, aortic stenosis, dissections and aneurysms [3]. Although higher doses of steroids are required to suppress inflammation in GCA, patients with isolated PMR usually show rapid response to low doses of corticosteroids [3]. Most patients with isolated PMR then withdraw steroids after 1–2 yrs [3], but up to one-third of patients have a more chronic, relapsing course requiring low doses of corticosteroids for a longer period of time [4, 5]. Corticosteroid-related adverse events are then common and strictly related to the cumulative dose: 65% of PMR patients show at least one serious corticosteroid-related event, such as osteoporotic fractures or diabetes mellitus occurring after an average of 1.6 yrs after treatment initiation [6]. Because of the severity of these corticosteroid-related side effects, it is essential to identify those patients requiring long-term treatment as early as possible. Reliable predictors for the duration of therapy, however, are elusive, and currently available studies on pretreatment acute-phase proteins including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and interleukin-6 (IL-6) are inconclusive [7–9].

Whether relapses in PMR patients are predictable using imaging techniques has now been addressed for the first time by Blockmans and colleagues [10]. In their study reported in this issue of Rheumatology, they evaluated the use of repeated 18F-Flourodeoxyglucose positron emission tomography (FDG-PET) in a cohort of newly diagnosed PMR patients [10]. Only a few data are available on the value of FDG-PET in rheumatology so far, and Blockmans et al. [10] have now provided an important, well-designed trial: the outcome of patients with isolated PMR was assessed performing FDG-PET scans at baseline, 3 and 6 months after diagnosis [11]. All patients followed a standardized treatment protocol, and temporal arteritis was actively excluded in all PMR patients by unilateral histological assessment. For objective quantification of FDG uptake in larger arteries and shoulders, hips and processi spinosi a semi-quantitative score was developed using values ranging from 0 (no uptake) to 3 (very marked FDG uptake) and zero (no uptake) to two (intense uptake), respectively. Interestingly, Blockmans et al. [10] found no correlation between the intensity of FDG uptake in the large vessels, shoulders, hips or processi spinosi of PMR patients and the risk of relapse. They conclude that repetitive performance of FDG-PET scans do not offer any advantage over the currently available, traditional follow-up methods in PMR patients. Because of the short duration of the study, however, it remains unclear whether patients with prolonged FDG uptake in large arteries are at higher risk for late complications such as aortic stenosis, dissections or aneurysms. Indeed, vascular inflammation is incompletely suppressed by corticosteroids even in PMR, and it has been suspected that complications predominantly occur at vessel sites with pathological changes in the FDG-PET examination [10, 12].

Unfortunately, the power of the Blockmans’ study was limited concerning the prediction of PMR relapses by incomplete follow-up data as only one-third of the patients enrolled into the study completed the planned three serial FDG-PET scans (type II error). A definite conclusion on the value of repeated FDG-PET is thus not possible. The careful reader observes higher FDG uptake 6 months after baseline in the shoulders [mean score 1.3 ± 0.8 (no units depicted) vs 0.5 ± 0.7; maximum score possible 2.0], hips (0.9 ± 0.9 vs 0.5 ± 0.7) and processi spinosi (0.4 ± 0.8 vs 0.0 ± 0.0) of relapsing patients compared with those without relapse, although differences did not reach statistical significance. An increased FDG uptake has been shown to correlate with levels of acute phase proteins. Elevated acute phase proteins (CRP and IL-6) at 3, 6 and 12 months after, but not at time of diagnosis, are linked with a higher risk of PMR relapse [12, 13]. Another prospective study with repeated FDG-PET scans in GCA patients by the same group had been unable to discriminate patients with recurrence of GCA from those without [14]. Between the 3rd and 6th month of treatment the mean total vascular score increased by 0.8 ± 3.6 and decreased by 2.5 ± 3.6 in patients with and without relapse, but the difference was also not significant. The low number of GCA patients completing all scheduled FDG-PET scans (n = 8) limited the power of this trial as well. In summary, it cannot be excluded that repeated FDG-PET scans facilitate the prediction of late complications of large vessel arteritis as well as relapses in PMR and/or GCA patients. The fact that the use of FDG-PET is limited even in clinical trial settings raises serious concerns about the feasibility of this technique in clinical practice. FDG-PET scans, however, may support diagnosing PMR in cases with atypical presentation and/or incomplete response to corticosteroids [15].

Apart from the limited clinical use of these findings, the present study provides additional insights into the pathogenesis of PMR and its suggested association with GCA. Using histological examinations of temporal arteries, approximately 40% of GCA patients have PMR and about 10% of patients originally presenting with isolated PMR have GCA. After clinical exclusion of temporal arteritis in combination with a normal biopsy, about 30% of patients with isolated PMR showed FDG uptake in their large arteries, suggesting a more frequent occurrence of large artery involvement than of temporal arteries in PMR [14]. Histological studies of temporal arteries in PMR and GCA patients revealed the presence of mature dendritic cells in the adventitial layer producing both IL-1 and IL-6 [16]. Fully developed vasculitis by histomorphological criteria and intimal hyperplasia, however, is absent in PMR and
interferon-γ-producing T cells are not recruited into the vascular tissue [16]. This infiltration with inflammatory cells in larger vessels of PMR patients further supports the close relationship between PMR and GCA. The incompleteness of the infiltration may explain the reduced vascular FDG uptake in PMR compared with GCA patients (mean total vascular score 2.5 ± 2.3 vs 6.0 ± 6.2 in the same centre, but not the same study) and the absence of characteristic arteritic symptoms. The pattern of vascular involvement (apart from temporal arteries) is similar in PMR and histologically confirmed GCA, with a preferential affection of both subclavian arteries, the thoracic and the abdominal aorta [10, 14].

Interestingly, polymyalgic symptoms appeared to correlate with (peri-)synovitis in the shoulders and hips in PMR patients, as indicated by increased FDG-uptake at these sites, whereas subclavian arteritis was unrelated to these symptoms. These findings support earlier magnetic resonance imaging and ultrasound studies showing the presence of shoulder synovitis, subacromial and subdeltoid bursitis as well as biceps tendon tenosynovitis in PMR patients [2, 10, 17]. Besides, Blockmans et al. [10] observed increased FDG-uptake in processi spinosi of PMR patients suggesting local inflammation of the spine. We agree with the authors that this additional site may contribute to patients’ discomfort and is well-suppressed by corticosteroids [10].

In conclusion, PMR is a complex disorder combining subclinical large vessel arteritis and (peri-)synovitis of the shoulders and hips causing polymyalgic symptoms. FDG-PET scans may be helpful for the diagnosis of PMR, but are of questionable value for the prediction of relapses.

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<td>• 18F-Fluorodeoxyglucose positron emission tomography scans are of questionable value for the prediction of relapses in patients with polymyalgia rheumatica.</td>
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<tr>
<td>• 18F-Fluorodeoxyglucose positron emission tomography findings support the close relationship between polymyalgia rheumatica and giant-cell arteritis.</td>
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References