Joint Involvement in Patients with Early Polymyalgia Rheumatica Using High-resolution Ultrasound and Its Contribution to the EULAR/ACR 2012 Classification Criteria for Polymyalgia Rheumatica

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ABSTRACT. ***Objective.*** To assess joint involvement and the contribution of musculoskeletal ultrasound (MSUS) to the novel European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) 2012 classification criteria in patients with polymyalgia rheumatic (PMR).

Methods. MSUS was performed in 54 consecutive patients with recent-onset PMR.

Results. Biceps tenosynovitis of at least 1 shoulder has been observed in 70.4% of patients, and 64.8% had a bilateral biceps tenosynovitis. Subdeltoid bursitis (27.8% unilateral, 5.6% bilateral), glenohumeral synovitis (22.2% unilateral, 9.3% bilateral), and hip involvement (22.2% unilateral, 16.7% bilateral) were observed less frequently. The sensitivities of the classification criteria were 85.2% for EULAR/ACR without MSUS and 81.5% for EULAR/ACR with MSUS.

Conclusion. The most common MSUS pathology was a biceps tenosynovitis. However, US findings had no effect on the sensitivity of the novel EULAR/ACR criteria for PMR. (First Release March 1 2014; J Rheumatol 2014;41:730–4; doi:10.3899/jrheum.130946)

Key Indexing Terms:
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Polymyalgia rheumatica (PMR) is an inflammatory rheumatic disease of middle aged and elderly patients (> 50 yrs), typically manifesting with bilateral pain and morning stiffness in the neck, shoulder girdle, and hip girdle. In Europe, the incidence rate ranges between 10 and 70 per 100,000 persons aged 50 years and older with lower rates in Southern Europe and higher rates in Northern Europe[1]. Moreover, there is a correlation of advancing age with a rising incidence. The exact pathogenesis of PMR has not been established; however, endogenous and exogenous factors might play a role in its pathogenesis[2]. Further, there is a lot of uncertainty when diagnosing PMR, and an important point is the exclusion of other diagnoses mimicking PMR[3]. Until 2012, several different sets of classification criteria for PMR were used: criteria by Bird and Wood (1979)[4], Chuang and Hunder (1982)[5], Healey (1984)[6], and Jones and Hazleman (1981)[7]. In April 2012, an initiative of the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) published new provisional classification criteria for PMR, and those criteria are the first to contain musculoskeletal ultrasound (MSUS) in an additional algorithm[8]. However, the relevance of MSUS to visualize joint involvement, as well as the pattern in PMR patients in daily clinical practice, has not been addressed. Therefore, we investigated joint involvement using MSUS in a cohort of patients with recent onset of PMR by analyzing the distribution of novel US criteria. In addition, the sensitivities of novel EULAR/ACR criteria with and without US were compared to the formerly established criteria.

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MATERIALS AND METHODS

All patients of our tertiary rheumatology center with newly established diagnosis of PMR between 01/2011 and 12/2012 were included in our study retrospectively. The study was conducted according to the guidelines for retrospective studies of the local ethics committee. It was analyzed for each patient whether the EULAR/ACR criteria for PMR with and without US as well as formerly used PMR criteria (i.e., Bird and Wood; Chuang and Hunder; Healey; and Jones and Hazleman) were fulfilled (Table 1A). MSUS was performed and interpreted by a physician with DEGUM (German Society for Ultrasound in Medicine) certification for MSUS in all patients with suspected PMR; and the physician who performed the MSUS

Table 1A. Comparison of polymyalgia rheumatica (PMR) criteria. Adapted from Dasgupta, et al. Arthritis Rheum 2006;55:518–20[9]; with permission.

		Bird & Wood	Chuang & Hunder	Healey	Jones & Hazleman	EULAR/ACR without MSUS	EULAR/ACR with MSUS
(1)	Age, yrs	> 65	≥ 50	> 50	—	≥ 50 (obligatory)	≥ 50 (obligatory)
(2)	Bilateral pain of neck, shoulders, and pelvic girdle	Shoulders	Any 2	Any	Shoulders and pelvic girdle	Shoulders (obligatory) Hips (1 point)	Shoulders (obligatory) Hips (1 point)
(3)	ESR	≥ 40 mm/h	> 40 mm/h	Elevated	> 30 mm/h and/or CRP > 6 mg/l	Elevated ESR and/or CRP (obligatory)	Elevated ESR and/or CRP (obligatory)
(4)	Morning stiffness	> 1 h	≥ 30 min	> 1 h	Yes	> 45 min (2 points)	> 45 min (2 points)
(5)	Duration of symptoms	Rapid onset < 2 weeks	≥ 1 mo	—	≥ 2 mo unless treated	—	—
(6)	Depression and/or weight loss	Yes	—	—	—	—	—
(7)	Bilateral upper arm tenderness	Yes	—	—	—	—	—
(8)	Exclusion of other diagnoses	—	Yes	Absence of RF and ANA	Yes	Absence of RF or ACPA (2 points) Absence of other joint involvement (1 point)	Absence of RF or ACPA (2 points) Absence of other joint involvement (1 point)
(9)	Rapid response to corticosteroids	—	—	≤ 20 mg prednisone	Yes	—	—
(10)	MSUS	—	—	—	—	—	1 shoulder and 1 hip (1 point) Both shoulders (1 point)
	Diagnosis	Any 3	All above	(1) and (8) obligatory, plus any 3 of (2), (3), (4) or (9)	All above	(1), (2) and (3) obligatory, plus a score of 4 or more points	(1), (2) and (3) obligatory, plus a score of 5 or more points

EULAR/ACR: European League Against Rheumatism/American College of Rheumatology criteria for PMR; MSUS: musculoskeletal ultrasound; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; RF: rheumatoid factor; ACPA: anti-citrullinated protein antibody; ANA: antinuclear antibodies.

Table 1B. Sensitivity of polymyalgia rheumatica (PMR) criteria in our cohort of patients with recent-onset PMR (n = 54).

	Bird & Wood	Chuang & Hunder	Healey	Jones & Hazleman	EULAR/ACR without MSUS	EULAR/ACR with MSUS
Sensitivity (no. patients)	87.0% (47/54)	40.7% (22/54)	66.7% (36/54)	83.3% (45/54)	85.2% (46/54)	81.5% (44/54)

MSUS: musculoskeletal ultrasound; EULAR/ACR: European League Against Rheumatism/American College of Rheumatology criteria for PMR.

scans was not blinded for clinical data of the patient. MSUS pathologies were defined as follows: tenosynovitis of the long biceps tendon (hypoechoic or anechoic thickened tissue with or without fluid in the tendon sheath as proposed by the Outcome Measures in Rheumatology group)[10]. Bursitis was defined as a distinct hypoechoic or anechoic distension of the subdeltoid bursa, whereas glenohumeral synovitis was defined as a clear delineation of a joint capsule distension in the posterior transverse scan. For the hip joint, a clear hypoechoic or anechoic joint capsule distension was considered as synovitis. Shoulders were examined using a Logiq e9 device (GE Healthcare) with a 6–15 MHz linear probe (ML 6–15). Biceps tenosynovitis, subdeltoid bursitis, and glenohumeral synovitis were evaluated as present or absent by greyscale US. Hip joints were examined using a linear transducer with 3–8 MHz bandwidth (9L–D) and scanned for coxitis and trochanteric bursitis. Representative MSUS scans are shown in Figure 1. The final diagnosis of PMR was established by an experienced rheumatologist according to medical history, physical examination, laboratory analysis, MSUS, and after exclusion of other conditions mimicking PMR. The response to corticosteroids was not used to verify the diagnosis of PMR. Statistical analyses were carried out using the Mann-Whitney U test, and $p < 0.05$ was considered significant.

RESULTS

A new diagnosis of PMR was established in 54 patients. The average age of these patients was 67.4 ± 9.4 years (mean ± SD) with 29 women (53.7%). The mean erythrocyte sedimentation rate (ESR) before treatment was 45.2 ± 25.7 mm/h; C-reactive protein (CRP), 47.2 ± 36.3 mg/l; duration

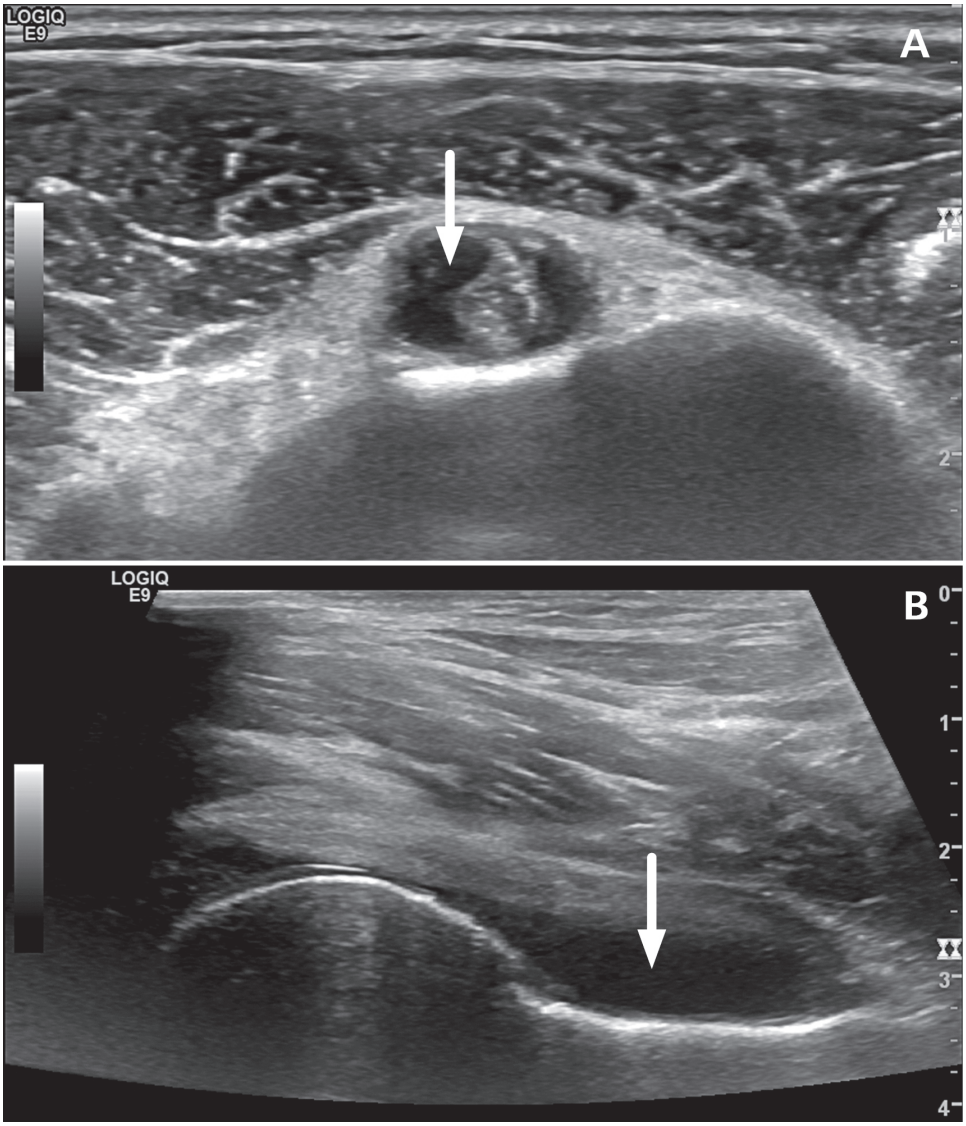

Figure 1. Representative musculoskeletal ultrasound scans. A. Ventral transversal scan of the shoulder joint showing tenosynovitis of the long biceps tendon (arrow). B. Ventral longitudinal scan of the hip joint showing an effusion with distinct capsule distension (arrow).

of morning stiffness, 84 ± 38 min. Forty-seven patients (87.0%) presented with hip pain or limited range of motion; 49 (90.7%) had normal values for rheumatoid factor and anticitrullinated protein antibodies (ACPA), with no patient being positive for ACPA, and 18 (33.3%) had no other joint involvement. Thirty-nine (72.2%) had pathological MSUS findings (see below) of both shoulders; 10 (18.5%) had pathological MSUS findings of at least 1 shoulder and 1 hip joint.

Further, the pattern of joint involvement was analyzed using MSUS (Figure 2). Pathological MSUS findings of shoulder or hip joints were present in 43 patients (79.6%). Biceps tenosynovitis, subdeltoid bursitis, or glenohumeral synovitis of at least 1 shoulder could be observed in 41 (75.9%). Biceps tenosynovitis of at least 1 shoulder was seen in 38 patients (70.4%), and 35 (64.8%) had a bilateral biceps tenosynovitis. Subdeltoid bursitis [15 (27.8%) unilateral, 3 (5.6%) bilateral], glenohumeral synovitis [12 (22.2%) unilateral, 5 (9.3%) bilateral], and hip involvement [12 (22.2%) unilateral, 9 (16.7%) bilateral] were observed less frequently. Of the patients with hip affection in MSUS, 66.7% (8/12) presented with pathological MSUS findings of both hips and both shoulders. In addition, we found that those patients had higher inflammatory activity (ESR 54.1 ± 25.2 mm/h, CRP 67.7 ± 33.3 mg/l) compared with the other subgroup (ESR 43.6 ± 25.8 mm/h, CRP 43.6 ± 35.9 mg/l, $p < 0.05$ for CRP).

The proportion of patients fulfilling the EULAR/ACR criteria without US was calculated at 85.2% (95% CI 73.4%–92.3%); and the proportion of the algorithm with US

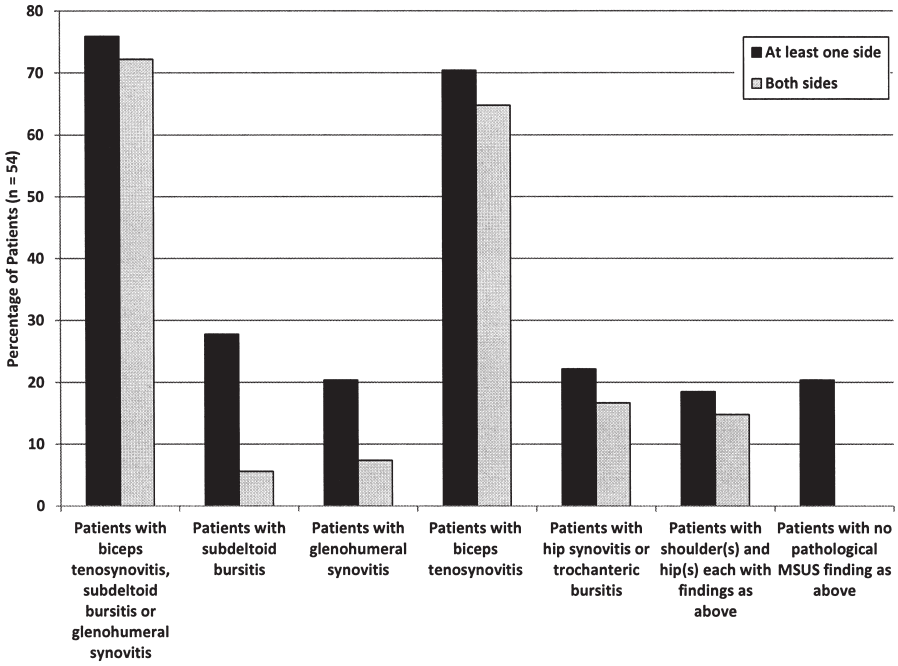

Figure 2. Joint involvement in our cohort of patients with polymyalgia rheumatica of recent onset according to musculoskeletal ultrasound. MSUS: musculoskeletal ultrasound.

at 81.5% (95% CI 69.2%–89.6%). We did not detect any patient fulfilling the EULAR/ACR criteria with US who did not fulfill the criteria without US. In addition, we determined the proportions of patients fulfilling formerly used criteria: 87.0% (95% CI 75.6%–93.6%) for criteria by Bird and Wood, 40.7% (95% CI 28.7%–54.0%) for Chuang and Hunder, 66.7% (95% CI 53.4%–77.8%) for Healey, and 83.3% (95% CI 71.3%–91.0%) for Jones and Hazleman (Table 1B).

DISCUSSION

Joint involvement in patients with early PMR. There are discrepant findings on joint manifestations in patients with PMR. Cantini, *et al* observed subdeltoid bursitis by MSUS in 96% of patients with untreated PMR, and in 93% of those patients the subdeltoid bursitis was bilateral. According to the authors, the frequency of glenohumeral synovitis and biceps tenosynovitis did not differ significantly between patients with PMR and controls[11]. Frediani, *et al* found subdeltoid bursitis by MSUS in 70%, biceps tenosynovitis in 68%, and glenohumeral synovitis in 66% of patients with untreated PMR[12].

Using MSUS, Jiménez-Palop, *et al* reported bilateral subdeltoid bursitis in 65%, bilateral biceps tenosynovitis in 45%, bilateral hip synovitis in 30%, and bilateral glenohumeral synovitis in 18% of patients with untreated PMR[13]. Recently, Ruta, *et al* reported that unilateral (55%) and bilateral (37%) subdeltoid bursitis as well as biceps tenosynovitis (unilateral 47%, bilateral 30%) were significantly more common in patients with flares of known PMR compared to rheumatoid arthritis (RA). In contrast, unilateral glenohumeral synovitis was more frequent in patients with RA, indicating that joint involvement in patients with PMR was primarily due to periarticular inflammation in contrast to intraarticular inflammation (synovitis) in patients with RA[14].

Consistent with these findings, our results demonstrate a periarticular (bilateral) biceps tenosynovitis being the most common pathological MSUS finding in patients with newly diagnosed PMR. Taking into account that 1 of the major clinical aspects in PMR is bilateral pain in the shoulder girdle, our results indicate that this bilaterality is most likely due to a bilateral biceps tenosynovitis and rarely related to bilateral subdeltoid bursitis or bilateral glenohumeral synovitis.

In contrast to the relatively high rate of pathological MSUS findings of the shoulders, we detected pathological MSUS findings of at least 1 hip in only 12 of the 54 patients. However, we observed pathological MSUS findings of both hips and both shoulders in 66.7% of patients with hip involvement according to MSUS. Those patients presented levels of CRP significantly higher than the other patients with PMR, indicating that hip involvement according to MSUS might reflect higher disease activity.

MSUS does not increase the sensitivity of the EULAR/ACR criteria for PMR. In our cohort of patients with recent-onset PMR, we found a slightly decreased sensitivity using the EULAR/ACR algorithm with US in

comparison to the algorithm without US (81.5% vs 85.2%). This is because there was no joint involvement detectable by MSUS in 20.4% of the patients. Those patients can still be considered as having PMR in the algorithm with US if they already scored 5 or more points in the algorithm without US.

Data presented in the report on the EULAR/ACR criteria demonstrate that, by adding US, the specificity of the criteria increases[8], and because one of the major points in diagnosing PMR is the exclusion of other diagnoses mimicking PMR, a higher specificity would be more beneficial.

Comparison of PMR criteria. When comparing the different sets of classification criteria (Table 1A), some criteria require all the included aspects to be fulfilled (Chuang and Hunder, Jones and Hazleman); some have obligatory aspects plus a certain number of other aspects (EULAR/ACR with and without MSUS, Healey) and 1 requires a certain number of the listed aspects with not a single aspect being obligatory (Bird and Wood). Therefore it is not surprising that Bird and Wood's criteria achieved the highest, and Chuang and Hunder's criteria the lowest sensitivity in our cohort of patients with recent onset PMR.

The sensitivity of Bird's criteria, the EULAR/ACR criteria with and without US, as well as Jones and Hazleman all were found to lie in the same range. When considering that the advantage of the algorithm with US is that it further increases specificity, we come to the conclusion that neither algorithm of the EULAR/ACR criteria is inferior to the formerly used criteria for diagnosing PMR.

Study limitations. This is a retrospective study and no followup was carried out, which means that the diagnosis of some patients might have changed in the course of followup. Further, the physician who performed the MSUS scans was not blinded for clinical data of the patient; moreover, the rheumatologist, who finally established the diagnosis of PMR, was not blinded for MSUS results. This lack of blinding might have introduced bias. Additionally, there was no control group of patients without PMR to evaluate the specificity of the PMR criteria.

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