Assessment of the New 2012 EULAR/ACR Clinical Classification Criteria for Polymyalgia Rheumatica: A Prospective Multicenter Study

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ABSTRACT. ***Objective.*** To assess the performance of the new 2012 provisional European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) polymyalgia rheumatica (PMR) clinical classification criteria in discriminating PMR from other mimicking conditions compared with the previous 5 diagnostic criteria in a multicenter prospective study.

Methods. Patients older than 50 years, presenting with new-onset bilateral shoulder pain with elevated acute-phase reactants (APR), were assessed for the fulfillment of the new and old classification/diagnostic criteria sets for PMR. At the end of the 1-year followup, 133 patients were diagnosed with PMR (expert opinion) and 142 with non-PMR conditions [69 rheumatoid arthritis (RA)]. Discriminating capacity, sensitivity, and specificity of the criteria sets were estimated.

Results. Discriminating capacity of the new clinical criteria for PMR from non-PMR conditions and RA as estimated by area under the curve (AUC) were good with AUC of 0.736 and 0.781, respectively. The new criteria had a sensitivity of 89.5% and a specificity of 57.7% when tested against all non-PMR cases. When tested against all RA, seropositive RA, seronegative RA, and non-RA control patients, specificity changed to 66.7%, 100%, 20.7%, and 49.3%, respectively. Except for the Bird criteria, the 4 previous criteria had lower sensitivity and higher specificity (ranging from 83%–93%) compared with the new clinical criteria in discriminating PMR from all other controls.

Conclusion. The new 2012 EULAR/ACR clinical classification criteria for PMR is highly sensitive; however, its ability to discriminate PMR from other inflammatory/noninflammatory shoulder conditions, especially from seronegative RA, is not adequate. Imaging and other modifications such as cutoff values for APR might increase the specificity of the criteria. (First Release February 1 2016; J Rheumatol 2016;43:893–900; doi:10.3899/jrheum.151103)

Key Indexing Terms:
POLYMYALGIA RHEUMATICA CLASSIFICATION CRITERIA RHEUMATOID ARTHRITIS

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Accepted for publication December 23, 2015.

Polymyalgia rheumatica (PMR) is a common inflammatory rheumatic disorder of the elderly that affects 0.1%–0.5% of the population over 50 years of age[1,2]. Diagnosis of PMR is challenging because there are several mimicking conditions without any specific test or clinical findings for PMR. Currently, diagnosis is almost exclusively dependent on a clinical construct, evidence of systemic inflammation, and exclusion of other causes. However, pelvic and shoulder girdle pain, morning stiffness, and constitutional symptoms may be observed in many rheumatic and nonrheumatic disorders. Differentiation at the disease onset or even after a certain followup period, particularly from elderly onset rheumatoid arthritis (RA) and other inflammatory diseases, is not always easy[3]. This difficulty in diagnosis led to the development of several diagnostic criteria sets[4,5,6,7,8]. These criteria mostly involve similar clinical variables such as the presence of bilateral shoulder and hip girdle pain, morning stiffness, age, and elevated markers of inflammation with different cutoff values. Some of these criteria have high sensitivity and low specificity and some vice versa[9,10]. The requirement of a standardized classification criteria resulted in the development of the new provisional classification criteria for PMR in 2012 by a collaborative effort between the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR)[11]. Although the new criteria set was developed to distinguish patients with PMR from patients with conditions that mimic PMR, the sensitivity and specificity in the derivation cohort remained at 68% and 78%, respectively, without ultrasound (US)[11]. With the addition of the optional US criteria (both shoulders and hips), specificity increased to 81%. A single-center retrospective study determined the performances of all previous diagnostic and the new classification criteria sets in a group of prospectively followed-up patients in which the prerequisite criteria for application of new criteria were fulfilled in only about 30% of the total control group[10].

The performance of this new classification criteria has not yet been prospectively determined in a group of patients who are ≥ 50 years of age presenting with new-onset bilateral shoulder pain and elevated acute-phase reactants (APR), i.e., fulfilling the prerequisite criteria. Therefore, in our multicenter prospective study we primarily aimed to assess the performance of the new 2012 provisional EULAR/ACR PMR clinical classification criteria in discriminating PMR from other mimicking conditions compared with the previous 5 diagnostic criteria sets.

MATERIALS AND METHODS

Study design, patients, and data collection. For our prospective multicenter study, patients ≥ 50 years of age presenting with new-onset (≤ 24 weeks) bilateral shoulder pain and erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) above the upper reference value were included from 18 rheumatology and physical medicine and rehabilitation clinics in Turkey. Patients were excluded if they had clinical features suggestive of giant cell arteritis at presentation with any diagnosis of mimicking inflammatory/noninflammatory diseases for more than 12 weeks before enrollment (except for fibromyalgia) and any glucocorticoid usage within 12 weeks of enrollment. After baseline eligibility evaluation, all patients were prospectively followed up for 52 weeks. Collected at baseline were clinical data involving the morning stiffness and its duration, shoulder and hip pain and ranges of motion, peripheral arthritis, constitutional symptoms, myalgia, 0–100 mm visual analog scale for pain, patient's and physician's global assessments, initial treatment modalities, ESR (mm/h), CRP (mg/l), creatine kinase, antinuclear antibody (ANA), rheumatoid factor (RF; positive if > 20 IU/ml), and anticyclic citrullinated peptide antibody (anti-CCP; positive if > 20 IU/ml) levels. Same clinical and laboratory data except for ANA, RF, and anti-CCP were also collected at the fourth, 12th, and 24th weeks of enrollment. At the 52nd week, all clinicians were requested to confirm the final diagnosis. At baseline or during followup, there was no standard evaluation protocol, and diagnostic investigations to exclude other mimicking conditions were performed according to the clinical decisions. The gold standard for diagnosis of PMR was the decision of an experienced clinician with the exclusion of other causes after a 1-year followup period. Patients with diagnosis other than PMR at the end of followup were designated as the control group. The control group mainly consisted of patients with RA who fulfilled the 2010 ACR/EULAR RA classification criteria[12]. The control group also included non-RA shoulder conditions and noninflammatory shoulder conditions, which were defined as patients with new-onset bilateral shoulder pain and diagnoses other than RA and any other inflammatory conditions, respectively.

All recruited patients were evaluated for fulfillment of each of the 6 different criteria for PMR (Chuang, *et al*[5], Bird, *et al*[4], Jones and Hazleman[7],

Nobunaga, *et al*[8], Healey[6], and the new 2012 EULAR/ACR classification criteria for PMR[11]).

At baseline evaluation, a subgroup of 48 patients from a single center (Marmara University, Rheumatology) underwent US examination of the shoulders and hips by an experienced sonographer (NI) using the MyLab70 US machine with multifrequency linear array transducers (6–12 MHz). The sonographer was blinded to clinical data and the physician evaluating clinical data/diagnosis was also blinded to the sonographic data.

Our study was approved by the local ethics committee for multicenter studies. Informed consent was obtained from all patients before study entry.

Statistical analysis. Statistical analysis was performed using the SPSS software version 16.0 (SPSS). Continuous variables were presented as mean ± SD unless otherwise indicated. The differences between the study and control groups were investigated using the chi-square and Student t test or nonparametric test (Wilcoxon's signed-rank test, Mann-Whitney U test), as applicable. Level of significance was chosen to be $p < 0.05$. Two-by-two classification tables were generated to estimate sensitivity and specificity at the proposed cutoff values for the diagnostic/classification criteria of PMR. To evaluate the capacity of the new and old PMR diagnostic/classification criteria sets to discriminate between patients with and without PMR, receiver-operating characteristic (ROC) curves with corresponding areas under the curve (AUC) were calculated. The AUC ranges from 0.5 to 1.0, with higher values indicating better accuracy. We performed sample size calculations to determine adequate power for ROC curve analysis. Using the preliminary data, a sample size of at least 125 patients in each group was estimated as necessary to achieve over 80% power to detect at least 80% difference in the AUC with the new 2012 EULAR/ACR PMR classification criteria using a 2-sided test at a significance level of 5%, assuming a prevalence of at least 0.5%[11,12].

RESULTS

Patient characteristics. The study cohort consisted of 275 patients (female/male = 212/63, mean age 64.9 ± 8.9 yrs) with new-onset (mean symptom duration 12.3 ± 7.6 weeks) bilateral shoulder pain. At baseline evaluation, 145 patients were diagnosed as PMR. Diagnosis was changed to non-PMR in 12 patients during the followup (5 patients at Week 4, 3 patients at Week 12, 2 patients at Week 24, and 2 patients at Week 52). The most common switch of diagnosis was from PMR to RA (n = 7). The remainder switches were Sjögren syndrome (n = 2), degenerative joint disease (n = 2), and spondyloarthritis (n = 1). Change of diagnosis also occurred in the non-PMR group (n = 17), but none were regarded as PMR. At the end of the 1-year followup, 133 patients (48.4%) were diagnosed with PMR and 142 (51.6%) were diagnosed as non-PMR. The non-PMR group consisted of 69 patients with RA and 73 non-RA shoulder conditions. In total, the non-RA group consisted of 16 other inflammatory and 51 noninflammatory shoulder conditions, 3 malignancies, and 3 infectious diseases. Baseline characteristics of patients who were diagnosed as PMR and non-PMR at the 52nd week are shown in Table 1.

Performances of the criteria sets for PMR. Discriminating capacity of the new 2012 EULAR/ACR clinical criteria for PMR between PMR and non-PMR conditions, as estimated by AUC, were moderate to good with an AUC of 0.736 (95% CI 0.676–0.796; Figure 1). The older criteria sets also had good discriminating capacities for PMR and RA (Table 2). The best discriminative capacity was for the Chuang criteria with an AUC of 0.842 (95% CI 0.792–0.892). Discriminative capacities of these criteria sets for PMR versus RA were also similar.

The sensitivity and specificity of each of the criteria sets for PMR are shown in Table 2. The 2012 EULAR/ACR clinical criteria for PMR had a sensitivity of 89.5% and a specificity of 57.7% when tested against all other non-PMR cases. Compared with this new classification criteria, only the Bird criteria had higher sensitivity (94%), with lower specificity (50%). However, the specificities of the other 4 criteria sets were significantly higher than the new 2012 EULAR/ACR clinical criteria, ranging from 83%–93%. The Jones criteria and the Chuang criteria had the highest specificities (93.7% and 88%, respectively).

When the new 2012 EULAR/ACR clinical criteria for PMR were tested against RA cases (n = 69), specificity increased to 66.7%. Similarly, the specificities of the Jones criteria, Chuang criteria, and Nobunaga criteria increased further. On the contrary, the specificities of the Bird criteria and Healey criteria decreased (Table 2). As a subgroup analysis, PMR versus seronegative (n = 29) and seropositive (n = 40) RA cases were also assessed. When PMR cases tested against seronegative patients with RA, the specificities of the previous 5 criteria sets were similar to PMR versus RA analysis (Chuang 82.8%, Bird 34.5%, Jones 96.6%, Nobunaga 89.7%, and Healey 75.9%). However, the specificity of the new 2012 EULAR/ACR clinical criteria for the differentiation of seronegative patients with RA from PMR decreased to 20.7%. The discriminative capacity of the new criteria between PMR and seronegative RA was also poor with an AUC of 0.551 (95% CI 0.430–0.672). The best criteria sets in discriminating PMR from seropositive RA (n = 40) were the new 2012 EULAR/ACR clinical PMR criteria and the Jones criteria (specificity for both 100% compared with Chuang 92.5%, Bird 40%, Nobunaga 92.5%, Healey 92.5%).

In discriminating PMR from non-RA shoulder conditions (n = 73) and noninflammatory shoulder conditions (n = 51), the specificity of the new 2012 EULAR/ACR clinical PMR criteria were 49.3% and 56.9%, respectively, whereas the specificities of the previous 5 criteria sets did not differ significantly.

Sensitivity and specificity of the new 2012 EULAR/ACR clinical PMR criteria were also analyzed in different age groups (50–64 yrs, ≥ 65 yrs) to determine whether age affected sensitivity or specificity of the new clinical PMR criteria. In the age group 50–64 years, the sensitivity of the new PMR criteria was 94.1%, specificity was 64.7%, and 70.7% in discriminating PMR from all non-PMR and patients with RA. In the age group ≥ 65 years, the sensitivity of the new PMR criteria was 86.6% whereas specificity was 47.3% and 60.7% in discriminating PMR from all non-PMR and patients with RA.

Last, we performed an analysis by separating patients into

Table 1. Baseline characteristics of patients who were diagnosed as PMR and non-PMR at the 52nd week. Values are mean ± SD or n (%) unless otherwise specified.

Characteristics	Patients with PMR, n = 133	Non-PMR Patients, n = 142	Patients with RA, n = 69	Noninflammatory Shoulder Conditions, n = 51	p, 1 vs 2	p, 1 vs 3	p, 1 vs 4
Demographic variables							
Age, yrs	66.9 ± 8.8	63.0 ± 8.7	63.6 ± 9.2	62.3 ± 7.6	< 0.001	0.015	0.001
Female	97 (72.9)	115 (81)	51 (73.9)	44 (86.3)	0.11	0.88	0.056
Symptom duration, weeks	11.1 ± 7.5	13.5 ± 7.5	15.2 ± 7.6	12.7 ± 7.5	0.008	< 0.001	0.19
Clinical characteristics							
Hip pain/limited ROM	98 (73.7)	67 (47.2)	27 (39.1)	25 (49)	< 0.001	< 0.001	0.001
Morning stiffness > 45 min	89 (66.9)	71 (50)	53 (76.8)	18 (35.3)	0.004	0.14	< 0.001
Peripheral arthritis	27 (20.3)	72 (50.7)	65 (94.2)	0 (0)	< 0.001	< 0.001	< 0.001
Myalgia	100 (75.2)	82 (57.2)	36 (52.2)	28 (54.9)	0.002	0.001	0.007
Moderate-severe myalgia	57 (42.8)	34 (23.9)	20 (28.9)	6 (11.8)	< 0.001	< 0.001	< 0.001
Constitutional symptoms	98 (73.7)	63 (44.4)	32 (46.4)	13 (25.5)	< 0.001	< 0.001	< 0.001
Pain VAS, 0–100 mm	85.6 ± 13.2	77.2 ± 19.3	83.0 ± 17.3	73.3 ± 17.4	0.002	0.24	< 0.001
PtGA, 0–100 mm	84.5 ± 12.9	77.1 ± 19.5	82.4 ± 17.3	67.4 ± 20.3	< 0.001	0.32	< 0.001
PGA, 0–100 mm	76.9 ± 13.2	68.5 ± 20.8	76.4 ± 15.9	56.7 ± 22.0	< 0.001	0.81	< 0.001
Laboratory variables							
ESR, mm/h, median (IQR)	76 (58.5–90.5)	42 (24–71.2)	55 (40–79)	25 (20–39)	< 0.001	< 0.001	< 0.001
CRP, mg/l, median (IQR)	19 (9.5–45.2)	9.6 (3.5–38.2)	15.8 (7.5–66)	3.8 (2.2–6.3)	< 0.001	0.92	< 0.001
RF positivity, > 20 IU/ml	4 (3)	41 (28.9)	37 (53.6)	2 (3.9)	< 0.001	< 0.001	< 0.001
Anti-CCP positivity, > 20 IU/ml	1 (0.8)	30 (21.1)	29 (42)	0 (0)	< 0.001	< 0.001	0.54
RF or anti-CCP positivity	4 (3)	44 (31)	40 (58)	2 (3.9)	< 0.001	< 0.001	0.76

PMR: polymyalgia rheumatica; RA: rheumatoid arthritis; ROM: range of motion; VAS: visual analog scale; PtGA: patient's global assessment; PGA: physician's global assessment; ESR: erythrocyte sedimentation rate; IQR: interquartile range; CRP: C-reactive protein; RF: rheumatoid factor; anti-CCP: anticyclic citrullinated peptide antibodies.

2 groups according to symptom duration: (1) ≤ 12 weeks, and (2) 13–24 weeks. The sensitivity and specificity of the new PMR criteria in discriminating PMR from non-PMR changed to 90.2% and 58.5% in the group with symptom duration ≤ 12 weeks and 87.1% and 56.7% in the group with symptom duration > 12 weeks, respectively.

Assessment of the new criteria with US evaluation. Bilateral shoulder and hip US were performed in a subgroup of 48 patients (23 PMR, 25 non-PMR patients; 13 patients with RA) from a single center. Two patients in the PMR group and 14 in the non-PMR group did not fulfill the optional US criteria of the new classification criteria set. Nine of the 13 US-evaluated patients with RA met the US criteria. With the use of the US criteria, the sensitivity of the 2012 EULAR/ACR criteria increased to 91.3%; on the other hand, the specificity was 52% for discriminating non-PMR conditions from PMR, 53.8% for discriminating RA from PMR, and 66.7% for discriminating non-RA shoulder conditions from PMR. US increased specificity of the new criteria especially in non-RA shoulder conditions (from 49.3% to 66.7%).

Assessment of the new criteria with different cutoff values for APR. Considering the poor performance of the new clinical criteria in differentiating PMR from noninflammatory conditions, we also tested the performance of the new criteria with adding an obligatory cutoff for APR. Because of the relatively higher ESR levels in elderly patients, as shown for patients in noninflammatory shoulder conditions (Table 3), we determined 4 different categories for APR: (1) ESR 2 times greater than the upper reference value, (2) CRP 2 times greater than the upper reference value, (3) both ESR and CRP 2 times greater than the upper reference value, and (4) either ESR or CRP 2 times greater than the upper reference value. Among these categories, the best performing cutoff was ESR 2 times greater than upper reference value in terms of sensitivity and specificity (Table 4). Adding a cutoff value for APR increased specificity of the new 2012 EULAR/ACR, particularly in discriminating PMR from non-RA and from noninflammatory control cases, with a decrease in sensitivity (Table 4).

DISCUSSION

Absence of a standardized classification criteria set for PMR limited PMR research compared with other inflammatory rheumatic diseases. To overcome this gap, provisional classification criteria have been developed by the EULAR/ACR in 2012[11]. However, the performance of this criteria set has not yet been adequately prospectively evaluated in patients older than 50 years presenting with new-onset bilateral shoulder pain and elevated APR.

In our present study, we evaluated the discriminative capacity of the new 2012 EULAR/ACR PMR clinical classification criteria compared with the older diagnostic criteria sets. We observed that the new classification criteria set had

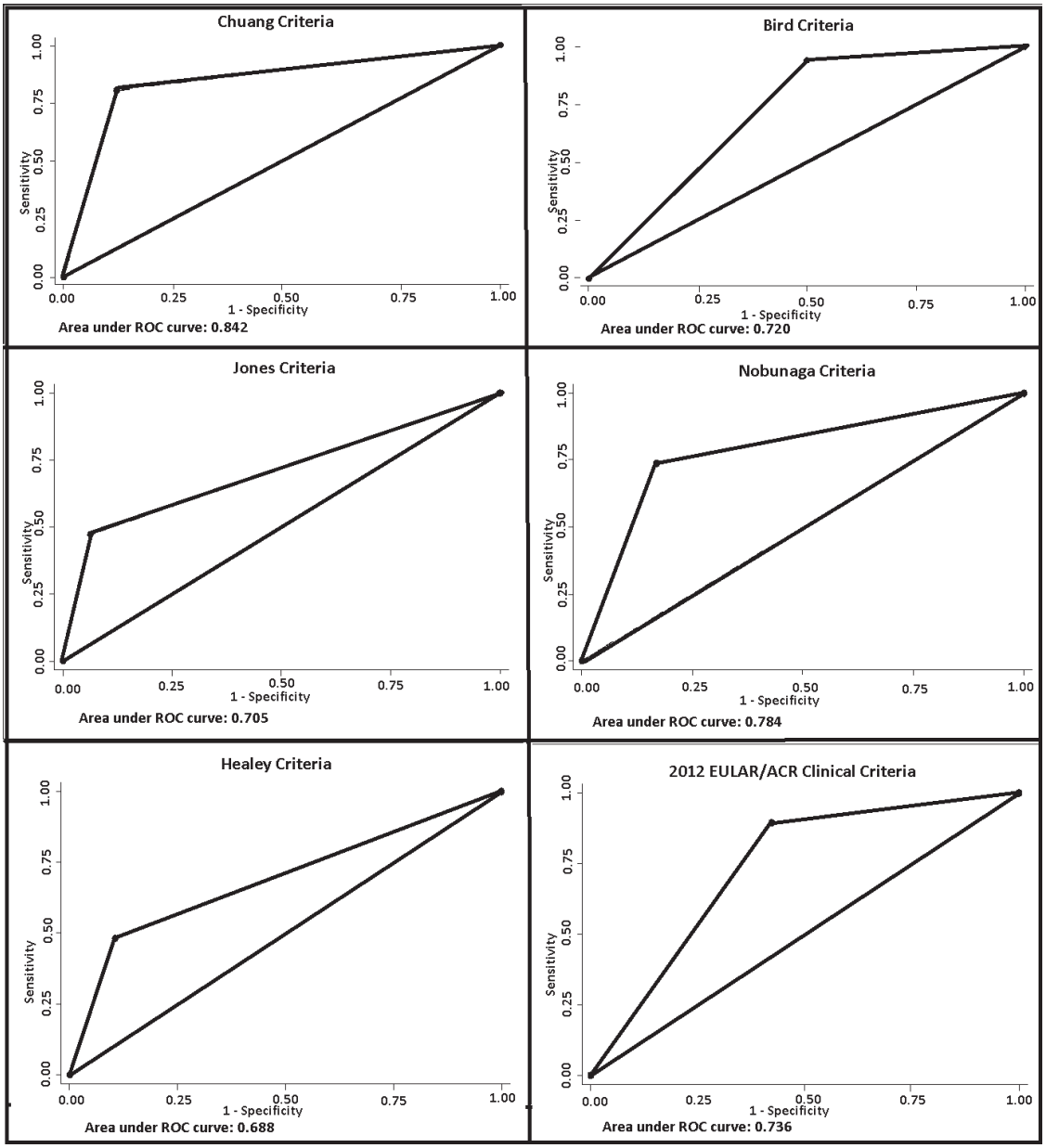

Figure 1. ROC curves of the different criteria sets for PMR. ROC: receiver-operating characteristic; PMR: polymyalgia rheumatica; EULAR: European League Against Rheumatism; ACR: American College of Rheumatology.

Table 2. Performance of each criteria set for PMR. Values are % unless otherwise specified.

Criteria	Sensitivity	Specificity	AUC (95% CI)	Specificity	AUC (95% CI)
	PMR vs Total Non-PMR Cases			PMR vs RA Cases	
Chuang, *et al*[5]	80.5	88	0.842 (0.792–0.892)	88.4	0.844 (0.785–0.903)
Bird, *et al*[4]	94	50	0.720 (0.659–0.781)	37.7	0.658 (0.574–0.743)
Jones, *et al*[7]	47.4	93.7	0.705 (0.642–0.768)	98.6	0.730 (0.662–0.797)
Nobunaga, *et al*[8]	73.7	83.1	0.784 (0.727–0.840)	91.3	0.825 (0.765–0.885)
Healey, *et al*[6]	48.1	89.4	0.688 (0.624–0.752)	85.5	0.668 (0.593–0.744)
2012 EULAR/ACR clinical criteria[11]	89.5	57.7	0.736 (0.676–0.796)	66.7	0.781 (0.707–0.854)

PMR: polymyalgia rheumatica; AUC: area under the curve; RA: rheumatoid arthritis; EULAR: European League Against Rheumatism; ACR: American College of Rheumatology.

Table 3. Elevations of acute-phase reactants in patients with noninflammatory shoulder conditions (n = 51)*. Values are n (%).

Variables	Fibromyalgia, n = 14	Osteoarthritis, n = 19	Rotator Cuff Lesions, n = 24	Adhesive Capsulitis, n = 2
ESR above the upper reference value	11 (78.6)	15 (78.9)	19 (79.2)	1 (50)
ESR 2 times greater than upper reference value	4 (28.6)	7 (36.8)	4 (16.7)	1 (50)
CRP above the upper reference value	8 (57.1)	8 (42.1)	12 (50)	1 (50)
CRP 2 times greater than upper reference value	2 (14.3)	2 (10.5)	3 (12.5)	0 (0)

* Because of the coexistence of noninflammatory shoulder conditions in some patients, sum of patient number in each group exceeds 51. ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

Table 4. Sensitivities and specificities of the 2012 EULAR/ACR clinical criteria for PMR with different cutoff values for acute-phase reactants. Values are %.

Criteria	Sensitivity PMR vs Total Non-PMR Cases	Specificity PMR vs Total Non-PMR Cases	Specificity PMR vs RA Cases	Specificity PMR vs Non-RA Control Cases	Specificity PMR vs Noninflammatory Control Cases
Original 2012 EULAR/ACR clinical criteria	89.5	57.7	66.7	49.3	56.9
2012 EULAR/ACR clinical criteria with ESR 2 times > upper reference value	82	71.8	69.6	74	84.3
2012 EULAR/ACR clinical criteria with CRP 2 times > upper reference value	69.2	75.4	73.9	76.7	90.2
2012 EULAR/ACR clinical criteria with both ESR AND CRP 2 times > upper reference value	66.2	78.2	73.9	82.2	96.1
2012 EULAR/ACR clinical criteria with either ESR OR CRP 2 times > upper reference value	88	67.6	69.6	65.8	76.5

EULAR: European League Against Rheumatism; ACR: American College of Rheumatology; PMR: polymyalgia rheumatica; RA: rheumatoid arthritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

a high sensitivity and specificity in discriminating PMR from seropositive patients with RA. However, its ability to discriminate PMR from seronegative RA and other inflammatory/noninflammatory shoulder conditions was not adequate.

The performance of the new 2012 EULAR/ACR PMR classification criteria has only been evaluated in 1 study thus far[10]. In that retrospective study, it was concluded that the 2012 EULAR/ACR criteria without US were the most sensitive criteria (92.6%) compared with the other 5 criteria sets. Specificity of the new criteria set was also comparable to other criteria sets and was 81.5% when tested against all other non-PMR patients and 79.7% when tested against patients with RA. The main possible reason for the discrepancy in the specificity of the new criteria between that study and ours was the difference in the selection of a control group. In contrast to our study, the control group of Macchioni, *et al* consisted of patients from an early arthritis cohort in which only about 30% of patients fulfilled the prerequisite features for the application of the new criteria set[10]. Additionally, a larger subset were seropositive patients with RA (94/149 patients were RA, 41.7% seronegative) in which the new criteria set performs best, whereas there were few patients (n = 14) with non-inflammatory shoulder conditions.

In our study, the specificity of the new criteria set was highest, 100%, in discriminating PMR from seropositive RA, whereas it was lowest in discriminating PMR from seronegative RA, followed by other shoulder conditions. High specificity of the anti-CCP antibodies for RA and their involvement in discriminating RA from PMR are well documented[13,14,15]. However, seropositivity for RF/anti-CCP is lower in elderly-onset RA than young-onset RA[16,17]. Therefore, for better differentiation of PMR from other shoulder conditions, especially seronegative cases, optional US criteria have been proposed for the EULAR/ACR criteria. In the original study, the use of bilateral shoulder and hip US increased specificity from 78% to 81%, 65% to 70%, and 88% to 89% in discriminating PMR from non-PMR, from RA, and from other non-RA shoulder conditions, respectively, with a slight decrease in sensitivity (68% to 66%)[11]. Similarly, Macchioni, *et al*'s retrospective study also revealed that US increased specificity (91.3% in PMR vs non-PMR and 89.9% in PMR vs RA)[10]. However, in our study, specificity of the new criteria decreased in differentiating PMR from all non-PMR and patients with RA with the use of US. On the other hand, US slightly increased specificity of the new criteria in discriminating PMR from non-RA shoulder conditions (from 49.3% to 66.7%). Data from US studies revealed that the majority of patients with PMR had some

degree of inflammation in the bursal, tenosynovial, and synovial tissue of the shoulder and/or hip region[18,19,20,21,22,23,24]. These periarticular or articular inflammatory changes are not specific to PMR. Although conflicting results have been reported about shoulder US findings of PMR versus patients with RA, those changes, especially glenohumeral synovitis and biceps tenosynovitis, may also be observed in patients with RA even in similar rates[19,20,23,24,25]. Our study, concordant with the previous US studies, indicate that US is more beneficial in differentiating PMR from other non-RA shoulder conditions than differentiation from RA[19,20]. The original study and Macchioni, *et al* reported that US increased the specificity of the criteria when tested against both total non-PMR and patients with RA. However, the change in specificity with US was not reported separately for PMR versus seronegative patients with RA or non-RA shoulder conditions. Therefore, future studies are required to determine the involvement of US in the differentiation of PMR from seronegative RA.

One of the main findings of our study was that the new criteria set was not better than the previously described PMR criteria sets in terms of specificity. All the previous and new diagnostic/classification criteria sets involve similar clinical or laboratory variables. However, the reason for higher specificities of the previous criteria sets, except for the Bird criteria, may be attributed to the involvement of a "cutoff" value for APR and exclusion of other diagnoses as a separate criterion. Further, the previous criteria sets require fulfillment of all criteria for diagnosis/classification of patients as PMR, unlike the new 2012 EULAR/ACR clinical criteria, which require only 4 points. However, this higher specificity of previous criteria sets with the fulfillment of all criteria seems to occur at the expense of sensitivity. In this regard, the new PMR classification criteria set offers an advantage without precluding the classification of patients with peripheral arthritis or less significant elevations in APR as PMR. On the other hand, with the new clinical criteria set, an elderly patient with degenerative joint disease can easily be classified as PMR when they present with new-onset bilateral shoulder and hip pain with slightly elevated ESR, such as 25 mm/h, without morning stiffness, peripheral arthritis, or seropositivity for RF or anti-CCP.

Because one of the main reasons for inadequate differentiation of PMR from noninflammatory shoulder conditions was the degree of APR elevation, we tested the new criteria set with additional obligatory cutoff values for APR, selecting ≥ 2 times upper reference values of ESR or CRP or both. This modification, with the best performing cutoff ESR ≥ 2 times upper reference value, increased specificity of the new criteria set with a slight decrease in sensitivity, especially in discriminating PMR from noninflammatory shoulder conditions. However, it has been reported that about 20% patients with PMR might not have elevated ESR or CRP[26,27,28]. Accordingly, instead of using elevated APR as a prerequisite criterion, it may be a useful approach to put a nonobligatory, scored criterion for the APR with a cutoff, such as ESR ≥ 1 or ≥ 2 times the upper reference value into the new criteria set.

Peripheral arthritis is another challenging feature of PMR that has been described in up to 38% of patients with PMR at the initial presentation[29,30,31,32]. Although several differences between RA and PMR joint involvement have been demonstrated such as the type of joint involvement, severity, and inflamed tissues[20,31,32,33], in the presence of peripheral arthritis, particularly in both hands, differentiation from RA is difficult. Therefore, instead of scoring the absence of peripheral arthritis as "1," addition of a category such as "peripheral joint involvement" that ranges from none to involvement of different joint types and joint counts (with plus and minus scores) may also be helpful. Further studies may reveal whether evaluation of peripheral arthritis in detail can overcome the low specificity of the new criteria set in differentiation of PMR from RA.

Several strengths and weaknesses of our study should be considered. To our knowledge, this is the first prospective study evaluating the performance of the new 2012 EULAR/ACR PMR classification criteria in patients fulfilling the original prerequisite features for the application of the new criteria. However, because this was a multicenter study with a lack of US facilities and expertise in all centers, determination of the effect of US criteria on the sensitivity and specificity in the entire cohort was hampered. Additionally, there was no predetermined standard glucocorticoid dose in the study protocol. For the assessment of "good response to glucocorticoids" included in previous criteria, only the physicians' decisions were taken into account. Nevertheless, the data about glucocorticoid response were not included in the analysis. The response to glucocorticoids was also not included in the new criteria set because it did not improve the performance of the criteria. Moreover, good response to glucocorticoids is not unique to PMR. RA, other inflammatory rheumatic diseases, and even some malignancies may respond to glucocorticoids. Lastly, the duration for the new-onset shoulder pain was determined as 24 weeks in contrast to 12 weeks in the original study. Considering the period of reaching a rheumatologist after symptom onset, the symptom duration was extended to 24 weeks. The analysis to assess the effect of this symptom duration extension showed no significant changes in sensitivity and specificity of the new PMR criteria.

Our results suggest that the new 2012 EULAR/ACR clinical classification criteria for PMR can classify patients with PMR with a high sensitivity; however, its ability to discriminate PMR from other inflammatory/noninflammatory conditions with shoulder pain, especially from seronegative RA, is not adequate. The new classification criteria set is also slightly more sensitive but less specific than the older criteria sets. For better discrimination, besides using imaging such as US, additional approaches such as a cutoff value for APR might be investigated in further studies.

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