Diagnostic evaluation of classification criteria for rheumatoid arthritis and reactive arthritis in an early synovitis outpatient clinic

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Abstract

Objective—To evaluate the diagnostic performance of classification criteria for rheumatoid arthritis (RA) and reactive arthritis (ReA) in an early synovitis outpatient clinic.

Methods—In a prospective two year survey consecutive patients with early synovitis of less than one year duration were documented using a standardised registry and were classified after an expert diagnosis. Of a total of 320 patients 39 (19%) were diagnosed as having RA, 24 (11%) patients had ReA, 117 (54%) patients did not have an unequivocal diagnosis, and were considered as undifferentiated arthritis.

Results—The retrospective application of the revised 1987 ACR criteria for the classification of RA in this data set revealed a sensitivity of 90% and a specificity of 90%. The positive predictive value was 0.67, the negative predictive value 0.98. Similarly, the criteria for ReA of the French Society of Rheumatology (FSR) showed a sensitivity of 80% and a specificity of 90% with a positive predictive value of 0.55 and a negative predictive value of 0.97. Both criteria sets had a satisfying likelihood ratio of 9 and 10, respectively.

Conclusion—Both the 1987 ACR criteria for RA and the criteria of the FSR for ReA have a reasonable diagnostic validity in patients with early synovitis, including a large portion of undifferentiated arthritis. (Ann Rheum Dis 1999;58:278–280)

In past decades rheumatologists have made efforts to standardise the classification and the nomenclature of rheumatic diseases. One of these efforts is the creation of classification criteria. In 1958 the American Rheumatism Association (ARA) had proposed diagnostic criteria for rheumatoid arthritis (RA).¹ In 1987 the American College of Rheumatology (ACR) published a revised set of seven classification criteria.² The term “diagnostic” criteria was replaced by “classification”. Since the introduction of the revised criteria, several studies^{3–5} have evaluated them, a few only in samples of patients with early disease.^{6,7} No study has investigated a cohort of patients including a sufficient number of unclassified arthritis, reflecting the normal clinical situation in early diagnosis of arthritis. The incidence of both reactive arthritis (ReA) and undifferentiated arthritis (UA) in adults below the age of 60 is at least of the same magnitude as RA.^{8,9} Further-

more, UA and other arthritides were seen more frequently than RA in early arthritis clinics.^{8,10} In addition it is crucial to differentiate RA as early as possible from the often benign and self limited forms of UA, as there is a need for early treatment of RA.¹¹

In this analysis our objective was to evaluate the diagnostic performance of the 1987 ACR classification criteria for RA and the criteria of the French Society of Rheumatology (FSR) for ReA¹² in a consecutive sample of patients with early arthritis as published previously.¹⁰

Methods

As published elsewhere in more detail¹⁰ 320 patients older than 15 years with a duration of rheumatic symptoms of less than one year were prospectively examined. All patients were referred to the early arthritis outpatient clinic in the tertiary university referral centre by general practitioners and rheumatologists who were specifically informed about this institution. Patients had a standardised interview and rheumatological examination. Besides routine blood and serum parameters, immunological investigations (CRP, IgG, IgA, IgM, C3, C4, RF, ANA, DNA, HLA B-27) and a microbiological programme was done to search for infectious agents, such as *Chlamydia trachomatis*, *Yersinia enterocolitica* and *pseudotuberculosis*, *Borrelia burgdorferi*, and *Campylobacter jejuni*. Virological studies were done including hepatitis A and B. Patients had chest radiography and hand and feet radiography if joints of these areas were involved.

Diagnoses were expert diagnoses made by one of us (HZ) and were not based on classification criteria. The classic format of the 1987 ACR criteria² for RA as well as the FSR criteria for ReA¹² were applied retrospectively to all patients, regardless of the primary diagnosis. For diagnosis of ReA three criteria were required instead of four criteria as proposed by Amor, as this increased sensitivity.¹³ Sensitivity,

Table 1 Frequency of expert diagnoses of early inflammatory rheumatic diseases

Diagnosis	Number	%
Undifferentiated arthritis	117	54
Rheumatoid arthritis	39	19
Reactive arthritis	24	11
Polymyalgia rheumatica	11	5
Ankylosing spondylitis	10	5
Psoriatic arthritis	7	3
Sarcoidosis	3	1
Sacroiliitis with peripheral arthritis	3	1
Systemic lupus erythematosus	3	1
Total	217	100

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Table 2 Number of patients (percentages) fulfilling the 1958 and the 1987 revised ACR criteria for rheumatoid arthritis and the FSR criteria for the diagnosis of reactive arthritis in the different diagnostic categories

Criteria sets	Expert diagnoses			Other diagnoses (n=37)
	UA (n=117)	RA (n=39)	ReA (n=24)	
1958 ARA criteria (≥ 5 positive)	23 (20)	39 (100)	4 (17)	3 (8)
1987 ACR criteria (≥ 4 positive)	15 (13)	35 (90)	0 (0)	2 (5)
FSR criteria (≥ 3 positive)	14 (12)	0 (0)	19 (79)	1 (3)

specificity, positive and negative predictive value, and positive and negative likelihood ratios were determined.

Results

During the study period of two years a total of 320 patients were referred of whom 217 had inflammatory rheumatic disease. Of these 217 patients, 117 (54%) were considered as having undifferentiated arthritis (UA), whereas 39 patients (19%) had RA, and 24 patients (11%) had ReA (table 1).

Application of the 1985 and retrospective application of the 1987 revised ACR criteria for RA to all patients with inflammatory rheumatic diseases shows, that the 1958 criteria have a higher sensitivity of 100% compared with 90% sensitivity of the 1987 revised criteria. In UA 20% of the patients fulfilled five or more of the 1958 criteria, in ReA 17%, and in the other diagnostic categories 8%. Patients with UA were only positive in 13% for four or more 1987 criteria, none were positive in the group with ReA, but 5% of the patients with other inflammatory rheumatic diseases. Thus, the specificity of the 1987 revised ACR criteria for RA reached 90% in this cohort of patients with early synovitis compared with a specificity of 83% of the 1958 criteria (table 2). The positive predictive value for the 1958 criteria is 0.57, the negative predictive value 1.0.

Similarly, with the application of the FSR criteria for ReA to the total cohort of patients with early synovitis, the sensitivity was 80%. Fourteen patients (12%) with UA and one patient (3%) with other inflammatory rheumatic diseases fulfilled three and more criteria for the diagnosis of ReA (table 2). Thus, specificity of three and more of the diagnostic criteria for ReA reaches 92% with a positive predictive value of 0.55, a negative predictive value of 0.97.

Discussion

The 1987 revised ACR criteria for the classification of RA had a good performance in the cohort in which they were initially tested.² They have been compared with the 1958 criteria in several cohort studies.⁴⁻⁶ Arnett *et al*² reported a sensitivity of 91%–94% and a specificity of 89% in patients with established, mostly advanced diseases. In the medical literature sensitivity and specificity have been reported varying between 66% and 95% for sensitivity and 74%–98% for specificity.^{3 5-7}

In this study the application of the 1987 revised ACR criteria for classification of RA revealed for both sensitivity and specificity a value of 90%. Thus, the criteria had a great

accuracy identifying patients with RA in this cohort of patients with early arthritis in contrast with most other reports.^{3 4 6 7} The subanalysis of the ACR subcommittee on patients with disease duration of less than one year showed an estimated sensitivity of only 81%, which was lower than the 91% obtained for the total of patients. The difference in sensitivities may be the result of different patient groups and may be influenced by the fact, that many patients, previously diagnosed as RA, were classified as UA in our cohort.

Finally, these results are substantiated by following up a limited number (24%) of patients with UA over a medium period of 26 (4–38) months as reported earlier.¹⁰ Only a few patients with active disease developed definite seronegative RA (7%) or AS (4%) during the follow up.

The negative predictive value of 0.98 for four or more fulfilled criteria is high. This means, that a high accuracy exists to exclude RA in this cohort, if less than four of the ACR criteria are positive. The positive predictive value of 0.67 means, that only about 7 of 10 patients with four or more ACR criteria can be diagnosed correctly as having RA. The positive predictive value for five or more of the 1958 criteria is higher with 0.77, while the negative predictive value is similar.

Clinically silent infections are increasingly recognised as a cause of seronegative arthritis.¹⁶ Diagnostic criteria for ReA have been proposed by the FSR¹² but have not been evaluated in cohorts with different inflammatory rheumatic diseases. We have retrospectively applied the criteria for ReA to our cohort of patients and found a sensitivity of 80% and a specificity of 92% for three and more criteria. The positive predictive value with 0.55 is rather low, while the negative predictive value of 0.97 is high. Thus, the criteria for ReA show a limited performance in patients with early synovitis. As only serology and culture techniques were used in this study, frequency of ReA could be higher using modern techniques, such as polymerase chain reaction in synovial fluid and in synovial tissue. In future, more sensitive diagnostic criteria including intra-articular identification of bacteria should be developed to advance the definite diagnosis of ReA. Meanwhile, many of the seronegative oligoarthritis with possible infectious aetiology can only be classified as UA.^{17 18}

In conclusion, in view of the good performance and the high accuracy found in this study, the 1987 ACR criteria are useful for the diagnosis of RA in an early arthritis outpatient clinic, where patients with undefined arthritis are frequently seen.^{8 10} It is important to be able to diagnose and treat RA very early and to differentiate RA from benign, often self limiting forms of UA to avoid overtreatment of these latter patients.^{11 19} ReA represents a third group of patients with increasing relevance to early differential diagnosis in clinical practice. Although the FSR criteria for ReA may miss patients with asymptomatic triggering infections, their future use in patients with early synovitis can be a first step towards a

criteria based diagnosis of this important group of patients, otherwise classified mainly according to unstandardised tests and local definitions.

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