

2016 ACR/EULAR Revised Criteria for too Early Diagnosis of Rheumatoid Arthritis

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Abstract

Rheumatoid Arthritis (RA) as a chronic progressive systemic autoimmune disease with hallmark of chronic erosive polyarthritis is the most common inflammatory articular disorder. Its overall prevalence is 1% and it is more common in middle to old aged women. Arthritis of peripheral synovial joints can be seen in almost all patients with RA. Chronic symmetric oligo/polyarthritis with especially small joints involvement of hand along with prolonged morning stiffness is the predominant feature of RA.

Extra-articular manifestations of RA usually can not be seen within initial presentation of it. High titer RF or Anti-CCP and both RF and Anti-CCP positivity are serologic hallmarks of disease.

Erosion is imaging hallmark of RA that can be detected in MRI much earlier than in plain X-Ray of involved joint. Positive family history of RA and HLA-DR4 positivity are associated with higher risk of future RA. Smoking is the most important environmental factor for development of RA. The 1987 ACR criteria and the 2010 ACR/EULAR criteria for RA ;both are designed for classification of RA but the Iran criteria for RA (2011) can be used for early diagnosis of RA with clinical synovitis during the acute to early chronic phase of disease. The corresponding-author of this letter wants to deliver a new criteria called "2016 ACR/EULAR revised criteria for too early diagnosis of RA" in the first week of initiation of RA especially subclinical cases.

Keywords: ACR Criteria; ACR/EULAR Criteria; IRAN Criteria; Criteria

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Letter to Editor

Rheumatoid Arthritis (RA) is the most common inflammatory articular disorder. It is a chronic progressive systemic autoimmune disease with hallmark of chronic erosive-polyarthritis. It can be seen in all races with overall prevalence of about 1 percent [1]. Its prevalence in old women is about 5 percent and female to male ratio is 3 to 1 in this disorder with the peak onset age of 50 ± 15 years [2].

The clinical feature of RA is divided to three categories:

- Articular
- Peri-articular
- Extra-articular (systemic)

Articular involvement can be seen in almost all patients with RA as arthritis of peripheral synovial joints.

Oligoarthritis may be common in initiation of disease but polyarthritis will be the final common picture of RA.

Monoarthritis is rare and there is not any axial involvement in this disease except cervical spine. The clinical articular hallmarks of RA are including [3]:

- Chronic symmetric polyarthritis
- Small > Small+Large > Large joints involvement
- Hand (wrist, MCP, PIP) joints are key joints involvement
- Morning stiffness ≥ 1 hour
- Uncommon to rare involvement of DIP joints
- Deformities in advanced (very late) phase

The different kinds of peri-arthritis can be seen in RA including deQuervain tenosynovitis, trigger finger, carpal tunnel syndrome, many bursitis and other tendinitis, and so on [4].

Sometimes during initial presentation of RA these peri-articular manifestations are predominant features of disease when the synovitis is subclinical.

The extra articular manifestations of RA are including [5]:

Rheumatoid nodule, Epi/Scleritis, Interstitial Lung Disease (ILD), pleurisy, Anemia of Chronic Disease (AOCD), coronary heart disease, Myocarditis/pericarditis, Myopathy and Myositis, Vasculitis (LCV, PAN), atherosclerosis, mononeuritis multiplex, Leg ulcer, nail fold infarcts, and finally Sjogren's syndrome, Renal amyloidosis, felty's syndrome and cervical myelopathy due to C1-C2 subluxations.

We know that Rheumatoid Factor (RF) has been the famous autoantibody in RA for many years. It can be seen in many other rheumatologic and non-rheumatologic diseases and even in normal population. Nowadays Anti-cyclic citrullinated peptide (Anti-CCP or ACPA) is the most specific autoantibody in RA with specificity of more than 95%. High titer RF or Anti-CCP and both RF and Anti-CCP positivity are serologic hallmarks of RA. It is well documented in the literature that the serum-levels of RF and Anti-CCP increase years prior to establishment of RA diagnosis. Also simultaneous presence of RF and Anti-CCP in the serum of an individual was highly specific for development of future RA [6]. Negative RF or Anti-CCP can be seen in 20% to 30% of cases with RA and both RF and Anti-CCP negativity can be seen up to 50% of cases in initial presentation and up to 20% in the course of RA [7].

Early X-Ray finding in involved joints is Juxta-articular osteoporosis but erosion in the X-Ray or MRI of joints is imaging hallmark of RA [8].

Sometimes articular synovitis is subclinical. In otherwords, physician can not clinically detect synovial swelling by just physical examination. In these cases musculoskeletal MRI or ultrasound can help us detect synovitis.

Considering the genetic background, it is estimated that the genetic contribution to RA ranges between 30% and 60%. The presence of HLA-DR4 allele in Caucasians is associated with a relative risk of almost 4 for RA [9]. It is shown that a positive family history of RA is associated with higher risk of future RA.

Smoking, as the most important environmental factor for RA, is associated with the risk of developing RA with an odds of 3 times for future RA in smokers compared to non-smokers [10].

We know that in initial presentation; RA can be seen as acute oligo/polyarthritis in about 95% of the cases, and extra-musculoskeletal manifestations including Rheumatoid nodule almost can never be seen in the initiation phase of disease. Sometimes synovitis is subclinical, therefore oligo/polyarthritis will be missed and RA will be presented as peri-arthritis or rarely

extra-musculoskeletal manifestations. Rarely RA presents as still's disease, palindromic Rheumatism or acute monoarthritis.

If the RA cases are not treated by compatible DMARDs therapy adjusted to the patient, they progress toward chronic symmetric erosive polyarthritis with hand involvement and prolonged morning stiffness, except some cases.

So, if we want to make an early diagnosis for RA in the acute phase of disease, we have to rule out other disorders presented as acute oligo/polyarthritis upon history and physical examination. These disorders are including; viral polyarthritis, Reactive arthritis, Systemic Lupus Erythematosus (SLE), Sarcoidosis, Psoriatic arthritis, Enteropathic (IBD) arthritis, Lyme arthritis, Brucellosis and etc.

The same as other disorders, the gold standard for diagnosis of RA is clinical/paraclinical judgement of an expert rheumatologist.

As you know there are some criteria for RA, here we mention three criteria among them including:

- The 1987 ACR classification criteria for RA [11].
- The 2010 ACR/EULAR classification criteria for RA [12].
- The Iran criteria for early diagnosis of RA (2011) [13].

It needs to be mentioned that the 1987 ACR criteria and the 2010 ACR/EULAR criteria both are designed for classification of RA and their sensitivity is not enough for early diagnosis. They can usually classify cases with RA during the chronic phase of disease especially after 6 months of initiation.

Iran criteria has been created for early diagnosis of clinical RA during the acute to early chronic phase of disease and its sensitivity is near to 100% [13].

But the corresponding author of this letter as the creator of "Iran criteria for early diagnosis of RA" wants to deliver a new criteria for too early diagnosis of RA in the first week of the initiation of disease and even early diagnosis of subclinical cases of RA.

This criteria is called "2016 ACR/EULAR revised criteria for too early diagnosis of RA" that is delivered by this letter and it is showed in table A.

And right now I'd like to ask you that; what is your idea about the case mentioned below?

A 65 year old smoker woman with polyarthritis of both wrists, right MCP2, both elbows, both knees and both ankles is admitted for the diagnosis to be established and beginning of the

treatment. Her initial presentation has been pain and swelling of both wrists that started 3 months ago. After that the arthritis of both wrists has been progressed towards above mentioned polyarthritis with adding pattern.

Her lab data are including: Hb: 11gr/dl, ESR: 35mm/hr, RF: Negative, Anti-CCP: positive; 12 (up to 5) HLA –DR4: positive

Hand X-Ray: Normal

Hand MRI: Synovial thickening along with multiple erosions within both wrists.

It has to be mentioned that; there are not any other clinical and paraclinical findings regarding this case.

I think, upon clinical/paraclinical judgement of all of the Rheumatologists in the world; this case is a typical/classic case of RA. But by using the ACR and ACR/EULAR criteria it can not be

classified as RA yet. In the first day of disease it could be diagnosed as RA by using ACR/EULAR revised criteria and 6 weeks after the initiation of disease, it could be diagnosed by using Iran criteria. Many cases have been visited by me with the diagnosis of RA upon clinical/paraclinical judgement that, they could not be classified as RA by using ACR and /or ACR/EULAR criteria but all of them could be diagnosed as RA by using Iran criteria during the acute phase of disease (first 6 weeks) and by using 2016 ACR/EULAR revised criteria in the first week of disease.

Finally I would like to ask ACR, EULAR, APLAR and all of the rheumatologists in the world to evaluate this new criteria for too early diagnosis of RA.

I would like to inform you that I cannot evaluate it due to financial restriction, the absence of proper research equipments and media

Table A. 2016 ACR/EULAR revised criteria for too early diagnosis of Rheumatoid Arthritis ^{a, b, c, d}

Domain I (Joints)	
• Joint pain with morning stiffness $\geq$ 1 hour	1.point
• Hand (wrist, MCP, PIP) synovitis ^e	2.points
• Synovitis ^e of $\geq$ 2 joints	1.point
• Symmetric synovitis ^e	1.point
• Duration of $\geq$ 6 weeks for synovitis	2.points
Domain II	
• Old female	1.point
• Positive history of RA in first-degree family ^f	1.point
• Positive history of smoking ^{f,g}	1.point
• RF/Anti-CCP positivity ^f	Up to 2.points
➤ Positive RF or Anti-CCP	1.point
➤ Positive RF and Anti-CCP	2.points
➤ High titer RF and/or Anti-CCP	2.points
• HLA-DR4 positivity ^f	1.point
• Involved joint imaging :	Up to 2.points
➤ Juxta-articular osteoporosis in X ray	1.point
➤ Erosion In X-ray or MRI	2.points

- Entry criteria ; No other prominent diagnosis is proposed according to the patient's history and physical examination .
- All peripheral joints are included
- ACR 66/68 counts for swollen and tender joints is applied (14).
- In the presence of 6 points or more out of 15 with at least 2 points belonging to domain I (joints) along with entry criteria the diagnosis of RA can be established.
- In the presence of pain along with morning stiffness of $\geq$ 1 hour in a joint if there is not any clinical synovitis in that, we can apply ultrasonography or MRI for detection of subclinical synovitis.
- They have been used in scoring system for pre-RA state too (15).
- Past history of heavy smoking or current smoking.

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