Current diagnosis and treatment strategies in rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease that preferentially targets the synovial lining of the joints but can affect other organ systems including the lungs, heart and blood vessels.

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RA affects an estimated 0.5 - 1% of the general population and twice as many women as men. The usual age of onset is between the third and fifth decade of life.

Patients with inflammatory arthritis should be seen early and treated at the earliest opportunity.

RA is the most common and most serious inflammatory arthritis that, if left untreated, will lead to irreversible joint damage, functional impairment and increased mortality. The outcome of the disease has improved considerably in recent years with the availability of effective therapies and the recognition that early intensive treatment strategies result in better outcomes.

Patients with inflammatory arthritis should be seen early and treated at the earliest opportunity. The initial aim should be to differentiate features of early RA from other diseases with similar presentations, such as psoriatic arthritis (PsA) or systemic lupus erythematosus (SLE) and from those that will remit spontaneously.

Patients with RA requiring therapy should be treated with the aim to induce remission to prevent joint damage, disability and long-term complications of the disease.[1] This article outlines the current diagnostic and therapeutic strategies in RA.

What is early RA?

There is no clear definition, but some authors refer to early RA as a disease with duration of 1 year or less, others up to 2 years.[2]

Why treat early?

The evidence is that 70% of patients with recent-onset RA develop bony erosions within the first 3 years and 25% develop erosions within 3 months of disease onset.[1] Therefore, early rather than delayed start of treatment results in less radiological damage and improves long-term functional outcome and mortality.[1]

Window of opportunity

There appears to exist a window of opportunity where the disease process can be effectively suppressed or reversed, resulting in prevention of damage progression and even a return to an asymptomatic state. This window may be an immunopathologically distinct phase compared with later disease, and may last as little as 12 weeks from initial presentation.[3] The American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) task force has developed new classification criteria to focus on features at earlier stages of disease that are associated with persistent and/or erosive disease,[4] rather than defining the disease by its late-stage features, as was the case with the 1987 ACR classification criteria for RA.[4] The new classification criteria are outlined in Table I.

Table I. The 2010 American College of Rheumatology/ European League Against Rheumatism classification criteria for rheumatoid arthritis[4]

Target population (who should be tested?)
Patients who have at least one joint with definite clinical synovitis (swelling) and those in whom the synovitis is not better explained by another disease

Classification criteria for RA
This is a score-based algorithm: add score of categories A-D: a score of ≥6/10 is needed to classify a patient as having definite RA

A. Joint involvement	Score
1 large joint	0
2 - 10 large joints	1
1 - 3 small joints (with or without involvement of large joints)	2
4 - 10 small joints (with or without involvement of large joints)	3
>10 joints (at least 1 small joint)	5
B. Serology (at least 1 test result is needed for classification)	
Negative RF and negative ACPA	0
Low-positive RF or low positive ACPA	2
High-positive RF or high-positive ACPA	3
C. Acute-phase reactants (at least 1 test result is needed for classification)	
Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1
D. Duration of symptoms	
< 6 weeks	0
≥ 6 weeks	1

Approach to early arthritis

Recognise features of inflammatory arthritis:

- early-morning stiffness >30 minutes
- pain worse at rest, relieved by activity
- swelling of joints.

It is important to first establish that the patient has arthritis. Pain in the joint does not equate to arthritis, as other structures like tendons and muscles may be the cause of pain (intra-articular v. extra-articular v. referred).

Sometimes it is a challenge to establish whether a patient has arthritis or not, especially where synovitis is not so obvious. A squeeze on the metarcarpophalangeal or metartarsal joints, if positive, may indicate subclinical synovitis.[1]

The pattern of joint involvement is important as this may give clues to other diagnoses:
- peripheral v. axial
- symmetrical v. asymmetrical
- small v. large joints.

Exclude other inflammatory arthritides (e.g. SLE, PsA, gout, infection).

Diagnosing RA

RA is largely a clinical diagnosis. Once synovitis is suspected or confirmed, one would proceed to do further tests to support the diagnosis of RA.

Laboratory tests

- Rheumatoid factor (RF) – important for diagnosis and prognosis.
- Anti-cyclic citrulinated peptide (ACCP) – can precede onset of symptoms by up to 10 years, particularly in the 2 years prior to development of symptoms. It is highly sensitive and specific and is a marker of disease as well as prognosis.[5]

Imaging

- X-rays (of the hands and feet) are the main imaging modality. In early disease they may be normal but osteopenia and soft-tissue swelling may be seen early before erosions.
- Ultrasound and/or MRI detect synovitis early on and demonstrate damage within weeks.[1] They are useful if the diagnosis is doubtful.

The predictors of disease persistence are listed in Table II.

Treatment

Non-pharmacological (lifestyle)

- Cessation of smoking
- Maintenance of physical activity
- Healthy diet
- Maintenance of appropriate body weight.

Recommended interventions

- Dynamic exercises
- Occupational therapy
- Hydrotherapy
- Patient education.

Pharmacological treatment

Symptom-modifying anti-rheumatic drugs (SMARDs)

- Simple analgesics
- NSAIDs (classic and COX-2, more effective than analgesics in active disease).

The evidence is that 70% of patients with recent-onset RA develop bony erosions within the first 3 years and 25% of develop erosions within 3 months of disease onset.

Glucocorticoids

In very early inflammatory arthritis steroids may be given as a single dose, either intramuscularly or intra-articularly to induce remission. Low-dose prednisone can be used to relieve short-term symptoms and signs of disease.

Disease-modifying anti-rheumatic drugs (DMARDs)

- Synthetic DMARDs – there is strong evidence that early treatment with synthetic DMARDs retards radiographic progression, and therefore DMARD therapy should not be delayed. In patients with early inflammatory arthritis before the stage of fulfilling ACR criteria for RA, treating with DMARDs (MTX) reduces progression of radiographic damage.
- Methotrexate (anchor drug)
- Salazopyrine
- Chloroquine is a weaker DMARD
- Leflunomide – similar efficacy to MTX and therefore best alternative.

Biological DMARD therapy

Biological DMARDs provide rapid control of inflammation and have proven efficacy both in terms of clinical outcomes and structural damage in early disease.[6] However, they are more expensive than traditional DMARDs, and this limits their use in early disease. They may also predispose to reactivation of TB and cause deep fungal infections.

Tumour necrosis factor inhibitors

- Infliximab – chimeric monoclonal antibody
- Etanercept – soluble fusion protein to TNF
- Adalimumab – fully human monoclonal antibody

IL-6 inhibitor

IL6 receptor blocker (tociluzimab)

B-cell depletion

B-cell therapy (rituximab)

Co-stimulation modulator

T-cell co-stimulation modulation (abatacept).

Monitor disease activity

The objective of treatment is to achieve a state of low disease activity (LDA), and ideally remission, to prevent structural damage and long-term disability. This can be achieved by regularly monitoring disease activity at 1-3-month intervals as long as remission is not achieved, using different indices of disease activity, e.g. DAS 28.[1]

The predictors of disease severity in RA are listed in Table III.

Table II. Predictors of disease persistence in early RA[1]

- Female gender
- Duration of symptoms (more than 12 weeks)
- High tender and swollen joint count
- Hand involvement
- Cigarette smoking
- Acute phase response
- Rheumatoid factor
- Anti-CCP antibodies
- Erosions on X-ray
- Fulfilment of 1987 ACR criteria for RA (sensitivity 88%; specificity 73%)

Table III. Predictors of disease severity in RA[1]

- Female gender
- High tender and swollen joint count
- HAQ score
- Acute phase reactants
- Rheumatoid factor
- Anti-CCP antibodies
- Shared epitope
- Erosive disease

References available at www.cmej.org.za

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- It is important to recognise early features of inflammatory arthritis.
- Patients with inflammatory arthritis should be reviewed by rheumatologists for further evaluation.
- Early treatment in RA can prevent or delay joint damage, functional impairment and mortality.
- RA is largely a clinical diagnosis and sometimes quite challenging but laboratoy and radiological tests can be useful.
- The new classification criteria focus on features at earlier stages of disease and are therefore useful in capturing patients with very early arthritis.
- Treatment is both pharmacological and non-pharmacological.
- Remission should be the target in RA treatment but low disease activity can be acceptable in some circumstances.
- Patients should be educated about their disease.