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Rheumatoid arthritis without deformities: fiction or reality?

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ABSTRACT

Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis, characterised by persistent synovial inflammation, progressive joint damage, and a wide range of extra-articular manifestations. Historically, RA was associated with significant disability and deformities. However, over the past two to three decades, advances in early diagnosis and the introduction of disease-modifying antirheumatic drugs (DMARDs) have transformed disease outcomes. Early recognition of inflammatory arthritis, prompt initiation of DMARD therapy within the "window of opportunity," and adoption of a treat-to-target strategy have enabled many patients to achieve sustained remission or low disease activity, thereby preventing irreversible joint damage. Consequently, the classical deforming phenotype of RA is now less frequently encountered in clinical practice.

Methotrexate remains the cornerstone of therapy, with escalation to combination conventional DMARDs, biologic agents, or targeted synthetic therapies in patients with inadequate response. Furthermore, RA is a systemic disease with significant extra-articular involvement and an increased burden of comorbidities, such as cardiovascular diseases, infections and osteoporosis. Therefore, comprehensive management requires not only control of inflammation but also proactive management of comorbidities and optimisation of overall health. However, delays in referral, under-recognition of early disease and delayed optimisation of DMARD therapy considerably influence patient outcomes. This review summarises the clinical features, diagnostic approach, and contemporary management of RA, and highlights how current strategies have made rheumatoid arthritis without deformities an increasingly attainable goal.

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Introduction

Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis, with a worldwide prevalence of approximately 0.5–2% and occurs more frequently in women, with a female-to-male ratio of approximately 3–4:1.[1] It is a systemic autoimmune disease characterised by persistent synovial inflammation and progressive joint destruction, resulting in severe joint deformities, functional disability, and reduced quality of life. Beyond articular involvement, RA is increasingly recognised as a condition with substantial systemic consequences. It is associated with the development of hypertension, accelerated atherosclerosis, dyslipidaemia, and broader immune dysregulation.[2] It is a systemic autoimmune disease with a range of extra-articular manifestations including lung, skin, eye, kidney and cardiac involvement.[3] Consequently, RA has been linked to a markedly increased risk of premature mortality, with earlier studies reporting up to a 50% excess in all-cause mortality.[4]

Over the past two to three decades, management of RA has undergone a major transformation. There has been a paradigm shift towards early and aggressive intervention, particularly within the immunological "window of opportunity," with the aim of rapidly suppressing disease activity.[5] This has been complemented by the widespread adoption of a treat-to-target strategy, where therapy is systematically adjusted to achieve remission or low disease activity.[6] The introduction of newer disease-modifying antirheumatic drugs (DMARDs), including newer biologic agents, has further strengthened this approach and significantly improved clinical outcomes. These advances have raised an important clinical question: is rheumatoid arthritis without deformities now achievable in modern practice?

This review summarises current concepts in the clinical presentation, diagnosis, and management of rheumatoid arthritis, and examines how contemporary treatment strategies have transformed disease outcomes. It also highlights key challenges and practical considerations in the Sri Lankan context, where delayed diagnosis, limited access to specialist care and advanced therapies, and resource constraints may influence disease outcomes. Emphasis is placed on pragmatic, context-appropriate approaches to early recognition and optimal management within available healthcare settings.

Clinical features

Articular manifestations

Rheumatoid arthritis typically presents as a symmetrical inflammatory polyarthritis predominantly affecting the small joints of the hands and feet. The metacarpophalangeal, proximal interphalangeal, and wrist joints are most frequently involved. Distal interphalangeal joints are typically spared. However, RA may involve most synovial joints, and atypical patterns, including large-joint involvement such as the knees and shoulders, or oligoarticular presentations, may occur. Axial involvement in RA primarily affects the atlantoaxial (C1–C2) joint, where synovitis, erosions, and potential subluxation may occur. In contrast, the remainder of the spine and the sacroiliac joints are characteristically not involved.[7]

Patients commonly present with joint pain, swelling, and prolonged morning stiffness lasting more than 30–60 minutes. Functional impairment may occur early in the disease course, with reduced grip strength and limitations in activities of daily living. On examination, synovitis is characterised by soft tissue swelling, warmth, tenderness, and reduced range of motion in the affected joints. Joint effusions may be evident in larger joints.

If left untreated, persistent synovitis leads to progressive joint damage and bone erosion, resulting in classical deformities such as ulnar deviation of the fingers, swan-neck and boutonnière deformities, and subluxation of joints. However, with early diagnosis and effective treatment, these deformities are now less frequently encountered. Some individuals may exhibit an episodic or palindromic course, or, less commonly, a transient, self-limiting illness early in the disease course.[8]

Extraarticular manifestations of rheumatoid arthritis

Although articular involvement is the dominant feature, extra-articular disease reported in approximately 50% of patients contributes significantly to overall morbidity and should be routinely evaluated in clinical practice. Extraarticular manifestations of RA are summarised in Figure 1.

Pulmonary involvement is among the most clinically significant, with interstitial lung disease (ILD) being one of the most important manifestations. The most common ILD patterns are usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP), although other forms such as organising pneumonia, desquamative interstitial pneumonia, lymphocytic interstitial pneumonia, diffuse alveolar damage, and acute interstitial pneumonia have also been described.[9] In addition to parenchymal disease, pleural involvement is common, most frequently presenting as pleuritis or pleural effusions. Airway disease may affect both large and small airways, with manifestations including bronchiectasis, bronchiolitis, airway hyperreactivity, and cricoarytenoid arthritis. Rheumatoid pulmonary nodules, which may be solitary or multiple, generally follow a benign course. They are often asymptomatic and may remain stable or regress spontaneously.

Cardiovascular disease is a major contributor to morbidity and mortality in rheumatoid arthritis, driven in part by chronic systemic inflammation that accelerates atherosclerosis and increases the risk of ischaemic heart disease and cerebrovascular events. Less commonly, direct cardiac involvement may occur, including pericarditis, myocarditis, endocardial disease (20-25%),[10] and cardiac autonomic dysfunction. Pericardial disease may occasionally lead to effusion or constrictive pericarditis, while endocardial rheumatoid nodules may result in valvular regurgitation or embolic complications.[11]

Renal involvement in RA is often under-recognised but not uncommon. A significant proportion of patients may have impaired renal function, typically due to multifactorial causes including advancing age, the use of non-steroidal anti-inflammatory drugs, and the nephrotoxic potential of certain disease-modifying therapies. A range of glomerular

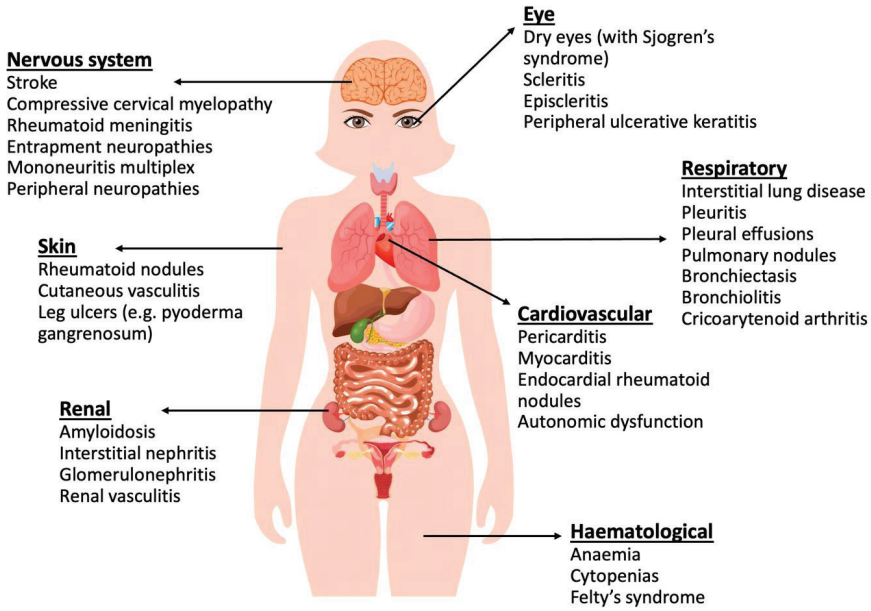

Figure 1. Extraarticular manifestations of rheumatoid arthritis.

pathologies have been described, with secondary amyloidosis (11%) being the most frequently reported, followed by other glomerular diseases including mesangioproliferative nephritis (8%) and focal segmental glomerulosclerosis (8%).[12]

Cutaneous manifestations in RA most commonly present as rheumatoid nodules, which typically occur over pressure points such as the elbows. Less commonly, patients may develop isolated cutaneous vasculitis or other forms of dermatoses such as pyoderma gangrenosum. Raynaud's phenomenon has also been described in a minority of patients, although it is infrequently encountered in routine clinical practice.

Ocular involvement is usually seen in the form of keratoconjunctivitis sicca, often associated with Sjögren disease in RA, while episcleritis and scleritis have also been reported. Scleritis is typically anterior and may be necrotising, with advanced cases progressing to scleromalacia perforans.[13]

Neurological manifestations are often due to entrapment neuropathies, such as carpal tunnel syndrome. Atlantoaxial instability with cervical compressive myelopathy may be seen in advanced disease. Rarely, rheumatoid meningitis may develop, presenting with a wide spectrum of clinical features, ranging from headache and meningism to cranial nerve palsies, seizures, or focal neurological deficit.[14]

Haematological abnormalities are also common in RA, with anaemia occurring in up to one-third to two-thirds of patients. This is typically multifactorial, with anaemia of chronic disease, iron deficiency and drug-related effects. Rarely, bone marrow suppression can result from DMARDs, leading to cytopenias that require urgent attention. Less commonly, autoimmune haemolytic anaemia or pure red cell aplasia may occur. Felty's syndrome, characterised by the triad of rheumatoid arthritis, neutropenia, and splenomegaly, is a rare but important complication, usually seen in patients with long-standing, seropositive disease.[15]

Systemic features such as fatigue, low-grade fever, and weight loss may be present in active disease. In addition, comorbid conditions including osteoporosis, sarcopenia, and fibromyalgia contribute significantly to functional impairment and reduced quality of life. Patients with RA are also at increased risk of infections due to disease-related immune dysregulation, immunosuppressive therapies, and associated comorbidities. Furthermore, there is a modestly increased overall risk of malignancy, particularly lymphomas.

Diagnosis

Early diagnosis of RA remains challenging because the classical textbook features of established disease may take months or years to develop and there is no gold standard diagnostic test for RA. Therefore, the diagnosis of RA remains fundamentally clinical, requiring integration of history, examination, investigations, and the exclusion of alternative diagnoses. Although serological markers and imaging findings are useful in supporting the diagnosis of RA, they should be interpreted in the clinical context and often provide valuable prognostic information regarding disease progression and outcomes.

Serological markers include rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA), commonly measured as anti-cyclic citrullinated peptide (anti-CCP) antibodies. Testing for both RF and anti-CCP increases diagnostic yield. Anti-CCP antibodies may be detectable several years before the onset of clinical disease and are associated with more aggressive disease and radiographic progression. However, some patients remain seronegative throughout the course of the disease.

Radiographic changes on plain X-rays often become apparent only after structural damage has occurred. Early findings may include periarticular osteopenia and subtle erosions. More sensitive imaging modalities, such

as musculoskeletal ultrasound and magnetic resonance imaging (MRI), may detect synovitis, bone marrow oedema, and erosions at an earlier stage.[16]

In patients presenting with early inflammatory arthritis without definitive features to point towards RA, alternative diagnoses should be considered before establishing a diagnosis of RA. Important differentials include post-infectious arthritides, psoriatic arthritis, systemic lupus erythematosus and other multisystem autoimmune diseases. Clinical evaluation, supported by appropriate investigations, is essential for distinguishing these conditions and facilitating timely initiation of appropriate therapy.

It is important to note that the 2010 ACR/EULAR classification criteria, developed primarily for research purposes, should not be used in isolation to establish a diagnosis of rheumatoid arthritis.[17] However, these classification criteria emphasise early disease features and may assist in identifying patients with RA at an earlier stage.

Nevertheless, clinical judgement remains central to the diagnosis of rheumatoid arthritis, and patients with suspected disease should be referred early for specialist evaluation, as timely diagnosis and management are critical in determining long-term outcomes.

Management

The management of rheumatoid arthritis (RA) has evolved considerably, with the current goal of achieving sustained remission or low disease activity to prevent joint damage, preserve function, and improve quality of life. Current management guidelines emphasise early, aggressive, and individualised treatment strategies delivered through a patient-centred approach.

Early initiation of DMARD therapy

Management should ideally be initiated and guided by a rheumatologist, in close partnership with the patient. Shared decision-making is central to care, considering disease severity, comorbidities, patient preferences, reproductive plans, and availability and affordability of medicines. Patient education regarding disease course, treatment options, adherence, and monitoring is essential to optimise outcomes.[18]

A few decades ago, RA treatment followed a pyramidal approach beginning with analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), with DMARDs introduced only in persistent disease. Current evidence demonstrates that most structural damage occurs early in the disease course. Early initiation of DMARD therapy during the "window of opportunity" significantly reduces disease progression and long-term disability. Therefore, treatment with DMARDs should begin as soon as the diagnosis of RA is established.[18]

Choice of initial DMARD

Methotrexate remains the anchor drug in the management of RA and is recommended as first-line therapy by most international guidelines including those of the American College of Rheumatology (ACR), the European Alliance of Associations for Rheumatology (EULAR), and the Asia-Pacific League of Associations for Rheumatology (APLAR). Methotrexate is typically started orally and escalated over several weeks to an effective weekly dose, accompanied by folic acid supplementation to reduce adverse effects.[19] In patients with contraindications or intolerance to methotrexate, leflunomide or sulfasalazine may be used as alternative conventional synthetic DMARDs. For patients with low disease activity, hydroxychloroquine may be considered due to its favourable safety profile, although its disease-modifying effects are relatively modest.

Combination therapy and treat-to-target strategy

Current management guidelines recommend a treat-to-target approach, in which therapy is adjusted until remission or low disease activity is achieved within a pre-defined timeframe. Patients should be reviewed regularly using validated disease activity scores such as the Disease Activity Score (DAS-28). If improvement is not observed within three months, or if the treatment target is not reached within six months, therapy should be modified. Delays in treatment escalation should be avoided, as persistent disease activity is associated with ongoing joint damage and poorer long-term outcomes.

Combination therapy using multiple conventional DMARDs (e.g. methotrexate, sulfasalazine, and hydroxychloroquine) may be considered in patients with inadequate response to monotherapy. For patients who do not achieve treatment targets with conventional synthetic DMARDs, biologic DMARDs or targeted synthetic DMARDs may be considered. Biologic DMARDs for rheumatoid arthritis available in Sri Lanka include tumour necrosis factor inhibitors such as etanercept, adalimumab, golimumab, and infliximab; anti-CD20 monoclonal therapy with rituximab; and the interleukin-6 receptor inhibitor tocilizumab. Targeted synthetic DMARDs comprise Janus kinase (JAK) inhibitors, of which tofacitinib is currently the only agent registered for use in Sri Lanka.

Traditionally, several factors have been considered markers of poor prognosis in rheumatoid arthritis, including persistent moderate-to-high disease activity despite conventional synthetic DMARD (csDMARD) therapy, elevated CRP or ESR, high swollen joint counts, RF and/or ACPA positivity (particularly at high titres), early erosive disease, and failure of multiple csDMARDs. These factors are associated with an increased risk of progressive radiographic damage and poorer long-term outcomes.[20] While such patients warrant closer monitoring and timely treatment escalation if targets are not achieved, emerging evidence suggests that poor prognostic factors alone should not necessarily prompt early escalation to biologic therapy.[21] Other factors such as quality of life, functional disability and emotional well-being should also be considered, and therapeutic decisions should be guided primarily by achievement of treatment targets with regular assessment of disease activity rather than by prognostic factors alone.

Role of glucocorticoids

Conventional synthetic DMARDs typically begin to show clinical benefit in approximately 4–6 weeks. Therefore, glucocorticoids are commonly used as bridging therapy to achieve rapid control of inflammation while awaiting the onset of DMARD efficacy and should be prescribed at the

lowest effective dose for the shortest possible duration. Intra-articular corticosteroid injections may also be useful in managing persistent monoarticular inflammation.[22]

Monitoring and safety considerations

Before initiating DMARD therapy, patients should undergo a baseline evaluation, including a full blood count, liver and renal function tests, and screening for active and latent infections, such as tuberculosis and viral hepatitis, particularly when biologic or targeted therapies are being considered. Additional baseline assessment should include cardiovascular risk evaluation and documentation of disease activity.

Regular monitoring is essential to assess treatment response and detect potential adverse effects, with the frequency determined by the specific therapy used and patient risk factors. Pre-treatment vaccination is also recommended in accordance with national and international guidelines, including immunisation against influenza, pneumococcal infection, hepatitis B (where indicated), and COVID-19. Live vaccines should ideally be administered prior to initiation of therapy as they are contraindicated once immunosuppressive therapy has commenced.[23]

Pregnancy and breastfeeding

Management of rheumatoid arthritis in pregnancy requires careful planning, with an emphasis on maintaining disease control using medications with established safety profiles. Methotrexate and leflunomide are contraindicated due to teratogenicity and must be discontinued well in advance of conception, with appropriate washout procedures for leflunomide where indicated. Methotrexate and leflunomide remain contraindicated during lactation as well.[23]

Hydroxychloroquine and sulfasalazine are considered safe and are recommended for use during both pregnancy and lactation. Low-dose glucocorticoids may be used when necessary, while non-steroidal anti-inflammatory drugs should be used with caution and avoided in the third trimester. All biologic DMARDs, particularly tumour necrosis factor inhibitors, may be continued during pregnancy and breastfeeding if required to control active or severe disease in certain patients.[24]

Management of comorbidities

Patients with RA have a substantial comorbidity burden that should be assessed and managed proactively as part of routine care. Cardiovascular risk factors should be systematically identified and treated, including optimisation of blood pressure, lipids, and glycaemic status, smoking cessation, weight management, and regular physical activity, alongside effective suppression of inflammatory disease activity.

Persistent pain should not automatically be assumed to reflect ongoing synovitis; coexisting fibromyalgia, mechanical pain, osteoarthritis, neuropathic pain, and fatigue should be actively considered, particularly before escalating DMARD therapy.[26] A holistic approach is therefore essential, incorporating patient education, shared decision-making, exercise, attention to mental wellbeing, vaccination, and optimisation of bone health and other relevant comorbidities, with input from other specialities where needed.

So, is rheumatoid arthritis without deformities a fiction or a reality?

Rheumatoid arthritis was once regarded as a relentlessly progressive disease leading to severe joint deformities and disability. However, advances in early diagnosis and the availability of effective disease-modifying therapies have significantly altered its natural history. With prompt recognition of inflammatory arthritis, early initiation of DMARD therapy, and adoption of a treat-to-target approach, many patients can now achieve sustained remission or low disease activity before irreversible joint damage occurs. As a result, the classical deforming phenotype of RA is increasingly less common in contemporary clinical practice.

Timely referral to specialist care remains a critical determinant of outcomes. In the Sri Lankan context, delays in referral may still occur due to under-recognition of early inflammatory arthritis or competing priorities across healthcare settings. Increasing awareness among clinicians and strengthening collaborative care pathways between generalist and specialist services are therefore essential to improving early diagnosis and optimising care. Public education is equally important. Misconceptions regarding rheumatoid arthritis and its treatment among the general public may result in delays in seeking appropriate medical attention, with some patients continuing to rely solely on traditional or alternative therapies despite the availability of effective disease-modifying treatments. While challenges remain, particularly in ensuring early diagnosis and equitable access to advanced therapies in a resource-limited setting such as Sri Lanka, the currently available therapies are often sufficient to meet treatment targets of most patients when used appropriately and optimally. Rheumatoid arthritis without deformities is therefore no longer a fiction, but an increasingly attainable reality in modern clinical practice.

Author declaration

Author declares no conflicts of interest.

Key messages

- Rheumatoid arthritis is a systemic disease with significant extra-articular manifestations and comorbidities that require comprehensive, multi-disciplinary management.
- Early recognition and prompt initiation of DMARD therapy within the “window of opportunity” are critical to prevent irreversible joint damage and disability.
- A treat-to-target strategy with regular disease activity assessment and timely treatment escalation improves long-term outcomes.
- Persistent symptoms should not always be attributed to active inflammation; coexisting conditions such as fibromyalgia and mechanical pain must be considered.
- With appropriate and optimal use of available therapies, including conventional DMARDs, rheumatoid arthritis without deformities is now an achievable goal in most patients, even in resource-limited settings.

References

1. Almutairi KB, Nossent JC, Preen DB, Keen HI, Inderjeeth CA. The Prevalence of Rheumatoid Arthritis: A Systematic Review of Population-based Studies. *J Rheumatol.* 2021;48(5):669–76.
2. Dougados M, Soubrier M, Antunez A, Balint P, Balsa A, Buch MH, et al. Prevalence of comorbidities in rheumatoid arthritis and evaluation of their monitoring: results of an international, cross-sectional study (COMORA). *Ann Rheum Dis.* 2014;73(1):62–8.
3. Misra DP. Clinical manifestations of rheumatoid arthritis, including comorbidities, complications, and long-term follow-up. *Best Pract Res Clin Rheumatol.* 2025;39(1):102020.
4. Dadoun S, Zeboulon-Ktorza N, Combescure C, Elhai M, Rozenberg S, Gossec L, et al. Mortality in rheumatoid arthritis over the last fifty years: systematic review and meta-analysis. *Joint Bone Spine.* 2013;80(1):29–33.
5. Burgers LE, Raza K, van der Helm-van Mil AH. Window of opportunity in rheumatoid arthritis – definitions and supporting evidence: from old to new perspectives. *RMD Open.* 2019;5(1):e000870.
6. Cardiel MH. Treat-to-target strategy in rheumatoid arthritis: real benefits. *Reumatol Clin.* 2013;9(2):101–5.
7. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet.* 2016;388(10055):2023–38.
8. Sanmarti R, Frade-Sosa B, Morla R, Castellanos-Moreira R, Cabrera-Villalba S, Ramirez J, et al. Palindromic Rheumatism: Just a Pre-rheumatoid Stage or Something Else? *Front Med (Lausanne).* 2021;8:657983.
9. Yunt ZX, Solomon JJ. Lung disease in rheumatoid arthritis. *Rheum Dis Clin North Am.* 2015;41(2):225–36.
10. Banks M, Ahmed F, Flint E, Forsey P, Bacon P, Kitas G. THU0135 Cardiac involvement in rheumatoid arthritis (RA). has it changed? *Annals of the Rheumatic Diseases.* 2001;60(Suppl 1):A408–A.
11. Sanghavi N, Ingrassia JP, Korem S, Ash J, Pan S, Wasserman A. Cardiovascular Manifestations in Rheumatoid Arthritis. *Cardiol Rev.* 2024;32(2):146–52.
12. Prata AR, Assunção H, Eugénio G, Sousa V, Duarte C. Renal abnormalities in rheumatoid arthritis: an insight on IgA nephropathy. *Rheumatology Advances in Practice.* 2021;6(1).
13. Zlatanovic G, Veselinovic D, Cekic S, Zivkovic M, Dordevic-Jocic J, Zlatanovic M. Ocular manifestation of rheumatoid arthritis – different forms and frequency. *Bosn J Basic Med Sci.* 2010;10(4):323–7.
14. DeQuattro K, Imboden JB. Neurologic Manifestations of Rheumatoid Arthritis. *Rheum Dis Clin North Am.* 2017;43(4):561–71.
15. Nikiphorou E, de Lusignan S, Mallen C, Khavandi K, Roberts J, Buckley CD, et al. Haematological abnormalities in new-onset rheumatoid arthritis and risk of common infections: a population-based study. *Rheumatology (Oxford).* 2020;59(5):997–1005.
16. Sahbudin I, Pickup L, Nightingale P, Allen G, Cader Z, Singh R, et al. The role of ultrasound-defined tenosynovitis and synovitis in the prediction of rheumatoid arthritis development. *Rheumatology (Oxford).* 2018;57(7):1243–52.
17. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, 3rd, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. *Arthritis Rheum.* 2010;62(9):2569–81.
18. Smolen JS, Landewé RBM, Bergstra SA, Kerschbaumer A, Sepriano A, Aletaha D, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. *Annals of the Rheumatic Diseases.* 2023;82(1):3–18.
19. Taylor PC, Balsa Criado A, Mongey AB, Avouac J, Marotte H, Mueller RB. How to Get the Most from Methotrexate (MTX) Treatment for Your Rheumatoid Arthritis Patient? – MTX in the Treat-to-Target Strategy. *J Clin Med.* 2019;8(4).
20. Ha Y-J, Shin S, Choi SR, Kang EH, Song YW, Lee YJ. Poor prognostic factors independently impact remission and treatment escalation in rheumatoid arthritis regardless of disease activity: A nationwide prospective cohort study. *Joint Bone Spine.* 2025;92(1):105798.
21. van der Pol JA, Allaart CF, Huizinga TWJ, Bergstra SA. Are poor prognostic factors a realistic basis for treatment decisions in patients with rheumatoid arthritis? Lessons from the IMPROVED study. *RMD Open.* 2024;10(2):e004382.
22. Fraenkel L, Bathon JM, England BR, St Clair EW, Arayssi T, Carandang K, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res (Hoboken).* 2021;73(7):924–39.
23. Bechman K, Song K, Abhishek A, Adas M, Ahmed A, Bray L, et al. The 2025 British Society for Rheumatology guideline for the prescription and monitoring of conventional synthetic disease-modifying anti-rheumatic drugs. *Rheumatology.* 2025;65(2).
24. Schreiber K, Frishman M, Russell MD, Dey M, Flint J, Allen A, et al. British Society for Rheumatology guideline on prescribing drugs in pregnancy and breastfeeding: comorbidity medications used in rheumatology practice. *Rheumatology (Oxford).* 2023;62(4):e89–e104.
25. Corrao S, Calvo L, Giardina A, Cangemi I, Falcone F, Argano C. Rheumatoid arthritis, cardiometabolic comorbidities, and related conditions: need to take action. *Front Med (Lausanne).* 2024;11:1421328.
26. Minhas D, Murphy A, Clauw DJ. Fibromyalgia and centralised pain in the rheumatoid arthritis patient. *Curr Opin Rheumatol.* 2023;35(3):170–4.