

## Management of Rheumatoid Arthritis

Shah P<sup>1</sup>, Trivedi J<sup>2\*</sup> and Shah P<sup>1</sup>

<sup>1</sup>Junior Resident, India

<sup>2</sup>Medical superintendent and professor of Medicine at Sal Hospital and Research Center, India

### \*Corresponding author:

Jayesh Trivedi,  
Medical superintendent and professor of Medicine  
at Sal Hospital and Research Center, Ahmedabad,  
Gujarat, India

Received: 06 Apr 2024

Accepted: 23 May 2024

Published: 28 May 2024

J Short Name: ACMCR

### Copyright:

©2024 Trivedi J. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially

### Keywords:

Rheumatoid arthritis; Synovectomy

### Citation:

Trivedi J, Management of Rheumatoid Arthritis. Ann Clin Med Case Rep. 2024; V13(18): 1-5

## 1. Abstract

Rheumatoid arthritis (RA) is a chronic inflammatory disease that primarily affects joints but can have systemic implications including increased cardiovascular risk. Effective management of RA involves a multifaceted approach encompassing pharmacologic treatments and lifestyle modifications. This review discusses various pharmacologic strategies including conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) like methotrexate and biologic DMARDs (bDMARDs) such as TNF inhibitors, alongside newer targeted synthetic DMARDs (tsDMARDs) like JAK inhibitors. Each medication category is evaluated for its mechanisms of action, efficacy, side effects, and specific indications. The review also explores surgical interventions for cases where pharmacologic treatment fails to halt disease progression or where significant joint damage necessitates procedures such as synovectomy or joint replacement.

Furthermore, the importance of physical therapy, including aerobic and strength training exercises, is highlighted as a critical component of comprehensive patient care. The article addresses the heightened risk of atherosclerotic cardiovascular disease in RA patients, outlining necessary preventative strategies such as improved cardiovascular risk assessment and the use of ASCVD risk-reducing medications. It advocates for a personalized, treat-to-target strategy that adapts to the individual patient's disease activity and comorbid conditions to optimize outcomes and enhance quality of life.

This review underscores the complexity of RA management and

the need for integrated care approaches to effectively address both the articular and extraarticular manifestations of the disease.

## 2. Treatment

### 2.1. Pharmacologic Treatment

Overview of drugs (1) Conventional Synthetic DMARDs (csDMARDs) Methotrexate (MTX)

- MOA: Inhibits dihydrofolate reductase, reducing folate and DNA synthesis, which decreases immune cell proliferation.

- Side Effects: Liver toxicity, bone marrow suppression, gastrointestinal discomfort, pulmonary fibrosis, and potential for teratogenic effects.

### 2.3. Hydroxychloroquine

- MOA: Interferes with lysosomal activity and antigen presentation in immune cells, among other effects.

- Side Effects: Retinal toxicity, gastrointestinal upset, skin rash, and rare neuromyopathy. Sulfasalazine

- MOA: Not fully understood; may involve inhibition of inflammatory cytokines and immune cell function.

- Side Effects: Gastrointestinal upset, headache, rash, hepatotoxicity, and hematological disorders.

### 2.4. Leflunomide

- MOA: Inhibits dihydroorotate dehydrogenase, leading to decreased pyrimidine synthesis and suppression of T cell proliferation.

- Side Effects: Diarrhea, hepatotoxicity, alopecia, and risk of ter-

atogenicity.

### 2.5. Biologic DMARDs (bDMARDs)

TNF Inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab pegol)

- MOA: Neutralize tumor necrosis factor (TNF), a key cytokine in the inflammatory process of RA.

- Side Effects: Increased risk of infections, potential for inducing autoantibodies, and rare lymphoma risk.

### 2.6. Interleukin-6 (IL-6) Receptor Inhibitors (tocilizumab, sarilumab)

- MOA: Block the IL-6 receptor, inhibiting the IL-6 pathway involved in inflammation.

- Side Effects: Increased risk of infections, elevated liver enzymes, and lipid abnormalities.

### 2.7. T Cell Costimulation Inhibitor (abatacept)

- MOA: Inhibits T-cell activation by binding to CD80 and CD86 on antigen-presenting cells, blocking interaction with CD28 on T cells.

- Side Effects: Increased risk of infections and headache.

### 2.8. B Cell Depletion Therapy (rituximab)

- MOA: Targets CD20-positive B cells, depleting them and reducing their role in inflammation.

- Side Effects: Infusion reactions, increased risk of infections, and rare progressive multifocal leukoencephalopathy (PML).

### 2.9. Targeted Synthetic DMARDs (tsDMARDs) Janus Kinase (JAK) Inhibitors (tofacitinib, baricitinib, upadacitinib)

- MOA: Inhibit Janus kinases, interfering with the JAK-STAT signaling pathway crucial for cytokine production and immune activity.

- Side Effects: Increased risk of infections, elevated liver enzymes, thrombosis risk, and lipid profile changes.

### 2.10. Glucocorticoids

- MOA: Broad anti-inflammatory and immunosuppressive effects by inhibiting gene transcription for multiple inflammatory cytokines and mediators.

- Side Effects: Weight gain, osteoporosis, diabetes, hypertension, increased infection risk, and potential adrenal suppression with long-term use.

These drugs are chosen and managed based on individual patient profiles, including disease activity, comorbidities, and tolerability, to optimize therapeutic outcomes while minimizing adverse effects.

## 3. Guidelines for Use [1]

### 3.1. Conventional Synthetic DMARDs (csDMARDs)

- Methotrexate (MTX): Central to RA treatment due to its effec-

tiveness as a disease-modifying agent. It's often considered the firstline therapy for patients with moderate to high disease activity.

- Hydroxychloroquine: Recommended for certain patient populations, particularly those with low disease activity.

- Sulfasalazine: Used in specific scenarios and is an alternative to methotrexate in certain cases.

- Leflunomide: An alternative to methotrexate, particularly when methotrexate is contraindicated or not tolerated.

### 3.2. Biologic DMARDs (bDMARDs)

- TNF Inhibitors: Including etanercept, adalimumab, infliximab, golimumab, and certolizumab pegol. Used in patients not responding adequately to csDMARDs.

- Interleukin-6 (IL-6) Receptor Inhibitors: Tocilizumab and sarilumab are mentioned as options, especially in patients for whom TNF inhibitors are not suitable.

- T Cell Costimulation Inhibitor: Abatacept, suitable for patients with moderate to high disease activity who have had an inadequate response to csDMARDs.

- B Cell Depletion Therapy: Rituximab, recommended for patients with a history of lymphoproliferative disorders or those who have had an inadequate response to TNF inhibitors.

### 3.3. Targeted Synthetic DMARDs (tsDMARDs)

- Janus Kinase (JAK) Inhibitors - Tofacitinib, baricitinib, and upadacitinib are included as options for patients with an inadequate response to csDMARDs or bDMARDs.

### 3.4. Glucocorticoids

- The guidelines conditionally recommend the cautious use of glucocorticoids, emphasizing the importance of minimizing their use due to potential toxicity. They may be used short-term for flare management or while waiting for DMARDs to take effect.

The current guidelines advocate for a personalized treatment approach, guided by disease activity, patient comorbidities, and drug safety profiles. Methotrexate remains the anchor drug for most RA treatment strategies, with other csDMARDs, bDMARDs, and tsDMARDs used based on specific patient circumstances, including disease severity, treatment history, and individual risk factors for adverse effects.

- A treat-to-target (TTT) approach, focusing on minimizing disease activity to prevent joint damage and other long-term sequelae, is strongly recommended over usual care for patients not previously treated with bDMARDs or tsDMARDs.

- Recommendations for DMARD tapering emphasize maintaining at least one DMARD and suggest that patients be in low disease activity or remission for at least 6 months before considering tapering.

Special Populations and Conditions

Recommendations should be tailored for patients with specific conditions such as heart failure, lymphoproliferative disorders, hepatitis B infection, nonalcoholic fatty liver disease (NAFLD), and history of serious infections, suggesting cautious use or avoidance of certain DMARDs in these groups.

## 4. Surgical Intervention Indications [2]

The indications for surgical intervention in Rheumatoid Arthritis (RA), are focused on addressing the various complications and failures of pharmacological treatments to manage the disease effectively. Here are the key indications for considering surgical treatment in RA patients:

### 4.1. Persistent Synovitis

Surgery may be indicated for patients with persistent synovitis that does not respond to medical therapy, including the use of Disease-Modifying Antirheumatic Drugs (DMARDs) and Biologic agents. In such cases, synovectomy, the surgical removal of inflamed synovial tissue, can be performed to alleviate pain and swelling.

### 4.2. Tendon Dysfunction

Tendon rupture or significant functional impairment due to RA can necessitate surgical repair or reconstruction. This is particularly common in the hands and feet, where RA can lead to tendon inflammation and subsequent rupture, affecting mobility and strength. Severe Joint Damage.

When RA leads to extensive joint damage, causing significant pain, loss of function, or both, surgical options like joint fusion (arthrodesis) or total joint replacement (arthroplasty) may be considered. These procedures are aimed at relieving pain, improving or restoring function, and enhancing the quality of life.

### 4.3. Joint Instability and Deformity

Surgical intervention may be required in cases of joint instability or deformities that significantly impair function or cause substantial pain.

Surgery can help correct deformities, stabilize the joint, and in some cases, restore function.

### 4.4. Failure of Conservative Management

Surgery is considered when conservative management, including pharmacological treatments and physical therapy, fails to provide adequate relief from symptoms or halt the progression of joint damage.

### 4.5. Improvement of Functional Status

In situations where RA severely affects the patient's functional status and quality of life, surgery may offer the best chance for improvement. This is especially true for interventions like joint replacement surgeries, which have been shown to significantly improve mobility and reduce pain in affected joints.

It's important to note that the decision to proceed with surgery in RA patients is made on an individual basis, taking into consideration the patient's overall health, the specific joints involved, the

severity of symptoms, and the expected outcomes of the surgical intervention.

Surgical treatments are typically considered when the benefits outweigh the risks and when there's a clear indication that surgery could improve the patient's quality of life.

## 5. Surgical Options

### 5.1. Function Synovectomy

Synovectomy involves the surgical removal of inflamed synovial tissue, aiming to reduce pain and swelling, and possibly slow down joint destruction. It is particularly considered when synovitis persists despite adequate medical therapy. This procedure can be performed on various joints, including knees, wrists, and elbows, to alleviate symptoms and potentially delay the need for joint replacement.

### 5.2. Tendon Repair

RA can lead to tendon inflammation and rupture, necessitating surgical repair. Procedures to repair or reconstruct tendons can restore function and reduce pain in affected joints, especially in the hands and feet, where tendons are critical for maintaining mobility and strength.

### 5.3. Joint Fusion (Arthrodesis)

For joints that are severely damaged, joint fusion may be recommended to alleviate pain.

Arthrodesis stabilizes and realigns the joint, offering pain relief but at the expense of joint mobility. This procedure is commonly performed on wrists and ankles, where joint replacement might not be as effective or durable.

### 5.4. Total Joint Replacement (Arthroplasty)

In cases of extensive joint damage where function is severely impaired and pain is significant, total joint replacement may be the best option. Hip and knee replacements are among the most common arthroplasty procedures performed in RA patients. The damaged parts of the joint are removed and replaced with artificial components, offering pain relief and improved joint function.

## 6. Physical Therapy in Rheumatoid Arthritis .Introduction to Physical Exercise in RA Management [3]

Physical exercise is recognized as a crucial component of RA management, aiming to reduce the multifaceted health consequences of the disease, which include joint symptoms, systemic effects, and psychosocial impacts. Despite historical reservations, there's growing consensus on the benefits of exercise in optimizing functional capabilities without exacerbating disease activity.

The European League Against Rheumatism (EULAR) and other health authorities recommend physical activity as part of standard RA care, acknowledging its role in mitigating inflammation, enhancing functional ability, and improving quality of life.

## 7. Indications for Physical Therapy [3]

Physical therapy in RA patients is indicated for various purposes:

- **Improvement of Aerobic Capacity:** Aerobic exercises, including walking, cycling, and swimming, are indicated to enhance cardiovascular fitness and potentially alleviate fatigue.

- **Muscle Strengthening:** Strength training, through free weights, machines, or bodyweight exercises, is recommended for improving muscle strength, joint stability, and reducing the risk of injuries.

**Enhancement of Physical Function and Reduction of Fatigue:** A combination of aerobic and strength training is indicated to offer comprehensive benefits in improving physical function, aerobic capacity, and reducing fatigue.

- **Improvement of Hand Function:** For patients experiencing hand impairments, targeted hand exercises are indicated to improve grip strength and overall hand function.

## 8. Types of physical Therapy- [3]

### 8.1. Aerobic Exercise

Aerobic exercise aims to improve cardiovascular fitness by increasing the heart rate and enhancing the body's use of oxygen. It includes activities like walking, jogging, cycling, and swimming. For RA patients, aerobic exercise has been shown to significantly improve aerobic capacity. It involves exercises that elevate the heart rate to 50%–80% of the maximum, designed to increase peak oxygen consumption (VO<sub>2</sub>max). The benefits observed include not just enhanced aerobic fitness but potentially reduced pain and fatigue, although the evidence for pain reduction is mixed.

### 8.2. Strength Training

Strength training focuses on improving muscle strength through exercises that gradually increase resistance. It can include the use of free weights, weight machines, or body weight. The review highlighted that strength training is beneficial for the erythrocyte sedimentation rate (ESR) and improves the 50-foot walking time in RA patients. It specifically designs routines to enhance muscle strength, which is crucial for maintaining joint stability and reducing the risk of injury.

### 8.3. Aerobic Exercise Combined with Strength Training

Combining aerobic exercise and strength training leverages the benefits of both cardiovascular fitness and muscle strengthening. This combination was shown to improve aerobic capacity, physical function, and reduce fatigue in RA patients. It suggests a holistic approach that targets multiple aspects of RA symptoms, providing comprehensive benefits.

### 8.4. Hand Exercise

Hand exercises are targeted activities designed to improve hand function and are particularly important for RA patients who experience hand impairments. These exercises may include stretching and strengthening routines focused on the hands, improving grip strength, and overall hand function. The review indicated that hand exercises could notably enhance hand function, making them a

critical component of RA management, especially given the prevalence of hand-related symptoms in RA patients.

### 8.5. Aquatic Exercise

Aquatic exercise, performed in warm water, offers a unique environment that reduces the load on the joints due to buoyancy, making it an ideal choice for patients with severe joint symptoms or a high risk of joint trauma. The review did not detail the effects of aquatic exercise specifically, but generally, such exercises can include water aerobics or swimming, focusing on improving flexibility, strength, and aerobic fitness in a low-impact setting.

## 9. Rheumatoid Arthritis and increased ASCVD Risk [4]

Rheumatoid Arthritis (RA) elevates the risk of atherosclerotic cardiovascular disease (ASCVD) through mechanisms beyond traditional cardiovascular risk factors. It identifies that increased disease activity and inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are associated with heightened ASCVD risk in RA patients. This association underscores the role of systemic inflammation in contributing to cardiovascular risk, highlighting that RA's inflammatory nature directly impacts cardiovascular health.

Moreover, medications commonly used in RA management, including glucocorticoids and targeted synthetic disease-modifying antirheumatic drugs (DMARDs), are linked with increased adverse cardiovascular events. These medications, while essential for controlling RA symptoms and progression, may exacerbate cardiovascular risk by affecting blood pressure, lipid profiles, and glucose metabolism.

In summary, RA increases cardiovascular risk through a combination of systemic inflammation, which is a hallmark of the disease, and the potential side effects of some RA treatments that can contribute to cardiovascular risk factors. This complex interplay underscores the importance of integrated care strategies that address both RA management and cardiovascular risk mitigation.

To prevent the elevated risk of atherosclerotic cardiovascular disease (ASCVD) in patients with Rheumatoid Arthritis (RA), the article outlines several recommendations and identifies care gaps that need addressing. Here's a summary of the preventive measures suggested:

1. **Improved Cardiovascular Risk Assessment:** The study highlights the need for better identification and assessment of cardiovascular risk in RA patients. Despite RA's association with increased cardiovascular risk, it's often underdiagnosed and undertreated. Implementing routine and comprehensive cardiovascular risk assessments during rheumatology encounters could help bridge this gap.

2. **Formal Guidelines for ASCVD Prevention in RA:** There's a call for the development of formal guidelines that specifically address ASCVD prevention in RA patients. Such guidelines would provide clear recommendations for screening, assessing, and managing

ing cardiovascular risk, similar to the established guidelines for diabetes mellitus.

3. **Integrated Care Approach:** The article suggests that a multidisciplinary approach involving both rheumatologists and cardiologists could improve the management of cardiovascular risk in RA patients. This could include early referral to cardiology for patients at high risk of ASCVD, ensuring that they receive specialized care for aggressive risk factor modification.

4. **Use of ASCVD Risk-Reducing Medications:** The research indicates that RA patients evaluated by cardiologists are more likely to be initiated on risk-reducing medications, such as lipidlowering drugs, antihypertensives, and aspirin. Ensuring that RA patients who are at elevated risk of ASCVD receive appropriate risk-reducing therapies is crucial for prevention.

5. **Educational Initiatives:** Raising awareness among healthcare providers, especially general practitioners and rheumatologists, about the increased risk of cardiovascular disease in RA patients and the importance of cardiovascular risk management as part of RA care.

6. **Patient Education:** Educating patients about their increased cardiovascular risk and the importance of lifestyle modifications, including diet, exercise, and smoking cessation, in conjunction with their RA treatment plan.

In summary, preventing increased cardiovascular risk in RA patients requires a coordinated effort to ensure comprehensive risk assessment, adherence to prevention guidelines, and a multidisciplinary approach to patient care. By addressing these areas, healthcare providers can better manage the complex needs of RA patients, ultimately reducing their risk of cardiovascular events.

## References

1. 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 & Rheumatology*. 2021; 73(7): 1108-23.
2. Radu AF, Bungau SG. Management of rheumatoid arthritis: an overview. *Cells*. 2021; 10(11): 2857.
3. Hu H, Xu A, Gao C, Wang Z, Wu X. The effect of physical exercise on rheumatoid arthritis: an overview of systematic reviews and meta-analysis. *Journal of advanced nursing*. 2021; 77(2): 506-22.
4. Aronov A, Kim YJ, Sweiss NJ, Nazir NT. Cardiovascular disease risk evaluation impact in patients with rheumatoid arthritis. *American Journal of Preventive Cardiology*. 2022; 12: 100380.