

# RHEUMATOID ARTHRITIS: Preoperative Medical Management

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## INTRODUCTION

Rheumatoid arthritis (RA) is a systemic inflammatory disease that involves the synovial membrane of joints (1). As the disease becomes more chronic, the inflammatory process progresses to include the cartilage and bone of the involved joints leading to destruction of articular cartilage and bony erosions (2). RA is not only a joint disease, but may also have extra-articular manifestations involving the skin, eyes, lungs, heart, gastrointestinal tract, nervous system, and hematologic system (1).

The diagnosis of RA is made based on the presence of the following criteria; morning stiffness, arthritis of 3 or more joint areas, arthritis in hand joints, symmetric arthritis, rheumatoid nodules, positive rheumatoid factor, and radiographic changes consistent with RA (3) (Table 1). Laboratory values may also be helpful in diagnosing RA although clinical findings should be correlated with these findings. Rheumatoid factor will be positive in 85% of patients with RA (1). Erythrocyte sedimentation rate and C-reactive protein values will commonly be elevated in these patients and can also be used to monitor the level of inflammation (1).

At the point when a patient with RA presents to the foot and ankle surgeon they may have already been diagnosed with RA and placed on a treatment regimen. Pain from the

inflammatory process may or may not be under control and they seek consult for the deformity that has resulted (4). Clinically, metatarsalgia and hammertoe contractures are commonly seen. Severe arthritis in the midfoot, hindfoot, and ankle are common.

Fortunately, procedures for rheumatoid arthritis in the foot and ankle have had good success and stand the test of time. Procedures such as hammertoe correction, pan-metatarsal head resection, and first metatarsophalangeal joint fusion or arthroplasty are commonly used for forefoot reconstructions. Using metatarsal shortening osteotomies instead of pan-metatarsal head resections has recently been introduced in the literature and has shown promising results when used in certain clinical situations (5). Arthrodesis procedures are most commonly used when deformity is present in the midfoot, hindfoot, and ankle. Ankle implant arthroplasty has been used in place of arthrodesis, although considerable controversy still remains on this topic as the search for the correct implant design continues.

While not much controversy surrounds procedure selection in the rheumatoid patient, there is considerable debate over how to preoperatively medically manage these patients. Mismanagement of these patients preoperatively can result in any of the following complications; wound healing, cervical spine subluxation, vascular compromise, edema, hematoma, DVT, and pain control issues (5). Rheumatoid patients should have a preoperative evaluation of their C-spine, a vascular examination, and their medications should be reviewed and adjusted as discussed below (5).

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**Table 1**

### CRITERIA FOR DIAGNOSIS OF RHEUMATOID ARTHRITIS

1. Morning Stiffness lasting at least 1 hour
2. Involvement of at least 3 joints
3. Arthritis affecting the wrist
4. Symmetric arthritis
5. Presence of rheumatoid nodules
6. Elevated rheumatoid factor
7. Radiographic changes consistent with rheumatoid arthritis

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\*4 of these need to be present (3)

## PREOPERATIVE MANAGEMENT

Preoperatively, patients with RA need to have a C-spine evaluation to check for atlantoaxial subluxation. This consists of flexion and extension lateral radiographs. An atlantodental interval of greater than 3mm or posterior atlantodental interval of less than 14 mm is positive for subluxation. These patients need to have a neurosurgical evaluation because they are at risk for spinal cord impingement while on the operating table (6). Symptoms of cervical subluxation include pain that radiates towards

the occiput, painless sensory loss in the hands and feet, and slowly progressive spastic quadriplegia (7). No studies exist that look at the risk of not evaluating for cervical subluxation preoperatively.

A vascular exam needs to be performed on all RA patients prior to surgery. The dorsalis pedis (DP) and posterior tibial (PT) arteries should be palpated. If these pulses are nonpalpable then noninvasive studies should be ordered; such as ABIs and segmental pressures. Segmental pressures need to be between 15-20 mmHg from arterial segment to arterial segment. Abnormal noninvasive studies may indicate that the patient will need a bypass before their reconstruction. The surgeon should keep in mind that smokers will often have palpable DP and PT arteries, but distal to the midfoot considerable intimal changes and media calcifications may exist with low flow states (4). To prevent postoperative gangrene, toe pressures and transcutaneous oximetry (TcPO<sub>2</sub>) values should be evaluated. Toe pressures should be greater than 40 mm Hg while TcPO<sub>2</sub> values should be greater than 40 mm Hg (5).

Patients may present on a variety of antirheumatic drugs that include; TNF-alpha inhibitors, NSAIDs, glucocorticoids, methotrexate, and many others. Of particular concern is how to properly manage your patients' antirheumatic drugs in order to prevent wound healing or postoperative infections.

TNF-alpha inhibitors work by binding to TNF alpha ligands on target cells and prevent release of inflammatory mediators. Etanercept and infliximab are two drugs in this class that are commonly used. Studies have shown that patients on TNF-alpha inhibitors do have a higher rate of serious infections when compared to those not on the drug (8-10), although these infections were usually respiratory rather than bone or soft tissue. Still determining how to adjust these drugs preoperatively has been somewhat controversial for foot and ankle surgeons due to the fact that no specific postoperative orthopedic studies have been previously available. Fortunately these studies now exist. Two smaller studies, one prospective with 31 patients and the other retrospective with 11 patients, compared complications between patients receiving TNF-alpha inhibitors prior to surgery and those not receiving the drug prior to surgery and both found that complication rates were the same (11, 12).

A larger study with 91 patients found that postoperative infections occurred in 20% of patients that were on TNF-alpha inhibitors prior to surgery and postoperative infections occurred in only 5% of patients that were not on these medications. While the evidence is still not complete on this medication it is certainly within reason to hold this medication 1 week preoperatively and resume it 1 week postoperatively.

Table 2

## RECOMMENDATIONS FOR DOSING

|                      |                            |
|----------------------|----------------------------|
| TNF Alpha Inhibitors | HOLD                       |
| Aspirin              | Discontinue 10 days pre-op |
| Naproxen             | Discontinue 4 days pre-op  |
| Ibuprofen            | Discontinue 1 day pre-op   |
| COX-2 Inhibitors     | No need to discontinue     |
| Methotrexate         | No need to discontinue     |
| Leflunomide          | HOLD 2 weeks prior         |
| Sulfasalazine        | HOLD 1 day prior           |
| Azathioprine         | HOLD 1 day prior           |
| Hydroxychloroquine   | No need to discontinue     |

Table 3

## ANTI-INFLAMMATORY PROPERTIES OF GLUCOCORTICOIDS

1. Opposes vascular permeability during acute inflammation
2. Causes leukocytosis
3. Causes depletion of circulations eosinophils and lymphoid tissue
4. Decreases production of IL-1 and IL-6 by macrophages
5. Inhibits production of lymphokines and prostaglandins
6. Inhibits production of bradykinin, platelet-activating factor, and serotonin
7. Reduces adherence of macrophage to vascular endothelium

NSAIDs should be discontinued preoperatively in order to prevent excessive bleeding during the procedure. Non-aspirin NSAIDs are usually discontinued 5 half lives prior to the procedure. Aspirin can be discontinued 10 days prior to the procedure, Naproxen 4 days, Ibuprofen 1 day, and COX-2 inhibitors do not need to be discontinued. It might be necessary to replace these with corticosteroids if the patient requires continued anti-inflammatory therapy (7) (Table 2).

Some patients with rheumatoid arthritis will be on glucocorticoid therapy. Unfortunately patients who have been on long-term steroid therapy may suffer from pituitary-hypothalamic suppression and adrenal atrophy. This suppression results from decreased levels of

endogenous ACTH. This physiologic process becomes problematic in the surgical setting because these patients could potentially have decreased levels of circulating cortisol. While cortisol has many different biologic functions, of most importance include its anti-inflammatory properties (Table 3) and its presence in the response to stress. It remains unknown why increased cortisol levels protect us from stress, but if deficient it can cause hypotension, shock, and death (13).

Ideally the dosage of the steroid should be tapered preoperatively so that the above mentioned anti-inflammatory properties will be limited at the time of the operation (7). Additionally these patients may need to be stress dosed on the day of surgery with either intravenous hydrocortisone or methylprednisolone to protect the patient from the serious complications of hypotension, shock, and death. This dose is tapered over the next few days following surgery (13). Several regimens for dosing these steroids can be found in the literature. Most of the regimens are based on the amount of stress that the procedure can be expected to create. Podiatric procedures will usually fall under a minimal stress category so the dosing regimen will require less steroid than that of a more major vascular procedure.

Current research has challenged the need to stress dose these surgical patients. The literature tends to support the fact that patients who have taken glucocorticoids for less than 3 weeks or who have received daily doses of less than 5mg/day of prednisone or its equivalent do not have HPA axis suppression (14-16). Patients can be assumed to have HPA axis suppression if they are on 20mg/day or more of prednisone or its equivalent for more than 3 weeks or have Cushing's syndrome (17).

Recommendations for stress dosing can be made based on the findings above. Patients that fall into the category of not having HPA axis suppression can continue on their normal dose of glucocorticoids perioperatively. Patients that do have HPA axis suppression should be stress dosed perioperatively, but return to their normal dosing schedule within 48 hours of their surgery (18, 19). Patients that fall in the intermediate risk group for developing HPA axis suppression can undergo an ACTH stimulation test preoperatively. Although this test may not always accurately predict the patient's stress response to surgery it can usually be assumed safe to not treat the patient with increased doses of glucocorticoids perioperatively as long as they respond normally to the test (20, 21).

Methotrexate will commonly be on the rheumatoid patients' medication list. Its mechanism of action is inhibition of the enzyme dihydrofolate reductase, which results in impaired DNA synthesis and its anti-inflammatory properties are seen through reduction in IL-1 production.

Hepatic fibrosis and leukopenia are potential side effects and so CBCs and liver enzymes need to be monitored when patients are on this drug (13). The same concern of post-operative infection complications exists with methotrexate as it does with other anti-rheumatic drugs. Studies exist to support holding (22, 23) methotrexate preoperatively as well as continuing therapy throughout the preoperative course (24-29). Other studies exist that make recommendations on various ranges of when to discontinue the drug preoperatively (30, 31). Preoperative decision making should be made on a patient by patient basis.

No clinical data exists regarding the perioperative use of leflunomide, sulfasalazine, azathioprine, and hydroxychloroquine. Currently it is recommended that leflunomide, sulfasalazine, and azathioprine are held prior to surgery. This recommendation is made based on the renal side effects of these medications. Leflunomide can be held 2 weeks prior to surgery due to its long half-life, and resumed 3 days after surgery. Sulfasalazine and azathioprine can be held 1 day prior to surgery and resumed 3 days after. Hydroxychloroquine has a non toxic profile and can be continued throughout the perioperative course (32).

The perioperative management of rheumatoid patients presents a significant challenge for foot and ankle surgeons. Certainly it is highly recommended that we work together with the patient's rheumatologist to properly manage these patients. Currently there is only evidence based research on continuing the use of methotrexate throughout surgery. Other recommendations lack the evidence and further research in this area is needed.

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