Accordant
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Clinical Practice Guidelines

Rheumatoid Arthritis

Program Update: 10/31/2014

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INTRODUCTION

The AccordantCare™ program works with health plans to assess, monitor, and support those with certain complex, chronic conditions. The focus of the program is to improve health outcomes and prevent or limit disease-related complications. AccordantCare offers unique services at no additional charge to patients, putting them in a strong position to adhere to their treatment plan.

There are several ways AccordantCare augments physicians' efforts. Through regular telephone contact, Accordant nurses:

- Keep patients informed about the disease process
- Coach patients in self-motivation and self-care skills
- Encourage patients to alert their physician when new symptoms arise
- Direct patients to resources that help pay for medication, transportation, home modifications, etc.
- Ensure preventive and screening measures are accomplished
- Provide emotional support to patients and caregivers
- Screen for depression
- Find local support groups

We invite physicians to make use of the services offered by AccordantCare and to suggest ways we can further patients' treatment goals. To offer feedback, get more information, ask questions or voice concerns, call toll-free 1-800-948-2497 to speak with a program representative from 8 a.m. to 9 p.m., Monday through Thursday, and from 8 a.m. to 5 p.m. on Friday, Eastern Time. Messages left after hours will be returned the next business day.

Intent of Guidelines

The purpose of this Clinical Practice Guideline is to describe current patterns of practice where there is no fully established national guideline for diagnosis and management. It is not meant to dictate care of patients. Decisions about care are made by the physician and the patient based on the individual needs of that patient.

A patient's health plan may or may not pay for the all medicines, tests, equipment, or services mentioned in this document. Benefits should be checked with the individual's health plan to assure payment.

DISEASE OVERVIEW

Although it can affect other parts of the body as well, rheumatoid arthritis (RA) is primarily a disease that causes inflammation, swelling, and pain of the joints between two bones. It is an autoimmune disease, in which, for reasons that are

not clearly understood, an individual's own immune system attacks otherwise healthy joints.

Currently in the United States alone, more than 1.3 million people suffer from the disease.[1] Prevalence is near 5% in women over age 55.[2] The average annual incidence in the United States is about 70 per 100,000.[2]

DIAGNOSIS OF DISEASE

Recognition of early RA remains a challenge. Diagnostic delay can lead to preventable erosive joint damage.[3] There is no single laboratory, histologic, or x-ray finding that indicates a definite diagnosis of RA. In addition to a detailed physical exam, a combination of the tests and studies below may be required.

Lab Tests[4]

- RF titer: limited prognostic value in the individual patient. Between 70% and 80% of people with RA have a positive RF.
- Anti-cyclic citrulinated peptide (anti-CCP2) antibody titer[5]
- Complete blood count (CBC): to check for anemia, infection, and inflammation
- ESR: to indicate degree of inflammation
- CRP: also to indicate degree of inflammation
- Electrolyte levels
- Creatinine
- Hepatic enzyme levels: aspartate aminotransferase (AST), alanine aminotransferase (ALT), and albumin
- Urinalysis
- Synovial fluid analysis

Imaging Studies

- X-rays show swelling of soft tissue and loss of bone density around the joints. They also show small erosions, narrowing of joint space, and are useful for comparison with later X-rays
- Magnetic resonance imaging (MRI) detects early inflammation/synovitis
- Ultrasound (U/S) can detect early synovitis as well

APPROACH TO MANAGEMENT OF RHEUMATOID ARTHRITIS

Goals of Treatment

Clinical remission is the physician's primary target of treatment for RA.[6] Clinical remission is the absence of signs and symptoms of significant inflammatory disease activity.

The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) have developed definitions of remission that can be used uniformly as an outcome measure in clinical trials:

The 2011 ACR/EULAR Definitions of Remission in Rheumatoid Arthritis Clinical Trials[7]

Boolean-Based Definition
At any time point, patient must satisfy all of the following:

- Tender joint count ≤1
- Swollen joint count ≤1
- C-reactive protein ≤1 mg/dl
- Patient global assessment ≤1 (on a 0–10 scale)

Index-Based Definition
Simplified Disease Activity Index score of ≤3.3

If remission is not achievable (e.g., patients with long-standing disease, considerable joint damage, several prior treatment failures), then reaching and maintaining low disease activity is an acceptable alternative goal.[6]

General Treatment Considerations

Patient participation in setting treatment goals and expectations is important for two reasons: to ensure finding the right medication treatment plan for that patient, *and* to show their commitment to that plan. Patients should discuss their priorities with their doctor and learn how their medication may help achieve those goals. Treatment goals may include[7]:

- Less pain
- More independence
- Ability to work
- Ease with activities of daily living
- Less visible joint damage
- Less fatigue
- Ability to do the things they enjoy

Patients should expect to see the doctor frequently while therapy is being adjusted and disease progress is being monitored. Comorbidities, such as fibromyalgia, should be carefully considered since they can contribute to measures of disease activity as well as patients' overall perception of RA.[6]

Patients with active, RF-positive disease involving multiple joints are at high risk (greater than 70%) of developing serious joint damage within two years of disease onset.[4] Aggressive early treatment with disease modifying antirheumatic drugs (DMARDs) is recommended for all patients with RA. The 2012 ACR

guidelines recommend more aggressive treatment for patients with early RA than the 2008 guidelines.[8]

For patients with early, poor-prognosis RA, initial methotrexate monotherapy with the option to step-up to combination therapy results in similar outcomes as treating these patients with immediate combination therapy.[9]

Progressive combination therapy is recommended over sequential monotherapy.[3,9]

Prevention of cardiovascular disease (CVD) should be an aim in the treatment of RA patients.[10] A high level of suspicion for CVD events is required as patients may present atypically. Patients with inflammatory arthritis need to be systematically screened and risk assessed for CVD.[10] The mortality associated with CVD in RA may be reduced by controlling the inflammation of RA using DMARD therapy and by controlling other, modifiable risk factors.[11-14]

Many different treatment options exist for RA. The ACR recommends that all patients with RA be followed by a rheumatologist.[4]

Nonpharmacologic Treatment[4]
Patients should participate in conditioning exercise programs that improve joint mobility, muscle strength, aerobic fitness, and overall function. There is moderate evidence that short- and long-term aerobic exercise (including aquatic) and muscle strength training have a positive effect on the aerobic capacity and muscle strength of patients.[15]

Patients should be encouraged to undertake both aerobic and strength training exercise and to discuss exercise programs with their doctor. Exercise programs should be carefully individualized, especially for patients with underlying large joint damage or pre-existing CVD.[16]

Physical therapists and occupational therapists may help patients experiencing difficulty with activities of daily living (ADL).

A wide variety of herbal medicines are used by some patients who believe them to be safer than conventional pharmaceuticals. For most herbal medicines, there is a lack of high-quality evidence to support their efficacy and little unbiased safety data. Some herbal medicines can interact with other medicines, so it is important that patients share a list of ALL medicines they take with their doctor and pharmacist.

Medications
<u>Pain Control</u>
NSAIDs
Salicylates[4]

Glucocorticoids [4]
Prednisone (e.g., Deltasone®) or delayed-release tablets (Rayos®)[17]
Methylprednisolone (e.g., Medrol®)

Disease Modifying Antirheumatic Drugs (DMARDs)
Methotrexate[18] (using the Methotrexate Intolerance Severity Score questionnaire can lead to early detection and treatment of symptoms and prevent the development of conditioned responses to methotrexate[19])
Hydroxychloroquine (e.g., Plaquenil®)[18]
Leflunomide (e.g., Arava®)[18]
Azathioprine (e.g., Imuran®)
Sulfasalazine (e.g., Azulfladine®)[4]
Cyclophosphamide (e.g., Cytoxan®)
Gold (e.g., oral Ridaura®, injectable gold sodium thiomalate)
D-penicillamine (e.g., Cuprimine®, Depen®)[4]
Cyclosporine (e.g., Neoral®)[4]
Tetracyclines (e.g., minocycline)[4]
Tofacitinib (Xeljanz®)[20]
Canakinumab (Ilaris®) for active systemic juvenile idiopathic arthritis in children aged 2 years and older[21]

Combination DMARD Therapy[18]
Methotrexate + hydroxychloroquine
Methotrexate + leflunomide
Methotrexate + sulfasalazine
Hydroxychloroquine + sulfasalazine
Methotrexate + hydroxychloroquine + sulfasalazine

Biologic DMARDs
Tumor necrosis factor (TNF) inhibitors
- Etanercept (Enbrel®)[4]
- Infliximab (Remicade®)[18]
- Adalimumab (Humira®)[18]
- Certolizumab pegol (Cimzia®)[22]
- Golimumab (Simponi® and Simponi Aria)[23,24]

Other Biologics
- Anakinra (Kineret®)[18]
- Abatacept (Orencia®)[18]
- Rituximab (Rituxan®)[18]
- Tocilizumab (Actemra®)[25]

Surgery[26]
Total joint replacement

Arthrodesis (fusion)
Synovectomy
Tendon reconstruction

PREVENTION AND MANAGEMENT OF COMPLICATIONS

Accordant helps patients prevent and manage complications by teaching early warning signs, encouraging adherence to treatment plans, offering supportive care, and recommending physician contact where needed.

The goals and cooperative interventions listed below are not a comprehensive list of complications but reflect some of the more common clinical situations specific to rheumatoid arthritis. Other health topics (e.g., specific age-appropriate vaccinations) are beyond the scope of this document.

Goal: Improve self-management skills
Cooperative interventions include teaching patients the importance of:

- personal motivation building
- prevention-focused, behavioral self-management skills development
- confidence and communication
- adhering to treatment plan
- knowledge development

Goal: Detect and correct anemia early
Cooperative interventions include teaching patients to:

- understand the significance of anemia of chronic disease and know the difference between it and iron deficiency anemia;
- recognize the symptoms of anemia (e.g., fatigue, pale skin, dizziness, clouded thinking, tachycardia, and dyspnea);
- know the importance of treating the underlying RA;
- recognize the symptoms of gastrointestinal (GI) bleeding (for chronic NSAID users);
- recognize ways to reduce the risk of having a GI bleed or ulcer (e.g., take NSAIDs with food or with a proton pump inhibitor);
- understand the significance of deficiencies of vitamins B_6 and B_{12} and folate, especially if taking methotrexate; and
- comply with routine lab work as scheduled.

Goal: Minimize the risk of cardiovascular disease (CVD)
Cooperative interventions include teaching patients to:

- discuss the overall risk for CVD with their doctor beginning at age 40;
- know the importance of treating underlying inflammation;
- understand the difference between modifiable and non-modifiable risk factors;

- understand the importance of their lipid profile and of controlling high cholesterol;
- understand the importance of regular blood pressure checks;
- know their blood glucose and A1c values if diabetic;
- discuss the risks and benefits associated with NSAIDs and COX-2 inhibitors with their doctor;
- recognize the signs and symptoms of a heart attack and stroke and understand the need to call 911 immediately;
- realize the importance of a low-fat, low-sodium, low-cholesterol diet;
- understand the need to quit smoking; and
- talk to their doctor about how to get about 30 minutes of safe exercise most days of the week.[16]

Goal: Prevent deterioration from entrapment neuropathy
Cooperative interventions include teaching patients to:

- control the underlying inflammation by complying with their physician's treatment plan;
- recognize the sensations associated with neuropathy (e.g., tingling, burning) and report them to their physician immediately;
- understand the benefits of occupational/physical therapy;
- stretch to increase blood flow to affected areas; and
- for carpal tunnel:
    - keep the wrist as straight as possible
    - avoid repetitive wrist motion
    - use splints as prescribed.[27,28]

Goal: Achieve and maintain a healthy weight
Cooperative interventions include teaching patients to:

- understand that a normal body weight reduces stress on weight-bearing joints and may prevent the need for hip and knee replacement surgery;
- understand that a healthy weight reduces the risk of other complications such as cardiovascular disease and diabetes;
- calculate their body mass index;
- consult their doctor or a registered dietician for ways to lose weight; and
- make better food choices (e.g., shop for and prepare healthy meals).

Goal: Manage symptoms of fatigue and decrease disability
Cooperative interventions include teaching patients to:

- **r**ecognize the symptoms of fatigue;
- discuss with their physician the symptoms they experience;
- treat underlying disease by complying with their physician's treatment plan;
- know the difference between fatigue and depression;

- realize that fatigue is the result of RA and treatment but that it may also be due to infection or anemia; and
- control factors that exacerbate fatigue
    - get eight hours or more of sleep each night
    - plan for rest periods throughout day
    - work exercise into daily activities
    - divide large tasks into several small steps
    - deal with stress.

Goal: Minimize the impact of Felty's syndrome
Cooperative interventions include teaching affected patients to:

- adhere to DMARD therapy as prescribed by their physician.
- know they are susceptible to recurrent infection (systemic and local)[29]; and
- recognize and seek immediate treatment for infections and leg ulcers.

Goal: Prevent progression of leg ulcers
Cooperative interventions include teaching patients to:

- report changes in skin integrity to physician;
- understand the different types of leg ulcers (e.g., vasculitis, pyoderma gangrenosa) and that symptoms and treatments differ;
- learn about the types of wound dressing/compression bandaging[24,25]
- accept the potential for recurrence of leg ulcers[30];
- understand that poor nutrition is both a causative and recurrent risk factor[30] and that adequate intake of zinc, vitamin C, protein, lipids, and carbohydrates helps healing[31];
- understand that smoking impairs healing[31];
- learn that improperly fitting footwear can cause skin abrasion and may exacerbate ulcers that occur secondary to foot and ankle deformities[30]; and
- recognize that treatment of peripheral edema can reduce recurrence and speed healing.[30]

Goal: Manage and decrease complications from mononeurtis multiplex
Cooperative interventions include teaching patients to:

- report abnormal sensations, unexplained injuries, or falls to their physician;
- understand the importance of exercise to increase muscle strength and control[16,32];
- recognize the benefits of physical/occupational therapy;
- check their lower extremities for bruises and other injuries that may go unnoticed and become prone to infection[32];
- avoid prolonged pressure on knees and elbows (e.g., crossing legs, leaning on elbows) because these areas are prone to new nerve damage[32];
- use braces, splints, and wheelchairs as prescribed; and

- recognize the need for a home safety evaluation, if appropriate.

Goal: Minimize the impact of ocular manifestations (e.g., scleritis, episcleritis)
Cooperative interventions include teaching patients to:

- understand the importance of reporting changes in vision or other eye problems to their physician;
- understand the symptoms of scleritis and episcleritis and the significance of each;
- understand the importance of an ophthalmologic exam; and
- use artificial tears for dry eyes.

Goal: Avoid hospitalization, surgery, and disability associated with osteoporotic fractures
Cooperative interventions include teaching patients to:[33]

- know the importance of risk assessment;
- know the importance of BMD testing[34];
- recognize the importance of calcium and vitamin D supplements[35];
- discuss treatment options to prevent and/or repair bone loss with a physician, especially if taking corticosteroids;
- talk about their risk for falling[35] and learn fall-prevention strategies;
- improve home safety;
- participate in exercise that improves balance, agility, strength, and posture[33,35] (encourage members to get physician approval of new exercise programs);
- understand the importance of smoking cessation; and
- learn the importance of reducing alcohol consumption.

Goal: Minimize pain and improve quality of life
Cooperative interventions include teaching patients to:

- understand the pain cycle, in which pain leads to inactivity and inactivity leads to weakness, stiffness, fatigue, and more pain;
- understand the importance of exercise to prevent constipation, high blood pressure, obesity, osteoporosis, and increased sensitivity to pain, anxiety, and depression;
- understand the need to lose weight to lower pressure on weight-bearing joints;
- understand the risks and benefits of pain relievers;
- rest during arthritis flares and participate in regular exercise between flares;
- get eight hours of sleep in a comfortable bed;
- use heat for stiffness and cold for pain relief[3]; and
- understand the benefits of meditation, prayer, positive self-talk, and relaxation techniques.

Cooperative interventions include teaching patients to:

- report shortness of breath or dry cough to their physician;
- understand the importance of controlling the underlying disease to minimize their risk;
- understand treatment options and the safety concerns regarding long-term corticosteroid therapy;
- access support systems as disease progresses;
- understand the importance of immunizations for flu and pneumonia; and
- realize the importance of smoking cessation.

Goal: Prevent complications from rheumatoid nodules
Cooperative interventions include teaching patients to:

- realize that smoking increases their risk for rheumatoid nodules[36,37];
- modify pressure to affected areas to reduce irritation;
- monitor for pressure ulcer or skin breakdown; and
- understand the potential for infection.

Goal: Prevent or minimize the impact of septic joint
Cooperative interventions include teaching patients to:

- recognize the symptoms of a septic joint and report them to a doctor;
- understand the importance of completing a regimen of antibiotics;
- understand the need to suspend TNF inhibitor or immunosuppressant therapy while infection is being treated;
- follow through with the physical therapy/passive motion exercises as prescribed;
- establish and maintain good oral health; and
- inform their dentist of any prior joint replacement surgery before scheduling high-risk dental procedures.

Goal: Minimize the impact of Sjögren's syndrome
Cooperative interventions include teaching patients to:

- recognize the symptoms of Sjögren's syndrome and report them to their physician;
- adhere to their physician's treatment plan;
- know the importance of good dental hygiene and regular dental visits;
- use artificial tears;
- rinse mouth regularly;
- use lozenges;
- sip water frequently;
- apply vaginal lubricants as needed;
- use a humidifier; and
- apply skin moisturizer regularly.

Goal: Detect spinal instability early and minimize disability
Cooperative interventions include teaching patients to:

- recognize neurological symptoms (e.g., decreased hand coordination, drop attacks) and understand the importance of reporting them to a physician; and
- understand that a home safety evaluation may help avoid injury.

Goal: Facilitate early diagnosis and treatment of vasculitis
Cooperative interventions include teaching patients to:

- recognize the symptoms of vasculitis (e.g., small brown spots on nail beds, dysesthesia) and understand the importance of reporting them to a physician; and
- understand the importance of adhering to DMARD therapy to control inflammation.

PATIENT FOLLOW-UP

The frequency of appointments is based on individual patient needs and will vary according to disease duration, level of disease activity, and medication issues. Many patients require regularly scheduled appointments that includes evaluation of[38]:

- Joint tenderness or pain on motion
- Morning stiffness
- Grip strength
- 50-foot walk time
- Range of motion
- Activities of daily living

Screen for and treat standard cardiovascular risk factors to decrease the risk of death from cardiovascular disease.[10,38]

Regularly monitor patients for medication side effects (e.g., osteoporosis, liver and kidney toxicities).[38]

Follow patients closely for signs of pulmonary infection and ensure they receive annual flu vaccine and the pneumonia vaccine at appropriate intervals.[38] Encourage smokers to quit.

Annual exams may be considered to monitor the impact of the disease on the musculoskeletal system, other body systems, and the patient's quality of life.[38]

PATIENT EDUCATION

The Accordant Health Communities website at https://www.accordant.com offers resources for patients with rheumatoid arthritis.

Other approved and informative Web sites for patient education include the following:

Arthritis Foundation at:
http://www.arthritis.org/

American College of Rheumatology at:
http://www.rheumatology.org/practice/clinical/patients/

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