REVIEW

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Osteoarthritis: No cure, but many options for symptom relief

ABSTRACT

Because curative disease-modifying medications for osteoarthritis are still not available, medical management strategies focus on pain relief. Other goals are to identify functional deficits early and to start restorative, if not preventive, rehabilitation. We review recent developments and summarize the clinical features and treatments currently available.

KEY POINTS

Do not automatically attribute musculoskeletal pain in older patients to osteoarthritis. The American College of Rheumatology has issued criteria for diagnosis.

All patients with osteoarthritis should receive nonpharmacologic therapies, whether or not they also receive pharmacologic therapy.

If a patient is to receive acetaminophen long-term, his or her liver function and hepatic enzyme profile should be evaluated.

If a nonsteroidal anti-inflammatory drug (NSAID) is used long-term, consider concurrent use of misoprostol or a proton-pump inhibitor or consider use of a cyclooxygenase-2 (COX-2) inhibitor to protect the gastric mucosa.

A newly approved therapy for osteoarthritis of the knee is a series of intra-articular injections of hyaluronic acid.

S EVERAL NEW THERAPIES for osteoarthritis and advances in our understanding of its pathogenesis hold promise for the development of disease-modifying drugs. For most patients, however, optimal therapy still consists of nonpharmacologic measures with or without an analgesic such as acetaminophen or a nonsteroidal anti-inflammatory drug (NSAID).

This update reviews the epidemiology, basic pathophysiology, and clinical features of osteoarthritis and summarizes the management strategies currently available.

PREVALENCE IS INCREASING

Osteoarthritis causes considerable suffering and functional compromise in older adults, and it places a heavy economic burden on the health care system.¹ It is the most common joint disease among adults 65 years and older in the United States, and its prevalence is expected to increase as the US population ages.^{2–4}

PATHOPHYSIOLOGY

In brief, osteoarthritis develops when the process of cartilage degradation outpaces cartilage repair.

The initiating events that trigger osteoarthritis remain unknown, although epidemiologic observations (see **RISK FACTORS**, below) provide insights into factors that contribute to its development.

A detailed review of the pathogenesis of osteoarthritis is beyond the scope of this article but is available elsewhere.^{5–7}

In the degradation process, the cartilage

TABLE 1

American College of Rheumatology criteria for diagnosing osteoarthritis

Hand

Pain, aching, or stiffness and Hard-tissue enlargement of at least two of the following joints: Distal interphalangeal Proximal interphalangeal First carpometacarpal and

Fewer than three swollen metacarpophalangeal joints and either

Hard tissue enlargement of ≥ 2 distal interphalangeal joints

or

Deformity in at least two of the following joints: Distal interphalangeal Proximal interphalangeal First carpometacarpal

Knee

Pain and Osteophytes on radiography and At least one of the following: Age \geq 50 years Morning stiffness lasting < 30 minutes Crepitus on motion

Hip

Pain and At least two of the following: Erythrocyte sedimentation rate < 10 mm/hour Femoral or acetabular osteophytes on radiography Joint-space narrowing on radiography

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matrix becomes depleted of polysaccharideprotein molecules called proteoglycans. As a result, the cartilage begins to break down into fibrils and to erode and crack, at first superficially but eventually deeper. Soluble proteins thought to contribute to this process include matrix and tissue metalloproteinases and inflammatory cytokines. The degraded cartilage becomes less viscoelastic and less compressive—ie, less able to serve as a smooth, cushioned, well-lubricated bearing surface for the joint. The reparative response is believed to involve metalloproteinase and cytokine inhibitors, growth factors, and perhaps oncogenes.

It is hoped that in the future we will have disease-modifying drugs that target these components to inhibit the degradation process, enhance the repair process, or both.

RISK FACTORS FOR OSTEOARTHRITIS

Advanced age is the strongest risk factor for osteoarthritis across all anatomic sites.^{3,8} An estimated 6.1% of the general population aged 30 years and older and 10% to 30% of those older than 65 years experience symptoms of osteoarthritis of the knee. In all age groups, symptomatic osteoarthritis of the hip is less common (0.7-4.4%).^{9–12}

Female gender.^{4,8,13} Women have a higher risk than men of developing osteoarthritis of the knee and hand and in multiple joints.¹⁴ Women are also more likely to experience pain at any site.^{8,13,14}

Excess weight plays a role in the development of osteoarthritis,^{15–19} and probably in its progression. It contributes to pain,²⁰ it leads to a decline in physical activity, and it is independently associated with physical disability.²¹

Estrogen deficiency is believed to be a contributing factor.^{4,22} Support for this theory comes from two studies^{23,24} that showed that women who took hormone replacement therapy had a lower incidence of knee and hip osteoarthritis, particularly bilateral radiographic osteoarthritis and more severe osteoarthritis.

Deficiencies of vitamins C and D. Framingham participants whose vitamin C intake was low had a significantly higher incidence of osteoarthritis of the knee.²⁵ Those with low levels of vitamin D intake had a greater risk of radiographic progression if they already had osteoarthritis, but they did not have a higher prevalence of osteoarthritis.²⁶

Physical activity. Framingham residents who engaged in heavy occupational physical activity had a higher incidence of radiographic and symptomatic osteoarthritis of the knee, especially if they were obese.²⁷ "Moderate" and "light" physical activity, although poorly defined, was not linked to the incidence of osteoarthritis. Likewise, persons who participate in sports that place a high torsional load on the knees have a higher risk of osteoarthritis, particularly those who have injuries to the meniscus or the supporting ligaments.²⁸

Trauma can be the cause of osteoarthritis in other peripheral joints such as the shoulder, elbow, wrist, and metacarpophalangeal joints, as can long-standing inflammatory arthritis.

CLINICAL FEATURES

The fundamental features of osteoarthritis are localized pain without systemic inflammatory or constitutional symptoms, and characteristic physical and radiographic abnormalities.^{29–31} The most common sites are the distal interphalangeal and proximal interphalangeal joints of the hands, the base of the thumb, the knees, and the hips.

Early in the disease the pain is relieved by rest, but later it may persist during rest. Stiffness, lasting less than 30 minutes, is noted upon arising in the morning and after periods of inactivity; this is called the "gel phenomenon" because of the subjective feeling of increased viscosity within the joint after a period of disuse.

Symptomatic osteoarthritis is easily identified and classified using criteria established by the American College of Rheumatology (TABLE 1).^{29–31}

Physical findings

The physical examination often reveals bony prominences, diminished or painful range of motion, and tenderness to palpation at the joint line.

Crepitus (audible or palpable joint grating) is common and may be elicited with passive range of motion or with compression; however, it is a nonspecific finding, even though it is one of the criteria for diagnosis of osteoarthritis.³⁰

Although many people with osteoarthritis have bony enlargement of the distal and proximal interphalangeal joints of the hands (Heberden and Bouchard nodes), hand osteoarthritis may not result in pain or functional impairment.³² Although knee and hip osteoarthritis may also be asymptomatic, a higher proportion is associated with painful symptoms.



FIGURE 1. Radiographs of the knees of a patient with osteoarthritis, showing the classic radiographic features of **(A)** osteophytes and joint-space narrowing, **(B)** subchondral sclerosis, and **(C)** cysts.

Frank joint deformities may develop due to progressive cartilage destruction, swelling, or disruption of supporting ligaments.

Radiographic findings

The classic radiographic findings are osteophytes, joint-space narrowing, subchondral sclerosis, and cysts (**FIGURE 1**).³³

Although the incidence of pain is higher among patients who apparently have more severe radiographic osteoarthritis, radiographic severity in itself is not a consistent predictor of the actual physical severity of symptoms or the degree of functional impairment.^{8–12,14,34} Early-stage symptomatic osteoarthritis does not always manifest radiographically.

Differential diagnosis

Clinicians should not automatically attribute musculoskeletal pain in older adults to osteoarthritis, because other conditions can mimic and coexist with it.³⁵ For example, bursitis, tendinitis, and periostitis are all marked by periarticular pain, but this symptom is not

TABLE 2

Therapeutic options for osteoarthritis of the hand, knee, or hip

Nonpharmacologic therapy

Patient education and support groups (for all patients with arthritis) Resistive and aerobic exercise (for knee osteoarthritis) Weight loss (for knee and hip osteoarthritis) Physical therapy Occupational therapy Use of a cane, heat therapy, taping Transcutaneous electrical nerve stimulation Electromagnetic therapy

Pharmacologic therapy

Acetaminophen Nonsteroidal anti-inflammatory drugs (consider prophylactic therapy to prevent gastrointestinal side effects) Cyclooxygenase-2 (COX-2) inhibitors Topical capsaicin Intra-articular steroid or hyaluronic acid injections (for osteoarthritis of the knee or hand for knee osteoarthritis; use judiciously)

typically reproduced by passive range-ofmotion maneuvers or palpation of the joint.

Atypical joint distribution in the absence of previous trauma suggests some other type of arthritis. Morning stiffness that persists for 1 hour or longer is a signal of an inflammatory process. Intense erythema, warmth, tenderness, and a tense effusion suggest an acute inflammatory illness such as infectious or microcrystalline arthritis. Systemic complaints such as weight loss, fatigue, fever, or anorexia are signs of other underlying processes, such as polymyalgia rheumatica, rheumatoid arthritis, lupus, sepsis, or malignancy.

MANAGEMENT OPTIONS

Until disease-modifying drugs become available, the best we can do for our patients is relieve their pain and help them maintain their mobility, independence, and quality of life.^{29,30,36} Nonpharmacologic and pharmacologic therapies should be used concurrently (TABLE 2).^{5,37}

Nonpharmacologic therapies for all

Nonpharmacologic therapy is an essential part of comprehensive treatment.^{38,39} Most studies of these methods focused on patients who had knee or hip osteoarthritis.³⁹ Weight loss, even if only modest, can dramatically alleviate symptoms of osteoarthritis of the knee in obese and overweight patients.⁴⁰ It should also benefit patients with osteoarthritis of the hip.

Strengthening exercise. Quadriceps weakness has been observed in patients with asymptomatic and early osteoarthritis, and it is thought to contribute to the development of painful symptoms.^{41,42} Other investigators have found that lower-extremity muscle strengthening not only eases pain, but improves gait dynamics, walking velocity, and overall function as well.^{43–45}

Aerobic exercise. Ettinger et al⁴⁶ reported exciting evidence that a 3-month program of aerobic activity significantly reduced the severity of pain in older adults who had disabling osteoarthritis of the knee. The reduction in pain was independent of any increase in quadriceps strength. The benefits of aerobic training have been documented in walking,⁴⁷ cycling, and treadmill programs.⁴⁶

Other options are joint-protection strategies (eg, use of a cane), heat treatments, patellar taping, and social support programs.⁵ Transcutaneous electrical nerve stimulation and pulsed electromagnetic therapy are two other possibilities. The efficacy of acupuncture has not yet been confirmed.⁴⁸

Osteoarthritis patients should all receive nondrug treatment

Drug therapies: Use judiciously

Pharmacologic therapies are the cornerstone of osteoarthritis management.^{29,30,36} The following drugs effectively relieve pain in osteoarthritis and are approved for its shortterm management.

Acetaminophen, in doses up to 4,000 mg/day, is the analgesic of choice for older adults.^{5,29,30} Before prescribing it as part of a long-term regimen, consider the patient's hepatic enzyme profile and function tests, as well as alcohol intake. Even modest levels of alcohol consumption can induce enzymes that favor generation of toxic acetaminophen metabolites. Detoxification of this metabolite is via a glutathione-dependent pathway, which may be impaired in malnourished patients. Deaths have been reported in alcoholic patients ingesting as little as 5 g per day. Although no direct data are available, patients with a history of three or more alcoholic drinks per day or signs of liver injury should not be given acetaminophen.

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit production of the enzyme cyclooxygenase, and thereby prevent the formation of inflammatory prostaglandins and thromboxanes.

NSAIDs are as effective as acetaminophen in relieving osteoarthritic pain, but they are significantly more likely to cause gastrointestinal bleeding.⁴⁹ An estimated 107,000 patients are hospitalized each year for NSAID-related gastrointestinal complications, and at least 16,500 arthritis patients die of NSAID-related adverse effects.⁵⁰

The risks of NSAID therapy can be ameliorated with concurrent treatment with antiulcer agents such as the prostaglandin analog misoprostol (Cytotec; also contained in Arthrotec) or a proton-pump inhibitor such as omeprazole (Losec, Prilosec) or lansoprazole (Prevacid).^{51–53} Misoprostol has been shown to reduce the number of bleeding episodes by 40%, and omeprazole appears to be effective in preventing NSAID-induced ulcers.^{51–53}

The cyclooxygenase-2 (COX-2) inhibitors celecoxib (Celebrex) and rofecoxib (Vioxx) are the newest of the NSAIDs. Small clinical trials suggested that COX-2 inhibitors are as effective as conventional NSAIDs while causing fewer ulcers, but we do not yet have any data on their long-term safety and efficacy.⁵⁴ A disadvantage of COX-2 inhibitors is expense: a 1-month supply can cost as much as \$85.⁵⁵

Topical capsaicin, applied to involved joints three or four times daily, has been shown to benefit patients who have osteoarthritis of the hand or knee.⁵⁶ This regimen can be used in addition to systemic analgesics.

Intra-articular steroids are indicated for painful osteoarthritis of the knee in patients who do not respond to or tolerate maximum therapy with other agents. Injections must be used judiciously, however, because their potential complications include bleeding, infection, and crystal-induced synovitis.

Intra-articular hyaluronic acid (Hyalgan) injections were recently approved by the Food and Drug Administration for treating symptomatic osteoarthritis of the knee. The rationale is that higher hyaluronic acid levels in the synovial fluid should replenish and preserve the extracellular matrix in the knee cartilage. A large randomized controlled trial⁵⁷ found this therapy as effective as naproxen in relieving pain and improving knee function. It is expensive, however: a series of three to five injections are required, each costing approximately \$600.⁵⁸

Dietary supplements. Glucosamine and chondroitin in combination has been touted in the lay press as a "cure" for osteoarthritis,⁵⁹ although credible evidence for this claim is lacking. In an analysis of a large pool of data published in March 2000, McAlindon et al⁶⁰ concluded that this combination has some efficacy, but its overall benefits have been exaggerated. Furthermore, the manufacture of these agents is unregulated in the United States, their long-term safety and benefits are unknown, and they are also expensive (\$50 a month).⁵

One dietary supplement that has been proven effective is S-adenosylmethionine, popularly known as SAM-e. This supplement has been studied for more than 20 years in Europe. In one of the early studies of SAM-e, in 734 patients with osteoarthritis, the supplement's efficacy in controlling pain was comparable to that of naproxen, with significantly fewer adverse effects.⁶¹ SAM-e has also been shown to be an effective antidepressant, NSAID-induced gastrointestinal toxicity can be reduced with antisecretory drugs

OSTEOARTHRITIS MCKINNEY AND LING

which could make it an attractive option for patients who have both somatic and depressive symptoms.⁶²

Many patients are using supplements and alternative therapies in their effort to alleviate the morbidity of osteoarthritis, reflecting our current lack of favorable treatment options. Physicians should inquire about the use of such nontraditional approaches in an open, unbiased manner.

Invasive procedures: If all else fails

An orthopedic consultation, and perhaps surgery, is appropriate for patients who continue to experience pain and have functional impairment despite maximal medical and nonmedical therapies. Surgery should also be considered for patients who are disabled by their condition or who have evidence of struc-

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tural instability.5

Before deciding on surgery, it is essential to carefully evaluate the patient to identify any factors that might impede his or her functional recovery and rehabilitation, such as cognitive impairment or depression.

Traditional surgical interventions include arthroscopy, osteotomy, hemiarthroplasty, and total joint arthroplasty.

Autologous chondrocyte transplantation has been shown to be effective in repairing isolated cartilage defects.⁶³ Similarly, osteochondral transplantation can be combined with osteotomy to repair osteoarthritic defects that are limited to a single compartment. However, it is unrealistic and inappropriate to use these techniques to repair the extensive damage that is typical of advanced osteoarthritis.

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The benefits of glucosamine and chondroitin appear to be exaggerated