Early Management of Osteoarthritis

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Abstract

Osteoarthritis (OA) is highly prevalent and increasing in frequency; the number of patients with OA has increased by nearly 30% over the past 10 years. The primary symptom of OA is pain. Pain and other symptoms of OA may have a profound effect on quality of life (QOL), affecting both physical function and psychological parameters. The economic costs of OA are high, and include those related to treatment, those for individuals and their families who must adapt their lives and homes to the disease, and those due to lost work productivity. These considerable humanistic and economic burdens of OA provide motivation for early identification and treatment. Early diagnosis is assisted by knowledge of risk factors. Classification criteria for OA of the hand, hip, and knee developed by the American College of Rheumatology assist in diagnosis. The European League Against Rheumatism has developed an elaborate system for diagnosis of OA of the hand. Several societies have developed therapeutic guidelines, with general overall agreement between publications. Therapy of OA is multimodal and requires a combination of pharmacologic and nonpharmacologic treatments.

(Am J Manag Care. 2010;16:S41-S47)

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The National Arthritis Data Workgroup estimates the prevalence of osteoarthritis (OA) in the United States as 26.9 million in 2005; this indicates a rise of nearly 30% over the course of the previous 10 years.[1,2] This remarkable increase in the prevalence of OA cannot be fully explained by the aging of the US population alone. However, this trend could be better understood by also considering the high and rising prevalence of obesity, an established risk factor.[3,4]

OA is associated with impaired quality of life (QOL) as well as high economic costs. Direct treatment costs include physician visits, medications, hospitalizations, surgery, and transportation costs. Indirect costs relate to comorbid conditions and lost productivity at home and work.[5-8]

Thus, for both humanistic and financial reasons, there is strong motivation to identify and treat OA as early as possible. The present article will address disease and economic burden, disease development and progression, risk factors, early identification, and early treatment of OA.

Disease Burden

Quality of Life

Patients with symptomatic OA commonly suffer reduced QOL.[9] In an Italian study in older patients (mean age, 64.6 years), individuals with OA were compared with healthy matched controls. QOL in patients experiencing recent-onset hip and knee OA symptoms was assessed by the Medical Outcomes Study Short Form-36 (SF-36) questionnaire. The authors found significant differences across all 8 QOL SF-36 domains ($P < .0001$ for all 8 domains).[7] The most dramatic losses in QOL were in physical function, role limitations because of physical problems, and pain; mental health and social function were also reduced in patients with OA.

The effects of OA on QOL are particularly pronounced in patients with more advanced disease. Greater pain and loss of physical function were common, particularly among those with a greater number of comorbidities. Greater pain and loss of physical function were also more common among women than men.[10]

Disability in OA is more than functional impairment. Emotions, such as feelings of helplessness and depression, influence function.[11] Pain itself is associated with reduced function among patients with OA.[11] Outcome is influenced by emotions, as patients with OA and

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psychological distress prior to knee arthroplasty have been shown to experience greater pain and functional impairment postoperatively compared with patients not experiencing such distress in the preoperative period.[12]

Data from focus groups in patients with OA shed further light on the pain experience. Patients with hip and knee OA describe their pain as intermittent, at times disappearing and reappearing on a daily or weekly basis, or coming and going for months at a time.[13] Pain can also be highly variable, for example, manifesting only in the morning, or consistently over the course of a week before dissipating. Patients with OA also describe experiencing pain elsewhere in the body, which they regard as integrated with, and not separable from, their joint pain—a perception that may be partly related to referred pain.[13] Pain among patients with OA is furthermore seen as entirely linked with function, with physical movements triggering pain, while pain, in turn, causes limitations in physical function.[13] To cope, patients will avoid certain movements and activities that they know will cause pain, and will engage in adaptive behavior to moderate the pain experience, such as organizing their homes to limit the need for movements or positions that are more likely to be painful.[13]

Economic Burden

The economic burden of OA is divided into direct and indirect costs, the latter much more difficult to measure. Direct costs include those related to physician visits, transportation to and from the physician's office, medication, hospitalizations, and surgery. Indirect costs result from comorbid disease and productivity loss at home and at work.[5] Moreover, financial costs are related to the degree of disease severity and symptoms. In a study of patients with hip and knee OA of varying levels of disability (based on Western Ontario and McMaster Universities osteoarthritis index [WOMAC]), a strong correlation was found between measure of self-rated disability and total costs (direct and indirect).[14] Patients with WOMAC scores of 35 to 44 had costs approximately 76% higher than those with WOMAC scores less than 15 (the reference group), whereas patients with WOMAC scores of 55 or greater had costs 342% higher than the reference group.

Estimating OA-related costs is difficult because of several variables, including differences in study populations, patient age, disease status, and insurance provider. That said, in a review of large groups of patients with OA and varying degrees of disability, the total annual costs of OA were estimated to be between $1750 and $2800. This number excluded costs for other medical expenditures that a given patient might incur.[6,8] The costs associated with more severe disease are much greater. The cost of end-stage knee and hip OA was explored using data from a national cohort of Medicare beneficiaries (ie, patients who were at least 65 years of age). Annual costs were determined to be $3800, almost double the cost in the general OA population.[15]

Direct costs include the costs of total knee arthroplasty (TKA), an increasingly common surgical procedure. The Agency for Healthcare Research and Quality calculates that more than 550,000 TKAs were performed in 2007.[16] The average cost associated with TKA, including rehabilitation, was estimated at $20,700. This increases to approximately $24,500 if revision is necessary.[15] An additional $12,600 in expenditures can be expected if perioperative complications occur. Early intervention in OA has the potential to delay surgery, and even a small reduction in the number of patients who need TKA could provide large cost savings.

Disease Development and Progression

Prior to age 40, most OA is secondary, such as OA due to trauma.[1] The incidence and prevalence of OA increases dramatically between ages 40 and 50 years, particularly among women.[1] There is a linear increase in the prevalence of OA up to age 70. The Framingham Osteoarthritis Study examined elderly patients (mean age, 70.8 years; range, 63-91 years), with a mean follow-up of approximately 8 years. After age 70, the prevalence of knee OA plateaued, as new-onset OA and the progression of disease was no more likely than in those younger than 70 years of age.[17]

The progression of disease severity in OA, although not occurring "overnight," does not require a great deal of time to manifest. A study published in 2004 followed a group of 32 patients with symptomatic knee OA to evaluate disease progression using magnetic resonance imaging procedures. These patients were followed over a 2-year period and overall reflected a significant (P <.0001) loss in global cartilage volume of 6.1% at the end of the study. Of particular interest was that movement to this figure was demonstrated statistically as early as 6 months after the start of the study, increasing at 18 and 24 months, reflecting a progression in the loss of cartilage volume over time.[18]

Anatomically, although OA invariably involves articular cartilage, it is now considered a disease of the entire joint. In addition to disruption and loss of articular cartilage, there is osteophyte formation at the joint margins, subchondral bony remodeling with cysts and sclerosis, ligamentous contractures and relaxation, muscle atrophy and spasm, and synovial inflammation.[19] Cartilage repair is inadequate because an imbalance develops between the normal anabolic and cata-

bolic processes within the cartilage. Inflammatory cytokines seem to drive this destructive imbalance, accentuated by synovial inflammation. Loss of the biomechanical properties of the articular cartilage accentuates abnormal pressures on both cartilage and subchondral bone.

Other factors that contribute to OA provide clues as to preventive therapy. For example, obesity is strongly related to OA of the knee in women, and less correlated to OA of the knee in men or OA of the hip in both sexes. Cooper et al suggest that obesity is related to both the prevalence of OA and the progression of OA.[20] Some data suggest prevalence but not progression of knee OA.[17]

Currently, the strongest predictor of progression of knee OA is malalignment. Varus malalignment, and to a lesser extent valgus malalignment, have both been shown to contribute to the development OA, whereas varus malalignment (but not valgus) has been shown to confer risk of OA progression.[21] A high body mass index (BMI), particularly one indicating obesity (BMI ≥30 kg/m^2), appears to account for additional risk of disease development and progression in patients with varus and valgus malalignment.[21]

Meniscal damage in the knee has also been shown to play a role in the development of OA. The Multicenter Osteoarthritis Study included 415 patients (aged 50-79 years) at high risk for OA but without radiographic evidence of the disease. After 30 months of follow-up, 54% of patients who later developed OA (n = 121) had meniscal damage at baseline compared with 18% who did not develop OA (P <.001).[22]

Risk Factors

As expected, increasing age is the strongest risk factor for virtually all types of OA.[1,23,24] Obesity is a risk factor common to knee, hip, and hand OA, although it appears to confer the greatest risk in knee OA, a somewhat lesser risk in hip OA, and the least risk in hand OA.[23-25] Elevated bone density is also a risk factor for hand, knee, and hip OA.[23,24,26] Women have an increased risk of OA, particularly for knee and hand OA, whereas men are more likely to experience cervical spine OA.[27] For knee OA, additional risk factors include prior knee trauma and presence of hand OA.[23] In the case of hip OA, prior hip injury and vigorous physical activity are risk factors.[25] Factors conferring greater risk of hand OA include family history, elevated bone density, menopausal status, joint laxity, previous hand injury, and work- or recreational-related activity.[24]

A systematic review of studies examining risk factors for disease *progression* in hip OA found that the strongest predictors were patient age, baseline joint space width, femoral head migration, femoral osteophytes, bony sclerosis, a Kellgren Lawrence hip grade of 3, baseline hip pain, and a Lequesne index score (an algofunctional index that measures disease activity in the hip and knee) of at least 10.[28,29]

Screening for OA

There have been several attempts to screen populations for OA. Some studies assessed the validity of telephone-administered questionnaires for screening of hip and knee OA. A 2007 study from Spain, in which more than 7500 participants were questioned by phone, found that the Knee and Hip OsteoArthritis Screening Questionnaire demonstrated a sensitivity of 87.4% and a specificity of 59.8% for hip OA, and a sensitivity of 94.5% and a specificity of 43.2% for knee OA.[30] A French study from 2008 applied a 2-step telephone-based questionnaire procedure that yielded 87% sensitivity and 92% specificity for detecting knee OA and 93% sensitivity and 93% specificity for hip OA.[31] A 2009 follow-up study from the same French group applied 3 screening strategies; the most reliable strategy produced more than 91% sensitivity for both hip and knee OA and 76% to 78% specificity.[32] This approach relied in part on a self-report diagnosis as part of the screening algorithm.

Another study of patients with end-stage knee OA found a positive correlation between self-reported physical function using WOMAC and objective functional measures, giving support to the validity of patient reports.[10] To the extent that patient reports can be relied upon to detect OA, this would represent an easier and less expensive means of identifying OA than by the use of objective measures.

The Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) grew out of World Health Organization efforts to increase understanding and research of chronic diseases.[33] Since its founding in 1981, COPCORD developed a survey protocol that has been successfully used to screen and survey people for arthritic diseases in Brazil, Kuwait, Vietnam, Shanghai, and an aboriginal community in Queensland, Australia.[33] Although the COPCORD surveys are primarily epidemiologic in content, they do serve the purpose of identifying patients with OA, among other arthritic conditions, who otherwise may not have been identified, and prioritizing resources for treatment.[33]

Diagnostic Criteria for OA

The 2009 European League Against Rheumatism (EULAR) recommendations for diagnosing knee OA state that 6 criteria—3 symptoms and 3 signs—could be used to

correctly diagnose 99% of knee OA patients when all 6 are present. The 3 symptoms are persistent knee pain, limited morning stiffness, and reduced function, and the 3 signs are crepitus, restricted movement, and bony enlargement.[34] These criteria are similar to those developed in 1986 by the American Rheumatism Association (now American College of Rheumatology [ACR]) that described OA based on clinical examination as knee pain in addition to 3 of the following 6 criteria: more than 50 years of age, less than 30 minutes of morning stiffness, crepitus, bony tenderness, no enlargement, or an absence of palpable warmth.[35] Sensitivity for these criteria is 95% with 69% specificity.

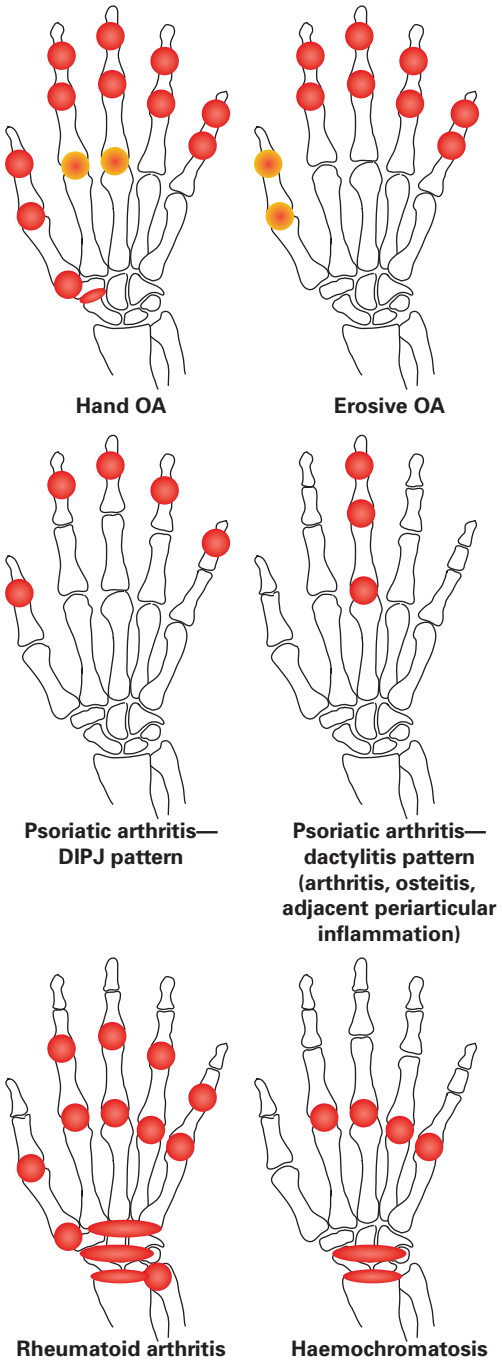
The ACR criteria for diagnosing hand OA have a sensitivity of 92% and specificity of 98%.[36] Diagnosis requires the presence of hand pain, aching, or stiffness *plus* hard tissue enlargement of at least 2 of 10 selected joints *plus* less than 3 swollen metacarpophalangeal joints *plus either* hard tissue enlargement of at least 2 distal interphalangeal joints *or* deformity of at least 1 of 10 selected joints. EULAR diagnostic recommendations for hand OA state that 88% of patients can be diagnosed when all of the following conditions are met: presence of Heberden's nodes, age more than 40 years, family history of nodes, and joint space narrowing in any finger joint.[24] Differential diagnosis between hand OA and other arthropathies can be made by assessing which joints are involved (**Figure 1**).

The ACR criteria for hip OA classification offer several methods for diagnosis. The standard approach requires the presence of hip pain and at least 2 of the following 3 criteria: radiographic evidence of femoral or acetabular osteophytes, radiographic evidence of joint space narrowing (superior, axial, or medial), and an erythrocyte sedimentation rate of <20 mm/hour. This approach yields a sensitivity of 89% and a specificity of 91%.[37]

Treating OA

Because no single therapy is adequate in OA, the major clinical guidelines for management of OA generally agree that therapy should involve a combination of nonpharmacologic and pharmacologic therapies (ie, multimodal therapy). The ACR recommendations for hip and knee OA management refer to nonpharmacologic therapies as the "cornerstone of OA management," and state that pharmacologic therapies should function as add-on therapy to nonpharmacologic treatment, the latter of which should be maintained throughout the course of the disease.[38] Revised criteria have been developed by the ACR, however, and are due to be published in early 2010.

Figure 1. Target Sites of Involvement With Hand Osteoarthritis (OA), Erosive OA, Psoriatic Arthritis, Rheumatoid Arthritis, and Hemochromatosis[24]



DIPJ indicates distal interphalangeal joint.
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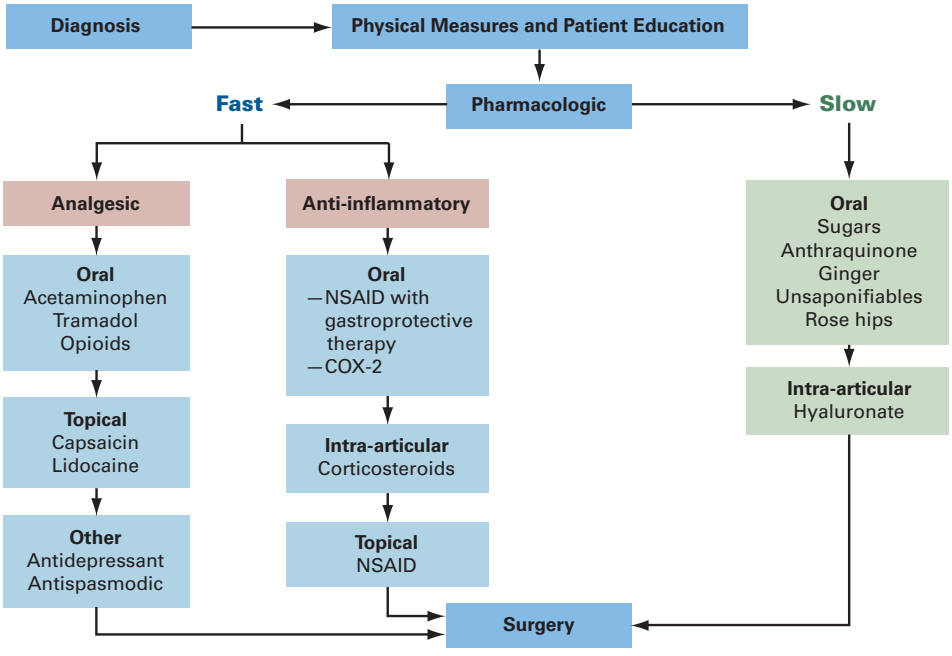
Table. American College of Rheumatology–Recommended Nonpharmacologic Therapies for Patients With Osteoarthritis

- Patient education
- Self-management programs (eg, Arthritis Foundation Self-Management Program)
- Personalized social support through telephone contact
- Weight loss (if overweight)
- Aerobic exercise programs
- Physical therapy
- Range-of-motion exercises
- Muscle-strengthening exercises
- Assistive devices for ambulation
- Patellar taping
- Appropriate footwear
- Lateral-wedged insoles (for genu varum)
- Bracing
- Occupational therapy
- Joint protection and energy conservation
- Assistive devices for activities of daily living

Figure 2. Algorithm for Present-Day Therapy of Osteoarthritis[a]



COX-2 indicates cyclooxygenase-2; NSAID, nonsteroidal anti-inflammatory drug.

[a]Once the diagnosis is confirmed, a nonpharmacologic program is initiated. If not effective, a pharmacologic program is initiated that is most often multimodal in its execution.

Nonpharmacologic Therapy

Nonpharmacologic modalities for OA are quite diverse (Table) but broadly divide into educational approaches and physical activities. Educational approaches are based on the premise that patients can be encouraged to change their lifestyle patterns—including diet and exercise—both for musculoskeletal strengthening and weight loss (where appropriate) to reduce the load on affected joints.[39] Physical exercises for hip and knee OA patients include aerobic activity, muscle strengthening, and range-of-motion exercises.[39] Consultation with a physical therapist to guide patient exercise regimens and, if necessary, advise symptomatic patients on the use of walking aids, is also recommended. Advice regarding proper footwear for patients with hip and knee OA, as well as the use of local heat for symptom relief, is further recommended. With regard to nonpharmacologic treatment for hand OA, the EULAR guidelines similarly call for education and exercise.[40] Use of local heat and, when necessary, splints, are also recommended. Identification and appropriate treatment of depression is also essential; if it is not addressed, some nonpharmacologic therapies will not be effective.

Pharmacologic Therapy

Pharmacologic treatments for OA of all kinds include, but are not limited to, analgesics (eg, acetaminophen, opioids, and capsaicin) and anti-inflammatory agents with analgesic properties (eg, nonselective nonsteroidal anti-inflammatory drugs [NSAIDs], cyclooxygenase [COX]-2 inhibitors, topical NSAIDs and, intra-articular corticosteroids) (**Figure 2**). Slower-acting pharmacologic options include intra-articular hyaluronate, as well as glucosamine sulfate and chondroitin sulfate.

The major clinical guidelines (including ACR, EULAR, Osteoarthritis Research Society International, and National Institute for Health and Clinical Excellence) are in general agreement that pharmacologic treatment of mild-to-moderate OA-related pain should begin with acetaminophen because of its efficacy and safety.[38-42] The EULAR guidelines state that if acetaminophen treatment is successful, it should be used for long-term analgesia. Topical NSAIDs and capsaicin are also recommended as alternatives to oral analgesics or in combination with them.[38-40] If acetaminophen does not provide sufficient analgesia, oral NSAIDs at their lowest effective dose are recommended, with the caution that long-term use should be avoided whenever possible because of their association with gastrointestinal side effects.[38,39] In patients with elevated gastrointestinal risk, COX-2 inhibitors or nonselective NSAIDs in combination with a proton pump inhibitor are recommended.[39,40,42] If acetaminophen, nonselective NSAIDs, and COX-2 inhibitors all prove insufficient (or intolerable), the clinical guidelines suggest the use of intra-articular modalities (corticosteroids and/or hyaluronate), glucosamine sulfate, chondroitin sulfate, or diacerein.[39,40,42] Opioids, with or without acetaminophen, may also be used should other oral analgesics fail, although stronger opioids are discouraged except when very severe pain is present and it cannot be treated with other analgesic agents.[38,39,42]

Conclusions

OA is a highly prevalent disease with potentially devastating effects on QOL, and a high economic burden in terms of both direct and indirect costs. Although our understanding of OA in its varying manifestations has expanded in recent years, clinical recommendations for diagnosing and treating OA are well established and provide clear guidance to allow for early identification and prompt appropriate therapeutic intervention. Although current therapeutic approaches for OA are primarily symptomatic in nature, there is nevertheless the potential to use available treatments to ameliorate the effects of OA on QOL and to potentially reduce the costs associated with the disease.

Acknowledgment: Editorial support for this manuscript was provided by James Borwick.

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Funding Source: Financial support for this work was provided by McNeil Consumer Healthcare.

Author Disclosure: Consultant: Endo, Ferring, Lilly, Novartis; Grants: Ferring, Novartis, Pfizer; Honoraria: Ferring, Forest, Lilly, Novartis; Lecturer: Forest.

Authorship Information: Concept and design; acquisition of data; analysis and interpretation of data; drafting of the manuscript; critical revision of the manuscript for important intellectual content; and statistical analysis.

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