

Osteoarthritis

David J Hunter, David T Felson

Osteoarthritis is the most prevalent form of arthritis, with an associated risk of mobility disability (defined as needing help walking or climbing stairs) for those with affected knees being greater than that due to any other medical condition in people aged ≥ 65 .^{w1} The societal burden (both in terms of personal suffering and use of health resources) is expected to increase with the increasing prevalence of obesity and the ageing of the community.

Osteoarthritis is a multifactorial process in which mechanical factors have a central role and is characterised by changes in structure and function of the whole joint.¹ There is no cure, and current therapeutic strategies are primarily aimed at reducing pain and improving joint function. We searched Medline for relevant articles (1966 to January 2006) and the Cochrane library (to first quarter of 2006) and consulted experts in rheumatology to produce a narrative review with an update on management for primary care doctors. We concentrated on osteoarthritis of the knee as this is associated with the greatest public health burden.

What is osteoarthritis?

Osteoarthritis is the clinical and pathological outcome of a range of disorders that results in structural and functional failure of synovial joints.² Traditionally, it has been considered a disease of articular cartilage. The current concept holds that osteoarthritis involves the entire joint organ, including the subchondral bone, menisci, ligaments, periarticular muscle, capsule, and synovium (fig 1).

Epidemiology of osteoarthritis

The reported prevalence of osteoarthritis varies according to the method used to evaluate it. In most epidemiological studies it is commonly assessed by radiography. Marked osteoarthritic damage must be present, however, to detect characteristic changes with plain radiographs, and they are therefore not sensitive diagnostic tests. About 6% of adults age ≥ 30 have frequent knee pain and radiographic osteoarthritis.

Osteoarthritis is caused by aberrant local mechanical factors acting within the context of systemic susceptibility. Systemic factors that increase the vulnerability of the joint to osteoarthritis include increasing age, female sex, and possibly nutritional deficiencies. While epidemiological studies have shown a major genetic component to risk that is probably polygenic, the genes responsible have not yet been identified.³ In people at

Summary points

Osteoarthritis is a disease of the whole joint, not just cartilage

The diagnosis of osteoarthritis is based on clinical presentation and supported by radiography

There are effective non-pharmacological and pharmacological treatments available for the management of osteoarthritis; non-pharmacological treatments should be tried first

Surgical intervention should be considered when medical treatment has failed

Boston University
Clinical
Epidemiology
Research and
Training Unit,
Boston University
School of Medicine,
Boston, MA, USA

David J Hunter
*assistant professor of
medicine*

David T Felson
*professor of medicine
and public health*

Correspondence to:
D J Hunter
djhunter@bu.edu

BMJ 2006;332:639-42

risk, local mechanical factors such as misalignment, muscle weakness, or alterations in the structural integrity of the joint environment (such as meniscal damage) facilitate the progression of the disease. Loading can also be affected by obesity and joint injury, both of which can increase the likelihood of developing osteoarthritis or experiencing its progression.

Diagnosis and investigation

The diagnosis of osteoarthritis can usually be made clinically and then confirmed by radiography. The main features that suggest the diagnosis include pain, stiffness, reduced movement, swelling, crepitus, and increased age (unusual before age 40) in the absence of systemic features (such as fever).

Typically osteoarthritis presents as joint pain. During a one year period, a quarter of people aged > 55 have an episode of persistent knee pain, of whom about one in six consults their general practitioner about it.⁴ About half of these have radiographic knee osteoarthritis. Many of the remainder also probably have disease as yet undetectable on plain radiography or another source of knee pain such as pes anserine bursitis or iliotibial band syndrome.^{w2}

The joint pain of osteoarthritis is typically described as exacerbated by activity and relieved by rest. In more advanced disease it is painful at rest and at night. The source of pain is not particularly well understood and is best framed in a biopsychosocial



References w1-w12 can be found on bmj.com.

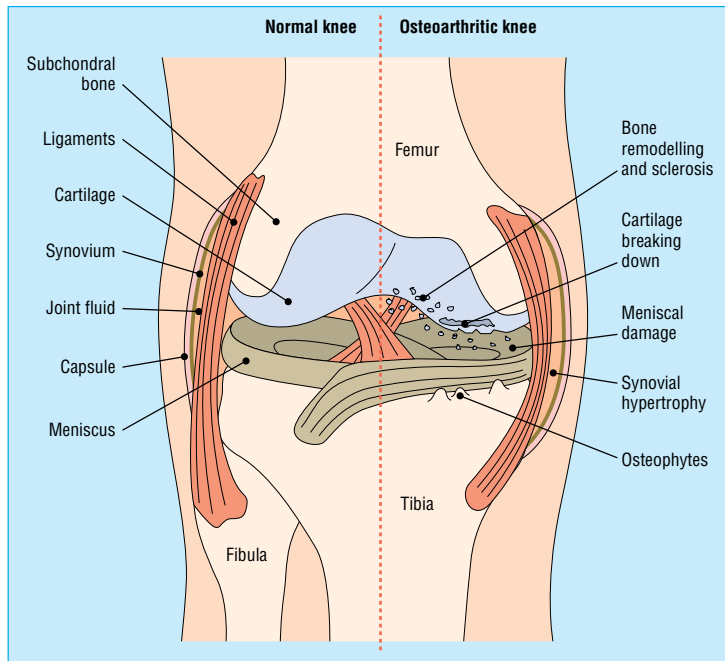


Fig 1 Pathogenic features consistent with osteoarthritis (“joint failure”)

framework.⁵ Of the local events in the joint, loss of cartilage probably does not contribute directly to pain as it is aneural. In contrast, the subchondral bone, periosteum, synovium, and joint capsule are all richly innervated and could be the source of nociceptive stimuli in osteoarthritis.

Clinical investigation

Physical examination should include an assessment of body weight, range of motion in the joint, the location of tenderness, muscle strength, and ligament stability.

Osteoarthritis can occur in any synovial joint in the body but is most common in the hands, knees, and hips. Diagnosis usually involves assessment of the range of presenting clinical features, including imaging. When disease is advanced, it is visible on plain radiographs, which show narrowing of joint space, osteophytes, and sometimes changes in the subchondral bone (fig 2).

Magnetic resonance imaging may be used to facilitate the diagnosis of other causes of knee pain that can be confused with knee osteoarthritis (such as osteochondritis dissecans and avascular necrosis). Nearly all people with knee osteoarthritis have meniscal tears, and these are not necessarily a cause of increased symptoms.⁶ The menisci should not be removed unless there are symptoms of locking or extension blockade.⁷

Do not rely on laboratory testing to establish the diagnosis. Because osteoarthritis is a non-inflammatory arthritis, laboratory findings are expected to be normal.

Clinical features of osteoarthritis

- Joint pain with activity
- Transient stiffness in the morning or after rest
- Reduced range of motion
- Joint crepitus or periarticular tenderness, or both
- Bony swelling

Because of the high prevalence of laboratory abnormalities in elderly people, such as a raised erythrocyte sedimentation rate and anaemia, however, these will commonly be detected and may prompt an unnecessary investigation. Consider obtaining a blood count, creatinine concentration, and liver function tests before starting the patient on non-steroidal anti-inflammatory drugs (NSAIDs), especially for elderly people or in those with other chronic illnesses.

Consider aspirating a joint if an effusion is present and a diagnosis other than osteoarthritis (such as septic arthritis, gout, pseudogout) is suspected. Synovial fluid from affected joints is non-inflammatory (leucocyte count < 2000/mm³, clear, viscous).

Treatment

The aims of management are:

- To educate patients about the disease and its management
- To control pain
- To improve function
- To alter the disease process and its consequences.

Osteoarthritis should be managed on an individual basis and will probably consist of a combination of treatment options. Treatment should be modified according to the response obtained. Unfortunately, nearly all treatments tested and used are drugs or surgery, or both. For example, in a recent meta-analysis, 60% of trials assessed the effect of drug treatment and 26% evaluated surgical procedures.⁸ The lack of studies evaluating rehabilitation techniques, including bracing and other self management techniques, has been labelled “research agenda bias”⁸ and is, in part, a consequence of lucrative opportunities for drug development. The toxicity and adverse event profile of the most commonly used existing treatments (such as NSAIDs, cyclo-oxygenase-2 (COX 2) inhibitors, and total joint replacement) is unfavourable compared with conservative interventions such as exercise, weight loss, braces, and orthotics.⁹

Some management guidelines are based on evidence from trials and expert consensus (see additional educational resources). The recommended



Fig 2 Frontal x ray of knee showing advanced osteoarthritis. Note the narrowing of the joint space, gas within the joint space, sclerosis, and bony spur formation along the margins of the distal femur and proximal tibia

hierarchy of management should consist of non-pharmacological treatments first, then drugs, and then, if necessary, surgery (fig 3). Too often the first step is forgotten or not emphasised sufficiently, to the patient's detriment.

The non-pharmacological approach includes:

Education—Encourage patients to participate in self management programmes (such as those conducted by the Arthritis Foundation in the United States and Arthritis Care in the United Kingdom), and provide resources for social support and instruction on coping skills.^{w3}

Weight loss—Encourage overweight patients with osteoarthritis of the hip and knee to lose weight through a combination of diet and exercise.¹⁰

Exercise increases aerobic capacity, muscle strength, and endurance and also facilitates weight loss.^{w4} All people capable of exercise should be encouraged to take part in a low impact aerobic exercise programme (walking, cycling, or swimming or other aquatic exercise). Exercises to strengthen the quadriceps lead to reductions in pain and improvements in function.

Physical therapy consists of several strategies to facilitate resolution of symptoms and improve functional deficits, including range of motion exercise, muscle strengthening, muscle stretching, and soft tissue mobilisation.

Knee braces and orthotics—For those with instability of the knee and varus misalignment, valgus bracing and orthotics shift the load away from the medial compartment and, in doing so, may provide relief of pain and improvement in function.¹¹ Though some research has shown that heel wedges can reduce medial compartment loads, there is no evidence that, used alone, they improve knee symptoms.¹² Appropriate supportive footwear should be worn by people who have osteoarthritis of the knee and hip.

Pharmacological approach

Analgesics

Paracetamol (up to 4 g/day) is the oral analgesic of choice for mild to moderate pain in osteoarthritis. NSAIDs should be added or substituted in patients who respond inadequately and are sometimes the first choice because of greater efficacy and patients' preference.^{13 w5} There are, however, certain disadvantages of routinely using NSAIDs—for example, all NSAIDs (non-selective and COX 2 selective) are associated with potential toxicity, particularly in elderly people.

COX 2 selective inhibitors have also been associated with an increased risk for cardiovascular disease. Rofecoxib, a COX 2 selective inhibitor, was recently withdrawn because of such concerns. In people with an increased gastrointestinal risk, non-selective NSAIDs plus a gastroprotective agent or a selective COX 2 inhibitor should be used.

Opioid analgesics are useful alternatives in patients in whom NSAIDs are contraindicated, ineffective, or poorly tolerated. Topical formulations of NSAIDs and capsaicin may be helpful.

Glucosamine compounds, in particular, have attracted a great deal of attention, mostly in the lay press. Possibly as a function of this publicity, osteoarthritis is the leading medical condition for which people use alternative therapies.^{w6} Glucosamine

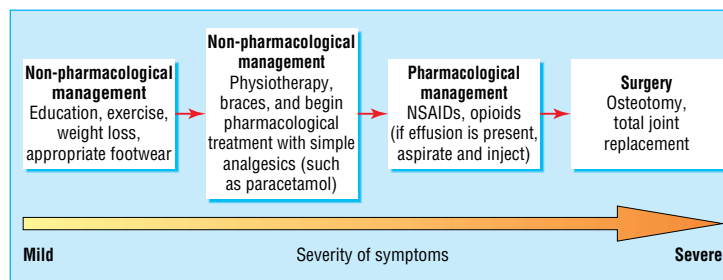


Fig 3 Stepwise algorithm for the management of patients with osteoarthritis. This is an example of a treatment algorithm that is modified according to patient's response and clinician's preference. It highlights the encompassing need to consider non-pharmacological management as first line for all patients

and chondroitin seem to have the same benefit as placebo,^{14 w7} and there is controversy over whether they also have structure modifying benefits.

Intra-articular steroids

In patients who present with acute exacerbations of pain and signs of local inflammation with joint effusion, analysis of synovial fluid is warranted to look for gout or pseudogout crystals and evidence of an inflammatory arthritis, such as rheumatoid arthritis. When not otherwise contraindicated, intra-articular corticosteroids are of short term benefit (one week) for pain and function.¹⁵

Intra-articular hyaluronan

Though the meta-analyses reviewing the efficacy of intra-articular hyaluronan are not in complete agreement, mainly because of variation in study methods, most suggest that the effect size is relatively small and the placebo response is significant.¹⁶

Surgery

Surgery should be resisted when symptoms can be managed by other treatment modalities. The typical indications for surgery are debilitating pain and major limitation of functions such as walking and daily activities or impaired ability to sleep or work.

Arthroscopic debridement and lavage

The role of arthroscopic debridement of the knee is controversial. In a well designed placebo surgery trial, improvement in symptoms could be attributed to a placebo effect.¹⁷ For a subgroup of knees with loose bodies or flaps of meniscus or cartilage that are causing mechanical symptoms, especially locking or catching

Tips for general practitioners

- Consider referral to a rheumatologist for patients who:
 - Display atypical features such as nocturnal pain, prolonged morning stiffness, or multiple affected joints and may have a different or concurrent rheumatological disease
 - Have not responded to standard treatment and may need a different combination of methods
 - May require arthrocentesis
 - May require an overall evaluation to address needs for non-drug treatment
- Consider referring patients to skilled therapists for help in initiating physical and occupational therapy and exercise programmes and in determining the need for orthotics and other devices
- Consider referring patients to an orthopaedic surgeon for joint replacement when medical treatment has failed

Additional educational resources**Medical articles from peer reviewed journals⁹**

Anonymous. Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. *Arthritis Rheumatism* 2000;43:1905-15.

Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med* 2000;133:635-46.

Zhang W, Doherty M, Arden N, Bannwarth B, Bijlsma J, Gunther KP, et al. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR standing committee for international clinical studies including therapeutics (ESCISIT). *Ann Rheum Dis* 2005;64:669-81.

Information resources for patients

National Institute of Arthritis and Musculoskeletal and Skin Diseases (<http://www.niams.nih.gov/hi/topics/arthritis/oahandout.htm>): an information source for patients and the public

Arthritis Foundation (US) (<http://www.arthritis.org/conditions/diseasecenter/OA/default.asp>): an information source for patients and the public

Arthritis Research Campaign (UK) (www.arc.org.uk): for people who want to know more about arthritis, the charity, and how to help to find a cure

American College of Rheumatology (www.rheumatology.org): for medical professionals, students, patients, and public

of the joint, however, arthroscopic removal of these unstable tissues may improve joint function and alleviate mechanical symptoms.

Osteotomy

A recent systematic review of studies comparing different types of osteotomy showed improvements in pain and function.⁸ Recovery is typically prolonged, but osteotomy may delay the need for total joint replacement for 5-10 years.¹⁸ Currently there is debate as to the relative merits of osteotomy versus unicompartmental knee replacement; this warrants further investigation in well designed clinical trials.⁹

Joint replacement

Development of modern total hip arthroplasty in the 1960s by John Charnley, a British surgeon, represents a milestone in orthopaedic surgery. Currently the most common indication for knee and hip replacement (about 85% of all cases) is osteoarthritis. Joint replacement is an irreversible intervention used in those for whom other treatments have failed.

Based on a survey of orthopaedic surgeons, indications for the procedure were severe daily pain and x ray evidence of narrowing of the joint space.¹⁹ With proper selection of patients, good to excellent results can be expected in 95%, and the survival rate of the implant is expected to be 95% at 15 years.²⁰ When overall health improvement is used to assess the cost effectiveness of total joint arthroplasty, hip and knee arthroplasty have similar results.¹⁰ Costs associated with long term medication, assistive care, and decreased work productivity may exceed the cost of arthroplasty. Total joint replacement has been shown to be cost effective compared with non-surgical treatments including NSAIDs.¹¹ Joint replacement was more cost effective in patients who had the most to gain (those with lower preoperative function). If left until functional status has declined, however, the postoperative functional status does not improve to the level achieved by those with higher preoperative function.¹²

Conclusion

We have summarised current knowledge about the epidemiology and management of osteoarthritis. Osteoarthritis is currently a major public health problem and the impact of the ageing baby boomers will further increase the burden to society. We anticipate, that with the current major research initiatives driving a better understanding of the course of symptomatic and structural change in the disease, that new treatments to retard the progress of osteoarthritis will be developed in the medium term. At present clinicians should manage patients with osteoarthritis with a combination of methods.

Contributors: DJH performed the literature search, wrote the manuscript, and is guarantor. DTF reviewed and approved the paper.

Funding: National Institutes of Health, grant No NIH AR47785.

Competing interests: None declared.

Ethical approval: Not required.

- Martin JA, Buckwalter JA. Roles of articular cartilage aging and chondrocyte senescence in the pathogenesis of osteoarthritis. *Iowa Orthop J* 2001;21:1-7.
- Nuki G. Osteoarthritis: a problem of joint failure. *Z Rheumatol* 1999;58:142-7.
- Peach CA, Carr AJ, Loughlin J. Recent advances in the genetic investigation of osteoarthritis. *Trends Mol Med* 2005;11:186-91.
- Peat G, McCarney R, Croft P. Knee pain and osteoarthritis in older adults: a review of community burden and current use of primary health care. *Ann Rheum Dis* 2001;60:91-7.
- Dieppe PA, Lohmander LS. Pathogenesis and management of pain in osteoarthritis. *Lancet* 2005;365:965-73.
- Bhattacharyya T, Gale D, Dewire P, Totterman S, Gale ME, McLaughlin S, et al. The clinical importance of meniscal tears demonstrated by magnetic resonance imaging in osteoarthritis of the knee. *J Bone Joint Surg Am* 2003;85-A:4-9.
- Englund M, Lohmander LS. Risk factors for symptomatic knee osteoarthritis fifteen to twenty-two years after meniscectomy. *Arthritis Rheum* 2004;50:2811-9.
- Tallon D, Chard J, Dieppe P. Relation between agendas of the research community and the research consumer. *Lancet* 2000;355:2037-40.
- Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: report of a task force of the standing committee for international clinical studies including therapeutic trials (ESCISIT). *Ann Rheum Dis* 2003;62:1145-55.
- Messier SP, Loeser RF, Miller GD, Morgan TM, Rejeski WJ, Sevick MA, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the arthritis, diet, and activity promotion trial. *Arthritis Rheum* 2004;50:1501-10.
- Kirkley A, Webster-Bogaert S, Litchfield R, Amendola A, MacDonald S, McCalden R, et al. The effect of bracing on varus gonarthrosis. *J Bone Joint Surg* 1999;81:539-48.
- Maillefert JF, Hudry C, Baron G, Kieffert P, Bourgeois P, Lechevalier D, et al. Laterally elevated wedged insoles in the treatment of medial knee osteoarthritis: a prospective randomized controlled study. *Osteoarthritis Cartilage* 2001;9:738-45.
- Pincus T, Swearingen C, Cummins P, Callahan LE. Preference for nonsteroidal antiinflammatory drugs versus acetaminophen and concomitant use of both types of drugs in patients with osteoarthritis. *J Rheumatol* 2000;27:1020-7.
- Towheed TE, Maxwell L, Anastassiades TP, Shea B, Houpt J, Robinson V, et al. Glucosamine therapy for treating osteoarthritis. *Cochrane Database Syst Rev* 2005;(2):CD002946.
- Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Intraarticular corticosteroid for treatment of osteoarthritis of the knee. *Cochrane Database Syst Rev* 2005;(2):CD005328.
- Lo GH, LaValley M, McAlindon T, Felson DT. Intra-articular hyaluronic acid in treatment of knee osteoarthritis: a meta-analysis. *JAMA* 2003;290:3115-21.
- Moseley JB, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. *N Engl J Med* 2002;347:81-8.
- Naudie D, Bourne RB, Rorabeck CH, Bourne TJ. The Install Award. Survivorship of the high tibial valgus osteotomy. A 10- to -22-year followup study. *Clin Orthop Relat Res* 1999;367:18-27.
- Mancuso CA, Ranawat CS, Esdaile JM, Johanson NA, Charlson ME. Indications for total hip and total knee arthroplasties. Results of orthopaedic surveys. *J Arthroplasty* 1996;11:34-46.
- Callahan CM, Drake BG, Heck DA, Dittus RS. Patient outcomes following tricompartmental total knee replacement. A meta-analysis. *JAMA* 1994;271:1349-57.

(Accepted 17 February 2006)