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Diagnosis and treatment of hip and knee osteoarthritis: A review

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Abstract

Importance: Osteoarthritis (OA) affects more than 240 million people worldwide and is the most frequent reason for activity limitation in adults. This review focuses on hip and knee OA.

Observations: OA is the most common type of arthritis. It can involve almost any joint but typically affects the hands, knees, hips and feet. It is characterized by pathologic changes in cartilage, bone, synovium, ligament, muscle, and periarticular fat, leading to joint dysfunction, pain, stiffness, functional limitation, and loss of valued activities. Risk factors include age, female sex, obesity, genetics and major joint injury. Persons with OA have more comorbidities and are more sedentary than those without OA. The reduced physical activity leads to a 20% higher age-adjusted mortality. Several physical examination findings are useful diagnostically, including bony enlargement in knee OA and pain elicited with internal hip rotation in hip OA. Radiographic indicators include marginal osteophytes and joint space narrowing. The cornerstones of OA management are prescribed exercises, weight loss if appropriate, and education—complemented by topical or oral NSAIDs, in those without contraindications. Intraarticular steroid injections provide short-term pain relief and duloxetine has demonstrated efficacy. Opiates should be avoided. Clinical trials have shown promising results for compounds that arrest structural progression (e.g. cathepsin K inhibitors, Wnt inhibitors, anabolic growth factors), or reduce OA pain (e.g. nerve growth factor inhibitors). Persons with advanced symptoms and structural damage are candidates for total joint replacement. Racial and ethnic disparities persist in the utilization and outcomes of joint replacement.

Conclusions and Relevance: Hip and knee OA are highly prevalent and disabling. Education, exercise and weight loss are cornerstones of management, complemented by NSAIDS (in those who are candidates), corticosteroid injections, and several adjunctive medications. In persons with advanced symptoms and structural damage, total joint replacement effectively relieves pain.

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Introduction:

Long characterized as a 'wear and tear' disorder, osteoarthritis (OA) is now understood to have a complex pathophysiology affecting multiple joints and joint structures, as captured by the Osteoarthritis Research Society International definition of OA: "The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation and loss of normal joint function), that can culminate in illness."[1]

Worldwide, an estimated 240 million persons have symptomatic, activity-limiting OA.[2,3] The knee and hip are two commonly affected joints and are the focus of this review. Nearly 30% of individuals greater than 45 years old have radiographic evidence of knee OA, about half of whom have knee symptoms.[4,5] The prevalence of symptomatic, radiographic hip OA is around 10%.[6,7]

The lifetime risk of symptomatic knee OA is greater in obese persons (BMI ≥ 30 kg/m^2) than nonobese persons (19.7% versus 10.9%).[8] Prior joint trauma, such as anterior cruciate ligament rupture and ankle fracture, increases risk, accounting for 12% of knee OA cases.[9] The prevalence of symptomatic, radiographic knee OA was 11.4% in women and 6.8% in men in one large cohort study[4] and 18.7% in women and 13.5% in men in another large cohort study.[5] As compared to males with OA, women have more severe radiographic findings and symptoms.[10] Older age and female sex are risk factors for hip OA as well as knee OA. In addition, congenital and acquired anatomic abnormalities (e.g. hip dysplasia) are risk factors for hip OA. Regarding race, African Americans and whites have similar prevalence of hip OA (accounting for race, sex and body mass index), while African Americans, especially women, have higher prevalence of knee OA.[5,7]

OA leads to substantial cost and mortality. Forty-three percent of the 54 million individuals in the US living with arthritis (most of whom have OA) experience arthritis-related limitations in daily activities.[11] Wage losses due to OA amount to $65 billion and direct medical costs exceed $100 billion.[2,12] Persons with knee OA spend, on average, around $15,000 dollars (discounted) over their lifetimes on direct medical costs of OA.[13] OA is commonly associated with comorbidities, which may stem from lack of physical activity, medication toxicity, and the effects of inflammatory cytokines. It has been estimated that 31% of persons with OA have ≥5 comorbid conditions.[2] Persons with hip and knee OA have ~20% excess mortality as compared with age-matched controls, due in part to lower levels of physical activity.[2]

Methods

We searched PubMed for English-language articles on the diagnosis and management of hip and knee OA, using the search terms osteoarthritis and treatment; osteoarthritis and epidemiology; osteoarthritis and diagnosis or imaging; osteoarthritis and disability or comorbidity. We reviewed these publications and relevant references in these papers. We based our conclusions on treatment efficacy primarily using the rigorous systematic

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literature syntheses and metaanalyses that support the Osteoarthritis Research Society International 2018 OA treatment guidelines.[14] The efficacy parameter in these studies is the standardized mean difference (SMD), the mean difference in improvement between active treatment and placebo, divided by the standard deviation of the difference. For questions not addressed by the metaanalyses, we provide results of pivotal trials.

Pathophysiology

OA arises from complex biological processes that include cartilage, bone, synovium, ligaments, periarticular fat, meniscus, and muscle.[15] The classic features of OA noted on radiographs include joint space narrowing due to loss of articular cartilage and meniscus, and bony changes including sclerosis of subchondral bone and osteophytes (Figure 1A). The effects of OA on cartilage, meniscus, syovium, subchondral bone and other structures can be appreciated on magnetic resonance imaging (Figure 1B).

The biomechanical environment influences the disease process. Varus alignment of the lower extremities (“bowlegged”) shifts load medially, increasing risk of medial compartment knee OA, while valgus alignment (“knocked knees”) shifts load laterally leading to lateral compartment OA. These abnormalities in alignment are risk factors for OA incidence and, more importantly, for OA progression.[16,17] Excessive loading of bone may result in bone marrow lesions, seen on magnetic resonance imaging (Figure 1B).[18] Histologically, bone marrow lesions contain microfractures with bone fragments, necrosis, fibrosis and abnormal adipocytes suggestive of focal areas of damage and remodeling due to abnormal loading.[19]

Synovitis is commonly noted in OA joints.[20] The synovitis seen in OA has a predominance of macrophages while the synovitis of rheumatoid arthritis (RA) has a predominance of T cells.[21] This reflects activation of the innate immune response in OA joints, likely due to damage of joint tissues resulting in a chronic wound type of environment.[22] OA synovitis is more focal than in RA; in the knee, it is commonly found in the suprapatellar pouch.[23] Synovitis plays a prominent role in joint destruction in RA, while its role in the progression of OA may be limited to a subset of individuals.

Many proinflammatory cytokines and growth factors have been identified in the OA joint (Figure 2.) Cytokines present at relatively high levels in OA synovial fluid include IL-6, MCP-1, VEGF, IP-10 and MIG.[24] The pro-inflammatory factors are responsible for the progressive destruction and remodeling of the joint through the stimulation of matrix-degrading enzymes, including the matrix metalloproteinases.[15,25] The growth factors that normally would stimulate matrix production and repair of joint tissues are overwhelmed by pro-inflammatory mediators. Certain growth factors including TGFβ and BMP-2 promote osteophyte formation and contribute to subchondral sclerosis. The pro-inflammatory mediators and anabolic factors are produced locally by the cells within the affected tissues including the articular chondrocytes, synovial fibroblasts and immune cells in the synovium, inflammatory cells in periarticular fat, as well as cells in bone, including osteoblasts, osteocytes, osteoclasts and bone marrow mesenchymal stem cells (Figure 3).[15,26] The cytokines are potential targets for disease modification in OA; however, currently it is not clear which cytokines are primary drivers of joint destruction, and which are involved secondarily.

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Clinical presentation

Patients with OA typically present with pain and stiffness in the affected joint(s). Stiffness is worse in the morning or on arising after prolonged sitting, and improves within 30 minutes. Pain is use-related early in the course, but can become less predictable over time. While sometimes viewed as a disease of inexorable worsening, natural history studies show that most patients report little change in symptoms over six years of observation.[27]

Assessment and Diagnosis

The clinician must distinguish symptomatic OA from other entities that can cause hip or knee pain, including inflammatory (e.g. rheumatoid and psoriatic) arthritis, infectious and crystalline (e.g. gout, pseudogout) arthritis and soft tissue lesions such as bursitis, tendonitis, and meniscal tear. The stiffness in inflammatory arthritis may last over an hour. The pain of infectious arthritis and crystalline arthritis is typically acute. Individuals with retropatellar pain may have patellofemoral OA, which can exist in isolation or in the presence of tibiofemoral OA. Because the patellofemoral joint is loaded when the knee is bent, patellofemoral OA is especially painful when patients ascend and descend stairs and get in and out of cars or a bath.[28] The syndrome of patellofemoral pain is common and often arises from malalignment of the patella in the femoral groove (due for example to asymmetric tension from the lateral and medial quadriceps) rather than from OA.

On physical exam, knee effusions are generally either absent or small and cool in persons with OA. Those with effusions may have popliteal or “Bakers” cysts, which are extensions of the synovial swelling that can be palpated in the posterior aspect of the knee. In contrast, the knee often has warm, easily palpable effusions in inflammatory, infectious and crystalline arthritis. Soft tissue lesions such as anserine bursitis and trochanteric bursitis are extra-articular and do not cause joint effusions; they are identified by local tenderness. Effusions cannot be detected on physical exam of recessed joints such as the hip. Infectious, crystalline and other inflammatory arthritides can be distinguished incisively from OA because the synovial fluid white blood cells exceed 2000 cells/cc in these disorders.

The sensitivities, specificities and likelihood ratios of various elements of the physical examination and radiographic features for hip and knee OA are shown in Table 1. Bony enlargement on physical examination is specific (95%) for knee OA, though somewhat insensitive (55%), while crepitus is sensitive (89%) though somewhat nonspecific (58%).[29] Osteophytes on knee radiographs are both sensitive (91%) and fairly specific (83%). The combination of osteophytes AND knee pain has good sensitivity (83%) and specificity (93%), with likelihood ratio of 11.9.[29] (The likelihood ratio = sensitivity / (1 – specificity). If the likelihood ratio is > 1, a positive test indicates that the post-test probability of disease is greater than the pre-test probability.

A recent review provided detailed data on the utility of physical examination maneuvers in the diagnosis of hip OA, and a video demonstration of the hip examination.[30,31] Hip internal rotation <15 degrees is moderately sensitive (66%) and specific (72%), as is limited hip adduction (80% sensitive, 81% specific).[30,32] Pain with hip internal rotation is more sensitive (82%) but less specific (39%). Osteophytes on radiographs are both sensitive (89%)

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and specific (90%). The combination of hip pain PLUS an osteophyte is also quite sensitive (89%) and specific (90%).[32]

These data suggest a presumptive diagnosis of hip or knee OA can be made on the basis of the history and physical exam. Radiographs portray the severity of structural damage and improve specificity when osteophytes or joint space narrowing are present. Pathologic features and symptoms of OA can occur before osteophytes are present on radiographs. Thus, a normal radiograph does not exclude OA. If the clinical presentation is highly suggestive of OA, clinicians should initiate management (detailed below) despite normal radiographs. Knee radiographs should be performed with the patient standing to reveal the extent of joint space narrowing of the tibiofemoral joint. For research purposes, hip and knee radiographs are typically assessed with the Kellgren-Lawrence grading system, with grade 0 representing no pathologic findings; Grade 1 questionable osteophytes; Grade 2 definite osteophytes; Grade 3, definite joint space narrowing; and Grade 4 advanced joint space narrowing.[33,34] The radiograph in Figure 1A is Kellgren-Lawrence Grade 3 and nearly K-L 4 because of the advanced medial joint space narrowing is nearly bone-on-bone.

Hip radiographs typically include an anteroposterior view and a lateral view. Weight-bearing is not necessary. The inter- and intra-rater reliabilities of hip radiographs for detecting joint space narrowing are high.[35] Hip radiographs involve greater exposure to ionizing radiation than radiographs of the chest or knee.

MRI is seldom indicated in the assessment or management of knee or hip OA. MRI detects changes in cartilage, meniscus (knee), labrum (hip), bone and synovium, providing a fuller picture of pathological involvement (Figure 1B).[36] Because of its high sensitivity[36], MRI is useful for research studies to identify early OA and document structural changes over time. In clinical care, MRI can be useful if there is suspicion of conditions such as subchondral insufficiency fracture, tumor or infection that would be treated differently and more urgently than OA.

Ultrasound can visualize joint effusion, osteophytes and other features.[37] As compared with MRI, ultrasound has sensitivity and specificity exceeding 85% for detecting osteophytes. Ultrasound is not as accurate as MRI in assessing joint space narrowing.[38] Because ultrasound is less expensive and more portable than MRI, it is used frequently in Europe and a growing number of US centers in the diagnosis of OA and assessment of progression.

Treatment

Several professional organizations have developed guidelines for OA management (Table 2). The guidelines suggest that patients with OA should be offered a core set of non-pharmacological interventions including education, weight loss (for those who are overweight), and exercises (strengthening, cardiovascular, and/or mind-body exercises such as Yoga or Tai Chi).[14,39–44]

Structured exercise interventions that typically focus on strengthening of lower extremity muscles offer improvements in pain and functional status (SMD of 0.52 for knee OA and 0.34 for hip OA; Table 3). A randomized controlled trial of a structured walking program

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showed a reduction in pain scores of 1.38 points (on a 0-10 scale) in the walking group and just 0.1 points in the control group (p=0.003).[45] Referral to a physical therapist is appropriate to initiate such a program, or to address lower extremity weakness or limitations in hip or knee range of motion. A combination of diet and exercise can result in substantial weight loss, pain relief, improvement in functional status, and reduction in inflammatory markers, as compared with exercise alone.[46]

While trials of lateral wedge shoe inserts have not been efficacious, a recent trial of an individualized external orthotic (attached below the sole) was associated with greater improvement in pain and functional status than a control orthotic.[47] This observation should be replicated before being advanced to routine use.

Non-steroidal anti-inflammatory drugs (NSAIDs) are first line pharmacologic treatment for OA. In numerous placebo-controlled trials, NSAIDs have resulted in greater pain relief than placebo, with standardized mean differences in pain and function scores of ~ 0.33 standard deviations, reflecting a moderate effect (Table 3). Many NSAIDs are available over the counter. Topical NSAIDs generally have less gastrointestinal toxicity than oral NSAIDs,[14,44] but are less useful in hip OA because the joint is recessed.

NSAIDs have important toxicities, including gastrointestinal irritation and ulceration, bleeding, and decreased renal blood flow with azotemia. Patients on anticoagulants who wish to take an NSAID should use a COX-2 inhibitor (such as celecoxib), which does not increase bleeding. Those with dyspepsia should use proton pump inhibitors and/or a COX-2 inhibitor. Patients with history of bleeding peptic ulcer are typically not prescribed NSAIDs at all. Risk factors for gastrointestinal bleeding from NSAIDs include older age, medical comorbidities, and concomitant use of corticosteroids and anticoagulants.[48] Individuals with cardiovascular or renal disease are at risk of renal toxicity; alternatives to NSAIDs should be discussed. Acetaminophen is less efficacious than NSAIDs in management of knee (SMD 0.05) and hip (SMD 0.23) OA.[49–53] It is a reasonable, safe alternative for those intolerant to NSAIDs but should not be used in persons with liver disease or risk factors such as heavy alcohol use. The Medical Letter table published in this issue of JAMA provides rich information on formulations, dosages and costs of many of the pharmacologic agents noted in this review.

Patients unable to take NSAIDs, or who do not respond, can try intra-articular corticosteroid injections, which typically relieve pain for a few weeks.[54] They are especially helpful in patients with OA of a single joint that can be injected easily, such as the knee. The hip is generally injected under imaging (fluoroscopy or ultrasound) guidance. Corticosteroid injections have no greater effect on pain than placebo after three months,[55] and may be inferior to physical therapy at one year.[56] A newer formulation of steroid injection (triamcinolone acetonide extended release) appears to have fewer systemic effects than traditional steroid injections.[57] Some studies have suggested that intraarticular steroid injections may have deleterious effects on cartilage[55,58]; the clinical meaning of these findings is not yet known.

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Injection of intra-articular hyaluronic acid (HA) products is another option for patients with persistent pain despite NSAIDs. Guidelines differ regarding recommendations of intraarticular HA (Table 2).[14,40–44] While efficacy of HA injections is similar to that of NSAIDs (SMD 0.37, Table 3), the highest quality trials showed weaker effects. Injection of growth factors, such as those found in platelet-rich plasma, and injection of stem cell preparations, are increasing in use. However, these products are non-standardized and studies of these agents are weak.

Osteoarthritis pain may be mediated in part by mechanisms in the central nervous system. Several medications have been used to address pain of central origin. Duloxetine, a serotonin-norepinephrine reuptake inhibitor, has been shown in randomized trials to result in greater pain relief than placebo in persons with knee OA (SMD 0.39).[59,60] Gabapentin may have efficacy in knee OA, but evidence is limited.[61] Opiate analgesics are used by over 20% of patients with OA, but have limited efficacy for hip and knee OA (SMD ~0.20) and considerable toxicity including constipation, falls, somnolence, respiratory depression and potential for addiction. OA treatment guidelines advise against use of stronger opiates, with conditional recommendation of tramadol, a synthetic opioid agonist that also inhibits reuptake of serotonin and norepinephrine.[44]

To date, trials of biologics to inhibit IL-1 or TNFα in knee OA failed to relieve symptoms or halt structural progression, as compared with placebo.[62–64] However, a secondary analysis of the CANTOS trial (canakinumab anti-inflammatory thrombosis outcome study) demonstrated a significant reduction in the incidence of hip and knee replacement in those receiving anti-IL-1β, with a pooled HR of 0.58 (CI 0.42-0.80, p=0.001).[65] Some areas of current investigation for disease modification that are being examined in early phase studies include Wnt inhibiton[66], intra-articular injection of an anabolic growth factor FGF-18[67] and a cathepsin K inhibitor.[68]

Patients with persistent pain and functional loss and advanced radiographic changes are candidates for total knee or hip replacement (TKR, THR). More than 700,000 primary TKRs and 330,000 primary THRs are done annually in the US, >90% for OA.[69] Ninety-day mortality is <1%, and serious complications at 90 days occur in <5%.[70–73] About 90% of recipients of THR and 80% of recipients of TKR report little to no residual pain following recovery from these procedures.[74] A randomized controlled trial of TKR vs. a rigorous physical therapy program showed that those receiving TKR improved in KOOS Pain score by 35 points (on a 0-100 scale), as compared with 17 points in those receiving PT (difference of 17 points (95% CI 10.4, 23.8).[75] Fewer than 10% of TKRs and ~20% of THRs need to be revised over 20 years.[76,77] The failure rate is higher in younger and more active recipients, those with comorbidities and those operated upon in low volume centers or by low volume surgeons.[78,79] The generally low revision rates mean that persons who receive TKR or THR in their 70's's are much more likely to die with their original implants in place than to need revision.[80] In the patient with unicompartmental knee OA, surgical options include unicondylar knee replacement and osteotomy as well as TKR. Arthroscopic debridement is not appropriate for treating OA; arthroscopic partical meniscectomy has a limited role in patients with OA and symptomatic meniscal tear, for whom nonoperative therapy was not helpful.[81–83]

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Blacks and Hispanics are ~25% less likely to receive TKR than non-Hispanic whites, even after accounting for age and socioeconomic status.[72,84] These patterns are seen for THR as well.[85,86] Proposed reasons for these disparities in utilization include less frequent offers of joint replacement to non-Whites,[87] less willingness to undergo TJR, implicit bias, and other factors.[88,89] Blacks and Hispanics also have higher risk of adverse outcomes including mortality after THR and joint infections following TKR.[90]

Several innovative interventions for OA have been introduced into clinical use but have not been evaluated with sufficient rigor to be recommended. The include geniculate artery embolization, water-cooled radiofrequency ablation and botox injections.

Evolving concepts in management of OA

OA consists of multiple phenotypes.[91] Knee OA developing after anterior cruciate ligament tear might have a mechanism distinct from OA associated with obesity. Individuals may have more than one mechanism at play, requiring multi-modal management. It will be important to determine which individuals with early OA are more likely to progress rapidly and would benefit from an intervention designed to slow disease progression. Machine learning approaches using datasets that include demographic, imaging and biomarker data are being harnessed to identify such subsets.[92]

Intensive research has identified potential targets for structure-modifying therapies,[66–68] including inhibitors of collagenases and aggrecanases that degrade cartilage, and of the cytokines and chemokines that contribute to the pro-inflammatory environment.[93] Pre-clinical evidence suggests that senescent cells in the joint contribute to OA by releasing pro-inflammatory mediators and matrix-degrading enzymes. Targeting these cells with senolytics that selectively kill senescent cells could be of value.[94] It remains unclear whether arresting progression of structural damage in OA will ultimately result in reduced pain and functional limitation.

In addition to structure modification, research in OA therapeutics has also focused on nerve growth factor (NGF), with several trials showing efficacy in pain relief with injections of anti-NGF antibodies.[95–97] However, individuals who received anti-NGF were more likely than those receiving placebo to experience rapid progression of OA requiring joint arthroplasty, especially if they were also taking NSAIDs. [98] If anti-NGF therapy is approved for OA, providers and patients will need to discuss risks and benefits carefully.

Prognosis

While some patients with OA follow a trajectory of steady increase in symptoms, others have waxing and waning pain over many years. There is also variability in the progression of joint damage. Model projections suggest that over 50% of persons in the US with symptomatic knee OA undergo TKR over their lifetimes.[13] Several factors influence the rapidity of radiographic and clinical progression including older age, reduced physical activity, the extent of cartilage damage, short term changes of cartilage damage, malalignment and more severe pain.[27,99,100]

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Conclusion

Evolving insights into pathophysiology portend a new age in OA therapeutics, with therapies that can curb structural progression and provide more potent and/or safer pain relief. The efficacy of diet and exercise interventions suggests that breakthroughs in efforts to sustain weight loss could move the field forward. Taken together these advances may change the outlook for patients with this painful, costly, disabling condition.

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Commonly Asked Questions about Osteoarthritis

How common is osteoarthritis?

Osteoarthritis (OA) is among the most frequently seen problems in adult office practice. It affects over 240 million persons worldwide and over 32 million in the US..

Who is mostly likely to get osteoarthritis?

The risk of OA rises markedly with age. OA is exceedingly rare in persons less than 30 years old, while one third of individuals over 75 have symptomatic knee OA. OA is more common in women than in men. Other important risk factors of OA include obesity, prior joint injury, genetics and malignment of joints.

How is osteoarthritis diagnosed?

The cardinal symptom of OA is pain, which is typically provoked by load bearing and relieved by rest. Stiffness occurs following inactivity. On physical examination, bony overgrowth can often be appreciated and pain can often be provoked by joint motion. Radiographs typically reveal osteophyte formation and narrowing of the joint space, the latter reflecting loss of cartilage.

Is osteoarthritis a wear and tear disease?

OA was long considered a ‘wear and tear’ disease of articular cartilage caused by prolonged use of joints, but our understanding of the disorder has advanced considerably. Pathologic changes in OA involve cartilage, bone, synovium, ligament, adipose tissue and meniscus, as well as neurologic pathways involving pain processing. These changes can arise from external mechanical loads (including obesity), joint malignment, joint injury and metabolic and genetic factors. Pathologic features include inflammation. These insights have prompted an array of therapies that may soon permit clinicians to arrest the progression of joint damage and attendant symptoms.

What treatments are used for osteoarthritis?

Management of OA begins with educating patients about its natural history, the benefits of excercise and weight loss, and strategies to reduce pain. Weight loss and physical therapy have well documented benefits in persons with knee OA. Nonsteroidal anti-inflammatory drugs, given either topically or orally, are the backbone of pharmacologic treatment. Duloxetine has proven efficacy. Intraarticular injections of corticosteroids provide temporary relief. Injection of hyaluronic acid products is also offered frequently, though evidence of benefit remains disputed. Injections of biologic therapies (such as platelet rich plasma, stem cells) have not been studied rigorously. Joint replacement is highly effective for advanced arthritis of the knee and hip.

How effective is total joint replacement? How dangerous it is? How long does the implant last?

About 90% of recipients of total hip replacement and about 80% of recipients of total knee replacement report substantial improvement in pain following surgery. Mortality following these procedures is less than 1% and serious problems such as pulmonary

embolus, myocardial infarction, pneumoinia and infection of the implant occur in less than 5%. The implants are durable with aobut 90% of knee implants and 80% of hip implants lasting 20 years. These procedures appear to be underutilized in African Americans and Hispanics with advanced OA.

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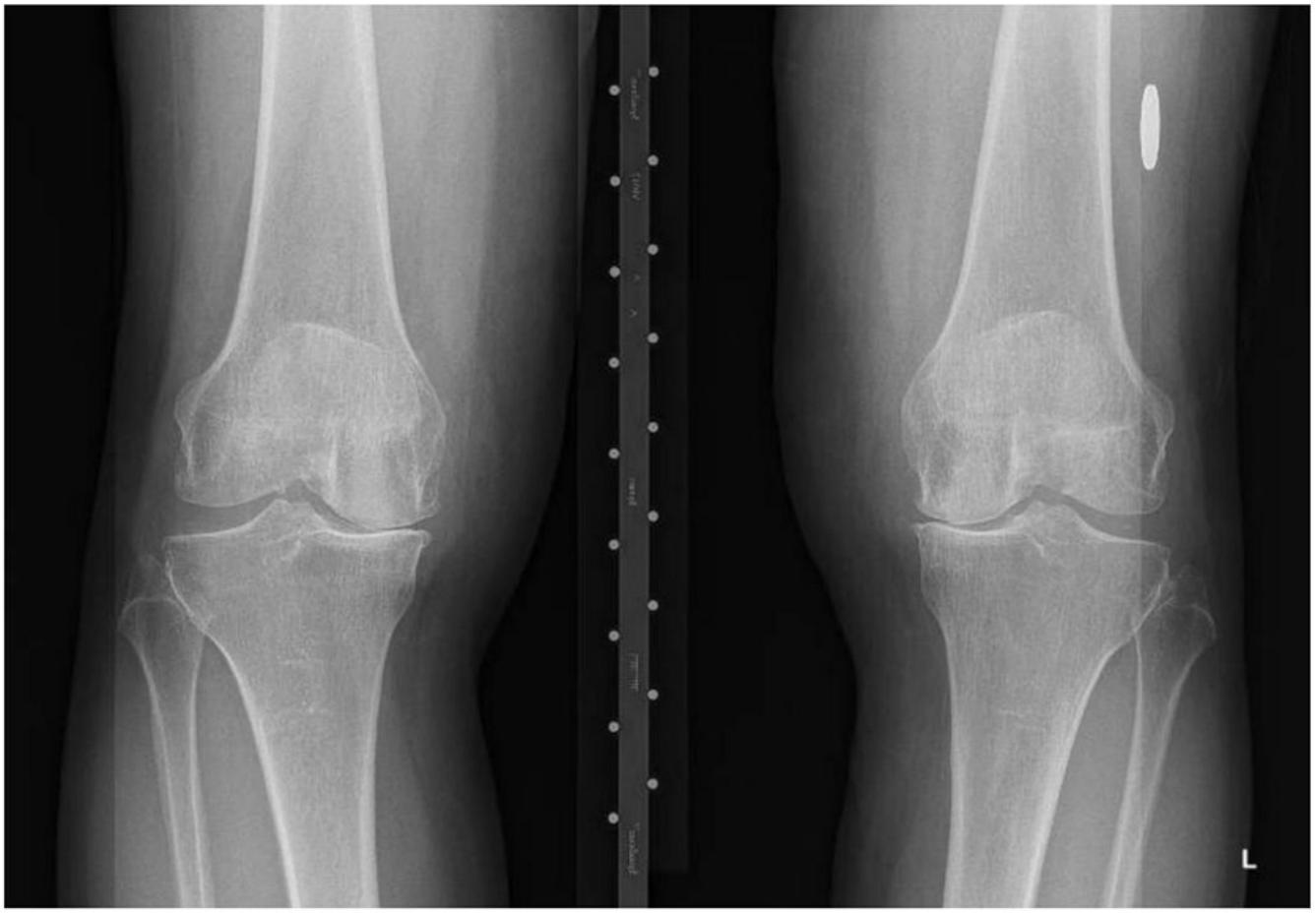

Figure 1A:
Bilateral varus deformity with medial joint space narrowing (nearly bone on bone) and osteophyte formation. Thin arrows show joint space narrowing and thick arrows medial marginal osteophytes.

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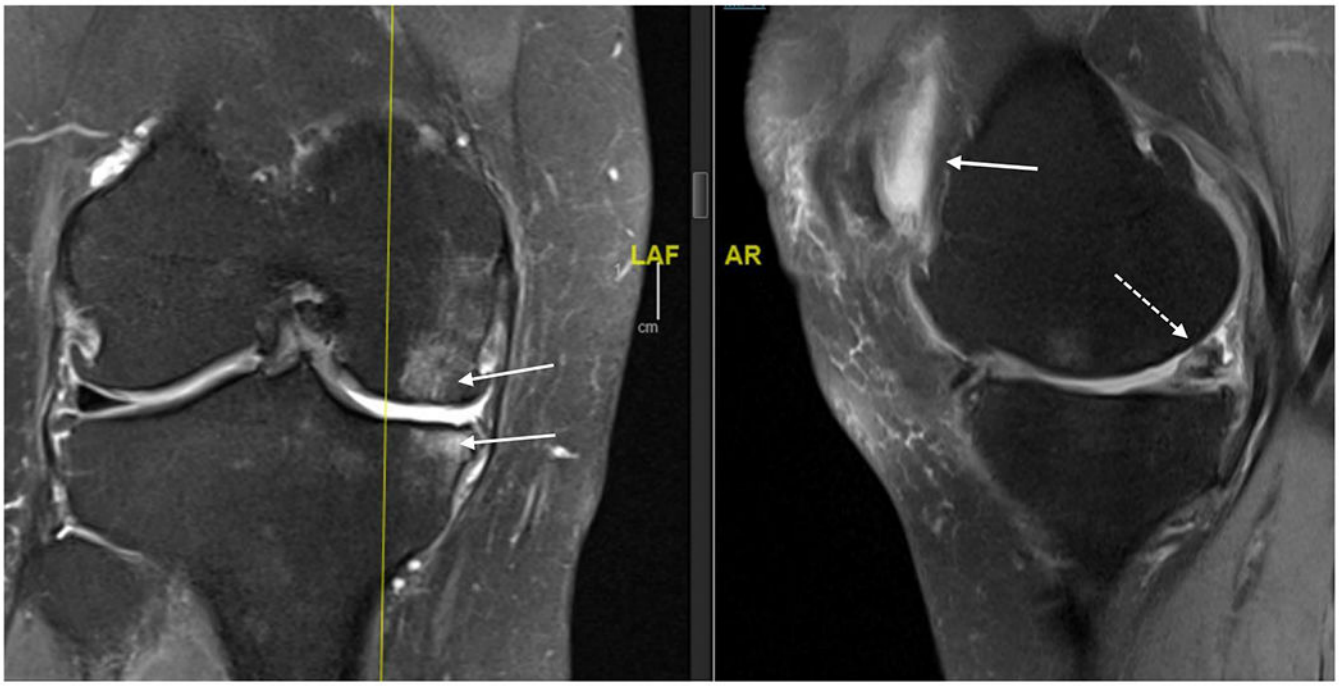

Figure 1B:
MRI (proton density, fat saturated) of right knee of 63 year old female. Coronal view on left and saggital view on right. Bone marrow lesions are identified with thin, solid white arrows on the coronal view; meniscal damage and cartilage damage are identified with dashed arrow on saggital view and retropatellar effusion as solid arrow on saggital view.

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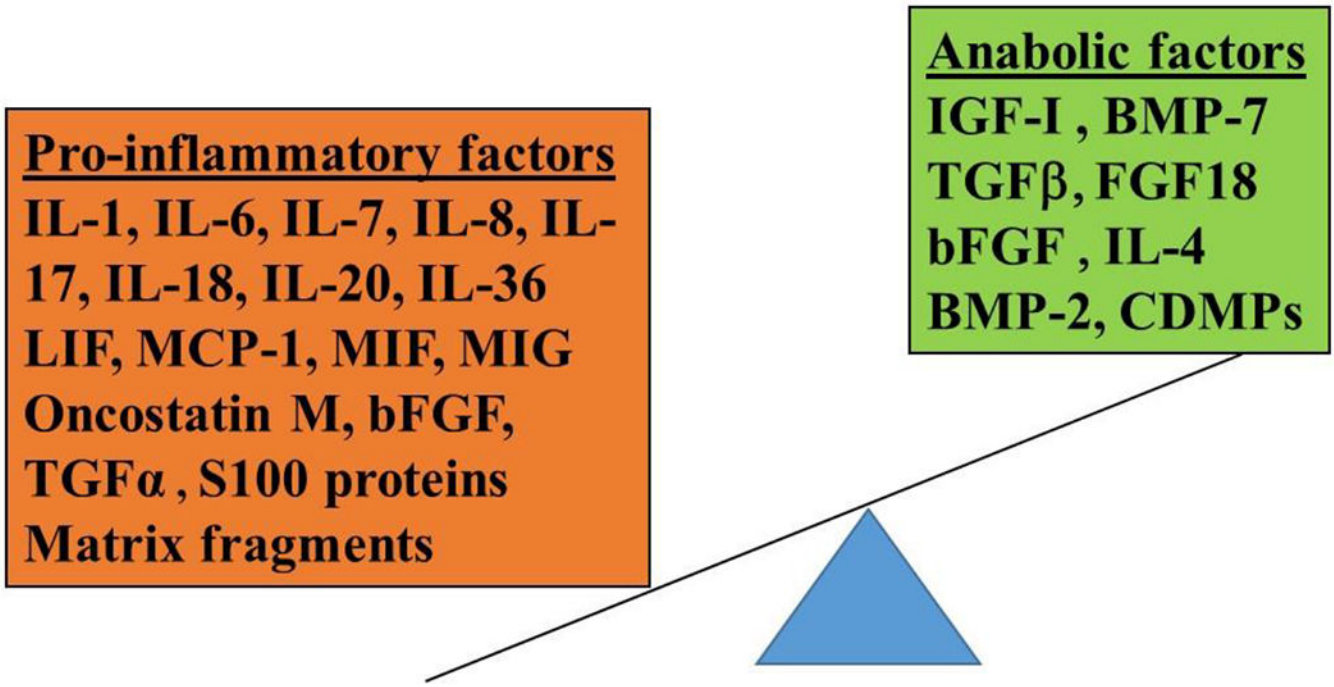

Figure 2.

Molecular Mediators of Osteoarthritis. A number of pro-inflammatory factors and anabolic factors are present in joint tissues and in the synovial fluid. Pro-inflammatory mediators contribute to joint tissue destruction in large part by stimulating production of matrix degrading enzymes, including the matrix metalloproteinases, but also through inhibition of matrix synthesis. The anabolic factors stimulate matrix production and, in some cases, also inhibit the catabolic signaling stimulated by pro-inflammatory mediators. Some factors including TGFβ and bFGF are capable of initiating either catabolic or anabolic activity depending on cell type and specific receptors expressed. TGFβ and BMP-2 can also stimulate osteophyte formation. The overall activity in the OA joint is tipped in favor of the pro-inflammatory side. (IL, interleukin; LIF, leukemia inhibitory factor; MCP, monocyte chemoattractant protein, MIF, macrophage migration inhibitory factor; MIG, monokine Induced By Interferon-Gamma; bFGF, basic fibroblast growth factor; TGF, transforming growth factor; IGF, insulin-like growth factor, BMP, bone morphogenetic protein; CDMP; cartilage-derived morphogenetic protein.)

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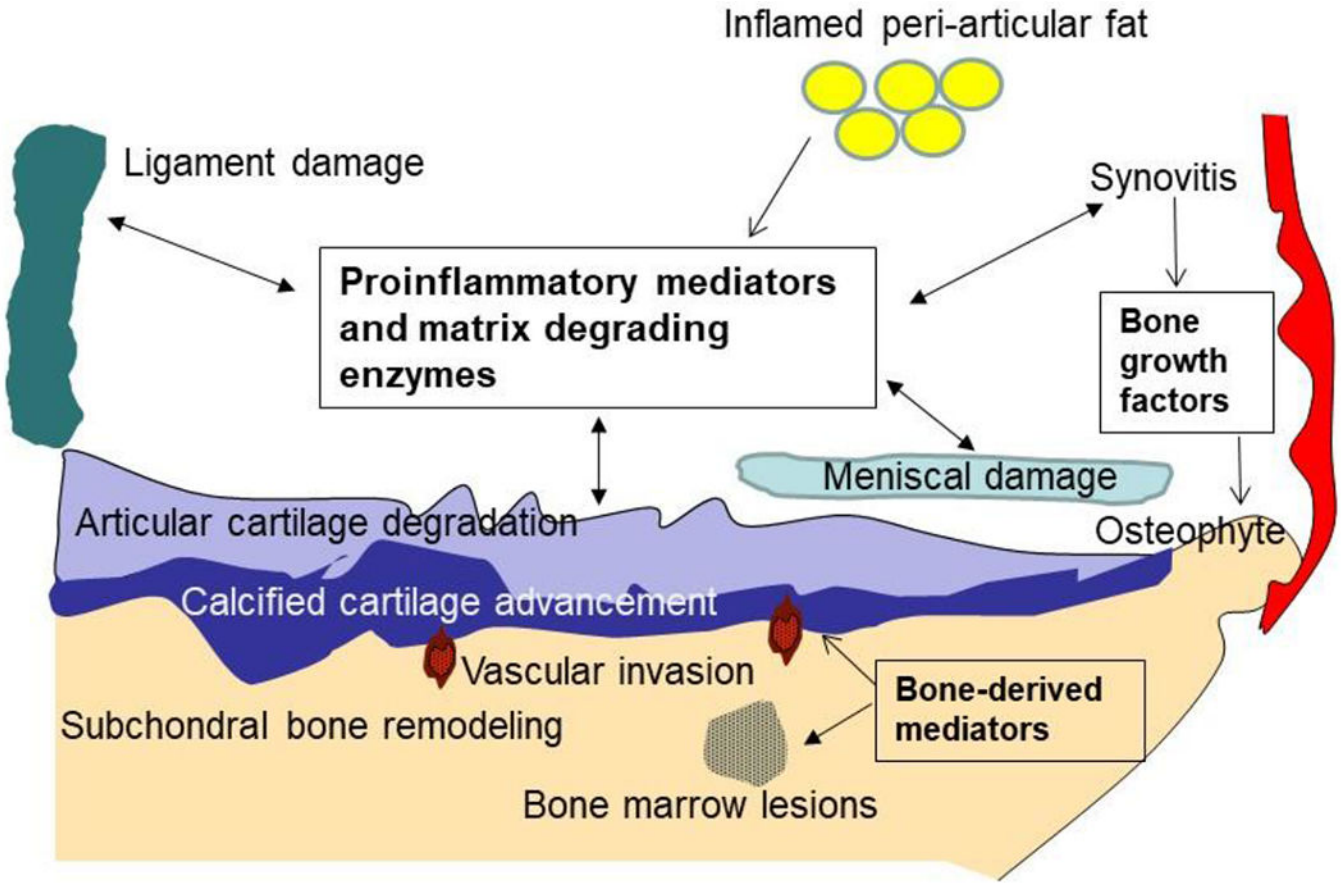

Figure 3.

Joint Tissue Involvement in Osteoarthritis. OA can involve all joint structures at some point in the disease process. Although articular cartilage degradation and loss is a central feature, changes in the neighboring bone accompany the cartilage damage. These include subchondral bone remodeling resulting in increased thickness, osteophytes, bone marrow lesions and vascular invasion into the overlying cartilage. Inflammatory cells, primarily macrophages, are present in the synovium and can also be noted in peri-articular fat. Meniscal and ligament damage is often found as well. All of these tissues are capable of producing a host of pro-inflammatory factors and matrix degrading enzymes and thus contribute to the progressive remodeling and destruction of the joint.

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Table 1:

Performance characteristics* of key physical examination and radiographic features of hip and knee OA

Feature	Sensitivity	Specificity	Likelihood Ratio
Knee			
Bony enlargement	55%	95%	11.0
Crepitus with passive motion	89%	58%	2.1
Osteophytes	91%	83%	5.4
Knee pain PLUS osteophyte	83%	93%	11.9
Hip			
Internal rotation < 15 deg	66%	72%	2.4
Pain with internal rotation	82%	39%	1.3
Decreased hip adduction	80%	81%	4.2
Femoral or acetabular osteophytes	89%	90%	8.9
Superior joint space narrowing	85%	66%	2.5
Hip pain PLUS osteophyte	89%	90%	8.9

*data from refs 30–32

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Table 2:

Summary of osteoarthritis treatment guidelines from major professional societies

Recommendation	ACR		EULAR		AAOS		OARSI	
	Knee	Hip	Knee	Hip	Knee	Hip	Knee	Hip
Non-Pharmacological Treatments								
Weight Loss recommended for individuals who are overweight or obese								
Self-Management/Education Programs which may include goal setting, skill building, education about exercise and medication								
Physical exercise Can include aerobic exercise, strengthening, neuromuscular training, isometric exercises; a combination of these exercises is advised.								
Balance Training								
Yoga								
Tai Chi								
Cognitive Behavioral Therapy								
Acupuncture								
Transcutaneous Electrical Nerve Stimulation (TENS)								
Pharmacological Treatments								
Oral NSAIDs								
Topical NSAIDs								
Acetaminophen Provides only short-term relief								
Tramadol								
Non-Tramadol Opioids								
Duloxetine								
Glucosamine or Chondroitin								
Hyaluronic Acid Injection								
Glucocorticoid Steroid Injection								
Growth Factor Injections and/or Platelet Rich Plasma								

*Recommendations taken from ACR, EULAR, AAOS, and OARSI Guidelines for the Management of OA.[14,43,44,101,102]

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LEGEND	
	Strongly recommended
	Conditionally recommended
	Conditionally recommended against
	Strongly recommended against
	Inconclusive

* EULAR does not distinguish between strong/conditional recommendations. In this table, any recommendation with a Level of Evidence of 1 (out of 4) and a level of agreement 8.5 (out of 10) or above is considered *strongly* recommended. AAOS includes 3 levels of evidence: strong, moderate, and limited. In this table, any recommendation that has moderate or limited evidence is considered *conditionally* recommended.

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Table 3:

Standardized mean differences in pain score from placebo controlled trials of 4-12 weeks duration

	Knee OA		Hip OA	
	SMD	**95% CI**	**SMD**	**95% CI**
Structured Exercise Program	0.52	0.37 – 0.68	0.34	0.19 – 0.49
Mind body programs *	0.63	0.32 – 0.95	0.35	−0.06 – 0.76
Dietary weight management ^	0.42	0.23-0.62	NT	
Acetaminophen	0.05	−0.11 – 0.21	0.23	0.13 – 0.33
Oral NSAID	0.28	0.22 – 0.35	0.33	0.24 – 0.43
Topical NSAID	0.20	0.11 – 0.29	NT	
Duloxetine	0.39	0.25 – 0.52	NT	
Opioids	0.20	0.05 – 0.35	0.21	0.10 – 0.32
IA Corticosteroids	0.41	0.21 – 0.61	1.65	0.16 – 3.47
IA Hyaluronic Acid	0.34	0.26 – 0.42	0.18	−0.13 – 0.50

* includes Tai-Chi, Yoga

^ dieteary weght management + exercise vs. exercise alone

From OARSI treatment guidelines Appendix.[14]

NT= no trials

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Table 4:

Approach to the patient with osteoarthritis

Type of therapy	Specific therapy	Comments
Non-pharmacologic therapies	Exercise Education Weight loss (if obese) Yoga or Tai Chi	-Physical therapist can provide structured exercise, especially if patient lacks confidence or knowledge -Weight loss effective but difficult to achieve and sustain -Yoga and Tai Chi beneficial, with few risks
Anti-inflammatory agents	Topical NSAIDs PO NSAIDS Cox-2 inhibitors	-Topical generally less toxic than oral -Cox-2 inhibitors if on anticoagulant or if GI toxicity
Intra-articular injections	Corticosteroids Hyaluronic acid compounds	-Injections most useful in monoarticular presentations -Steroid injections: risk of hyperglycemia, infection; benefits last a few weeks to months -Long-acting steroid compound may offer advantages -HA compounds more costly, conflicting evidence of efficacy -Stem cells, Platelet rich plasma, other growth factors not recommended because of lack of efficacy data
Additional medications	Duloxetine Opioids	-Duloxetine efficacious, though may be difficult to tolerate -Oioid side effects numerous and serious; reserve for short-term use or if no other options; tramadol preferred over stronger opioids
Surgery	Arthroscopy Total joint replacement	-Arthroscopy not indicated for OA per se; reasonable in OA and meniscal tear if no response to PT -Joint replacement effective; cost effective; underutilized in Blacks and Hispanics