Osteoarthritic Pain: A Brief Review of Nonsurgical, Surgical, and Alternative Treatment Approaches

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INTRODUCTION

Osteoarthritis (OA) is thought to be the most common chronic joint disease, with the hip, knee, and hand most commonly affected.[1] Although estimates of prevalence vary, 67% of women and 55% of men demonstrated radiographic signs of hand OA in a cohort of nearly 4000 individuals older than 55.[2] Among those older than 80, 53% of women and 33% of men had radiographic knee OA. It is well known that not all patients with radiographic OA experience pain, and the estimates of the prevalence of osteoarthritic pain are varied. One study reported that 26% of women and 13% of men experienced pain due to OA of the hand, and, in general, 17% and 10% of people experience pain due to OA of the knees and hips, respectively.[3,4] Pain from OA is known to have a significant effect on quality of life, with women more affected than men.[5] This effect is modulated negatively by depression and poverty, and positively by education and treatment of underlying disease. Along with back pain, OA accounts for the two most common causes of chronic pain in the US.[6]

The mechanisms of osteoarthritic pain can be generally divided into two pathways, peripheral and central. Early controlled studies demonstrated that pain was correlated with joint space narrowing and other structural abnormalities.[6] Later studies pointed towards synovium and bone as more likely pain generators, because cartilage lacks nerve endings. It is now understood that the intraarticular milieu of growth factors and cytokines also contributes significantly to the experience of pain. Notably, nerve growth factor (NGF), which promotes axon growth and survival of peripheral neurons, has been implicated in osteoarthritic pain. NGF decreases the firing threshold of vanilloid receptor 1, causing depolarization of nociceptive neurons. Its expression is increased in cartilage in response to mechanical stress and leads to haphazard innervation of previously aneural cartilage with peripheral sensitization to pain. Cytokines such as Tumor Necrosis Factor α (TNF–α) and Interleukin-6 (IL-6) are also upregulated in arthritis, leading to inflammation and pain.[6]

The central mechanism of osteoarthritic pain deals mainly with the spinal cord. Increased glutamate receptor sensitivity leads to the formation of closed synaptic loops, which widens the receptive field for noxious stimuli and enhances both temporal and spatial summation of pain signals. The impairment of descending inhibitory pain pathways further exacerbates pain. Finally, involvement of central pain processing pathways as well as the limbic system, which is responsible for the fear response to pain, also aggravates osteoarthritic pain.[6]

The numerous treatment options for painful OA all involve modulation of these pathways in some manner, although all the effects of some individual treatments are not fully understood.[6] The purpose of this review is to explore the traditional treatments for painful OA, including nonsurgical and procedural or surgical options, as well as nontraditional methods.

NONSURGICAL MANAGEMENT

There is a robust body of literature describing the nonsurgical management of osteoarthritic pain. In 2013, the American Academy of Orthopaedic Surgeons (AAOS) released updated guidelines for the treatment of the osteoarthritic knee (**Table 1**).[7] Current evidence demonstrates that exercise

Table 1. AAOS Consensus Guidelines for Nonsurgical Management of Knee Osteoarthritis[7]

Recommendations For	Strength
Self-directed exercise and strengthening program	Strong
NSAIDS and Tramadol	Strong
Weight loss	Moderate
Recommendations Against	**Strength**
Acupuncture	Strong
Glucosamine and chondroitin	Strong
Lateral wedge insoles	Moderate
Electrotherapy (e.g. TENS, etc.)	Inconclusive
Manual Therapy (e.g. chiropractic therapy, myofascial release)	Inconclusive
Medial compartment unloader brace	Inconclusive
Acetaminophen, opioids, pain patches	Inconclusive

is strongly associated with decreased pain and self-reported disability in patients with knee arthritis.[7] A systematic review of 13 randomized controlled trials compared aerobic exercise with resistance training and found that both modes of exercise produced significant improvements in pain and disability, with no difference between the two.[8] Patients may be encouraged to choose their preferred mode of exercise in order to maximize adherence, which is a key predictor of good outcomes.[8] Home-based and clinic-based physical therapy are equally effective at producing clinically significant improvement in pain, although previous studies have found that clinic-based therapy can lower medication utilization and increase patient satisfaction.[9]

Another common treatment measure with moderate evidence is weight loss for obese patients.[7] These patients have excess adipose and muscle tissue and their strength is generally inadequate to bear the load placed through their joints; contributing to this lack of strength is intramuscular fat deposition, which is associated with a 10-fold increase in systemic pro-inflammatory cytokines.[10] Together, these changes alter the composition of cartilage and likely contribute to osteoarthritic progression and worsening pain. Studies have demonstrated significant pain reduction in the hip, knee, ankle, spine, neck, shoulder, elbow, wrist, and hand after weight loss in obese individuals.[10] Weight-loss options include exercise, FDA-approved medications like Orlistat and Sibutramine, and bariatric surgery in the form of laparoscopic gastric banding, sleeve gastrectomy, and vertical banded gastroplasty.[10]

There is strong evidence for the use of NSAIDs (oral and topical) and tramadol for arthritic pain in the knee.[7] Topical NSAIDs such as diclofenac and ketoprofen are associated with a 50% pain reduction in 60% of OA patients, with the benefit of avoiding gastrointestinal side effects, while several placebo-controlled trials also demonstrated good efficacy of oral NSAIDs.[11] There is strong evidence in support of tramadol,[7] but a direct comparison showed that NSAIDs produced a superior analgesic effect[11] (and lack the former drug's risk of dependence).

On the other hand, there is inconclusive evidence in support of acetaminophen, opioids, pain patches, and corticosteroid injections.[7] Intra-articular steroid injections are frequently utilized for their anti-inflammatory and analgesic effects, with effects lasting anywhere from 1 week to 24 weeks.[11] Despite their widespread use, more research is necessary to validate their role in the treatment of osteoarthritic pain. Other treatments with inconclusive evidence include growth factors, platelet-rich plasma, stem-cell injections, electrotherapeutic modalities, manual therapies like joint manipulation and chiropractic therapy, and valgus-directed force braces.[7] Treatments with evidence suggesting a lack of efficacy include acupuncture, glucosamine, chondroitin sulfate, hyaluronic acid, and lateral wedge insoles.[7]

SURGICAL MANAGEMENT

Surgical management plays an important and well-established role in the treatment of osteoarthritis when non-surgical modalities have failed. Among all joints treated for osteoarthritis, hip and knee arthroplasty remain the most prevalent. There is a preponderance of data demonstrating success in reducing pain and improving function in the short- and long-term, with the most significant improvement within the first three months.[12] Certain predictive factors have been shown to affect post-surgical outcomes in surgical candidates. In a comprehensive study of patient-reported outcomes[13] after total hip (THA) and knee arthroplasty (TKA), age and gender did not have any predictive value, whereas high expectations of pain relief had a positive effect in both hip and knee patients. Interestingly, severe radiographic evidence of OA had a positive predictive effect for TKA patients, but no predictive effect for THA patients.

Resurfacing operations for hip osteoarthritis have also been studied. Unlike total hip arthroplasty, in which the femoral head is removed, resurfacing techniques for hip arthritis involve reshaping the femoral head in order to fit a metal cap. The acetabulum is trimmed to accept a metal shell with which the femoral cap articulates. This technique preserves bone compared to, and may be easier to revise than, total hip arthroplasty. It has a decreased risk of dislocation and leads to more normal walking patterns than total hip arthroplasty as well, and was initially developed for younger and more active patients with hip arthritis. However, disadvantages of hip resurfacing include a greater risk of femoral neck fracture and adverse local tissue reactions related to metal-on-metal wear and the resulting buildup of metal ions in the local tissues, followed by lymphocytic inflammation and pain.[14] Hip resurfacing remains less frequently performed when compared to total hip arthroplasty in part due to this complication profile.[14]

Unfortunately, some patients are poor candidates for arthroplasty for various reasons, including medical comorbidities. An alternative to arthroplasty in patients with hip and knee osteoarthritis is radiofrequency peripheral nerve ablation. Radiofrequency ablation (RFA) is a two-step procedure that is typically performed under light sedation, and is also used in the treatment of lumbar facet pain. In the treatment of knee arthritis, the genicular nerves are targeted for ablation. The first step is a diagnostic anesthetic injection to the peripheral extraarticular sensory branches of the genicular nerves. If this trial provides significant pain relief, then a radiofrequency probe is used to apply thermal energy to ablate the peripheral nerve endings. In a double-blind, randomized controlled trial[15] comparing radiofrequency genicular neurotomy to sham surgery, the neurotomy group showed significant improvement in both visual analog (VAS) and Oxford Knee Scores (OKS). Nearly 60% of all patients reported at least 50% pain reduction at 1, 4, and 12 weeks. Similarly, a prospective observational study[16] demonstrated

significant improvement in VAS and Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores following radiofrequency genicular neurotomy. Although the therapeutic effect declined after 6 months, 32% of patients reported at least 50% improvement in pretreatment VAS scores after 1 year.

Patients with hip osteoarthritis may also benefit from radiofrequency ablation of articular branches of the obturator nerve, femoral nerve, or sciatic nerve dependent on the location of pain. Reported techniques are similar to those for treatment of knee arthritis, with a diagnostic anesthetic injection followed by application of thermal energy to ablate the targeted nerve endings. A recent systematic review reported pain relief ranging from 30% to 90% from baseline scores, although the durability of this effect remains unclear, with some studies reporting recurrence of pain within 1–2 years.[17]

Complications following radiofrequency ablation are rare. Kumar et al. described loss of cutaneous sensation in the distribution of the lateral femoral cutaneous nerve in a small number of patients treated with RF ablation for hip arthritis.[17] In a recently published systematic review of RF ablation for knee arthritis, Jamison et al. discovered no major adverse complications reported in the literature, although they refer to unpublished cases of skin burns in some patients with nerve branches in near proximity to the skin.[18] Strand et al. recently published a case report of medial thigh hematoma after RF ablation for knee arthritis.[19] Longer-term follow-up studies are required to better characterize the role of nerve ablation in treating pain associated with OA.

Arthroscopy is an alternative to arthroplasty and nerve ablation, especially for the treatment of knee osteoarthritic pain. The mechanism of pain improvement after arthroscopy of the knee is thought to be related to lavage as well as removal of debris. Lavage of the knee decreases the concentration of inflammatory cytokines and degradative enzymes in the synovial fluid, leading to diminished inflammation of the cartilage and surrounding synovium. Removal of tissue debris, inflamed synovium, and damaged cartilage and meniscus also removes sources of synovial and cartilage inflammation, which is thought to improve pain.[20] Although arthroscopy was previously used more widely in the treatment of OA, it has received more scrutiny in recent years. A review of arthroscopic management of osteoarthritis found that it tends to benefit young, active patients with mild to moderate arthritic changes without deformity.[21] Thus, arthroscopy may play a role in the management of early OA in select patients. However, a paucity of high-quality studies makes it difficult to produce thorough guidelines with respect to the treatment of OA with arthroscopy.

ALTERNATIVE TREATMENTS

A number of alternative therapies have tried to address osteoarthritic pain (**Table 2**). These include practices that have a rich tradition in other cultures, like acupuncture and yoga, as well as nontraditional pharmacological interventions. OA frequently leads to a sedentary lifestyle, which further exacerbates joint stiffening, pain, and muscle weakness.[22]

Table 2. Alternative Therapies for Treatment of Symptomatic Knee Osteoarthritis[7]

Alternative Therapy	AAOS Recommendation	Rationale
Yoga (Hatha or Chair)	For; Strong	Improved WOMAC and SF-36 Physical Functioning and Bodily Pain Subscales in yoga + physical therapy treatment group when compared to physical therapy alone
Acupuncture	Against; Strong	Based on evidence of lack of efficacy rather than evidence of harm
Glucosamine/ Chondroitin	Against; Strong	Based on evidence of lack of efficacy rather than evidence of harm

Hatha yoga (HA) is a form of yoga that reduces pain and stiffness in OA patients by realigning the skeleton, strengthening muscles around joints, and stretching out joints.[23] For patients unable to perform HA, chair yoga is an option. A significant reduction in pain was appreciated in patients with lower extremity OA who performed yoga for 3 months.[22] Regardless of the specific form, yoga has been shown to increase sleep quality and decrease sleep disturbances in patients with OA.[22] Coupled with breathing and relaxation, yoga can help patients cope with the reactive aspects of chronic pain.[23]

Similarly, acupuncture has been shown in some studies to help patients with OA pain. The proposed mechanism is that small diameter muscular afferent nerves are stimulated to send impulses to the spinal cord to release endorphins and monoamines involved in the pain messaging pathway.[24] Studies examining the immediate effects of electroacupuncture and manual acupuncture on pain and mobility in patients with knee OA have demonstrated a significant reduction in pain intensity and time-to-run test scores in both groups compared to controls.[25] Acupuncture has consistently been shown to be an effective treatment modality for pain and dysfunction associated with knee OA.[24]

Alternative pharmacologic interventions, such as glucosamine, chondroitin, capsaicin, and cannabidiol, are gaining popularity among patients with painful OA. While both glucosamine and chondroitin are over-the-counter supplements in the United States, they are registered as medications in Europe.[26] In-vitro models suggest that chondroitin sulfate and glucosamine sulfate exert a beneficial effect on the metabolism of synovial joint cells, including chondrocytes, synoviocytes, and cells from subchondral bone.[26] They increase the expression of type II collagen and stimulate proteoglycan synthesis in human articular chondrocytes while

reducing the production of pro-inflammatory cytokines and proteases.[26] Studies using MRI have demonstrated that these supplements reduce the loss of cartilage volume and associated joint space narrowing.[26] The Osteoarthritis Research Society International (OARSI) considers glucosamine and chondroitin to be low-risk medications with a moderate to high effect. There is a favorable risk/benefit ratio for the treatment of older patients with OA and co-morbidities, in contrast to the long-term administration of drugs like NSAIDs and acetaminophen.[26] It should be noted, however, that the 2013 AAOS consensus guidelines for the treatment of knee osteoarthritis recommend against the use of acupuncture or glucosamine/chondroitin due to lack of efficacy, although they do not conclude that either treatment modality is harmful.

Capsaicin, a highly lipid-soluble compound available in topical formulations, is thought to help alleviate osteoarthritic pain through the "defunctionalization" of nociceptive nerve fibers, a process that involves temporary loss of membrane potential, inability to transport neurotrophic factors, and a reversible retraction of epidermal and dermal nerve fiber terminals. According to the 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee,[27] capsaicin is conditionally recommended for the treatment of osteoarthritic knee pain due to low effect sizes in the available literature, and conditionally recommended against in terms of its use in osteoarthritic hand pain due to lack of available literature in hand OA.

Finally, the effects of cannabidiol on the treatment of osteoarthritic pain are poorly studied. Cannabidiol is the most abundant non-psychoactive compound in extracts of the *Cannabis sativa* plant, and various cannabinoids have been shown to have anti-inflammatory, anti-tumorigenic, and analgesic effects through action on a variety of receptors, but mainly cannabinoid receptors 1 and 2 (CB1, CB2). In animal models cannabinoids have shown to modulate OA pain manifestations and stress-related responses, and CB2 receptor activation has been shown to attenuate the development of pain and sensitization in an OA rat model.[28,29] However, the only known study to assess the effects of cannabidiol on human articular chondrocytes demonstrated that exposure to high levels of cannabidiol induces apoptosis in chondrocytes in-vitro.[28] No clinical trials exist studying the effects of cannabidiol in the treatment of osteoarthritis in humans.

CONCLUSION

Osteoarthritic pain is relatively common and is mediated by both peripheral and central pain mechanisms. Treatment options for osteoarthritic pain are numerous and include nonsurgical treatments such as in-home or clinic-based physical therapy, NSAIDs, and tramadol. Joint arthroplasty for appropriate patients is a durable and successful surgical treatment option. Other surgical options such as radiofrequency genicular nerve ablation and arthroscopy have also shown to be beneficial in certain patient populations. Finally, alternative treatment options such as yoga, acupuncture, and over-the-counter supplements like chondroitin and glucosamine have also shown benefits in the treatment of OA pain.

Although the literature surrounding arthroplasty and traditional nonsurgical treatment options is robust and continues to grow, the research surrounding alternative treatments is relatively sparse. Future research is needed in this field as many patients with either cultural preferences or those with contraindications to traditional approaches could benefit from alternative treatments. Osteoarthritis (OA) is a common cause of disability and pain. A patient-centered approach to the treatment of osteoarthritis is necessary as there are myriad nonoperative and operative treatment options for osteoarthritic pain.

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