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PAIN ASPECTS OF ARTHRITIS (ALLISON BAILEY, SECTION EDITOR)

Effects of Exercise and Physical Activity on Knee Osteoarthritis

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Abstract Exercise is one of the most discussed and controversial nonpharmacologic management strategies for osteoarthritis (OA) of the knee. Health care providers and patients share varied and often pseudoscientific beliefs regarding the effects of exercise on knee OA formulated on outdated notions of the etiology, pathophysiology, and progression of the condition. Based on the contemporary literature, regular light to moderate physical activity has both preventive and therapeutic benefits for individuals with knee OA. Exercise regimens with strong evidence of benefit include those that focus on aerobic/cardiovascular conditioning and lower extremity strength training. Health care providers should confidently incorporate exercise recommendations into clinical management and offer patients evidence-based and individually tailored exercise prescriptions to help manage the painful and often disabling symptoms of this condition.

Keywords Pain · Arthritis · Knee osteoarthritis · Exercise · Physical activity · Quadriceps strength · Weight management · Weight loss · Diet · Traumatic injury · Cycling · Aerobics · Cardiovascular exercise · Therapy

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Introduction

Osteoarthritis (OA) of the knee is one of the top five causes of disability among noninstitutionalized adults in the United States and is commonly encountered in the clinical setting [1]. About 12% of Americans over the age of 60 years experience symptomatic knee OA, and the financial, physiologic, emotional, and functional effects of this ailment are varied and significant [2].

Individuals over the age of 65 years are more commonly affected, and due to a decline in fertility and an increase in life expectancy over the past century, the number of persons over 65 years of age is expected to increase from about 35 million in 2000 to an estimated 71 million in 2030, while the number of persons over 80 years of age is expected to increase from 9.3 million in 2000 to 19.5 million in 2030 [3]. This "graying" of America will result in an increase in the prevalence of OA of the knee and other primary joints.

Clinicians should be prepared to address patient concerns regarding the appropriate pharmacologic and nonpharmacologic management of knee OA. One of the most discussed and controversial nonpharmacologic management strategies for OA is exercise. "Should I exercise?" and "Will exercise make my arthritis worse?" are questions clinicians frequently are asked. Traditional responses promote the theory that knee OA is a "wear and tear" phenomenon. According to this model, increased physical activity, by definition, will accelerate the degenerative process. A contemporary understanding of the pathophysiology of knee OA and the associated epidemiology suggest this proverbial understanding is incomplete, if not inaccurate.

Definition of Osteoarthritis

OA is a chronic and often progressive joint disease characterized by focal loss of articular cartilage and marginal bone formation, resulting in joint space narrowing and osteophytosis [4]. The clinical syndrome of OA is diagnosed when symptoms and signs of the disease are present in the setting of these classic radiological findings.

Scope of the Problem

OA affects 13.9% of adults aged 25 years and older and 33.6% (12.4 million) of those over 65 years; an estimated 26.9 million adults in the United States in 2005, an increase from 21 million in 1990 [5]. It is now estimated that half of all adults will develop symptomatic OA in his or her lifetime, and this number will increase to two of three obese adults [6•]. With more than 34% of adults aged 20 years and over in the United States meeting the criteria for overweight, 33.8% meeting the criteria for obesity, and 5.7% categorized as extremely obese, the rates of knee OA are predicted to climb exponentially [7•].

The financial cost of OA care is estimated at $2600 per capita out-of-pocket expenses [8] and $5700 total per person costs [9], with a total annual national cost estimate of $15.5–$28.6 billion per year. This includes 11.1 million outpatient visits and 632,000 joint replacements annually [10]. Job-related OA costs are estimated between $3.4 and $13.2 billion per year [11], making job-related OA more costly than asthma and pulmonary diseases, and also more than renal and neurologic diseases combined. According to some researchers, these estimates are low and total annual OA costs may presently exceed $89.1 billion [12].

In addition to financial costs, OA has a powerful negative effect on vocational and recreational function and quality of life (QOL). OA of the knee is one of five leading causes of disability among noninstitutionalized adults [13]. Some degree of mobility limitation is experienced by 80% of patients with OA; 25% cannot perform major activities of daily living (ADLs); 11% of adults with knee OA need help with personal care; and 14% require help with routine needs. OA ranks third as a cause of years lived with disability, above ischemic heart disease, diabetes, and rheumatoid arthritis [14].

Etiology and Pathogenesis: Moving Beyond the "Wear & Tear" Hypothesis

The pathophysiology of OA is incompletely understood. Although abnormal biomechanical stressors on the articular cartilage clearly play a role, this is now recognized to be at best a partial explanation for the disease. Current science suggests that a host of factors induce biochemical changes within the articular cartilage leading to altered chondrocyte metabolism and imbalance between cartilage synthesis and degradation [15, 16]. Genetics likely influence individual susceptibility to these etiological factors.

Although the initial pathology appears to be within the cartilage matrix, all joint structures are involved in advanced disease, including cellular adaptations in the subchondral bone, accompanied by inflammation, thickening, and tightening of the joint capsule and eventual capsular stretching with resultant ligamentous laxity, joint instability, and periarticular muscle dysfunction and imbalance. This in turn results in a cyclic pattern of pain and accelerated degeneration unless the cycle is interrupted.

The pain due to OA is significant and for many patients severely impairs ADLs and QOL. Pain generated by progressive OA is now thought to be due in part to angiogenesis associated with the disease, as new blood vessel formation coincides with the growth of peripheral nerves [17]. Imbalanced chondrocyte homeostasis, progressive soft tissue dysfunction, and eventual bony erosion are promoted by a rich proinflammatory chemical environment [16].

Diagnosis: Signs, Symptoms, and Radiographic Findings

The diagnosis of OA is classically determined by a combination of both clinical examination findings and radiographic evidence (Table 1). The astute health care provider must use these findings to differentiate OA pain and dysfunction from other common causes of knee pain, such as meniscal tears, patellofemoral syndrome, anserine bursitis, rheumatoid arthritis, gouty flairs, and ligamentous sprains among others.

Symptoms and signs patients may present with include joint pain, stiffness, crepitus, restricted range of motion, effusions, bony hypertrophy, joint malalignment (such as a change in varus/valgus knee contour), surrounding muscle weakness, disordered gait, and, eventually, functional limitations and disability.

Radiographs may demonstrate joint space narrowing as native cartilage is degraded. The medial joint space is more commonly affected, resulting in a tendency toward progressive varus deformity in advanced OA. Reactive osteophytes also may be seen, and some studies suggest their presence is more closely correlated with knee pain than joint space narrowing [18]. As the joint space narrows, increased forces will be distributed across the bone surface, causing bony reactions. The reactive bone increases calcium deposition, and eventually, subchondral sclerosis may be visible on plain films.

Table 1 Diagnostic criteria for knee osteoarthritis

Clinical and laboratory	Clinical and radiographic	Clinical
Knee pain	Knee pain	Knee pain
+ at least 5 of 9:	+ at least 1 of 3:	+ at least 3 of 6:
–Age>50 y	–Age>50 y	–Age>50 y
–Stiffness <30 min	–Stiffness <30 min	–Stiffness <30 min
–Crepitus	–Crepitus	–Crepitus
–Bony tenderness	+ Osteophytes	–Bony tenderness
–Bony enlargement		–Bony enlargement
–No palpable warmth		–No palpable warmth
–ESR <40 mm/h		
–RF <1:40		
–SF OA		
92% sensitive	91% sensitive	95% sensitive
75% specific	86% specific	69% specific

ESR erythrocyte sedimentation rate; *RF*—rheumatic factor; *SF OA* synovial fluid signs of osteoarthritis (clear, viscous, or white blood cell count <2000/mm^3).

(*From* Altman et al. [87], *with permission*.)

Unraveling the Role of Exercise

When diagnosis is determined and patients are seeking advice, health care providers are called on to offer evidence-based recommendations for both pharmacologic and nonpharmacologic management. Although the American College of Rheumatology includes exercise in its recommendations for the nonpharmacological management of knee OA [19], both practitioners and patients have mixed beliefs on the effects of physical activity on knee OA development, prevention, progression, and symptom management [20].

Knee cartilage has impressive tensile strength. By some estimates, the average 48-year-old knee may withstand about 15.4 MPa before cartilage fatigue [21]. Average forces in knee cartilage during running, jumping, and throwing are around 4–9 MPa [22]. However, the influence on cartilage experiencing chronic repetitive loading or extreme torsional strains is less well identified. Unhealthy, previously injured cartilage or cartilage in a malaligned or excessively lax or taut knee joint also may experience increased pressures while having less adaptability.

Mature cartilage cells receive nourishment via the diffusion of substances through synovial fluid, a process that is enhanced by physical activity [23]. Cartilage loading in the form of regular moderate exercise enhances glycosaminoglycan content in knee cartilage of both humans and other mammals [24–27]. The cartilaginous matrix adapts to loading stresses by enhanced crosslinking analogous to osteoblastic activity in bones under moderate duress. What is not known is if a genetically predetermined "sweet spot" exists above which injury outweighs benefit [28].

Traumatic Beginnings

Trauma to the knee may disrupt the fine balance of chondral integrity, impairing adaptability to stress and increasing the risk for progressive degeneration. Studies show that radiographic OA is significantly increased after all knee injuries compared with the uninjured joint of the same patient [29]. The exact increase in OA risk after knee injury has become less clear over the past decade. Gillquist and Messner's 1999 study [29] suggested that "isolated meniscal tears and subsequent repair, or partial or total ruptures of the ACL [anterior cruciate ligament] without major concomitant injuries, increased the risk of knee OA 10-fold" (15–20% incidence of knee OA) compared with an age-matched, uninjured population (1–2%). More recent reviews suggest these numbers may be inflated. In a 2009 systematic review, Øiestad et al. [30•] reported the prevalence of knee OA for patients with isolated ACL injury was 0–13%; for patients with ACL and additional meniscal injury, the prevalence varied between 21% and 48% more than 10 years postinjury. Several studies looking at the incidence of knee OA in competitive athletes suggest that 50% of female soccer players and 41–78% of male soccer players who sustain ACL injuries will develop knee OA over the next 15 years [31, 32].

Although exact risk increase is still hotly debated, it is clear that altering the normal cartilage matrix through traumatic injury or surgical intervention will increase the risk of knee OA. For this reason, sports with increased risk of traumatic knee injury, such as American football, soccer, and ice hockey, have increased rates of knee OA as compared to the average population [33–35]. However, it is the increased incidence of knee injury in the athletic population rather than participation in physical activity itself that appears to increase the risk of knee OA [36].

Everything in Moderation

The overwhelming majority of literature supports the conclusion that there is no increased risk of knee OA with regular light or moderate physical activity [37–39]. Large epidemiologic studies and ongoing prospective trials both confirm these findings. In fact, moderate recreational physical activity may be associated with a decreased risk of knee OA [40]. Because most health benefits (including improved cardiovascular health, reduced diabetes and

neoplastic risk, improved mood and self-efficacy, and reduced disability) can be achieved through moderate levels of physical activity, health care providers have clear mandates to encourage physical activity. They should not defer recommending exercise due to concern that the prescription will result in increased knee OA.

Skeptics may argue that the increased incidence of knee osteophytes in regular exercisers as compared to controls is evidence that physical activity increases risk of knee OA [41]. However, the presence of knee osteophytes does not correlate well with pain or dysfunction and cannot be considered interchangeable terminology with symptomatic knee OA. Furthermore, prospective studies show a negative association between increased weight-bearing exercise and changes in the rate of spur development in both mature men and women [42]. Even in mature long-distance runners followed over 20 years, there is no increased risk of knee OA as compared to age-matched control patients [43••].

Exercise as Treatment of Knee Osteoarthritis

The American College of Sports Medicine categorizes exercise into several forms, including stretching/range of motion, aerobic/endurance, resistance/strength training, and balance/proprioceptive exercise, with frequent areas of overlap [44]. Patients with knee OA may be hesitant to participate in these health-engendering activities for fear of worsening their OA. Based on the available evidence, they should do just the opposite. Participation in regular physical activity has been shown to provide significant benefits in the treatment of knee OA, while failure to remain active and disuse of the affected limb may accelerate impaired joint mechanics and potentially result in articular cartilage softening and matrix dysfunction, leading to more rapid cartilage degeneration [45•].

Immobility and disuse also result in a loss of flexibility at or around the knee joint, including the overlying soft tissues, and can lead to impaired gait mechanics, unequal distribution of force across the proximal and distal joints, and the associated clinical findings of pain and dysfunction [46, 47]. Alteration in the function of soft tissue structures has been shown to independently generate pain in the affected limb. In view of this, it could be theorized that improving range of motion of the joint and the overlying muscles and soft tissue structures should improve gait mechanics, joint movement, fascial tension, and tissue circulation, as well as reduce sensory nerve sensitivity [48, 49].

Aerobic or cardiovascular exercise has been shown to improve the symptoms of knee OA and physical function. Even simple aerobic walking can reduce pain and improve function [50–52]. In Ettinger et al.'s classic Fitness Arthritis and Seniors Trial (FAST) [53], 439 patients (age>60 y) were randomly assigned to aerobic versus resistance exercise versus a health education control group. Participants in the aerobic exercise group reduced their mean score on the physical disability questionnaire by 10%, demonstrated a 12% lower score on the knee pain questionnaire, and performed better on functional tasks, including the 6-minute walk test, stair climbing, and car transfer time as compared to the health education group.

Cycling has shown similar benefits. The low-impact nature of the activity and potential for high cardiovascular returns make it a popular recommendation. Both high- and low-intensity cycling show benefit, are well tolerated, and do not appear to increase daily acute pain [54].

Resistance/strength training also has positive effects on pain scores and functional outcomes in knee OA [55–60]. Both home and gym therapy–based resistance training appear to be effective, and patient preference, education, and access should be considered when developing a plan of care [61]. Because quadriceps weakness has been identified as a potential risk for knee OA [62, 63] and is closely associated with disability [64, 65], many of the resistance-training protocols have focused on quadriceps strengthening and stabilization and have shown good clinical benefit. However, in individuals with malaligned or excessively lax knees, increased quadriceps strength is associated with progression of tibiofemoral OA [66]. Therefore, quadriceps strengthening alone may not be sufficient as an exercise-based treatment of this subgroup of patients. Future research should focus on the effect of preferential hamstring or hip abductor strengthening as compared to quadriceps-only programs to more precisely guide therapeutic interventions.

Aquatic therapies are frequently recommended to patients who are hesitant to begin a regular weight-bearing, land-based program. Because aquatic therapy entails less joint impact, many practitioners believe therapy will be more readily tolerated and less likely to flare symptoms. Evidence does support these perspectives [67–69], but fails to provide convincing data that benefits are sustained long term [70]. Health care providers may wish to consider using aquatic therapies as a bridge to land-based activity for those patients especially reticent to start moving.

A growing body of literature also supports the use of proprioceptive or balance-focused activities, including tai chi, in the management of knee OA. Regular participation can positively influence pain, balance, self-efficacy, and physical functioning [71–73].

It is clear that light- to moderate-intensity exercise positively influences knee OA. There is significant evidence that many forms of exercise, including aerobic conditioning, resistance training, and aquatic therapies as well as less conventional approaches, all provide benefit.

The combination of improved balance, muscle strength, and joint and soft tissue flexibility likely contribute to improvements in pain and function. Because the literature is still imprecise on exactly which form of exercise is the "best," health care providers should be encouraged to make recommendations based on patient preferences, cost of care, convenience, and patient access. Future areas of research include clarifying the mechanisms by which exercise has its positive effects on the prevention and treatment of knee OA and determining if one form of exercise should be the "standard of care" for specific clinical presentations. As the patient increases the level of physical activity, appropriate pharmacologic pain management must not be overlooked. The patient should be clearly counseled that it is not an "either/or" treatment plan, but that both nonpharmacologic and pharmacologic modalities will be used to maximize function and QOL. If pain increases, the appropriate medication modifications should be made and the activity program evaluated and modified accordingly. If pain improves, then pain medication should be carefully titrated, with a preference to reduce those medications with greatest risk and cost. Interval re-evaluation should be undertaken and appropriate modifications made at each visit.

Weight Loss and Knee Osteoarthritis

Over 34% of adults in the United States are overweight, 33.8% are obese, and 5.7% are extremely obese [74]. Excess adiposity increases the risk for knee OA through both biomechanical and biochemical processes. During ambulation, three to five times the body weight passes through the knee joint [75]. Small changes in weight result in large increases in force across the joint. Obesity also increases circulating levels of tumor necrosis factor–α, interleukin-6, C-reactive protein, and other proinflammatory cytokines that may promote cartilage matrix degeneration [76]. Some authors suggest there is up to a 10% increase in risk per kilogram increase in body weight [77]. Fortunately, a reduction in weight can result in equally significant reductions in risk [78].

In the Framingham Study, a 12-lb weight loss reduced knee OA risk by 50% [79]. Christensen et al. [80] found that rapid diet-induced weight reductions of 10% improved function by 28% with each percent body fat reduction, equating to 9.4% improvement in WOMAC (Western Ontario and McMaster Universities Arthritis Index) scores. In their 2007 meta-analysis, Christensen et al. [81] concluded that disability could be significantly improved with a weight reduction of as little as 5%. It is evident that weight loss has positive clinical results on knee OA whether achieved via bariatric surgery or lifestyle measures [82]. Excess body weight is a primary risk factor for knee OA, on par with a history of knee injury, and should be a target for both prevention and treatment [83–86].

Conclusions

There is overwhelming evidence that light to moderate physical activity does not cause or accelerate knee OA; in fact, exercise may prevent its onset, and is clearly effective in the management and treatment of the pain and functional decline associated with OA. Health care providers should not hesitate to include recommendations for exercise as part of the clinical management of knee OA. Exercise regimens with strong evidence of benefit include those that focus on aerobic/cardiovascular conditioning as well as lower-extremity strength training.

Specific recommendations should be guided by individual factors uncovered on history and physical examination and by patient preference and accessibility. Special attention should be given to patients with joint malalignment, excessive joint laxity, a history of knee injury or surgery, medical comorbidities, or exercise phobias. In these settings, it may be preferable to have patients begin a supervised exercise regimen under the supervision of a skilled physical therapy. Progress made in this setting then can be transitioned to a home-, gym-, or community-based exercise program. Exercise prescriptions provided by the health care provider should be tailored to the individual needs and goals of each patient. Clinicians should play an active role in encouraging patients to take this step by providing patients with specific information regarding the benefits of doing so.

As health care providers, we do a better job of promoting exercise in our patients when we effectively communicate to them the array of symptoms that exercise helps to prevent and treat. This may mean stepping out of our comfort zone of offering "quick fix" pharmaceutical solutions to patients' complaints and considering exercise as an intervention with measurable benefits. We may need to discuss specific forms of appropriate exercise given patients' overall fitness and physical limitations. Exploring this with patients will help to improve their confidence and interest in exercise as a valid treatment. Exercise truly can be a powerful "medicine," and as health care providers, we have unparalleled opportunities to use this powerful modality for the prevention and treatment of the pathology, dysfunction, pain, and disability associated with OA of the knee.

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