Osteoarthritis of the Knee in Women

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Continuing Medical Education

Goal

To discuss current concepts concerning the prevalence, pathogenesis, risk factors, and treatment of knee osteoarthritis (KOA) in women.

Objectives

1. To emphasize the high prevalence of KOA in women aged > 65 years, and highlight risk factors including obesity, occupation, and sports activity/injury.
2. To clarify the role of mechanical factors such as knee malalignment, laxity, and muscle strength in women.
3. To explore the therapeutic possibilities of analgesia and surgery in women.

Accreditation

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Arthritic deterioration of the knee joint is not an inevitable consequence of aging, and knowing the female-specific differences in prevalence and risk factors can contribute significantly to effective management.

Osteoarthritis (OA) is the leading cause of disability among older adults in the developed world. In the peripheral joints, OA most frequently involves the knee, and may affect the medial tibiofemoral, lateral tibiofemoral, and/or patellofemoral compartments. Osteoarthritic changes decrease the effectiveness of load transfer across the joint, impairing mobility. Knee OA (KOA) greatly limits daily activities,[1] and is associated with an increase in major depressive episodes in older adults.[2]

Men are more likely than women to report KOA symptoms before age 50 years, but the incidence rises among women after menopause; by age 65 years, the prevalence is at least 2-fold greater in women (Figure).[3,4] Estimates of prevalence differ due to varying disease definitions and cohort characteristics. White populations in developed countries have similar rates, but black women may be 2-fold to 3-fold more likely to have KOA.[5] The prevalence of KOA is 45% higher in Chinese women[6] and 100% higher in Japanese women[7] than in age-matched white women.

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DEFINITION

Osteoarthritis is a dynamic disease of the synovial joint that destabilizes the degradation-synthesis cycle of the articular cartilage chondrocytes, extracellular matrix, and subchondral bone. These changes lead to softening, fibrillation, ulceration, loss of articular cartilage, sclerosis, and eburnation of subchondral bone, osteophytes, and subchondral cysts[8]—ie, the whole joint and surrounding soft tissues are involved. Effects range from asymptomatic radiographic findings to severe pain and functional disability.[9]

Common symptoms of KOA are pain, stiffness after activity, and instability. Physical findings include crepitation, bony enlargement related to osteophyte formation, deformity, and effusion in approximately 30% of individuals. The American College of Rheumatology (ACR) has developed diagnostic criteria for KOA (Table 1),[10] but many researchers apply other standards—eg, radiographic features alone. This can confound results, as > 50% of individuals with radiographic KOA do not report joint pain.[11]

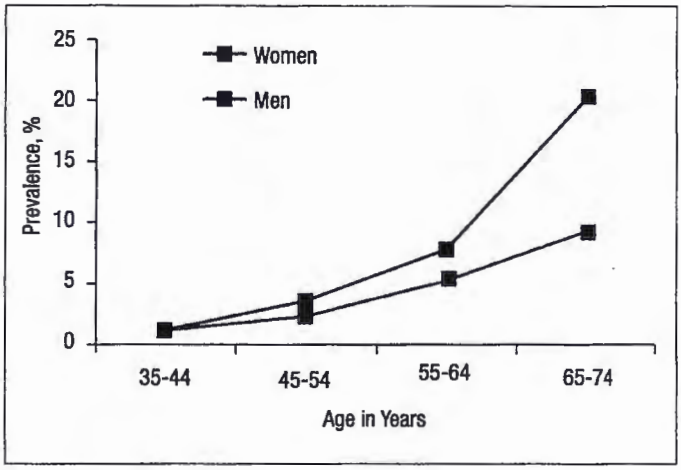

FIGURE. Prevalence of radiographic knee osteoarthritis in the US population—NHANES I.

Source: Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first National Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *Am J Epidemiol*. 1988;128(1):179-189.

RISK FACTORS

In addition to age, gender, and race/ethnicity, susceptibility to KOA depends on a variety of "local" factors that can influence load distribution across the joint.[12,13]

Obesity

Obesity is a strong risk factor for KOA among women.[12] Any increase in body weight increases the load across the joint by a force 3-fold to 7-fold greater than the actual weight gain. Knee alignment can contribute to this stress; for instance, knees with varus alignment are especially vulnerable to excess body weight, resulting in more severe medial tibiofemoral KOA.[13] When the highest tertile for body mass index was compared with the lowest in women aged 45 to 64 years to assess odds ratio (OR) and 95% confidence interval (CI) for radiographic KOA, the OR was 6.2 (95% CI, 3.3-11.7) for any OA; 18.0 (95% CI, 6.3-51.7) for bilateral OA; and 8.6 (95% CI, 3.3-22.5) for symptomatic OA.[14]

Weight change can be significant; subjects who gained ≥ 5 lb had an almost 4-fold greater risk for incident OA compared with those who gained or lost < 5 lb. Those who lost > 5 lb halved their OA risk.[15]

Obesity also exacerbates pain and functional limitations from KOA. Conversely, weight loss in obese patients with KOA—particularly if accompanied by an increase in physical activity—improves physical function and quality of life.[16]

Physical Activity

While light or moderate physical activity does not increase the risk of KOA,[12,17] heavy activity is strongly associated with incident KOA (OR 7.2, 95% CI, 2.5-20).[18] Similarly, female runners and

TABLE 1. American College of Rheumatology Diagnostic Criteria for Osteoarthritis of the Knee[10]

- Knee pain
- Osteophytes on radiography

PLUS at least one of the following

- Age > 50 y
- Stiffness < 30 min after activity
- Crepitus on physical examination

tennis players were 3-fold more likely to develop tibiofemoral and patellofemoral KOA than were age-matched controls.[17]

Occupations requiring repetitive overuse of the knee confer an increased risk of KOA. Crouching, kneeling, squatting, climbing stairs, and lifting heavy loads all cause abnormal loading across the joint and tissue damage. Few studies have included women, but all the evidence suggests that the risk factors are similar in both sexes.[19]

With regard to knee laxity, varus-valgus laxity increases with age, and tends to be greater in women.

Knee Injury

Any knee injury preventing unaided walking for ≥ 1 week is a strong predictor of KOA.[13] Such injuries usually involve rupture of the anterior cruciate ligament (ACL), which is often associated with tearing of the meniscus or the medial collateral ligament. Both ACL damage and meniscal rupture are strongly linked to early arthritic degeneration. As ACL injury is 2-fold to 8-fold higher among female than male athletes,[20,21] the rising number of women participating in sports can be expected to result in higher rates of KOA in women. Early ACL reconstruction with meniscal preservation may help to protect against KOA. The poorest postoperative outcomes were seen following meniscectomy.[22,23]

Mechanical Environment

Knee alignment has a strong influence on load distribution across the joint. Varus alignment is associated with progressive medial OA, and valgus with lateral OA. The degree of malalignment is correlated with the magnitude of joint-space narrowing.[24]

Proprioception, which helps to establish and maintain joint stability, is decreased in both the involved and uninvolved knees of patients with unilateral KOA. Thus, loss of proprioception may precede pathology.[13]

With regard to knee laxity, varus-valgus laxity increases with age, and tends to be greater in women. Patients with unilateral KOA have greater varus-valgus laxity in both the involved and contralateral knees, so that such laxity may also precede KOA.[13,25]

Muscle Strength

Many patients with KOA have quadriceps weakness.[13,26] This is attributed to disuse atrophy secondary to knee pain, but such extensor weakness is present in women with asymptomatic tibiofemoral OA—suggesting that quadriceps weakness is a risk factor for KOA. In a study of subjects with no KOA at enrollment, women who developed KOA during follow-up had 18% less quadriceps strength at baseline than those who remained OA-free. Muscle strength did not influence disease progression.[13]

TREATMENT

Pain is intermittent in early KOA and progresses in severity, often with locking or giving way of the knee. Joint stiffness (gelling) may occur after physical activity relative to interstitial edema.[2,20] Gradual deterioration is common, and > 50% of patients with joint-space narrowing report worsening symptoms and radiographic changes over a 7-year period.[21]

There is no cure for KOA, but the ACR has established nonpharmacologic and pharmacologic management guidelines.[3] Therapy is directed at controlling pain and maintaining functional activity.[2,20,22] Nonpharmacologic options focus on reducing knee stress, and include weight reduction, job/activity modifications, quadriceps strengthening, and assistive devices. Targeted physical therapy can improve knee strength and flexibility, delaying or eliminating the need for total knee replacement. Canes, braces, and orthotics can ameliorate knee stresses, but may limit function. Occupational therapy may be appropriate as well.

Pharmacologic therapy for KOA is directed at pain management (Table 2). While no medications can significantly influence disease course, the ACR recommends acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) as primary agents.[22] Studies have suggested a therapeutic advantage of NSAIDs over acetaminophen for analgesic efficacy in OA, but NSAIDs can cause adverse gastrointestinal and cardiovascular effects. Hepatic toxicity is possible with chronic acetaminophen administration, especially in patients who consume alcohol.

Response to different NSAIDs is variable and not clinically predictable, with approximately 70% of individuals benefiting from one of these agents. Lower NSAID doses are primarily analgesic, while larger doses are required for anti-inflammatory

TABLE 2. Medical Management of Knee Osteoarthritis

Nonpharmacologic Therapy

- Patient education/self management
- Weight loss
- Exercise (physical therapy, aerobic, strengthening, range of motion)
- Assistive devices (braces, orthotics, taping, footwear)

Pharmacologic Therapy

- Oral (acetaminophen, COX-2 selective NSAIDs, nonselective NSAIDs, opioids [rarely], propoxyphene, tramadol)
- Intra-articular (corticosteroids, hyaluronic acid)
- Topical (capsaicin, methyl salicylate)

COX-2 = cyclooxygenase-2; NSAIDs = nonsteroidal anti-inflammatory drugs.

effects. A therapeutic trial of ≥ 2 weeks is recommended to assess the effect of a particular agent. Tolerance can develop to NSAIDs, and switching among agents can be beneficial. Because of the frequent need for continuous, long-term use in KOA, compliance is better with once- or twice-daily dosing than with more frequent administration.

Intra-articular injections of corticosteroids and hyaluronic acid may relieve symptoms, but the improvement is usually transient. The role of oral glucosamine and chondroitin, which are components of articular cartilage, is uncertain and at best modest.

Surgery

Patients with KOA rarely show radiographic improvement, but the rate of progression is highly variable.[27] Progression occurs in 3% to 12% of patients annually, with a mean decrease in joint space of 0.18 to 0.60 mm. Obese patients and those with contralateral KOA are most likely to show exacerbation. When medical treatment fails to alleviate KOA symptoms, arthroplasty may be considered. Candidates are usually limited to those with severe joint-space narrowing.

Although knee arthroplasty is cost-effective and improves quality of life, only 8% to 15% of patients with a demonstrated need elect to undergo the procedure.[28,29] This underuse is particularly marked in women, who usually have more severe symptoms at surgery than do men. Surgical success is enhanced in nonobese women who are over age 60 years.[30]

CONCLUSION

Because KOA has several modifiable risk factors, interventions should target primary prevention—ie, weight loss, directed physical activity, and repetitive stress reduction. Challenges include an appreciation of the spectrum from asymptomatic to severe, and selection of the most effective management approaches. Treatment plans, including pharmacologic and nonpharmacologic measures, should be assessed in the context of evidenced-based medicine. Specific evidence-based interventions have the potential to modify the burden of disease, as well as reduce health care costs.[24]

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