

OA Pathogenesis & Risk Factors

Osteoarthritis Prevention and
Management in Primary Care

OA

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PATHOGENESIS

Much has been learned about the pathogenesis of osteoarthritis (OA) in the last two decades. While this research has not yet produced effective disease-modifying treatment options for OA, it has given direction to providers and patients alike for identifying the presence of and the risk factors for OA and helping manage the disease and slow its progression.

Osteoarthritis Research Society International (OARSI) defines osteoarthritis as: **“a disorder involving movable joints characterized by cell stress and extracellular matrix degradation initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. 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

HEALTHY JOINT

Healthy articular (hyaline) cartilage is a frictionless, aneural, and avascular substance that covers the ends of bones in a joint. Cartilage is only 2–5 mm thick and may be compressed as much as 40% when bearing a load.² Water is the primary component of cartilage, but it also contains collagen, proteoglycan aggregates (aggrecans), proteins, and chondrocytes. Cartilage is metabolically active and undergoes continual internal remodeling under the control of the chondrocytes. Synovial fluid, found in the joint capsule, is viscous, aids in the lubrication and movement of a joint, and allows vital nutrients to reach the cartilage while blocking harmful substances. Along with muscles and subchondral bone, synovial fluid is an important component for joint stress reduction or load absorp-

tion. Hyaluronic acid is a key component of both synovial fluid and cartilage which facilitates the viscosity of the synovial fluid, acts as a shock absorber under sudden joint loading, and filters potentially damaging cells and molecules.³

DISEASED JOINT

Following joint injury (e.g., trauma or repeated loading), proinflammatory mediators (e.g., cytokines and chemokines) are naturally produced, leading to extensive matrix degradation and loss. As part of this process proteoglycans attract water, and articular cartilage expands. Chondrocytes, which are normally dormant, begin to proliferate due to the loss of matrix. When cartilage degeneration exceeds the rate of chondrocyte remodeling, OA occurs. When collagen is degraded and lost, the cartilage has limited ability to repair and chondrocytes die.

Within the joint, soft tissue damage leads to thickening of the joint capsule which can result in visible, but often minor joint swelling. Bone sclerosis and osteophyte (bone spur) formation can also result when OA is more moderate to severe.⁴ Such alterations to the joint often precede the onset of clinically or

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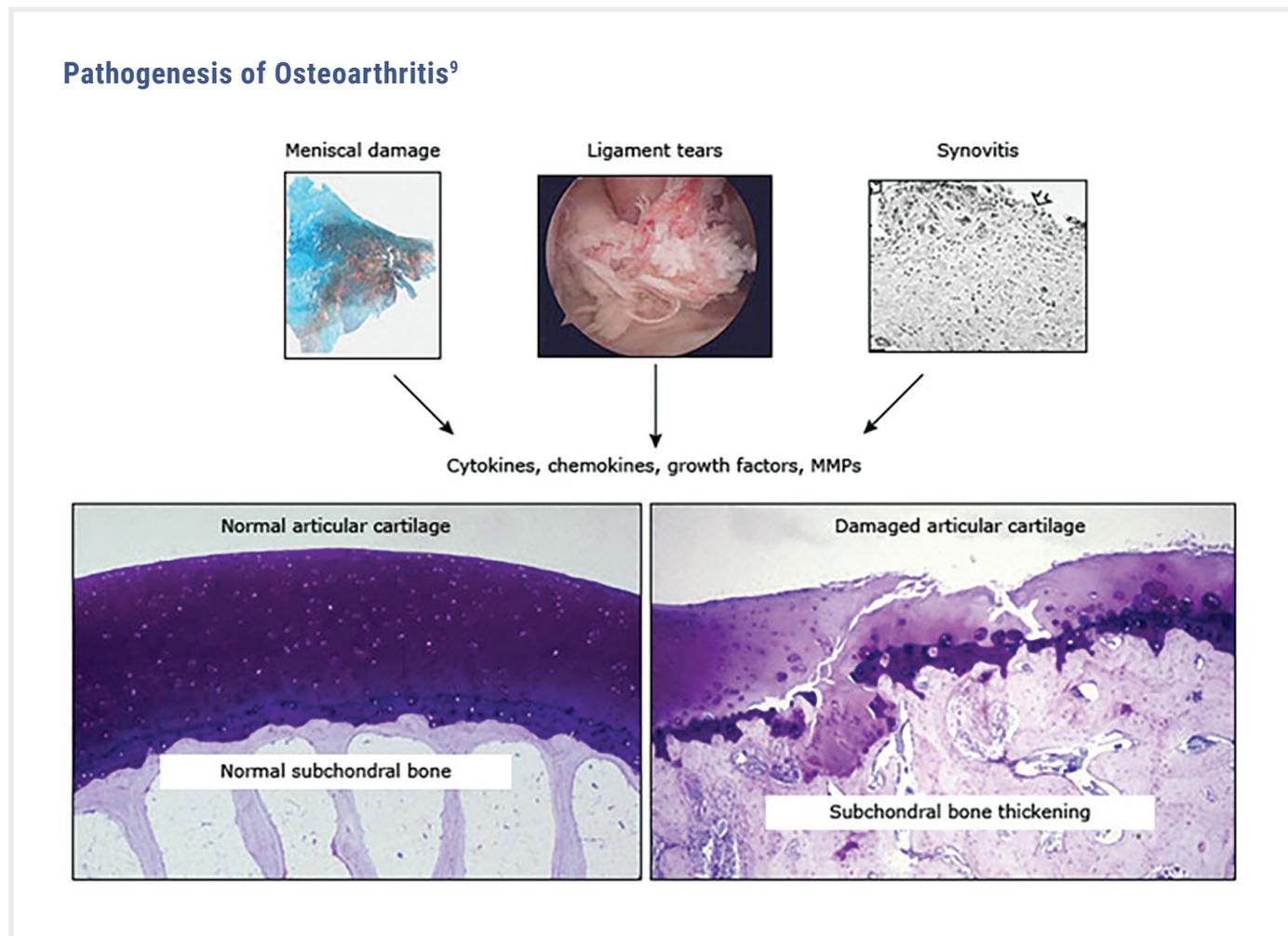
radiographically detectable OA.⁵⁻⁷

Age-related changes within a joint can increase the risk of developing OA due to the joint's susceptibility to injury and decreased capacity for repair. Cellular senescence and mitochondrial dysfunction due to advancing age also contribute to the development of OA.⁴

Patient-reported symptoms—that is, the illness—do not necessarily align with this underlying disease pathology.⁸ Pain in OA is likely the result of a complex interplay of factors including mechanical, inflammatory, and centralized pain pathways.²

FIGURE 1

Osteoarthritis involves all of the joint tissues including the menisci in the knee, ligaments, synovium, articular cartilage, and bone. Damage to the menisci and ligament tears not only alter joint mechanics but, along with the inflamed synovium (synovitis), produce proinflammatory factors (cytokines and chemokines) and matrix-degrading enzymes (eg, matrix metalloproteinases [MMPs]). These factors are also produced by chondrocytes and serve to promote joint tissue destruction.



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RISK FACTORS

For most patients, OA is linked to multiple risk factors that can be grouped into modifiable and non-modifiable. Non-modifiable risk factors for OA include age, sex, ethnicity, genetics, previous history of injury or joint trauma. Potentially modifiable risk factors for OA include excess weight, certain occupations and sports, joint injury (injury prevention), joint malalignment and quadriceps weakness.

Non-Modifiable Risk Factors

AGE, ETHNICITY, SEX & GENETICS

Age is the best-known risk factor for OA, but advancing age does not automatically lead to the development of OA. Furthermore, OA is occurring in younger adults at increasing rates. In 1997, the incidence of OA in people between the ages of 25 and 34 years was reported to be less than 1%, and in those over the age of 55 years, the rate was 80%.¹⁰ In 2018, among US adults with self-reported OA, 11.7% were 18–44 years of age, 45.7% were 45–64 years old, and 42.6% were 65 years of age and older.¹¹ It is important to note that the prevalence and incidence of OA vary depending on the definition used in the analysis, the specific joints being evaluated, and whether the diagnosis is self-made or medically confirmed.

Sex and ethnicity are also risk factors; however, the frequency and severity of OA differ among the types of OA being considered. Female sex is associated with an increased risk of OA, especially OA of the hand, foot, and knee. Older women are more than twice as likely to develop OA of the hand as their male counterparts.¹² The Women's Health Initiative revealed that older African-American, Native American, and non-white Hispanic women were more likely to develop OA than white women.^{13,14} African-Americans are more likely to develop symptomatic knee and hip OA compared to other races.¹⁵ Hip OA is 33% more prevalent in older African-American men than white men.¹²

OA, like many common chronic conditions, is likely influenced by many genetic loci, each with only a small effect.¹⁶ Twin studies have shown the heritability of hip OA to be approximately 60%, knee OA greater than 40%, hand OA 65%, and spine OA 70%.¹⁷ Multiple gene interactions within collagen, cartilage, and bone may contribute to the development of OA.

PREVIOUS INJURY

Previous traumatic injury to cartilage, ligaments, and/or meniscus also increases the risk of developing OA in the affected joint(s). Post-traumatic arthritis makes up approximately 12% of all OA cases and can result from injuries sustained in automobile or military accidents, falls, or sports.¹⁸ Someone with a history of a previously torn anterior cruciate ligament (ACL) or meniscus is 2.5 times more likely to develop knee OA and 4 times more likely to undergo an eventual total knee arthroplasty.^{2,15,19} Among young athletes who sustain an ACL injury, 10–90% will develop OA within 10–20 years. Furthermore, surgical reconstruction and rehabilitation do not appear to mitigate the risk of developing OA following ACL injury.²⁰

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Potentially modifiable risk factors

Modifiable risk factors for OA include weight, certain occupations and sports, joint injuries, and malalignment.

OBESITY

Obesity is regarded as the strongest modifiable risk factor for the development of OA of the knee; moreover, it has been associated with higher rates of disability.^{21,22} Men and women who are obese have a 2.8-fold and 4.4-fold increase in developing knee OA, respectively. For each kilogram (2.2 pounds) of excess weight, the risk of developing OA increases by approximately 10%.²¹ Someone with ten pounds of additional weight increases the force exerted on their knee by up to 60 pounds with each step.²³ Not only does obesity contribute to OA through increased joint load, but there are metabolic factors involved as well. Indeed, excess body weight is also associated with an increased risk of OA of the hand, giving credence that certain metabolic changes (not just excessive weight-bearing activities) contribute to the development of OA. In the IDEA trial (Intensive Diet and Exercise for Arthritis), subjects with knee OA who were overweight and who achieved a modest weight loss (10% of body weight) through diet and exercise, achieved a 50% reduction in pain scores.²⁴

Obesity is regarded as the strongest modifiable risk factor for OA and is associated with higher rates of disability among patients with OA.

OCCUPATIONS & SPORTS

Research has clearly demonstrated the health benefits of light to moderate physical activity in reducing OA-related joint pain; however, the extent to which participation in non-contact recreational sports or repetitive occupational activities may increase the risk of OA has not been fully elucidated.²⁵ It is evident that certain occupations (e.g., construction, healthcare, farming, law enforcement, first responders, military) involving prolonged standing, squatting, lifting, kneeling, and repetitive motion where the result is the application of excessive mechanical stress on a joint, raises the risk of OA and can worsen symptoms.^{26,27} Osteoarthritis and back pain are the most common diagnoses related to disability-caused separation from the military, both during periods of peacetime and war.^{27,28}

High impact professional sports (e.g., hockey, soccer, and football), where there is repetitive loading or excessive force,

in addition to joint trauma, puts players at risk of OA.²⁹ In a systematic review, Driban et al found that in addition to elite-level athletes (soccer, long-distance running, weight lifting and wrestling), nonelite soccer athletes were also at risk of developing OA.²⁵ Proper precautions such as stretching and strengthening exercises, appropriate footwear and other supportive devices, along with supportive workplace policies can help reduce onset and progression of OA in occupational and sports settings.

JOINT INJURY (INJURY PREVENTION)

As previously discussed, injuries resulting from occupational activities, sports, or accidental falls, are known to be risk factors for subsequent OA development. While these injuries may not be entirely preventable, steps can be taken to reduce their incidence or impact in later life. Injury prevention activities such as stretching, strengthening, and neuromuscular training exercises can be implemented in all levels of sports—from youth to professional levels—to protect athletes' joints. See the OA Prevention module for more information. Patients at risk of falling can build strength and improve balance to reduce their risk of fall-related injuries and should be counseled to engage in or increase their physical activity. The CDC's STEADI initiative (Stopping Elderly Accidents, Deaths, & Injuries) includes educational materials for providers and handouts for patients on preventing falls. Implementing workplace policies such as job-switching, reduced work time, and paid sick leave could potentially help reduce symptomatic knee pain in workers with OA.³⁰

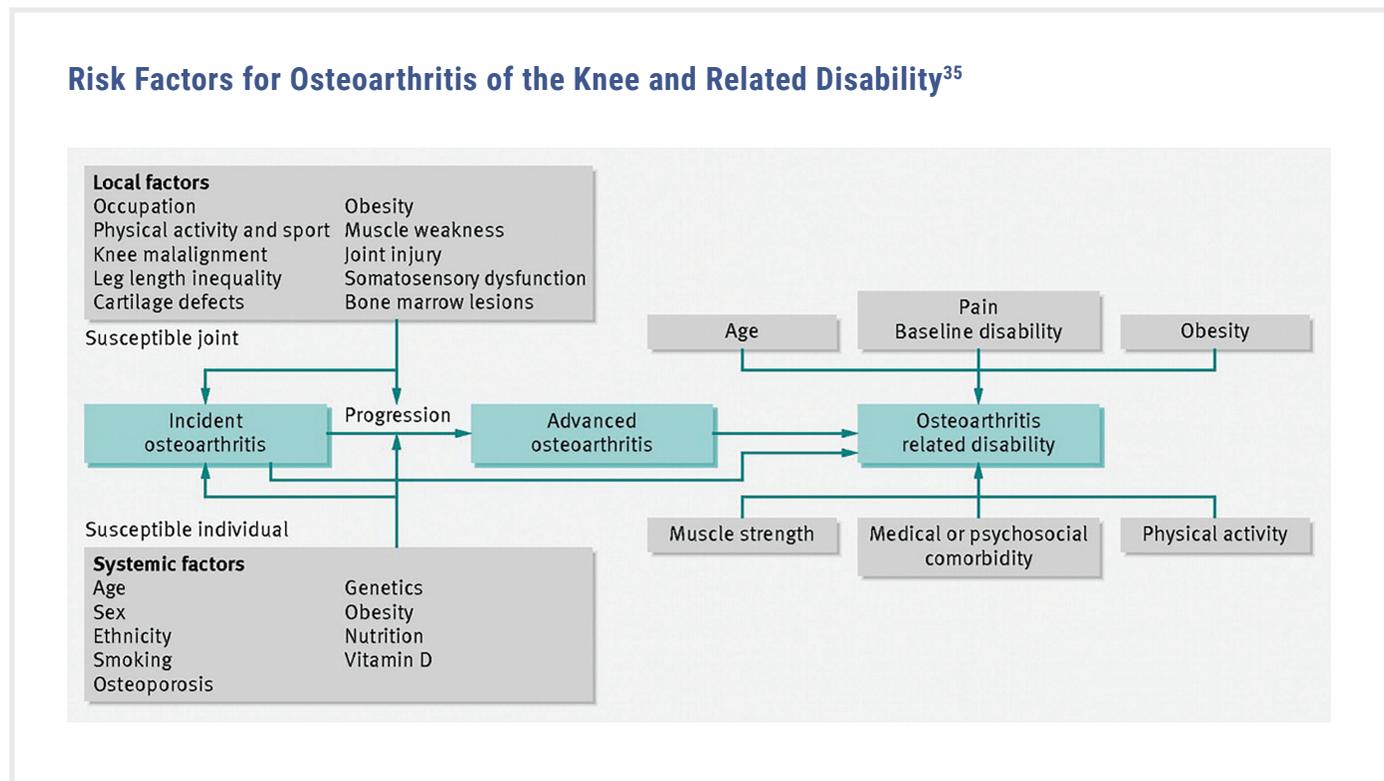
JOINT POSITION AND MUSCLE STRENGTH

Knees that are not mechanically aligned properly—resulting in either varus (bowlegged) or valgus (knock-kneed) alignments—can result in increased risk of knee OA. Additionally, the worse the malalignment, the greater decline in physical function likely to be experienced by patients.³¹ Knee braces or shoe inserts may help with pain and stiffness when these conditions exist.^{31,32} Weaker quadriceps strength has been connected to increased functional disability and pain in people with knee OA.^{33,34} Muscle-strengthening exercises with a physical therapist or through a community-based intervention program can help reduce pain and functional limitations.

The Prevention & Self-Management handout may be useful for patients with OA or at risk of developing OA.

FIGURE 2

Figure 2 demonstrates the relationship between non-modifiable and modifiable risk factors in the context of the progression of OA and associated increasing functional limitations.



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Clinical Take-Home Points

- OA is not simply “wear and tear” or “degeneration” of the joint, but rather a complex disorder characterized by a variety of molecular, anatomic, and physiologic changes leading to disease.
- Non-modifiable risk factors should be considered, and modifiable risk factors addressed, to reduce disease burden.

ADDITIONAL READING

Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. Lancet. 2019;393(10182):1745–1759.

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