Osteoarthritis of the Knee

4

Aaron Bolds and Subhadra Nori

Introduction and Pathophysiology

Osteoarthritis (OA) remains the most common type of arthritis, with over 6% of U.S. adults aged 30 and over being clinically affected [1]. The prevalence of knee OA in the US is approximately 34%, with women representing roughly 10% more [2]. As populations continue to age, an increase in the prevalence of osteoarthritis is inevitable. There is a large economic burden associated with osteoarthritis secondary to the impact on disability. Many of the risk factors linked to osteoarthritis cause significant comorbidities as well, thus increasing risk for functional disability. The increasing prevalence of obesity continues to be of concern as it leads to increased "wear and tear" on large joints, specifically the knee. The knee is the largest synovial joint in the body and the most common site of OA associated with disability.

The joint is covered by an articular cartilage and surrounded by a synovial bursa. Extracellular matrix components such as type II collagen and other proteoglycans house receptors that allow chon-

A. Bolds
Mount Sinai Hospital, New York, NY, USA

S. Nori (✉)
NYC Health + Hospitals, New York, NY, USA
e-mail: NORIS@nychhc.org

M. Leong et al. (eds.), *A Case-Based Approach to Knee Pain*,
https://doi.org/10.1007/978-3-031-15356-3_4

drocytes to detect mechanical stress. Metalloproteinases are key players in cartilage matrix degradation. Their upregulation is secondary to repeated mechanical or inflammatory stimulation [3]. Chondrocytes can undergo phenotypic transformation and express inflammatory mediators such as cytokines and chemokines, in response to repeated stimulation. During the remodeling process there is new blood vessel formation, known as vascular channels. These channels have sensory nerve endings and their articular cartilage innervation is a pain generator [3]. This cycle of cartilage damage and remodeling is the primary pathological feature of osteoarthritis.

Unique to the morphology of the knee joint is the infrapatellar fat pad, also referred to as Hoffa's fat pad. This structure is composed of a fibrous network, including a layer of adipose tissue. It is located beneath the patella and within close proximity of other structures including bone, articular cartilage and synovium [4]. Hoffa's fat pad contains many immune cells that are involved in producing inflammatory mediators. There are nociceptive nerve fibers present in Hoffa's fat pad. Inflammatory mediators, such as cytokines, may play a role in altering the sensitivity of nerve fibers and decreasing pain threshold [4]. Thus, the infrapatellar fat pad must be considered a significant factor in the pathology of knee OA.

Risk Factors

OA is more than just a "wear and tear" disease process. It is better defined as a multifactorial process influenced by, but not limited to, genetic history, inflammation, mechanical forces, immune-mediated cellular processes, biochemical processes, age, sex, and body composition. Risk factors are split into non-modifiable and modifiable. The most common modifiable risk factor is obesity which leads to increased joint loading and early disease progression of OA. For every pound of bodyweight gained, there are two to four pounds of load bearing pressure added to the knee joints [2]. The added load bearing is not the only contributing factor of obesity to knee OA. Obesity is also associated with negative

effects related to inflammation and psychological factors, such as sedentary lifestyle leading to loss of protective muscle mass surrounding the joint.

There is an association of estrogen deficiency and high incidence of OA in post-menopausal women. There are conflicting studies in regard to these mechanisms, as some studies show effects of estrogen, such as increased bone mass, may counteract the effect of estrogen on OA [1]. It has been established that there are sex differences in the incidence and severity of knee OA. Knee and hand OA appears to be more prevalent in women and African-American population. In addition to increased prevalence, women typically report higher pain burden and decreased overall function compared to men [5]. Understanding the mechanisms responsible for the above mentioned sex differences in OA will require further epidemiologic and pathophysiologic studies in the future.

There have been nutritional factors implicated in the disease process of OA. Chondrocytes are sources of reactive oxygen species (ROS), which can influence cartilage collagen and synovium degradation [1]. Therefore, antioxidant consumption may play a role in protection against OA, given its defense against tissue injury. Vitamin C has been found to decrease apoptosis and the expression of pro-inflammatory mediators, such as cytokines and metalloproteinases [6]. It also has antioxidative properties which can protect against reactive oxygen species created by chondrocytes during knee OA disease progression. Vitamin D deficiency can impact the bone response in OA and lead to increased severity. The Framingham cohort study on OA showed the risk for OA progression was increased threefold in persons with vitamin D deficiency, thus indicating the nutritional value of vitamin D in the knee OA disease process [1].

A small percentage of knee OA cases are genetically predisposed. Some of the genes previously studied for their up/down regulatory involvement in OA include, but are not limited to: insulin-like growth factor I genes, vitamin D receptor gene, neuronal growth factor, cytokine receptor-like factor 1, and tumor necrosis factor alpha-induced protein 6 [1]. Future studies are needed to understand the mechanisms by which these genes affect

disease occurrence. This will allow for proactive strategies to be utilized to prevent disease occurrence or progression.

There are also biomechanical risk factors associated with knee OA, such as varus–valgus laxity, knee–hip–ankle alignment, joint injury or alteration of anatomy, muscle weakness, job and sporting activities [1]. Increased joint instability secondary to articular surface fractures, ligamentous injury (ACL, PCL, MCL, and LCL), and menisci can lead to development of knee OA. High impact, high intensity sports have been shown to increase risk of knee OA. American football and soccer are common sports that involve repetitive pivoting and explosive horizontal and vertical forces. Decreasing risk of OA among sports participants is a growing topic. In conjunction with joint stability training; modifications to protocols, equipment, and playing surfaces can help lower risk [1]. It is vital that the aging population stays active and incorporates some level of physical activity at least 3–4 days per week. Including lower extremity strength training will help reduce obesity and also help maintain protective mass to muscles surrounding the knee joint, specifically the quadriceps.

Clinical Presentation

Patients with knee OA can present in various ways depending on the etiology. However, pain is the most common symptom, with various characters and/or temporal patterns. Patellofemoral area may be involved with anterior knee pain and joint line pain with activity could suggest meniscal involvement. Patients may experience crepitus, knee buckling, leg weakness, and locking. Swelling can also intermittently accompany pain, especially following high impact activities. Decreased functional ability can be a symptom, often reported as difficulty ambulating stairs, prolonged sitting, and performing activities of daily living (ADLs).

As a result of pain, patients may report difficulties with tolerating physical activity. This may lead to a sedentary lifestyle, exacerbating the modifiable risk factors associated with knee OA. As a clinician, it is important to screen these patients for depression, as a psychosocial component can be linked.

Physical Exam

Inspection should include evaluating for edema, skin changes, erythema, and deformities. Palpation should be used to locate any point tenderness proximal to the medial and lateral joint lines. Posterior and anterior aspects of the knee should be palpated to assess for baker's cyst or patellofemoral point tenderness, respectively. Range of motion should be tested, paying close attention to patellar maltracking, known as the J-sign. Instability of the joint can be detected by applying varus and valgus stress to the knee joint. Functional tests such as squatting, hopping, calf raises, and jumping can be used to see which mechanical movements illicit pain. Lower extremity strength should be tested bilaterally, being careful to differentiate true weakness versus pain limited weakness. Gait testing should be used to identify any malalignment and instability.

Special tests can be used to identify any superimposed ligamentous or meniscal pathology. There are many special tests with varying sensitivity and specificity. With respect to knee OA, the integrity of the patellofemoral and meniscal structures can be evaluated with some of the following tests: Meniscus (McMurrays, Apley's test, Thessaly test) and patellofemoral (Apprehension and Grind test/Clarkes sign).

Diagnosis

History taking and physical exams are utilized for diagnosis but definitive diagnosis is typically found radiographically. However, the American College of Rheumatology suggests that the diagnosis of knee OA can be made without radiographic evidence [2]. The clinical diagnosis must include at least 3 of the following: mechanical crepitus, morning stiffness lasting less than 30 min, age 50 and older, bony enlargement or tenderness on the knee exam, and no palpable warmth. The most frequently used grading system is the Kellgren and Lawrence system, including 4 grades. Grade 1 does not include joint space narrowing, but the initial formation of osteophytes on articular surfaces. Grade 2 is charac-

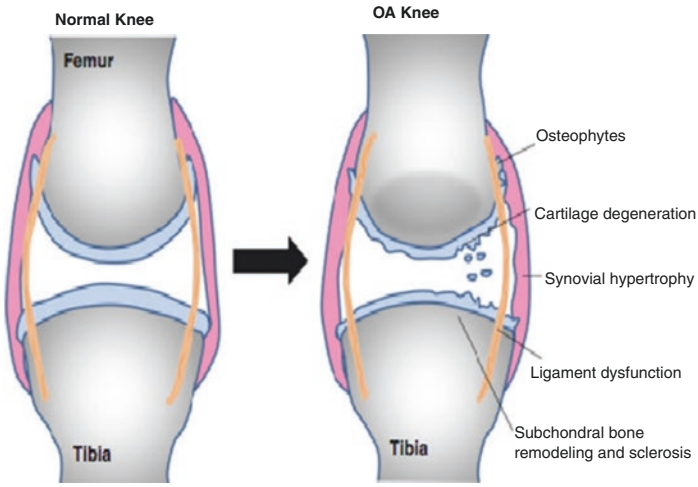

Fig. 4.1 Depiction of degenerative changes in knee OA [4]

terized by mild joint space narrowing and definite osteophytes. Grade 3 is similar to grade 2 except the joint space narrowing is worse and osteophytes are more abundant. Also, in grade 3 there may be sclerosis and bony deformity. Grade 4 reveals severe joint space narrowing and bony sclerosis, large osteophytes, and definite bony deformity at the tibial plateau [2]. Figure 4.1 depicts various pathological changes seen with knee OA.

Although plain radiographs and MRI are imaging techniques most frequently used for knee joint evaluation, ultrasound use is becoming more popular. There are advantages to ultrasound such as low cost, no radiation exposure, portable, and high sensitivity. It is also possible to evaluate structures dynamically. Limitations to ultrasound use include its user dependence, inability to display deep structures within the joint, and limited evidence on reliability [7]. Typically, ultrasound is not used for definitive diagnosis of knee OA and instead is used diagnostically or to guide the needle for therapeutic injections. However, as more research is conducted on the validity and reliability of ultrasound, development of standardized diagnostic methods may follow.

Treatment

Some of the conservative methods for treating OA are also methods for preventing OA. Exercising for weight loss and lower extremity muscle strengthening should be considered first-line. These exercise programs can be done solely by the patient or under supervision from a therapist or trainer. Supervised exercise programs may be more beneficial for those without significant experience with aerobic or strengthening exercises, in order to prevent injuries. A supervised program will allow for strength deficits, poor technique, and malalignment during dynamic exercises to be corrected. It is important that patients with knee OA participate in low impact exercises such as cycling, elliptical machines, and swimming. A systematic review and meta-analysis showed that stationary cycling exercise relieves pain and improves sport function in patients with knee OA, but may not be as clinically effective for improving stiffness, daily activity, and quality of life [8].

A structured physical therapy program will allow patients to participate in supervised aerobic and strengthening exercises, as well as utilize other noninvasive treatment modalities. Cold and hot compression, transcutaneous electrical nerve stimulator (TENS), and neuromuscular electrical stimulation are available. Structured programs will allow for the evaluation of gait and potential need for an assistive device or bracing.

Oral and topical NSAIDs are used as first-line medications in patients with knee OA. In a meta-analysis, diclofenac at a dose of 150 mg per day was found to be the most effective NSAID for pain and function [2]. Patients must be monitored for side effects of NSAID use such as gastrointestinal and renal issues. Opioids are usually not prescribed for knee OA but tramadol is sometimes used on a case by case basis, especially in patients with debilitating pain. Tylenol can be used safely at a dose of 3000 mg per day, typically taken as 1000 mg three times a day. A literature review showed that capsaicin has a good safety profile and efficacy in reducing knee OA, despite the studies having limitations [9].

Common interventions for treatment of knee OA include intra-articular injections with corticosteroids, viscosupplementation,

and platelet-rich-plasma (PRP). Corticosteroid injections help to disrupt the inflammatory cascade and reduce pain. There is often short-term pain reduction with corticosteroid injections, which is why they should be coupled with physical therapy to maximize overall benefit. Pain can be a limiting factor for patients not tolerating a physical therapy program. Viscosupplementation injections with hyaluronic acid are used to compensate for lack of cushion and lubrication in the knee OA joint. There are different brands of hyaluronic acid that can be used depending on insurance coverage, some including a series of injections. Platelet-rich plasma (PRP) is derived from the patient's blood and then injected into the knee joint. PRP is not currently FDA approved for the treatment of knee OA. However, studies have shown the benefits of PRP to include reduced pain, improved joint function, and potential cartilage repair, although more studies are required to validate the efficacy [10]. Corticosteroid and PRP injections are commonly performed under ultrasound guidance for visualization of the needle and to scan for any other pathology that may be associated with the knee OA. Figure 4.2 shows an intra-articular corticosteroid injection with effusion in suprapatellar recess.

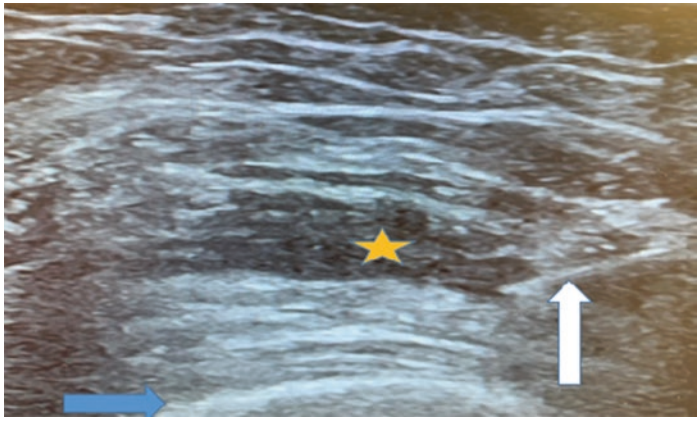

Fig. 4.2 Blue arrow—patella, yellow star—suprapatellar recess, white arrow—needle tip

References

1. Felson D, Lawrence R, et al. Osteoarthritis: new insights part 1: the disease and its risk factors. Ann Intern Med. 2000;133:635–46.
2. Lespasio M, Piuzzi N, Husni E, Muschler G, Guarino AJ, Mont M. Knee osteoarthritis: a primer. Perm J. 2017;21:183. https://doi.org/10.7812/TPP/16-183.
3. Jang S, Lee K, Ju J. Recent updates of diagnosis, pathophysiology, and treatment on osteoarthritis of the knee. Int J Mol Sci. 2021;22(5):2619.
4. Kapoor M, Mahomed N, et al. Osteoarthritis: pathogenesis, diagnosis, available treatments, drug safety, regenerative and precision medicine. Cham: Springer International; 2015. https://doi.org/10.1007/978-3-319-19560-5_1.
5. Boyan B, Tosi L, Coutts R, et al. Sex differences in osteoarthritis of the knee. J Am Acad Orthop Surg. 2012;20(10):668–9.
6. Chiu R, Hu Y, et al. Vitamin C protects chondrocytes against monosodium iodoacetate-induced osteoarthritis by multiple pathways. Int J Mol Sci. 2016;18(1):10038. https://doi.org/10.3390/ijms18010038.
7. Lee L, Yan C, Chiu K, Fung W, et al. Imaging of knee osteoarthritis: a review of current evidence and clinical guidelines. Musculoskelet Care. 2021;19(3):363–74. https://doi.org/10.1002/msc.1536.
8. Luan L, Bousie J, Pranata A, Adams R, Han J. Stationary cycling exercise for knee osteoarthritis: a systematic review and meta-analysis. Clin Rehabil. 2021;35(4):522–33.
9. Guedes V, Castro JP, Brito I. Topical capsaicin for pain in osteoarthritis: a literature review. Reumatol Clin (Engl Ed). 2018;14(1):40–5. https://doi.org/10.1016/j.reuma.2016.07.008.
10. Kennedy M, Whitney K, Evans T, LaPrade R. Platelet-rich plasma and cartilage repair. Curr Rev Musculoskelet Med. 2018;11(4):573–82.