Knee arthrosis

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Knee Arthrosis

Graduate thesis

Zagreb, 2019.

The graduate thesis was made at the department of orthopedics, Salata, Zagreb and was mentored by Orthopedic Surgeon, Prof. Mislav Jelic and was submitted for evaluation in 2019.

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Summary

Osteoarthritis of the knee, Mr. Joshua Munonye.

Knee osteoarthritis a common disease of the geriatric population. It affects women more than men and is one of the leading causes of disability. With knee osteoarthritis, there is a progressive destruction of articular cartilage. Common risk factors include age, sex, weight, trauma to the knee joint due to repeated movements, in particular squatting and kneeling. Clinical symptoms include pain around the knee, stiffness particularly in the morning and swelling around the joint, grinding or cracking sounds during joint movement and functional deterioration of the joint. Treatment plans for knee osteoarthritis begins with a nonsurgical, conservative approach. If this method becomes refractory, surgery is considered. This thesis will discuss osteoarthritis of the knee.

Key words: knee, osteoarthritis, cartilage.

Sažetak

Osteoartritis koljena. Mr Joshua Muonye.

Osteoartritis koljena je česta bolest gerijatrijske populacije. Ona više pogađa žene nego muškarce i jedan je od vodećih uzroka invaliditeta. Kod osteoartritisa koljena dolazi do progresivnog razaranja zglobne hrskavice. Uobičajeni rizični čimbenici uključuju dob, spol, težinu, traumu koljenskog zgloba zbog ponovljenih pokreta, osobito čučanj i klečanje. Klinički simptomi uključuju bol oko koljena, ukočenost osobito u jutarnjim satima i oticanje oko zgloba, brušenje ili zvuk pucanja tijekom pokreta zglobova i funkcionalnog pogoršanja zgloba. Planovi liječenja osteoartritisa koljena započinju bez operacije, konzervativnim pristupom. Ako ova metoda postane refraktorna, razmatra se operacija. U ovom radu raspravljat će se o osteoartritisu koljena.

Ključna rijeci: koljeno, osteoartritis, hrskavica

Introduction

Osteoarthritis also known as degenerative joint disease is one of the most common causes of chronic knee pain. It is a disease involving inflammation of the bone and joint cartilage. A healthy knee joint consists of three bones: femur, tibia and patella each with its own layer of articular cartilage, a type of connective tissue that allows the bones to glide against each other, without pain and friction. With osteoarthritis, there is a progressive loss of articular cartilage. It is most common in the geriatric population with women affected more than men. Knee osteoarthritis can be divided into primary and secondary. In primary osteoarthritis, there is a progressive loss of articular cartilage without any clear underlying cause, whereas in secondary osteoarthritis, several factors like post-traumatic injury or abnormal articular cartilage are risk factors to developing secondary osteoarthritis. Common clinical symptoms include knee pain, stiffness particularly in the morning and swelling around the joint, grinding or cracking sounds during joint movement and functional deterioration of the joint. The intensity of these symptoms may vary from person to person. Management and treatment options for knee osteoarthritis begins with conservative methods and then surgical treatment when conservative treatment becomes refractory (1, 5, 6).

Knee Anatomy

To better understand how knee problems occur, it is important to understand the anatomy of the knee joint and how the parts of the knee work together to maintain normal function. The knee joint is made up of three bones: the femur, the patella and the tibia. The femur has the medial and lateral condyle. The patella articulates with the femur. A well-functioning knee joint is critical to mobility including standing, walking and running. The important structures of the knee can be divided into several categories. These include cartilage, ligaments, tendons, muscles, nerves, blood vessels and synovium (2). Synovial fluid is a viscous fluid found in the cavities of synovial joints, including the knee. It is secreted by synovial cells located in the inner membrane of synovial joints. Synovial fluid contains hyaluronic acid that is synthesized by the synovial membrane and secreted into the knee joint space to increase the viscosity and elasticity of articular cartilage. This viscous fluid helps with reducing friction in the knee joint by lubricating the surfaces between synovium and cartilage (2).

The knee is the joint where the femur and the tibia meet. The patella or knee cap is made of bone and cartilage and sits in front of the knee. The knee joint is a synovial joint. Synovial joints are enclosed by a ligament capsule and contains a fluid called synovial fluid that lubricates the joint. The distal part of the femur joins the top of the tibia to create the knee joint. Two round knobs called femoral condyles are found on the end of the femur. These condyles rests on the top surface of the tibia. The surface is called the tibial plateau. The outside half, furthest away from the other knee is called the lateral tibial plateau and the inside half closest to the other knee is called the medial tibial plateau. The patella glides through a special groove formed by the two femoral condyles called the patellofemoral groove. The smaller bone of the lower leg, the fibula, never really enters the knee joint. It does have a small joint that connects it to the side of the tibia. This joint normally moves very little. Articular cartilage is the material that covers the ends

of bones of any joint. It is a slippery substance that allows the surfaces to slide against one another without damage to either surface. The function of articular cartilage is to absorb shock and provide an extremely smooth surface to facilitate motion. In the knee, articular cartilage covers the ends of the femur, the top of the tibia and the back of the patella (2).

Ligaments are tough bands of tissue that connects the ends of bones together. Two important ligaments are found on either side of the knee joint. They are the medial collateral ligament (MCL) and the lateral collateral ligament (LCL). Inside the knee joint, two other important ligaments stretch between the femur and tibia, the anterior cruciate ligament (ACL) and the posterior cruciate ligament (PCL). The ACL and PCL prevent the knee from moving too far in the side to side direction. They control the front to back motion of the knee joint. The ACL keeps the tibia from sliding too far forward in relation to the femur. The PCL keeps the tibia from sliding too far backward in relation to the femur. Working together, the two cruciate ligaments controls the back and forth motion of the knee. The ligaments all taken together are the most important structures controlling the stability of the knee (2).

Two special types of cartilage called menisci sit between the femur and tibia. The two menisci are important for two reasons. Firstly, they work like a gasket to spread the force from the weight of the body over a larger area and secondly, they help the ligament with stability of the knee. Without the menisci, any weight of the femur will be concentrated to one point on the tibia but with the menisci, weight is spread across the tibial surface. Weight distribution by the menisci is important because it protects the articular cartilage on the ends of the bones from excessive forces. Without the menisci the concentration of force into a small area on the articular cartilage will damage the surface leading the degeneration over time. The menisci make the knee joint more stable by acting like a wedge. The menisci are thicker around the outside and this thickness helps the round femur from rolling on the flat tibia. The menisci convert the tibial surface into a shallow socket. The socket is more stable and more efficient in transmitting the weight from the upper part of the body. In osteoarthritis of the knee, all components of the knee joint are affected and not only the articular cartilage (2).

Etiology and risk factors

Osteoarthritis has traditionally been subdivided into two groups according to its etiology: primary (idiopathic or non-traumatic) and secondary (usually due to trauma or mechanical misalignment). The severity of the disease can also be graded according to the radiological findings by Kellgren-Lawrence (KL) system described in 1957. It was believed that osteoarthritis was exclusively a degenerative disease of the cartilage, however, latest evidence has proven that osteoarthritis is a multifactorial entity, involving multiple causative factors like trauma, mechanical forces, inflammation, biochemical reactions, and metabolic derangements. It is a complex disease affecting the whole joint and not only the cartilaginous tissue. Due to its lack of blood vessels and nerve supply, the cartilage, by itself is not capable of producing inflammation or pain at least on the early stages of the disease. Thus, the cause of the painful knee joint originates from sources outside the cartilaginous component of the joint such as the joint capsule, synovial membrane, periosteum, ligaments and periarticular muscles (2, 5)

Osteoarthritis is a condition once thought to be a normal consequence of aging and mechanical consequence of wear and tear on the cartilage of a joint leading to the term degenerative joint disease. However, the disease is now known to be multifactorial in origin and involves a complex interplay of constitutional and mechanical factors, including joint integrity, genetic predisposition, local inflammation, mechanical forces and cellular and biomedical processes. Knee osteoarthritis is closely linked with age, as x-ray evidence of osteoarthritis occurs in people over the age of 65. Although till this day, the mechanism of osteoarthritis has not been fully clarified, it has been reported that the incidence and prevalence of osteoarthritis is higher in women than men. Excess weight on the knee can have a negative impact on the knee joint (1,2)

An association between obesity and the prevalence and incidence of knee osteoarthritis has been consistently demonstrated in several studies. Although, excess weight leads to increased loading of the weight-bearing joint, this is not the only factor involved in the association between osteoarthritis and obesity. Obesity increases the risk of knee osteoarthritis by multiple mechanisms: increased joint loading; changes in body composition, with negative effects related to inflammation; and behavioral factors, such as diminished physical activity and subsequent loss of protective muscle strength (1, 2, 18) (see Figure 1).

Risk of osteoarthritis

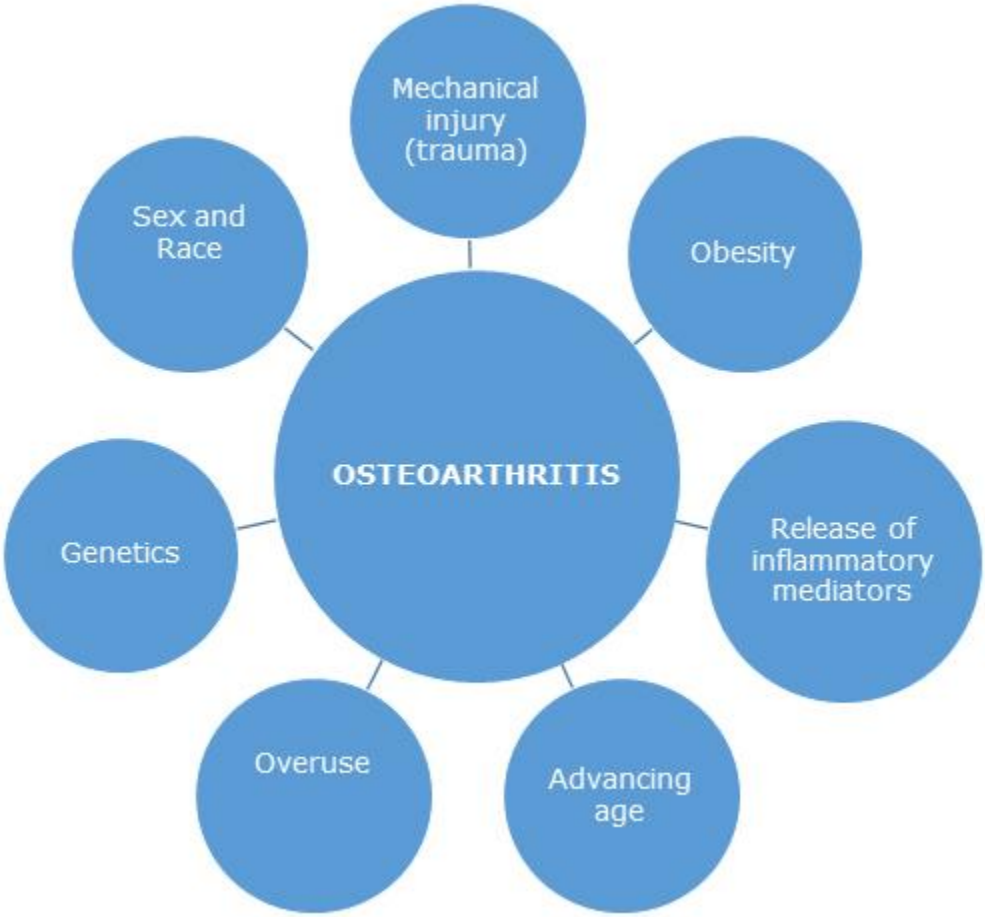

Figure 1. Osteoarthritis risk factors. Source: Wikidoc (32).

Pathophysiology

Both primary and secondary osteoarthritis have the same pathological basis with bilateral symmetry often observed in primary osteoarthritis (4). Although osteoarthritis has been classified as a noninflammatory arthritis, recent studies have shown that inflammation occurs as cytokines and metalloproteinases are released into the joint (5, 6). These agents cause increased catabolic activities in the extracellular matrix leading to cartilage degeneration and osteoarthritis. Studies have shown that high levels of interleukin-17 (IL-17), a proinflammatory cytokine were found in the synovium of osteoarthritic joints. Other inflammatory molecules that have been associated with osteoarthritis include 15-hydroxyeicosaetraenoic acid, prostaglandin E2, IL-1beta, IL-receptor antagonist, and uric acid (7, 8).

In the early phases of osteoarthritis, swelling of the articular cartilage usually occurs, because of the increased synthesis of proteoglycans. This reflects a flawed attempt to repair damaged cartilage. This stage may last for several years and the chondrocytes can assume a hypertrophic phenotype. However, as the disease progresses, proteoglycan levels reduce significantly, causing the cartilage to soften and lose elasticity. Thus, further compromising the integrity of the joint space. Microscopically, flaking and fibrillation of the articular cartilage develop on the surface of the osteoarthritic knee joint. As the disease progresses, the joint space diminishes due to loss of cartilage. The greatest loss of joint space is commonly seen in the medial femorotibial compartment because it experiences the highest loads in comparison with the lateral femorotibial and patellofemoral compartments. Varus and valgus deformities may occur if the medial or lateral compartments are severely affected (9, 10, 11).

Over time the damaged cartilage breaks down until the underlying bone is exposed. Bone stripped of its protective cartilage continues to articulate with the opposing surface. Eventually, the stresses exceed the ultimate strength of the bone tissue. After cartilage loss, the subchondral bone responds with vascular invasion and increased cellularity to becoming eburnation at pressure areas. The traumatized subchondral bone may also undergo cystic degeneration, which is attributable either to pressure necrosis or synovial intrusion into bone. At non-pressure areas along the articular margin, vascularization of subchondral marrow, osseous metaplasia of synovial connective tissue, and ossifying cartilaginous protrusions lead to irregular outgrowth of new bone (osteophytes) (see figure 4). Loose bodies (joint mice) are present in the intra-articular space as a result of fragmented cartilage or osteophytes. Along with joint damage, osteoarthritis may also lead to pathophysiological changes in associated ligaments and the neuromuscular apparatus (9, 10).

Stages of osteoarthritis

Osteoarthritis can be classified as mild, moderate and severe. With mild knee osteoarthritis, there is mild discomfort of the knee joint. Though the joint space appears normal, the cartilage matrix has begun to break down from a combination of wear and tear and increased production of degrading enzyme. In addition, bone spurs known as osteophytes may begin to develop on the edge of the joint. These small, smooth, dense growth of bone are part of the body's natural response to the loss of cartilage. Progression of the disease can be slowed at this stage by increased exercise and weight loss. With moderate knee osteoarthritis, changes in the joint are much more evident. The cartilage surface between the bones has begun to erode, narrowing the gap between the femur and tibia. Hyaluronic acid (HA), which helps synovial fluid lubricate the joint is now becoming less viscous, elastic and concentrated. Osteoarthritis often affects the subchondral bone located just underneath the cartilage. Subchondral bone provides hydration and oxygen to the cartilage. As subchondral bone flattens and tries to repair itself, cytokines and proteins are released into the synovial fluid. Osteophytes may increase in number and size making the bone rougher. All these factors combine to make joint pain more severe and long lasting both with movement and at rest. Weight loss, exercise, pain relievers, HA or steroid injections are commonly prescribed treatments. With severe osteoarthritis, conditions worsen dramatically. The joint has become far narrower causing more rapid and severe destruction of the cartilage. The knee becomes inflamed and sore. Synovial fluid is decreased, increasing friction

and pain during movement. Within the synovial membrane, destructive proteins are produced, which degrade cartilage and soft tissue around the knee. Osteophytes continue to develop and bone moves against bone not cartilage. Mobility, activity of daily living and quality of life are severely impacted. Treatment for severe osteoarthritis is typically surgery (12, 13) (see Figure 2, 3 & 4).

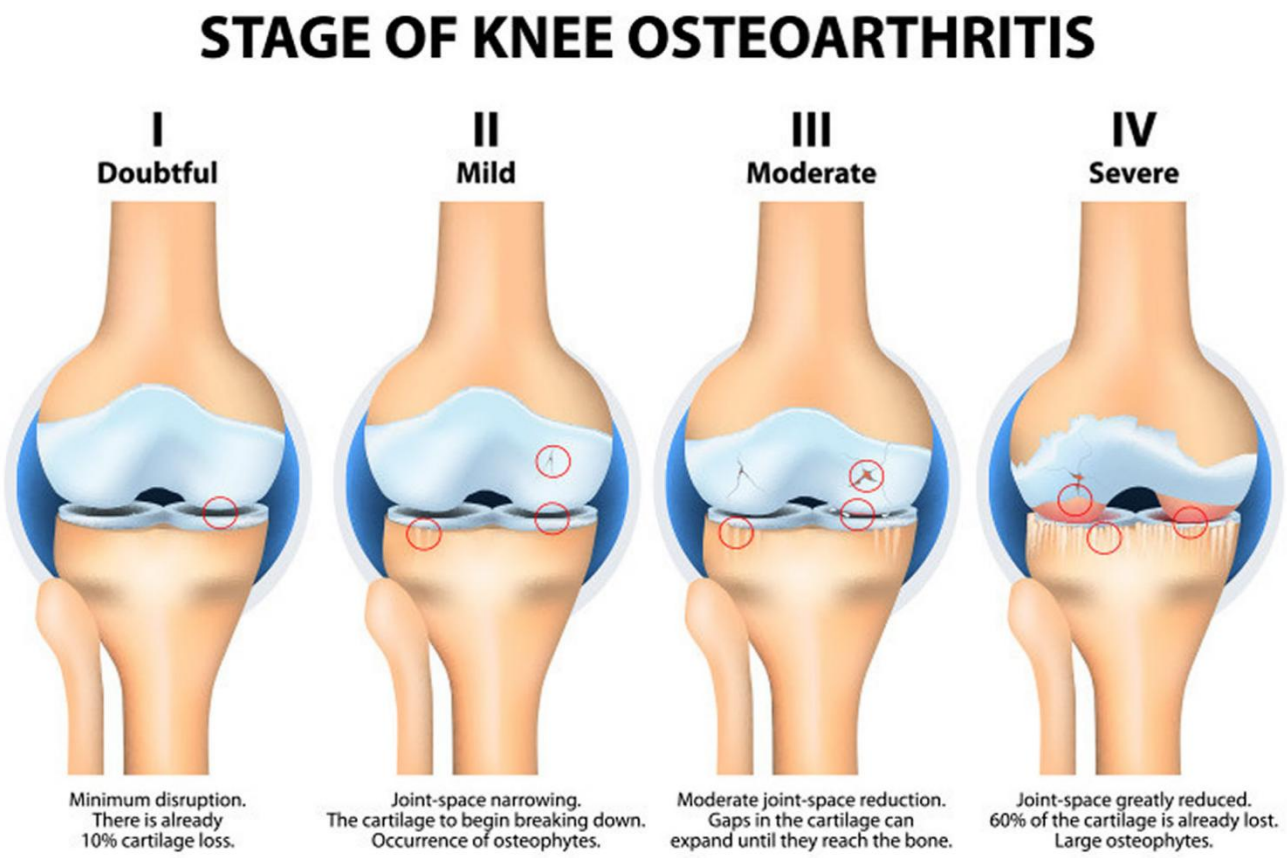

Figure 2. Osteoarthritic changes in the knee. Source: Health Jade Team (33).

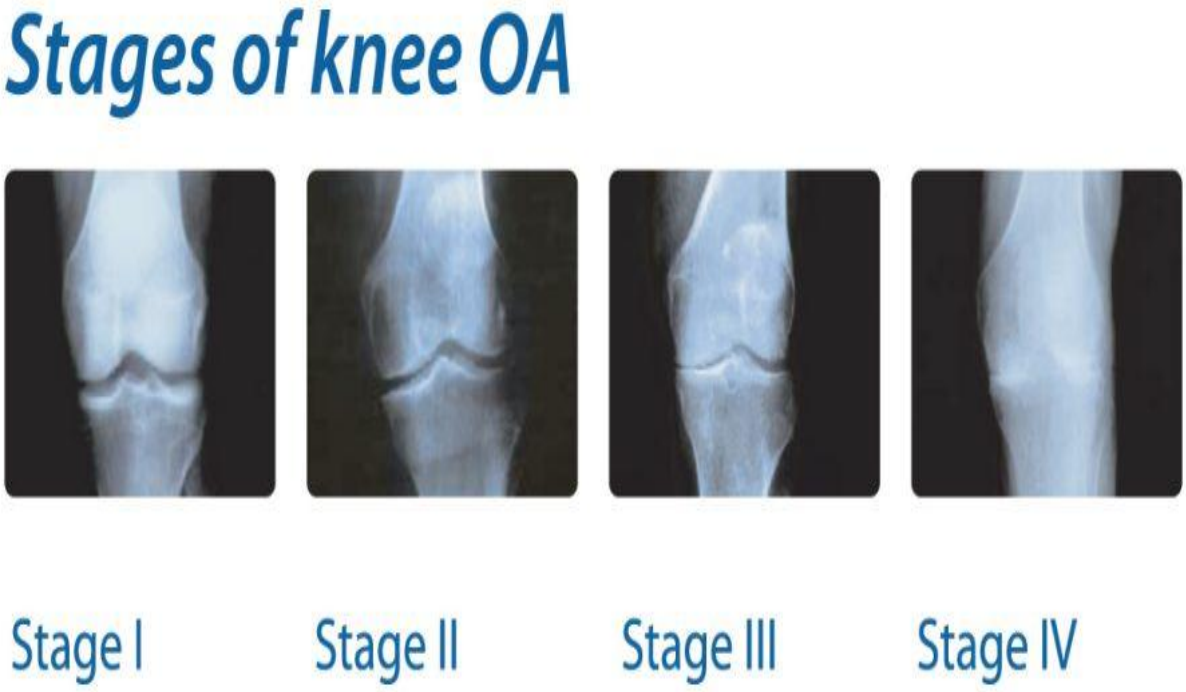

Figure 3. Radiological changes in osteoarthritic knee. Source: NorrisHealthUk (34).

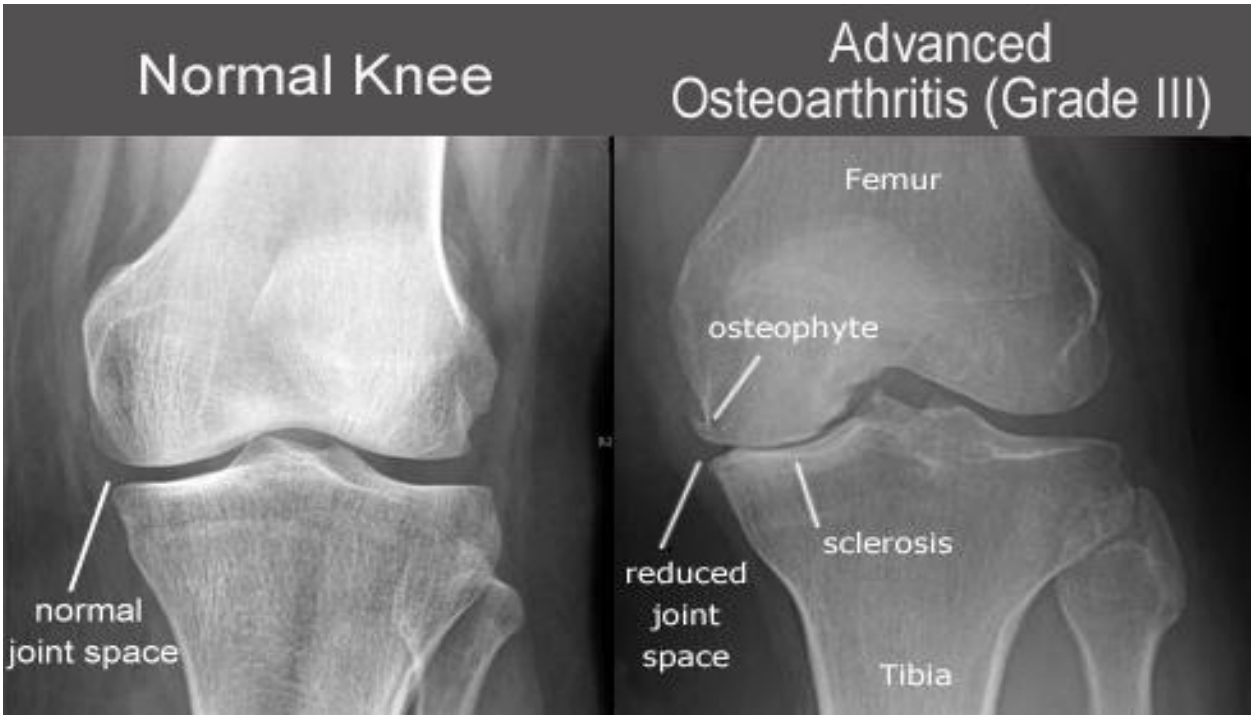

Figure 4. Normal knee and a grade 3 knee osteoarthritis. Picture also shows outgrowth of bone spurs (osteophytes). Source: Centre for Advanced Orthopedics, MOSC Hospital and Medical College, Kolenchery, Kochi, Kerala (35).

Treatment

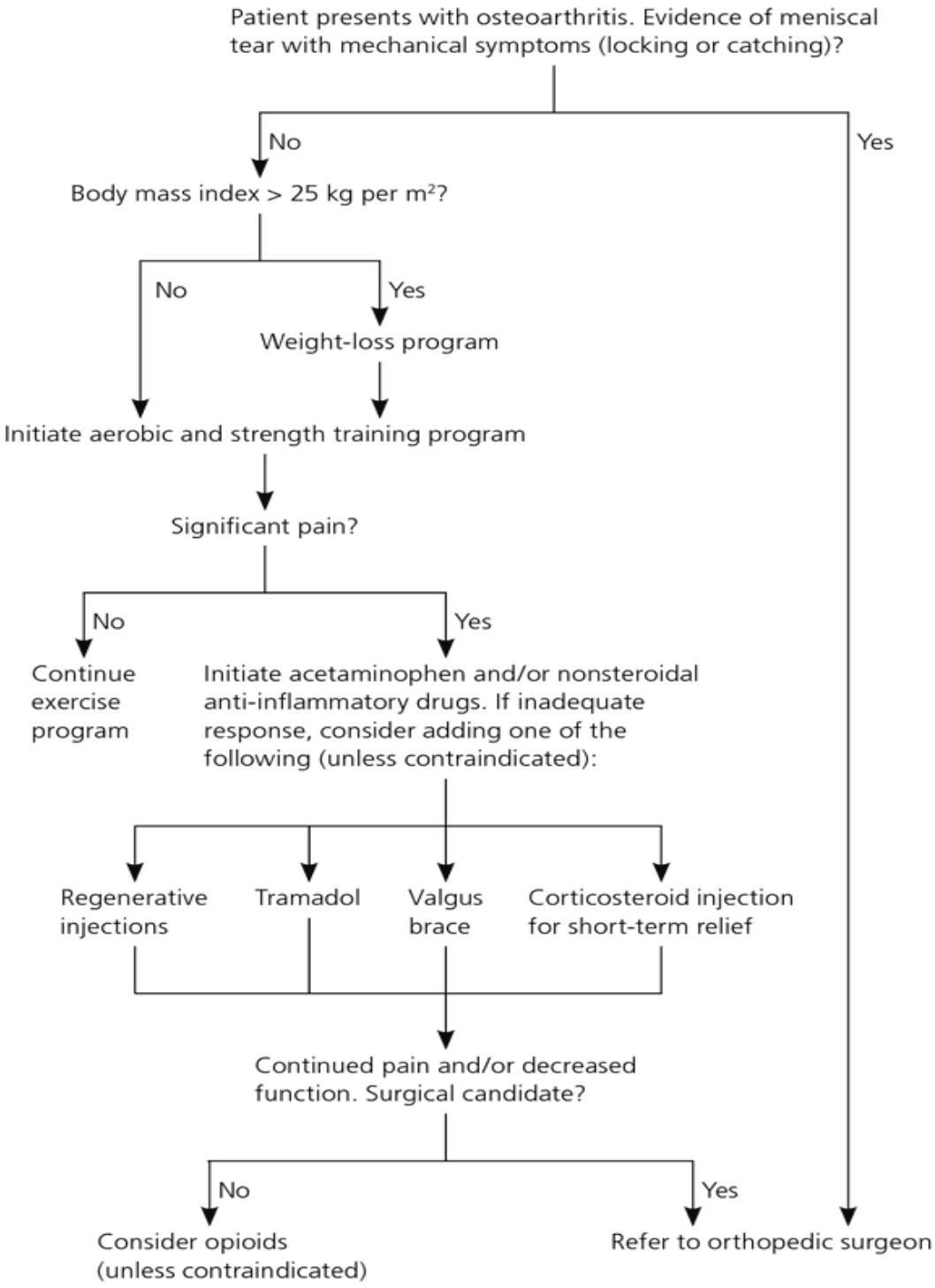

Figure 5. Algorithm for the management of knee osteoarthritis. Source: American Family Physician (37).

Management and treatment of osteoarthritis involves nonsurgical and surgical treatment options. Nonsurgical or conservative treatments include modalities like losing weight and exercise as well as physical therapy. Pharmacological treatments focus on reducing pain and inflammation. If neither of these approaches are successful, some patients might benefit from injections of HA into the joint or they might need surgery to replace the affected joint. Non-surgical treatments are useful for patients with Grades 1-3 osteoarthritis, whereas surgical treatment options are typically for patients with advanced or grade 4 knee osteoarthritis (14,15) (see figure 5 and 6).

Nonsurgical options

Nonsurgical treatment strategies are for patients who present with the initial symptoms of knee osteoarthritis. There are several therapeutic options. Heat and cold therapy can be effective in managing chronic knee pain. Heat treatments such as heating pads or warm baths enhance circulation, reduce joint stiffness and soothe tired muscles, whereas cold therapy reduce circulation, which slows inflammation, thus alleviating acute pain. The patient may need to experiment with heat and cold remedies to identify which is better to treat his/her specific symptoms (2, 16).

Treatment may include weight loss, orthotics, osteopathic treatment, muscle strengthening exercises, application of ice or heat, pharmacological treatment including NSAIDs, and viscosupplementation and hyaluronic acid injections, corticosteroid injections, glucosamine, and platelet-rich plasma (PRP). Platelet-rich plasma therapy attempts to take advantage of the blood's natural healing properties. PRP are harvested from the patient's own blood and then injected directly into the painful knee joint to provide effective pain relief, improve joint function and possibly repair cartilaginous lesions. In most cases, a simpler approach is to be aware of the activities that make the symptoms worse and minimize those activities (e.g., climbing stairs).

Avoiding high-impact activities such as jogging or football, which put stress on bones should be substituted with low-impact activities like swimming or cycling that may reduce stress on the knee and improve joint functionality. Therapeutic exercise is recommended for reducing pain and improving health status in people with osteoarthritis. Specific exercises can reduce joint pain, increase strength and flexibility and can increase range of motion. In most cases, combination of tailored exercise program with behavioral weight loss programs may be the most beneficial for improving painful joint in overweight patients. Both can be tough, especially in people who find it hard to exercise because of their knee pain (3, 16, 17, 18).

Weight loss

Obesity is one of the modifiable risk factors for incidence and progression of osteoarthritis and addressing it is crucial for successful management. Weight loss alleviates the risk of onset of the disease and in established disease, slows disease progression and improve joint function and symptoms. Evidence suggests that nonpharmacological treatment modality is overlooked and underused by physicians in both primary and secondary care. To resolve these issues, interprofessional collaboration among physicians and other health care providers within the healthcare system may provide the most effective solutions (3, 18).

Electrical Stimulation and Assistive Devices

Four nonsurgical treatment modalities for knee osteoarthritis were identified in a systemic review of the literature. Those modalities identified significantly alleviated pain associated with knee osteoarthritis. They included TENS (Transcutaneous Electrical Nerve Stimulation), neuromuscular electrical stimulation, insoles and bracing. Of note, there are no follow-up studies examining long-term outcome in most of the studies reviewed. A cheap electrical stimulator may be beneficial for treating knee osteoarthritis. The stimulator is particularly useful for those who are unable or find it difficult to perform an exercise program. Transcutaneous Electrical Nerve Stimulation uses low-voltage electrical current to alleviate knee pain. This therapy uses a small, battery-operated device that is connected via electrodes from the machine to the skin. The electrodes are typically placed on the area of pain such as the knee joint, creating a circuit of electrical impulses that travels along nerve fibers. The electrical current generates a sensation that is thought to block the pain signal from the nerve to where it is perceived in the brain as pain (3, 19).

Neuromuscular electrical stimulation also utilizes a device that transmits an electrical impulse transcutaneously via electrodes over selected muscle groups. The selected muscle groups contract under electrical stimulation. This therapeutic approach is designed to strengthen or maintain muscle mass of treated muscles. Electrical stimulation on the muscles supporting knee like the quadriceps and hamstrings may provide pain relief and strengthen the muscles. It also may delay the need for total knee arthroplasty (3).

The use of walking aid devices such as wearing a slip-on knee brace, wearing a well-cushioned shock-absorbing shoes or inserts or using a cane can help improve symptoms. Assistive devices like a cane or a crutch can help alleviate pain by reducing the force transmitted to the knee joint. Patients should be given instructions on the optimal use of a cane or crutch in the contralateral hand (20). Although the effectiveness of knee bracing is inconclusive, braces placed over the arthritic knee often assist with mobility and function and patients may find them helpful in improving their symptoms (21). Unloader knee braces unload the affected, painful side of the knee, shifting weight away from the affected side of the knee. This system "unloads" the pressure from the affected area, providing pain relief. A “support” brace redistributes the weight-bearing load, helping reducing pain. Braces are designed to reduce symptoms, improve gait mechanics and correct knee malalignment. Using pneumatic brace with extension assist resulted in significant improvements in quadriceps and hamstring muscle strength. More research is required because the optimal choice for an orthosis and their long-term effectiveness remain unclear (22, 23).

Medication

Nonsteroidal anti-inflammatory *drugs* (*NSAIDs*) such as ibuprofen, naproxen, diclofenac, or aspirin are among the most widely used medications for knee osteoarthritis. A current network meta-analysis concluded that diclofenac at a dose of 150 mg per day is the most effective NSAID for treating osteoarthritic knee. These medications should be taken with caution to prevent excessive use. In addition, the health care practitioner needs to consider the patient’s

comorbidities and safety information when selecting any of the aforementioned medications for a patient (1, 3)

Intra-articular knee injections

Intra-articular injections into the knee are an appealing option for patients because they present a low risk of harm while providing potential relief of pain and improvement of joint function. These knee injections are a tempting successful alternative in younger people with less severe arthritic knee. Most reported intra-articular knee injections for treatments of osteoarthritis can be categorized into three groups: viscosupplementation with hyaluronic acid (HA), Intra-articular corticosteroids and biologics.

Viscosupplimention with hyaluronic acid (HA)

People with knee osteoarthritis have reduced amounts of HA in their joint fluid (24). Injection into the knee with HA has been shown to alleviate pain temporarily. The pain relief effects and improved mobility typically last for three months. Evidence on the efficacy of HA in knee osteoarthritis is still debated and treatment recommendations remain uncertain. The American Academy of Orthopedic Surgeon recently recommended against using HA for patients with symptomatic end-stage degenerative knee joint disease. There is lack of reliable evidence that HA injections will cause regression of osteophytes, regeneration of cartilage and remodeling of subchondral bone. More studies are needed to ascertain whether high-molecular-weight and cross-linked preparation of HA have superior efficacy with other HA preparations or other currently available treatments. In addition, further investigations involving long-term outcomes of efficacy, safety, and economical cost-benefit analyses are needed (25, 26).

Intra-articular corticosteroids

Intra-articular injection of corticosteroids is a common therapy for knee osteoarthritis, but studies evaluating their efficacy have been inconsistent. The American Academy of Orthopedic Surgeon does not recommend for or against the use of intra-articular corticosteroids into the knee for conservative treatment modalities. Clinically important benefits of one to six weeks of corticosteroids injections remain uncertain because of the overall quality of the studies, large amount of heterogeneity between trials and evidence of small- study effects (26).

Biologics

Multiple studies and systemic reviews have reported on the use intra-articular PRP for the treatment of knee osteoarthritis. Platelet-rich plasma contains concentrated growth factors. It is believed that PRP accelerates and promotes healing and stimulates the repair process (3). Initial findings suggest that PRP procedure is safe and efficacious. Although, some patients have experienced temporary pain or swelling after PRP use, these symptoms usually subside within 72 hours, and no long-term side effects have been reported. Patients treated with lower leukocyte concentration known as leukocyte-poor PRP (LP-PRP) showed a sustained improvement in knee function in comparison HA and placebo. The effect of leukocyte-poor PRP begin about 2 months after application and lasting up to 12 months. While the current evidence has demonstrated the efficacy PRP injections in improving symptoms in knee osteoarthritis compared with control

studies, the quality of evidence is lacking and more investigations are needed to establish the efficacy of using PRP as a treatment option. There is no large study to document the value of PRP to become the standard of care (27).

Surgical options

If conservative treatment option for knee osteoarthritis fails, surgery is a valid option. The switch to surgical alternative is considered when conservative management for at least three months becomes ineffective or futile and when quality of life is greatly affected. Surgical interventions for the treatment of knee osteoarthritis include arthroscopy, cartilage repair, osteotomies and joint arthroplasties, which includes total and partial knee replacement. Several variables or parameters are taken into consideration and must be evaluated when determining which of these surgical procedures is the most suitable for a particular patient. The location and extent or severity of the knee osteoarthritis along with patient comorbidities and risk factors must be contemplated for any surgical candidate (3, 25, 26, 30).

Arthroscopic lavage and debridement

Arthroscopic techniques include lavage and debridement of the knee to treat symptomatic knee osteoarthritis. Theoretically, knee arthroscopy should improve symptoms by removing debris and inflammatory cytokines that cause synovitis. Debridement can shave off rough articular cartilage or trim torn or degenerated meniscal fragments. Arthroscopy is one of the most commonly performed procedures in knee osteoarthritis, however, its role in the management of knee osteoarthritis is debatable. A controlled trial study by Moseley et al. demonstrated that there was no benefit comparing arthroscopy lavage and debridement with placebo-controlled surgical trial (38). Patients with less extensive arthritis as seen on radiology, moderate arthritic changes of articular cartilage, and a younger age at the time of the surgery have higher chance of improvement. Little radiographic evidence of osteoarthritis with a short duration of pain and mechanical symptoms correlate with a favorable outcome. On the basis of detailed clinical and/or radiographic evidence, arthroscopic washout seems to provide only short-term benefit to selected patients with mild radiographic osteoarthritis and joint effusion. For most patients with knee osteoarthritis, arthroscopic lavage and debridement offers little benefit (29). Arthroscopic debridement is not recommended as routine treatment for knee osteoarthritis, although patients with mechanical symptoms such as degenerative meniscus tears and loose bodies with locking symptoms could benefit (29).

In general, arthroscopic surgery is not a good treatment for arthritis. Quantification of the benefits of arthroscopy has been limited by methodological problems and limited analysis in many studies. Knee arthroscopy is an outpatient procedure with relatively less serious complications and the procedure can last less than 30 minutes, or over an hour. The postoperative course is predictive, and the risk of complications associated with knee arthroscopy remain small for most patients. If arthroscopy fails, it will not prevent the patient from having a THR or other definitive surgery and so patient and surgeon may feel it is “worth a try”. However, it cannot change the course of the disease; it may only be a helpful instrument to minimize pain in well-selected patients (28, 29).

Osteotomies around the knee

High tibia osteotomy (HTO) is performed when medial unicompartmental osteoarthritis is accompanied by varus malalignment. The goal is to unload the medial compartment by a lateral transfer of the weight-bearing axis. This procedure delays THR in young and physically active patients and produces good results. It is commonly used to relieve pain when nonoperative treatments have failed. High tibia osteotomy is commonly recommended for patients under 55 years of age with a mobile knee. It has proven beneficial for the young who want to delay TKR. Good candidate for HTO include young, active arthritic patients who are unable to have arthroplasty due to excessive wear, patients with good vascular support, non-obese patients with only one knee compartment affected and the patient who is able to follow the postoperative protocol. The goal of the surgery is to release the involved joint compartment by correcting the malalignment of the tibia and to maintain the joint line perpendicular to the mechanical axis of the leg. There are two techniques that can be used: closing wedge osteotomy and opening wedge osteotomy. The surgeon determines the choice of the technique based on the requirement of the patient. Closing wedge osteotomy is the most commonly used technique to perform HTO. In this procedure, the surgeon makes an incision in front of the knee and removes a small wedge of bone in the upper part of the tibia. This manipulation brings the bone together and close the space left by the removed bone. The surgeon then uses plates and screws to bind the bone together while the osteotomy heals. This procedure unloads the pressure off the damaged joint area and helps to transfer some of the weight to the outer part of the knee, where the cartilage is still intact. In opening wedged osteotomy, the surgeon makes an incision in front of the knee just below the knee cap and makes a wedged shape cut in the bone. Bone grafts is used to fill the space of the wedged-shaped opening and if required plates and screws can be attached to further support the surgical site during the healing process (30).

Joint Arthroplasty

Total knee replacement is indicated in stage 4 knee osteoarthritis, when more than one compartment is involved and when conservative treatment options have failed. Total knee replacement is correlated with improved quality of life and overall patient function. Until now it has been the first-line procedure for end-stage knee osteoarthritis. Multiple studies have documented 15 years survival rate of TKA of up to 98%. In contrast, results in younger patients are mostly reported to be inferior with 76% survival rate at 10 years. Although TKA has become an effective means for treating advanced arthritis, postsurgical pain remained in 1 of 8 patients despite an absence of clinical or radiological abnormalities. The main complications of TKA include femoropatellar problems, loosening of prosthesis or prothesis malposition, infections and stiffness of the knee. There is an association between existing comorbid conditions of patients and the range of motion and condition of the knee postoperatively. However, there have been significant refinement of understanding in the treatment of complications. The importance of patient-related factors to outcome of TKA is shown, and these factors should influence preoperative counseling of patients awaiting TKA (31).

For those patients with osteoarthritis mainly in only one compartment of the knee, partial knee replacement offers an attractive alternative approach to TKR or osteotomy. In this procedure,

only the degenerated cartilage in an isolated part of the joint is resurfaced. The choice between partial knee replacement and TKR is not well defined. Partial knee replacement is associated with a remarkable reduced risk of postoperative complications and mortality as well as better functional and patient satisfaction outcomes after 6 months. It may also save costs compared with TKR, given a shorter hospital stay. In addition, partial knee replacement tends to have quicker recovery, reduced invasiveness and blood loss, fewer and lower incidence of severe complications like infection and lower mortality than TKR (31).

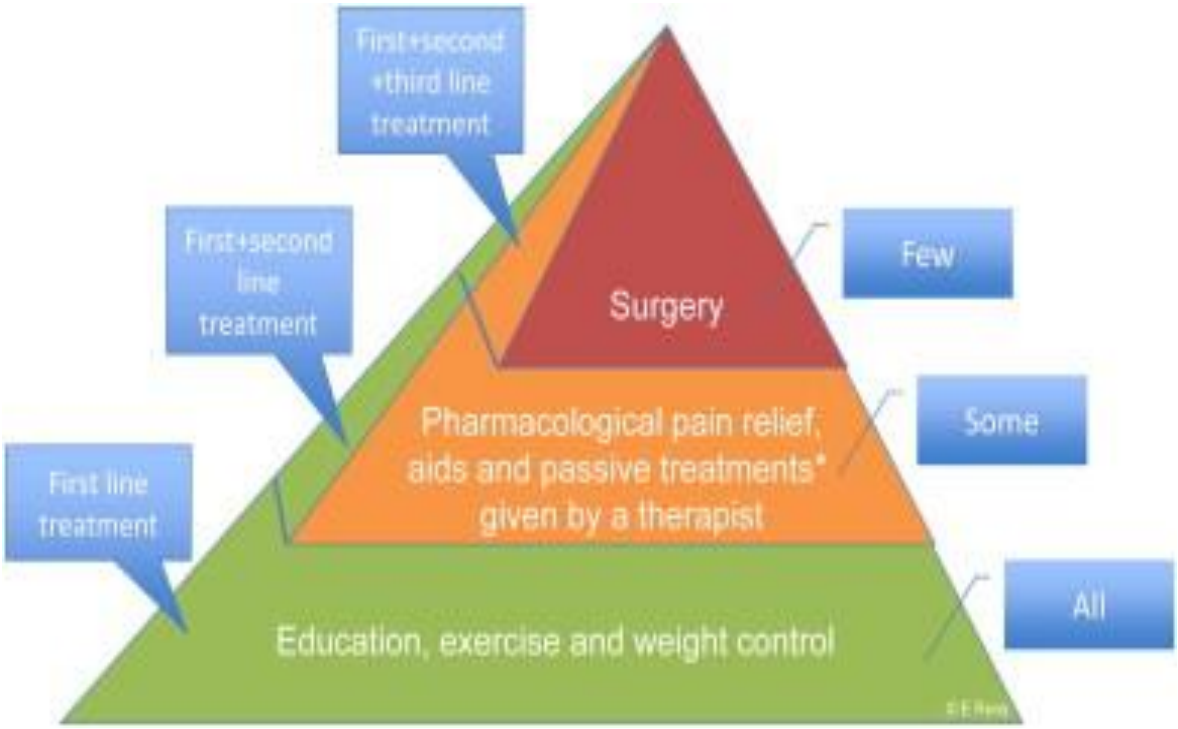

Figure 6. Global clinical guidelines suggest the above type of management for knee osteoarthritis starting with education, exercise and weight control to everyone who seeks medical care because of pain from knee joints. If that is not enough, it should be added on with pharmacological pain relieve aids, braces or orthopedic shoes. If conservative treatment modalities fail, consider surgical options. Source: Osteoarthritis and Cartilage Journal (36).

Conclusion

Knee osteoarthritis is a degenerative joint disease and is one of the leading causes of disability worldwide largely due to pain, the primary symptom of the disease. Although the root cause of knee osteoarthritis is still unclear and is under current investigation, it is accepted that it is a multifactorial disease affecting the whole joint. Knee osteoarthritis has a multi-factorial etiology. They can be described as either nonmodifiable or modifiable. Non-modifiable risk factors are those

that are heredity or congenital that may predispose a joint to developing knee osteoarthritis. Modifiable risk factors are conditions that can be managed effectively and therefore can be altered. Current treatment aims at controlling pain, improving joint function and limiting disabilities. Non-operative treatments are first-line therapy for patients with initial presentation of knee osteoarthritis. Treatment may include avoiding physical activities that puts strain on the knee and switching to low-impact aerobic exercises, shading excess weight, participating in muscle strengthening exercises, use of orthotics and braces, application of cold or heat, treatment with medications such as NSAIDs and intra-articular injection treatments. Surgery should be considered when a patient is refractory to nonoperative treatment options and patient's quality of life is significantly impacted. Surgical intervention for osteoarthritis of the knee includes minimally invasive arthroscopic debridement, cartilage repair, osteotomies and knee arthroplasty (partial and total knee replacement).

Acknowledgements

I would like to thank my mentor, Prof. Mislav Jelic for his guidance and constructive criticism throughout the course of my thesis. I am thankful to Prof. Domagoj Delimar for his time in examining my work.

References

1 Hsu H, Siwiec RM. Knee Osteoarthritis (2018). *StatPearls.*

2 Flandry F, Hommel G. Normal anatomy and biomechanics of the knee. *Sports Med Arthros*c Rev. 2011 Jun;19(2):82-92

3 Lespasio, M. J., Piuzzi, N. S., Husni, M. E., Muschler, G. F., Guarino, A., & Mont, M. A. (2017). Knee Osteoarthritis: A Primer. *The Permanente journal*, *21*, 16–183.

4 Buckland-Wright C, Verbruggen G, Haraoui PB. Imaging: radiological assessment of hand osteoarthritis. *Osteoarthritis Cartilage*. 2000. 55-6

5 Mora JC, Przkora R, Cruz-Almeida Y. Knee osteoarthritis: pathophysiology and current treatment modalities. *Journal of Pain Research. (*2018). 2190

6 Poole AR. An introduction to the pathophysiology of osteoarthritis. *Front Biosci*. 1999 Oct 15. 4

7 Mabey, T., & Honsawek, S. (2015). Cytokines as biochemical markers for knee osteoarthritis. *World journal of orthopedics*, *6*(1), 95–105.

8 Krasnokutsky S, Oshinsky C, Attur M, Ma S, Zhou H, Zheng F, et al. Serum Urate Levels Predict Joint Space Narrowing in Non-Gout Patients With Medial Knee Osteoarthritis. *Arthritis Rheumatol*. 2017 Jun. 69 (6):1213-1220.

9 Man, G. S., & Mologhianu, G. (2014). Osteoarthritis pathogenesis - a complex process that involves the entire joint. *Journal of medicine and life*, *7*(1), 37–41.

10 Chan PMB, Wen C, Yang WC, Yan C1, Chiu K (2017). Is subchondral bone cyst formation in non-load-bearing region of osteoarthritic knee a vascular problem? *Science direct,* 80-83.

11 Nakagawa, Y., Mukai, S., Yabumoto, H., Tarumi, E., & Nakamura, T. (2015). Cartilage Degeneration and Alignment in Severe Varus Knee Osteoarthritis. *Cartilage*, *6*(4), 208–215.

12 Kohn, M. D., Sassoon, A. A., & Fernando, N. D. (2016). Classifications in Brief: Kellgren-Lawrence Classification of Osteoarthritis. *Clinical orthopaedics and related research*, *474*(8), 1886–1893.

13 Case, R., Thomas, E., Clarke, E., & Peat, G. (2018). Prodromal symptoms in knee osteoarthritis: a nested case-control study using data from the Osteoarthritis Initiative. *Osteoarthritis and cartilage*, *23*(7), 1083–1089.

14 Vaishya R, Pariyo GB, Agarwal AK, Vijay V. Non-operative management of osteoarthritis of the knee joint. *J Clin Orthop Trauma* 2016 Jul-Sep;7(3):170-6.

15 AAOS: American Academy of Orthopaedic Surgeons. Treatment of osteoarthritis of the knee: Evidence-based guideline. 2nd edition [Internet]. Rosemont, IL: American Academy of Orthopaedic Surgeons; 2013 May 1

16 Blagojevic M, Jinks C, Jeffery A, Jordan KP. C2010 Jan;18(1):24-33. of osteoarthritis of the knee in older adults: A systematic review and meta-analysis. Osteoarthritis Cartilage 2010 Jan;18(1):24-33.

17 Van Manen MD, Nace J, Mont MA. Management of primary knee osteoarthritis and indications for total knee arthroplasty for general practitioners. J Am Osteopath Assoc 2012 Nov;112(11):709-15.

18 Christensen R, Bolvig J, Lund H, Bartels EM, Astrup AV, Hochberg MC, Singh JA, Lohmander S, Bliddal H, Juhl CB. Weight loss for overweight patients with knee or hip osteoarthritis. Cochrane Database of Systematic Reviews 2017, Issue 11. Art. No.: CD012526. DOI: 10.1002/14651858.CD012526.

19 J. J. Cherian, J. J. Jauregui, A. K. Leichliter, R. K. Elmallah, A. Bhave, M. A. Mont (2016). The effects of various physical non-operative modalities on the pain in osteoarthritis of the knee. *Bone Joint J* 2016;98-B (1 Suppl A):89–94.

20 Hagen KB. Canes for knee osteoarthritis: Is a randomised trial necessary? Ann Rheum Dis 2012 Feb;71(2):159-60

21 Duivenvoorden T, Brouwer RW, van Raaij TM, Verhagen AP, Verhaar JA, Bierma-Zeinstra SM. Braces and orthoses for treating osteoarthritis of the knee. Cochrane Database Syst Rev 2015 Mar 16;(3)

22 Kapadia BH, Cherian JJ, Starr R, et al. Gait using pneumatic brace for end-stage knee osteoarthritis. J Knee Surg 2016 Apr;29(3):218-23.

23 Cherian JJ, Bhave A, Kapadia BH, Starr R, McElroy MJ, Mont MA. Strength and functional improvement using pneumatic brace with extension assist for end-stage knee osteoarthritis: A prospective, randomized trial. J Arthroplasty 2015 May;30(5):747-53

24 Kusayama, Y., Akamatsu, Y., Kumagai, K., Kobayashi, H., Aratake, M., & Saito, T. (2014). Changes in synovial fluid biomarkers and clinical efficacy of intra-articular injections of hyaluronic acid for patients with knee osteoarthritis. *Journal of experimental orthopaedics*, *1*(1), 16. doi:10.1186/s40634-014-0016-7

25 Yaftali, Nina A. et al. Corticosteroids and Hyaluronic Acid Injections (2019). Clinics in Sports Medicine, Volume 38, Issue 1, 1 - 15.

26 Hulsopple C (2018). Musculoskeletal Therapies: Musculoskeletal Injection Therapy. *FP Essent.* Jul;470:21-26.

27 Alves R, Grimalt R: A Review of Platelet-Rich Plasma: History, Biology, Mechanism of Action, and Classification. Skin Appendage Disord 2018;4:18-24

28 Siemieniuk Reed A C, Harris Ian A, Agoritsas Thomas, Poolman Rudolf W, Brignardello-Petersen Romina, Van de Velde Stijn et al. Arthroscopic surgery for degenerative knee arthritis and meniscal tears: a clinical practice guideline BMJ 2017; 357 :j1982

29 Lee JC et al,. (2019). Asia-Pacific Journal of Sports Medicine, Arthroscopy, Rehabilitation and Technology. *science direct*. 23-28.

30 Gao, L., Madry, H., Chugaev, D. V., Denti, M., Frolov, A., Burtsev, M., … Korolev, A. (2019). Advances in modern osteotomies around the knee: Report on the Association of Sports Traumatology, Arthroscopy, Orthopaedic surgery, Rehabilitation (ASTAOR) Moscow International Osteotomy Congress 2017. *Journal of experimental orthopaedics*, *6*(1), 9. doi:10.1186/s40634-019-0177-5

31 Burn, E., Liddle, A. D., Hamilton, T. W., Pai, S., Pandit, H. G., Murray, D. W., & Pinedo-Villanueva, R. (2017). Choosing Between Unicompartmental and Total Knee Replacement: What Can Economic Evaluations Tell Us? A Systematic Review. *PharmacoEconomics - open*, *1*(4), 241–253.

32 https://www.wikidoc.org/index.php/File:Osteoarthritis_risk_factors.jpg

33 https://healthjade.com/*osteoarthritis*/

34 http://www.norrishealth.co.uk/knee-arthritis/

35 http://www.docjoints.com/knee-replacement/

36 Roos, E.M. and C.B Juhl (2012). Osteoarthritis 2012 year in review: rehabilitation and outcomes. *Osteoarthritis and Cartilage,* Volume 20, Issue 12, 1477 – 1483

37 Jones BQ, Covey CJ, Sineath MH Jr (2015). Nonsurgical Management of Knee Pain in Adults. *Am Fam Physician.* 2015 Nov 15;92(10):875-83.

38 Moseley JB, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, Hollingsworth JC, Ashton CM, Wray NP. A Controlled Trial of Arthroscopic Surgery for Osteoarthritis of the Knee (2002) *N Engl J Med.* 11;347(2):81-8.