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Osteoarthritis: physiology, disease, treatments, market analysis

Abstract

Osteoarthritis is a degenerative joint disease. As osteoarthritis begins to develop, it damages all areas of the joint including cartilage, tendons, ligaments, synovia, bone and meniscus.[1] Symptoms of Osteoarthritis often begin slowly with few joints. Symptoms include swelling, pain and stiffness. There is no current cure for Osteoarthritis. Current treatments include lifestyle changes, painkillers and therapy.[2] Few cases require surgery.[2] The therapeutics market size for osteoarthritis is expected to double by 2032.[3] In this review, we will cover an analysis of the osteoarthritis therapeutics market including market size and trends. We will also go over an overview of current treatments and products available for osteoarthritis patients. Finally, we'll conclude with emerging treatments recently approved or in clinical trials.

Keywords: osteoarthritis, cartilage, degenerative joint disease

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Abbreviations: OA, osteoarthritis; NSAIDs, non-steroidal anti-inflammatory drugs; ACI, autologous chondrocyte implantation; BMAC, bone marrow aspirate concentrate; MSCs, mesenchymal stromal cells

Introduction

Cartilage is a strong, connective tissue that protects joints and bones.[4] Its purpose is to prevent the bones from rubbing against each other and creating friction. Cartilage serves three main functions: absorbing shock, reducing friction, and supporting structures in the body. Cartilage acts as a cushion for your bones and joints when you move. Osteoarthritis is degenerative joint disease that occurs due to the breaking down of cartilage and other tissue in joints.[1] It most commonly occurs in the weight-bearing joints in the knees, hips, and spine. Osteoarthritis causes cartilage in the joint to lose its elasticity and therefore become stiffer. If the condition worsens, bones will rub against each other.[5,6] As cartilage weakens, tendons and ligaments stretch causing pain.[5] Due to the pain and inflammation caused by osteoarthritis, patients look for ways to reduce this pain through painkillers or treatments.

Physiology of cartilage

Cartilage is a strong, connective tissue that protects joints and bones. Its purpose is to prevent the bones from rubbing against each other and creating friction. Cartilage serves three main functions: absorbing shock, reducing friction, and supporting structures in the body. Cartilage acts as a cushion for your bones and joints when you move. It absorbs the force and reduces the stress exerted on the bone. Cartilage also lubricates the joints, allowing bones to slide past each other. This reduces the amount of wear and tear on them. Finally, cartilage helps keep their shape during movement. It also connects other tissue together and to other bones.[4]

Cartilage is found almost anywhere two bones meet. There are three types of cartilage found in the body. Hyaline is the most common one. It is smooth to the touch and made up mostly of type II collagen and proteoglycans. It has a pale blue color but becomes yellow with age. It goes from being moist to dry as a person ages. The second type is elastic cartilage which provides flexibility and is resilient in response to pressure. This type of cartilage appears yellow is most commonly found in the ear, larynx, and eustachian tube. The final type is fibrocartilage. It is is composed of type I collagen and proteoglycan. It is commonly found in tendons and ligaments. Fibrocartilage can resist high degrees of compression and tension.[7]

Disease

Osteoarthritis occurs due to the breaking down of cartilage and other tissue or a change in joints.[1] It most commonly occurs in the weight-bearing joints in the knees, hips, and spine. Certain factors, such as aging, obesity, family history, and previous injury, make it more likely to develop.[1] Osteoarthritis causes cartilage in the joint to lose its elasticity and therefore become more stiff. As cartilage weakens, tendons and ligaments stretch causing pain.[5] If the condition worsens, bones will rub against each other as can be seen in Figure 1.[5,6]

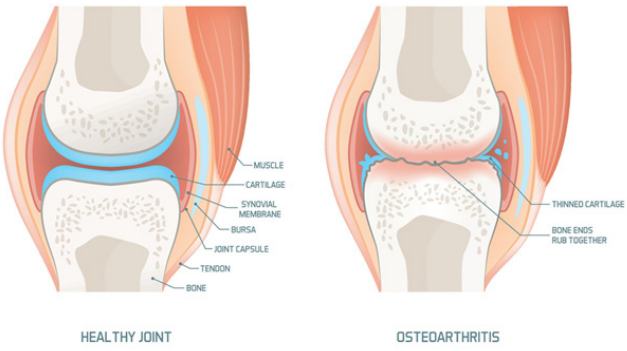

Figure 1 Difference between a health joint and one impacted by Osteoarthritis.[6]

For patients still in the early stages, they might experience joint pain following activity but that is relieved with rest. However, patients with a severe condition may experience pain at rest and have reported to feel the most pain at the end of the day due to activity and movement. Physical signs of osteoarthritis include body enlargement, decreased range of motion, and crepitus. Furthermore, radiographic signs of osteoarthritis include joint space narrowing, subchondral sclerosis, osteophyte formation, and cysts.[8]

Osteophytes are bony lumps that grow on the bone around joints (Figure 2). Osteophytes can cause put pressure on your nerves, affect your movement and rub against the bone. Some symptoms of osteophyte formation is a pins and needles feeling in the arms or legs, as well as lumps on the joint.[9]

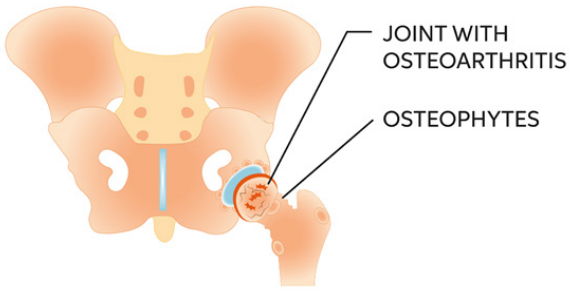

Figure 2 Osteophytes formed bone next to joint with osteoarthritis.[10]

Market size and trends

Osteoarthritis affects over 32.5 million adults in the United States.[11] Furthermore, high BMI and the fact that osteoarthritis in the knee is extra mutual as people age are believed to be two current public health developments that play the most significant role in the increase of osteoarthritis. Additionally, osteoarthritis is the most prevalent cause of discomfort and incapacity amongst the senior population.[3]

This year, the market size for Osteoarthritis therapeutics is 8.9 billion USD.[3] By 2032, the estimated market size is expected to be 18.36 billion USD (Figure 3).[3] The Osteoarthritis treatment market is expected to grow as the senior population rises since osteoarthritis is the most prevalent form of arthritis in older adults.[3] Additionally, the market is anticipated to be stimulated by the increase in need for cell-based research and the widespread use of pain killers.[3,12] Personalized osteoarthritis drugs have been conceptualized which would lead to improved diagnosing, treating and monitoring of the disease in patients.[12]

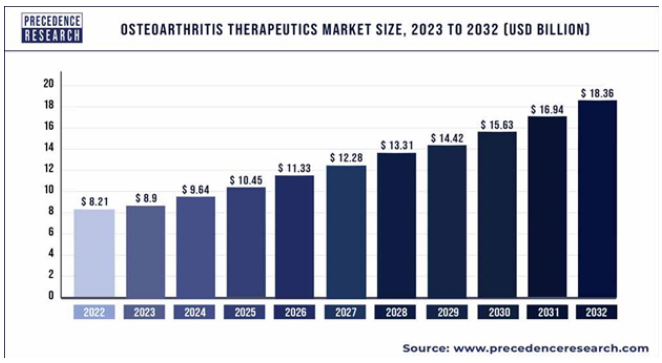

Figure 3 Osteoarthritis therapeutics market size from 2023 to 2032.[3]

Globally, the largest market for osteoarthritis therapeutics is in Europe.[3] Osteoarthritis is estimated to affect over 40 million people across Europe.[13] In a study conducted by Stanford, humans from Europe and Asia were found to have evolved to form shorter bones.[14] This genetic variant seems to have favored those in colder climates.[13] However, having shorter bones lead to an increased risk of osteoarthritis. Increased life expectancy and obesity across Europe are contributing to the growth of Osteoarthritis prevalence worldwide.[13]

Furthermore, the market for cartilage repair globally accounted for $1.47 billion in 2022 and is expected to increase to 4.62 billion by 2032 (Figure 4). Due to the increase in osteoarthritis over the past few decades, the cartilage repair industry has grown. Additionally, due to these trends, there is significant government funding for medicines and technology for cartilage repair and regeneration.[15]

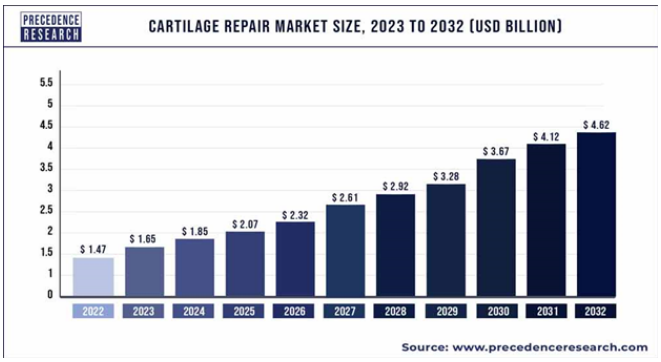

Figure 4 Cartilage repair market size from 2023 to 2032.[15]

Existing treatments

The main treatments for osteoarthritis include lifestyle changes, medication and supportive therapies. In terms of lifestyle changes, exercise and losing weight are recommended because they will help strengthen your joints and relive some of the strain on the joint. Paracetamol is a common medication suggested for short term pain relief. Another common medication are non-steroidal anti-inflammatory drugs (NSAIDs) which can be available as creams as well as tablets. If NSAIDs are ineffective, capsaicin cream may be prescribed. Capsaicin cream works by blocking nerves that send pain messages to the treated area. Additionally, hot or cold packs can be used to help treat the pain and symptoms of osteoarthritis.[2] Assistive devices are also useful for patients facing mobility problems or difficulty with everyday tasks.

Surgery is only needed for a small number of cases when other treatments are ineffective.[2] Arthroplasty is a surgical procedure used to restore the function of a joint.[16] The joint can be restored by resurfacing the bone or in some cases, an artificial joint can be used.[16] If joint replacement isn't suitable, arthrodesis, or fusion of joints, may be suggested.[2] Arthrodesis is an orthopedic surgery in which bones in a joint are fused into one larger bone.[17,18] This treatment eliminates instability or pain caused by arthritis.[17] Additionally, for patients with osteoarthritis in the knees but ineligible for knee replacement surgery, they may be able to have an osteotomy.[2] Osteotomy refers to the cutting of the bone.[19,20] In the knee, either the femur or tibia are cut and reshaped. By doing this, the weight on the knee is shifted, relieving pain in the joint.[19]

Microfracture is a technique used to treat an articular cartilage injury that is most often performed in the knee. In this procedure, a small pick creates hole in the base of the cartilage injury, allowing the blood to clot. Overtime, this clot turns into fibrocartilage which fills in the injured area. Micro fracture is a simple but cost effective procedure. However, the tissue formed is not as durable as is with other methods and thus micro fracture works best for initial treatments.[21]

Furthermore, another fairly new treatment is Autologous Chondrocyte Implantation (ACI). ACI is utilized to isolated full thickness articular cartilage damage of the knee. ACI is a two-step procedure with the first starting with the surgeon harvesting a small piece of cartilage from the patient's knee. Chondrocytes are isolated from this cartilage biopsy expanded, and sent back to the surgeon. The second step is an open procedure. In this step, a patch is sewn over the defect and the chondrocytes are injected onto it. This method

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has had a success rate of approximately 85% of patients returning to pain-free activity.[22]

Additionally, hyaluronic acid visco-supplementation is another treatment used to treat pain due to osteoarthritis. During this treatment, hyaluronic acid is injected into the joint. This thick fluid can reduce pain and swelling. To experience pain relief, you must undergo 3-5 treatments.[23] Relief from these injections lasts for about 4-6 months.[24] HA visco-supplementation may not work as well for older adults and those with severe osteoarthritis.[25] (Table 1)

Table 1 Treatments for osteoarthritis [21,23,37]

Treatments	Bone	Advantages	Disadvantages
Micro-fracture	knee, elbow, hip, other joints	simple procedure, cost effective	not durable, only suitable for initial treatment
Autologous Chondrocyte Injection	knee	uses patient's own cells, high success rate	two stage procedure, takes several weeks, requires open incision
HA visco-supplementation	knee, hip	minimal recovery time, minimal side effects	series of injections, short term

Products in development

Zilretta is a product from Flexion Therapeutics that utilizes polymeric microspheres to treat pain due to Osteoarthritis.[26] Zilretta is an extended-release corticosteroid and is the first and only FDA-approved osteoarthritis knee pain treatment that uses extended-release microsphere technology. The microspheres used contain triamcinolone acetonide and are injected directly into the knee. The microspheres stay in the knee and slowly release the medicine over a 3 month period. Once the medicine has run, they decompose and turn into carbon dioxide and water.[27]

Another product comes from iCeutica Inc. and is called Zorvolex.[26] Zorvolex is a low-dose, quick dissolving nanoparticle form of diclofenac.[28] This product is meant for adult patients with mild to moderate acute pain. The recommended dosage of Zorovalex is 35 milligrams three times a day. This drug is taken orally.[29]

Products in clinical trials

A product currently in clinical trials is the Bone Marrow Aspirate Concentrate (BMAC) treatment. This treatment is for those with moderate and severe knee osteoarthritis. Before total knee replacement, patients will have a sample of bone marrow removed from their pelvic region and concentrated using an Arthrex Angel Concentrated Platelet Rich Plasma system. The concentrated bone marrow is then immediately delivered back into the patient to the knee.[29] BMAC is a fairly safe treatment, requires minimal invasion and provides robust healing of damaged tissue.[30]

Another product in trials, amniotic fluid injections, would be used to treat inflammation and pain due to osteoarthritis.[31] Amniotic stem cells are injected near the damaged tissue.[32] Amniotic fluid contains various growth factors and other nutrients that encourage soft tissue regeneration.[33] These injections can be performed during an office visit and require little to no downtime afterwards.[34]

Mesenchymal stromal cell-based therapy is being looked at as a form of regenerative treatment for knee osteoarthritis.[35] Mesenchymal stromal cells (MSCs) and secreted exosomes hold therapeutic potentials for cartilage regeneration, such as chondrogenic differentiation and balancing activity of cartilage.[35] MSCs also have anti-inflammatory and immune-modulatory properties that suggest they might reduce joint inflammation and pain. It has also been suggested that the paracrine growth factors released by MSCs play a role in neo-cartilage formation.[36]

Conclusion

Osteoarthritis is a degenerative joint disease, affecting 32.5 million Americans.[1,11] Osteoarthritis causes cartilage in the joint to lose its elasticity and therefore become more stiff.[5] As cartilage weakens, tendons and ligaments stretch causing pain.[5] The pain and inflammation brought about due to osteoarthritis can be treated, but not cured, with a variety of treatments and drugs. Specifically looking at tissue engineering, micro fracture, HA viscosupplementation and autologous chondrocyte implantation are utilized for pain relief, most commonly in the knee. Furthermore, new products and treatments are in the works to encourage cartilage regeneration in the damaged joints due to osteoarthritis. Overall, Osteoarthritis holds a fairly large market size in the U.S. and worldwide.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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