

Cartilage of Knee: Anatomy, Function and Recent Conservative Treatments

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Abstract. Damage to the knee's cartilage, notably the menisci, is thought to be a substantial contributor to musculoskeletal morbidity. The unique anatomical, biomechanical, and functional properties of knee cartilage make it vulnerable to injury and destruction. Knee cartilage is essential for both everyday use and long-term health. Due to its importance and its injury susceptibility, treatment toward this injury also is important. Considering the contraindications of surgery and the requirements of anesthesia, and the characteristics of the disease in the age distribution, surgery might unsuitable for some people then conservative treatment is worth consider. The purpose of this review is to summarize and analyze recent conservative treatment toward the injury of cartilage in knee and some of the current developments in order to search for the future target. By analyzing several conservative treatments, including pharmacotherapy, physical therapy, Kinesio tape and tissue engineering, it can be clear that conservative treatments have significant effect on symptoms and part of its function but can hardly rebuild its structure and all physiological functions.

Keywords: Menisci, Cartilage Injury, Conservative Treatment, Tissue Engineering.

1. Introduction

The fibrocartilaginous structures that make up the knee cartilage aid in static weight bearing, compressive force distribution during joint motion, joint lubrication, joint stabilization, and proprioception. A frequent musculoskeletal injury that affects all age groups is cartilage damage in the knee, with accidental radio-graphic pathologic alterations occurring in the asymptomatic population [1]. Given the significance of cartilage, treatment paradigms have changed significantly from the time when they were thought of as unimportant, non-functional structures. Recent advances in cartilage repair procedures allow for the preservation of meniscal tissue whenever possible while conservative therapy remains a hallmark of treatment for knee injuries. Additionally, there is increased interest in the use of tissue and cell engineering, such as mesenchymal stem cells (MSCs) and platelet-rich plasma (PRP), to improve the potential healing properties of cartilage and articular tissue. This article provides an introduction to knee anatomy as well as an updated review of available therapies for treating cartilage damage.

1.1. Anatomy of knee cartilage

Hyaline cartilage and fibrocartilage are the two main forms of cartilage found in the knee. The surface of numerous joints is covered in hyaline cartilage, which is vitreous translucent cartilage. Additionally, the ribs, nose, voice box, and trachea are where it is most frequently discovered. The structure of hyaline cartilage, which is pearly gray in color, has a lot of collagen but no nerves or blood arteries. A fibrous membrane known as the perichondrium, or the synovial membrane when it runs along the surface of the joint, covers the outer surface of hyaline cartilage. Blood veins located within this membrane diffuse nutrients into the cartilage. The bone that envelopes the hyaline cartilage joint, sometimes referred to as the synovium, is called hyaline cartilage. Hyaline cartilage is not regarded as a constituent of the meniscus and articular discs, which are made exclusively of fibrocartilage despite being frequently in close proximity to them. The extracellular matrix (ECM) of hyaline cartilage has a highly specialized structure that is divided up into various regions. To resist shear forces, the superficial layer is primarily composed of collagen II fibers that are arranged parallel to the articular surface, whereas the deep region is made up of the same fibers that are arranged

perpendicular to the articular surface. The compressive load is absorbed by the bone contact. The most prevalent disease of the joint, osteoarthritis, might result from the biochemical breakdown of hyaline cartilage. In terms of fibrocartilage, it is well known that the menisci are what are found in the knee. The fibrocartilage wedges known as knee menisci are located between the tibial plateau and the femoral condyles. They have a crescent form. The menisci have a convex outer edge with attachments to the joint capsule and a concave free edge on the inside. Water makes up the majority of the menisci (72%), utilizing the leftover 28% consisting of collagen, glycosaminoglycans, DNA, and glycoproteins [2]. A few of the factors that determine how much of each of these components there is are age, accidents, and illnesses. The medial and lateral geniculate arteries, posterior and anterior, which come via means of popliteal artery, are the primary source of blood flow for the menisci. Within the synovial and capsular tissue, these blood vessels group together to form a perimeniscal capillary plexus that nourishes the meniscus' perimeter. The remaining meniscus is supplied by synovial fluid since only 10%–30% of the medial meniscus border and 10%–25% of the patellar ligament border are suitably vascularized. The treatment plan is influenced by the vascular supply and may partially account for the difficulties in rebuilding.

1.2. Recent therapy

Due to its special anatomy, recently there is conservative treatment and surgery. For hyaline cartilage injury, especially osteoarthritis, conservative treatment might be the best way to choose. For early osteoarthritis, conservative treatment is recommended. Resting, physical therapy and releasing weight and taking drugs like NSAIDs can relieve its symptoms. When conservative treatments do not have effect toward the symptoms, patients can take arthroscopic surgical treatment, mainly through arthroscopic removal of some joint synovial hyperplasia, hyperplastic bone. If it still does not work, then artificial replacement of the joint will be the way to solve the problem. For menisci injury, there are also conservative treatments and surgery depending on the severity of injury. However, most of the menisci injury recently are treated with surgery as the first choice. In specific cases, due to its severity, partial meniscectomy or meniscus suture repair is selected. For menisci injury, other conservative treatments are quite the same to osteoarthritis.

It is certain that for a particular kind of injury, there are both conservative treatments and surgery. However, for some groups of people, it is impossible for them to do the surgery, such as patients with severe cardiovascular disease. Other situation might also be a block for taking surgery. It is well-known that after surgery it is necessary to take physical therapy in order to rebuild the function of the knee. For some of the patients, it may be impossible to go through the whole process, and it will be possible that the situation may be worse than before. Therefore, for people with those difficulties, an effective conservative treatment may be suitable. Recently, there are several conservative treatments, for example pharmacotherapy, physical therapy, Kinesio Taping and tissue and cell engineering. This article's goal is to offer a summary of current conservative therapies as well as to examine and identify potential future research directions for conservative therapy [3].

2. Pharmacotherapy

For knee cartilage problems, especially inflammation related problems, as primary pharmaceutical therapy, local medicines are preferred. It is important to keep focusing on the patient during this process, in order to prevent the appearance of adverse effects.

2.1. Non-steroidal anti-inflammatory drugs (NSAIDs)

Both the OARSi8 and ACR13 guidelines strongly advise using conventional NSAIDs as first-line treatment due to their low risk of side effects. In addition, OARSi8 advises using NSAIDs for treatment in patients with gastrointestinal or cardiovascular problems as well as individuals who are fragile. The ACR guidelines strongly advise oral NSAIDs and intraarticular glucocorticoid injection in addition to topical NSAID use. In vitro studies using both bovine and human explants showed that

the common glucocorticoid drug dexamethasone increases proteoglycan production and decreases GAG loss in injured cartilage. It is believed to possess anti-inflammatory qualities. It also has an impact on how diseases develop. Dexamethasone's anti-inflammatory, anti-degenerative, and pro-regenerative effects are felt in the knee joint [4]. The effects of dexamethasone, however, are unclear because some study indicates that it decreases cell apoptosis, while other research reveals that it has toxic and proteolytic adverse reactions that markedly increase chondrocyte apoptosis and decrease chondrocyte proliferation [5]. But only when dexamethasone is repeatedly administered at high levels does this circumstance arise. This may make articular cartilage degeneration worse. By employing the proper dosage, treatment length, and timing, dexamethasone consumption can be regulated to result in more favorable benefits than negative ones.

2.2. Opioids

Opioids, another widely used class of medications that are commonly seen as effective pain relievers, should be strongly avoided when contemplating painkillers. Opioids have very marginal effects on pain and physical function in people with knee issues, according to recent studies. In addition, compared to placebo, patients may take on three to four times as much risk and/or discontinue due to negative side effects.

2.3. Platelet-rich plasma (PRP)

PRP is an allogenic product being used as a therapeutic assessment for musculoskeletal disorders, including meniscus injuries [6]. It contains a variety of growth factors and cytokines. Through the promotion of meniscus cell proliferation and migration, angiogenesis, and matrix formation, the increased concentration of platelets and growth factors is said to promote the natural wound-healing process. The use of PRP is becoming more and more common in the field of orthopaedics. 86,000 athletes are reportedly treated with PRP each year just in the United States [7]. Recent research have suggested several potential explanations for how PRP can treat knee cartilage. Recent studies have shown that PRP injections massively increased serum growth factors, which may assist in enhancing the healing response [7]. It was reported that the impact of PRP may be mediated by immunological and growth factor-related responses, which may show that PRP promotes regeneration by elevating growth factors and cytokines at the expected sites [8].

3. Physical therapy

The fundamental component of rehabilitation therapy is physical therapy, which targets local or systemic dysfunction or disease of the human body using physical variables such as sound, light, cold, heat, electricity, and force (movement and pressure). It is a type of non-invasive, drug-free treatment that can revert the body to its initial physiological condition. People who do not have substantially limited range of movement, locking, or stiffness of the affected knee are typically the only ones who can receive the initial nonoperative treatment for cartilage injury. Based on the clinical presentation, a decision is made. Those who are deemed suitable contenders for the conservative care following a severe knee injury should initially be treated with relaxation, cold, compression, and elevation of the injured knee. Physical therapy can then gradually aid in symptom alleviation over the course of six weeks [9]. Early on in a physical therapy program, control and swelling management should be the main priorities, moreover, knee range of motion must be ensured. Strengthening of the hamstrings and quadriceps muscles should be incorporated later in the program, followed by the introduction of dynamic postural controlled training. It can keep up its health by working out and cycling before engaging in jogging or other regular exercises [10]. It is recommended to bear weight, reduce edema, delay the emergence of post-injury symptoms, and have a minimally restricted range of motion in order to ensure the success of conservative treatment.

Several adjunct therapies are utilized in conjunction with conservative treatment in order to help the treatment and maximize results. Thermal modalities, laser therapy, therapeutic ultrasonography,

electrical stimulation, manual therapy methods, taping, and acupuncture are a few of the techniques that are regularly used.

3.1. Thermal modalities

The use of thermal modalities including cold and heat therapy is not backed by any evidence [11]. Patients may prefer to receive heat, cold, or contrast treatments to reduce pain and enhance physical function, according to study [12]. Women typically respond to thermal modalities with greater increases within the realms of physical and subjective quality of life because they enjoy heat treatments. Men prefer cold or contrast therapy, albeit they are less likely to claim success [12].

3.2. Laser, therapeutic ultrasound, and electrical stimulation

For laser therapy, the stimulation of tissue metabolism and the control of the inflammatory process are the two potential mechanisms of pain alleviation by laser therapy. However, due to its improbable biological mechanism and likely lack of efficacy with weak data, the OARSI strongly opposes utilizing laser to treat knee OA [13]. Recent research, however, demonstrate the opposite effects of laser therapy. Low-level laser therapy (LLLT) appears to lessen pain and impairment in people, according to a meta-analysis that examined its impact on symptoms and function in knee OA patients [14]. It exhibits a positive benefit for therapeutic ultrasonography but has methodological limitations [15]. The ACR recommendations nevertheless encourage employing therapeutic ultrasonography even if there isn't enough data to back it up [13]. Additionally, there is a lack of evidence to support the utilization of electrical stimulation [16]. The ACR guidelines also strongly advised against the use of transcutaneous electrical stimulation in all patients suffering from osteoarthritis [17].

4. Kinesio Taping (KT)

KT developed by Dr. Kenzo Kase was characterized by its specific thickness and high elasticity, as well as its capability of stretching up to 130–140% of its resting static length, ensuring free mobility of the applied muscle or joint [18]. Numerous studies support the idea that KT can lessen pain by activating skin's mechanoreceptors and boosting afferent feedback [19]. In addition to its pain-relieving effects, KT also aims to increase sports performance and muscle performance [18]. Patients with functional disabilities and muscle weakness can benefit from this normal trait.

According to recent studies, there are conflicting views regarding the efficacy of KT. Some people believe that KT has a beneficial impact on lower extremity discomfort and muscle weakness. A research stated that KT administration improved electromyographic activity during the recovery stage of anterior cruciate ligament surgery in the quadriceps muscles, and another study asserted that muscle contraction may be aided by KT applied from the muscle's origin to its insertion [18,20]. However, a recent study found that KT application to the quadriceps was unable to alter healthy women's peak knee extensor torque, one-footed static balance, or lower limb function [21].

For persons with osteoarthritis and damaged knee cartilage, pain might be the most incapacitating condition because it not only hinders day-to-day tasks but also encourages muscle atrophy. Recent studies have demonstrated that KT has a pain-reducing effect on a variety of knee issues [22]. The most widely recognized theory for this pain-relieving action is the gate control theory, which claims that the tape activates neuromuscular circuits by raising afferent feedback [21]. The enhanced afferent inputs from large-diameter nerve fibers may be able to block the input from small-diameter nerve fibers conveying nociception, causing pain alleviation, according to this notion.

Along with pain, people with knee pain frequently experience bilateral muscle weakness of the lower extremities. There has been conflicting evidence in the past about the therapeutic effects of KT on muscle function; some trials indicated a benefit, while others did not. Recent studies suggest that patients with chronic musculoskeletal conditions like OA should benefit more from KT's capacity to increase muscular strength than those who are healthy [22]. Every previous study has indicated that KT can ease discomfort. By reducing the pain-induced muscular inhibition of the quadriceps,

which has been found to selectively weaken the quadriceps in people with knee OA, it may be possible to promote movement by decreasing pain and eventually increase the muscle strength of people suffering osteoarthritis of the knee [23].

Overall, KT conventional therapy significantly improves isokinetic muscular strength but not isometric muscle strength. Given the significance of muscular strength for knee stability, KT can be crucial to recovery. Additionally, it may be a viable and efficient treatment option for individuals with knee injuries who have discomfort and muscle weakness in their lower extremities.

5. Cartilage tissue engineering

The tissue's limited capacity for regeneration makes today's repair techniques still ineffective, partly because they hardly ever succeed in restoring the tissue to health and restoring its normal function. Even though it appears to be merely a simple tissue, replicating it can be difficult. Recently, advances in tissue engineering have opened up new possibilities for reconstructing the anatomical structure of cartilage and, to some extent, giving it functionalities.

In reality, the manufacture of biomaterials has advanced significantly over the last 20 years, which could have a positive effect on cartilage regeneration. Regarding biomaterials, there are many formulations being developed, from the use of biostable and biodegradable compounds to the modern use of polypeptides with improved chemistry, which can be used to naturally induce regeneration [24]. The methods used to cure joint cartilage defects, however, have some drawbacks. Regenerative techniques (such as ACI/MACI) have better results in treating joint cartilage degeneration [25]. Because the structural coherence of the tissue surface is less than that of real tissue, the results now appear to be palliative rather than therapeutic. Additionally, based on the regeneration of cartilage, it will be ideal for the regenerated tissue to have a structure comparable to that of the original tissue and some of its normal functions [26]. It is only possible to achieve functional regeneration with specific hierarchical structures and the appropriate cells.

There are numerous options available because of the source of the cells being used. Primary articular chondrocytes appear to be the best option, however getting a sufficient number of cells can be challenging. While in vitro cell growth can help generate large numbers of cells, it is likely to cause those cells to lose their chondrogenic character quickly. As an alternative to the original articular chondrocytes, non-articular chondrocytes like costal or nasal chondrocytes are being studied. For instance, the neocartilage formed by costal chondrocytes has mechanical and biochemical characteristics similar to natural articular cartilage. Additionally, chondrocytes taken from the nasal septum have a stronger capacity to form cartilage tissues that resemble hyaline. Stem cells have also been seen as a sophisticated alternative. The biological specialty of these cells, which makes it simple to separate, get, and multiply them to the required number before differentiating into chondrocytes, is the basis for their use. The three main cell types that make up cartilage tissue are mesenchymal stem cells (MSCs), embryonic stem cells, and progenitor cells, the first of which will be discussed below [27].

MSCs could conceivably encourage cartilage regeneration. Pluripotent stem cells, also known as MSCs, can be found in skeletal muscles, the pancreas, adipose tissues, the placenta, bones, and bone marrow, to name a few human organs. Without taking into account the origins of those cells, all MSCs are capable of chondrogenesis, adipogenesis, and osteogenesis. MSCs are typically produced from dental pulp, adipose tissue, umbilical cord blood, and bone marrow for usage in clinical settings. Research has shown that bone marrow MSCs can repair both human and animal tissue differently, and meniscus lesions in certain animals can eventually heal entirely on their own without any further care. MSCs can enhance meniscal regeneration, according to several animal studies and a small number of human studies, however many issues remain unresolved because to the paucity of human evidence and the shortcomings of animal studies.

6. Discussion

Since various types of cartilage injury can occur in people of all ages, not considering the particular reason and the type of the injury, it is important to seek early strategies to protect and cure such injury before it causes a more severe problem. This review describes various therapeutic approaches that can be used to stop or reverse early disease progression toward cartilage damage in the knee joint. These approaches can control inflammation and concurrent cartilage degeneration, as well as other symptoms of the disease. Some of these approaches, such as PRP, can also have regenerative effects.

For pharmacotherapy, there are traditional drugs and all tissue/ cellular engineering. According to traditional drugs, like NSAIDs and opioids that are mentioned above, they undoubtedly possess anti-inflammatory, anti-degenerative, and pro-regenerative properties, also pain relief effect in the knee joint. However, the drawbacks here are also obvious, for they can just address the symptoms but they do not really treat the cause. Besides, for NSAIDs, take dexamethasone as an example, they can have an opposite effect toward cells, which may exacerbate the damage to articular cartilage. For cell engineering, in most cases, animal and clinical studies have reported favorable effects using PRP but firm statements can hardly be made. It still needs a long-time and high-quality study to further usage, comparing to other standard treatments using present [28]. In addition, physical therapy as another main part of conservative treatments, can make a difference without invasive and drugs. However, it has limitation toward the crowd and it truly needs a long-term adherence. Kinesio Taping, which also functions as a form of conservative therapy, significantly improves isokinetic muscular strength but not isometric muscle strength, which turns out to be a major downside. Apart from those above-mentioned therapies, tissue engineering is also a promising approach. It is still challenging to pinpoint the precise impact of biomaterials due to the absence of human scientific proof and problems in animal experimentation that have left numerous issues unresolved, despite the fact that the science and manufacturing of biomaterials have advanced significantly over the course of the extensive research and the sources of cells have also made significant strides in development.

By using conservative treatments, it can be possible to cure patients who are unsuitable to surgeries and to some extent it can relieve some symptoms such as pain in daily life. However, the drawback of conservative treatments is also obvious. It has lack power toward the basis of the injury, for it can just remit superficial symptoms but has no idea with the basis, such as the deficient cartilage and the recovering of the tissue's function. At present there is surgery that can remove the damaged part, but it has strict limit, especially for elder patients, and there is also difficulty after surgery mainly in postoperative rehabilitation. There are conservative treatments that can relieve symptoms temporarily. Yet it is hard for conservative treatments at present to have a radical effect on the tissue itself, which can be the biggest problem and also the main goal in future study.

For further studies, it is expected to focus on its radical effect on rebuilding the structure of the cartilage and the tissue's physiological function instead of only superficial symptom therapy. It can give patients who have no opportunity to do surgery and are not able to achieve postoperative rehabilitation.

7. Conclusion

For present conservative therapy, it has several embranchments, such as pharmacotherapy, physical therapy, Kinesio Taping and tissue engineering. Each of it has its own advantages and disadvantages. Though it is certainly excellent in pain relief or other aspects, the common shortcomings are its lack of effect on the tissue, without the effect on rebuilding, **except tissue engineering mentioned above**. Therefore, it is necessary for future studies to focus on its effect on tissue itself rather than the superficial symptoms, which can remedy the defect of surgery.

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