

Comparison of the treatments of osteoarthritis

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Abstract. Osteoarthritis is one of the most prevalent diseases in the world, which affects a wide range of age groups, ranging from children to the elderly. More than 300 million people worldwide suffer from osteoarthritis, which may cause pain, stiffness, tenderness, loss of flexibility, grating sensation, bone spurs and swelling, and other diseases. Medication, surgery, and therapy are the main treatments. For medication, there are Analgesics and Nonsteroidal anti-inflammatory drugs, which have the function of reducing pain and inflammation. Nonsteroidal anti-inflammatory drugs can also reduce pain. For surgery, there are arthroplasty, arthrodesis, and osteotomy. In addition, there are physical therapy and occupational therapy. Those different kinds of therapies have their own advantages. Recent studies have shown that mesenchymal stem cells (MSCs) can be used to treat osteoarthritis, which has the properties of differentiating into chondrocytes and having anti-inflammatory and immunomodulatory effects. These cells are ideal for treating osteoarthritis that requires anti-inflammatory and cartilage replacement. This paper provides a brief overview of the different treatment approaches and aims to compare the pros and cons of each approach.

Keywords: Osteoarthritis, Arthroplasty, Physical Therapy, Mesenchymal Stem Cell.

1. Introduction

Osteoarthritis is a disease that usually affects the joints of the body. Osteoarthritis usually results from bone growth due to the loss of cartilage and subsequent collision of the two bones that make up the joint. The symptoms of osteoarthritis include pain, stiffness, tenderness, loss of flexibility, grating sensation, bone spurs, and swelling. Osteoarthritis is one of the most important and prevalent diseases in the world. Osteoarthritis also affects a wide range of age groups, ranging from children to the elderly. Most of them are elderly. More than 300 million people worldwide suffer from osteoarthritis, according to data released this year. Patients with osteoarthritis must be treated in time, otherwise not only knee joint deformation will lead to crooked legs, but also may cause depression, osteoporosis, coronary heart disease, and other diseases due to long-term disability, bringing economic and spiritual double blows to patients and families.

Cartilage is a semi-rigid but flexible avascular connective tissue found at various sites within the body. The role of cartilage in joints is to protect bone, smooth the friction between bones, and prevent friction between bones. To be more specific, due to long-term wear or osteoclasts, the cartilage in the joint gradually disappears. The consequence of the loss of cartilage in the joint is the narrowing of the joint space. The bone and bone start to move closer and grow because there isn't cartilage anymore. This event leads to an increase in the friction between two bones of the joint. Finally, this friction will lead to the inflammation of the portion or whole of the joints, joint deformation, and joint intumescencia. Inflammation leads to increased permeability of local blood vessels, resulting in local swelling caused by fluid and cellular components leaking out. The exudation and swelling press on nerve endings, leading to pain. At the same time, the glands release inflammatory mediators (mainly PGE₂, bradykinin, and substance P) that act on sensory nerve endings and cause pain.

This paper mainly discusses these treatment options for osteoarthritis: medication, surgery, and therapy, the factors that can affect the recovery rate of osteoarthritis: calcium intake, vitamin K intake, moisture, and amount of exercise, and the expectation of future treatment of osteoarthritis.

2. Current treatment

2.1. Medication

For medication, there are two kinds of drugs: Analgesics and Nonsteroidal anti-inflammatory drugs. Analgesics, commonly known as painkillers, are medications that alleviate a variety of pains, including headaches, injuries, and arthritis. While opioids change the way the brain interprets pain, anti-inflammatory analgesics lower inflammation. One example of analgesics is Acetaminophen. It is one of the most common active drug ingredients in the United States and was found in more than 500 over-the-counter and prescription drugs [1]. Acetaminophen is transformed to p-aminophenol, which crosses the blood-brain barrier easily and is converted to AM404 by fatty acid amide hydrolase. Transformed acetaminophen works to relieve pain through two main mechanisms.

First, AM404 causes analgesia by binding to TRPV1 receptors in the brain. By activating the TRPV1 receptor, AM404, for example, generates an outward current. In the formalin test, intraventricular injection of AM404 also generated analgesic effects. As a result, these brain receptors are largely thought to be the primary mediators of acetaminophen-induced analgesia. Second, in addition to their functions in the brain, acetaminophen and its metabolite AM404 may cause analgesia in the spinal dorsal horn by directly activating TRPV1 and CB1 receptors. Previous research has revealed that AM404 lowers the positive immunological reactivity of neuronal c-fos - produced by innocuous spinal cord stimulation in a rat model of neuropathic or inflammatory pain - and that TRPV1 or CB1 receptor antagonists suppress these responses [2].

Nonsteroidal anti-inflammatory medicines (NSAIDs) inhibit the formation of specific molecules in the body that cause inflammation. Pain caused by chronic tissue damage, such as arthritis, can be effectively treated with NSAIDs. Back discomfort, dysmenorrhea, and migraines can all be treated with NSAIDs. Aspirin, ibuprofen, and sodium naproxen are examples of NSAIDs.

Ibuprofen is meant to prevent pain, not numb existing pain, or address the root cause. It works by inhibiting prostaglandins, lipids that cause inflammation, in order to locate and boost the body's defense and repair mechanisms. Ibuprofen blocks inflammation (and pain) caused by prostaglandins by blocking their synthesis. Ibuprofen works by blocking two COX isomers, which has anti-inflammatory and analgesic properties. Ibuprofen also eliminated HO radicals, NO, and ONOO-, and by acting on the nitric oxide synthase (NOS) subtype, it can promote or inhibit nitric oxide synthesis. By attaching to cannabinoid receptors and blocking the enzyme fatty acid amide hydrolase (FAAH), which metabolizes endocannabinoids, ibuprofen may activate the antinociceptive axis [3].

2.2. Surgery

For surgery, there are mainly three types of surgeries: arthroplasty, arthrodesis, and osteotomy. Arthroplasty is a surgical procedure to restore the function of a joint. A joint can be restored by resurfacing the bones; an artificial joint may also be used. The surgeons will make incisions and remove the damaged joint, then they will replace it with an artificial joint. They use stitches, staples, or surgical glue to close the incisions. The advantages of arthroplasty include helping the patient move without pain and stiffness, helping people take part in activities they once enjoyed, and improving the quality of life and overall health of the patient.

Arthrodesis is a surgical procedure in which the surgeons will fuse the damaged joints. This procedure can reduce pain, but movements of the joints are difficult. Hence, this procedure is only performed when arthroplasty is not possible.

The osteotomy is a surgery in which one or more bones are cut without replacement. There are many types of osteotomies, which are used to treat various orthopedic conditions and injuries. Osteotomy is more like a way to prevent excessive bone growth or correct the wrong angle of the joint, rather than dealing with inflammation or cartilage damage. The version, for example, is the angle between the femoral neck and the shaft of the femur. This can be considered to be the "twist" of the femur bone. The standard version has a 12-15-degree forward angle. The femoral neck can be turned too far forward, which is called excessive anteversion, or too far backward, which is called

retroversion, in people with version abnormalities. Both of these abnormalities cause the ball component of the hip joint to be at an unfavorable angle to the socket cup, which can cause injury to the hip joint surfaces and surrounding structures. [4]. With an osteotomy, doctors will remove excess bone in a joint or polish the bone of a joint that is too large. This is a way to keep the patient's joints at a good, healthy angle.

Therefore, osteotomy is more like a protective measure to protect the normal growth of bone, which is more effective in controlling the growth and reducing the compression of bone in the body, rather than being used for the treatment of osteoarthritis (table 1). The open-wedge high tibial osteotomy (OWHTO) and noncompartmental knee arthroplasty (UKA) were compared in a study undertaken by a Chinese doctor team. They discovered that there was no significant difference in OA progression between the two groups. However, after a 10-year follow-up, UKA patients had a greater survival percentage (96.2 percent) than OWHTO patients (87.7 percent). The results concluded that arthroplasty is more effective in curing OA than osteotomy [5].

Table 1. Comparison of three types of surgeries

Type	Function	Efficiency	Advantage	Limitations
Arthroplasty	Treatment of arthritis, joint damage, broken bones.	It takes a lot of preparation and it takes a long time. It requires precise cutting and artificial joint filling. Artificial joints need to be made.	The joints can move freely, reducing a lot of pain.	The body needs to adapt to the artificial joint, and there may be subsequent reactions. You may not be able to completely resolve the inflammation.
Arthrodesis	Fusing joints.	The time is short and the need for surgical techniques is not great.	It solves the pain problem fundamentally.	No movement of the joints at all.
Osteotomy	Ensure healthy bone growth and remove the excess bone.	It requires a precise cut. It doesn't take that long.	It allows people to move normally and protect bone growth.	The inability to perform extensive incisions on some joints limits the effectiveness of surgery.

2.3. Physical therapy and occupational therapy

One of the allied health professions is physical therapy, usually known as physiotherapy. Physical therapy is a medical specialty that tries to prevent disease and injury-related mobility and pain problems. It is offered by physical therapists who use physical examination, diagnosis, prognosis, patient education, physical intervention, rehabilitation, disease prevention, and health promotion to promote, maintain, or restore health [6]. It encompasses all non-drug, non-invasive treatments with a medical or scientific foundation. Non-drug and non-invasive treatments are important for the recovery of inflammation. In the case that the cause of the disease is not eradicated after surgery, therapy can prevent the recurrence of the disease and restore the function of the body.

A team of researchers studied the effects of physical therapy on recovery from osteoarthritis. They were looking for 83 people who had knee osteoarthritis. They then randomly assigned them to the therapy group :(42 people of 15 men and 27 women, mean age of 60 ± 11 years) and the placebo group :(41 people of 19 Men and 22 women, mean age of 62 ± 10 years). In the clinic and at home, the therapy group received manipulative treatment of the knee, as well as lumbar, hip, and ankle joints when needed, as well as a standardized knee exercise regimen. Subtherapeutic ultrasound was used on the knee joint of the placebo group at an intensity of 0.1 W/cm² in a 10% pulse mode. For four weeks, both groups received treatment at the clinic twice a week. At the end of the treatment, the researchers monitored the patients' physical and joint performance, including distance walked in 6 minutes, some of the function, pain, and stiffness sub scores of the Western Ontario and McMaster

Universities Osteoarthritis Index (WOMAC). The two groups were compared by uninformed testers before the initial visit, at week 4, week 8, and year 1. After testing, the 6-minute walk and WOMAC scores at weeks 4 and 8 in the therapy group showed significant clinical and statistical improvements, but not in the placebo group. At 8 weeks, the therapy group had a 13.1% improvement in mean 6-minute walking distance and a 55.8% improvement in WOMAC scores from baseline ($P < 0.05$). Patients in the therapy group walked an average of 170 m (95 percent CI, 71 to 270 m) more for 6 minutes at week 8 than those in the placebo group, with an average WOMAC score of 599 mm after correcting for potential confounding variables (95 percent CI, 197 to 1002 mm). After observing the results of this study, it is obvious that after physical therapy, people with osteoarthritis recover much faster than those without physical therapy [7].

Occupational therapy is quite different from physical therapy. Physical therapy focuses on the recovery of physical functions, such as bone-bearing capacity and muscle strength. But occupational therapy pays more attention to whether patients can reintegrate into society through therapy, into the former circle of patients, in daily life. In general, occupational therapy is a client-centered health profession that promotes health and well-being through occupation. Occupational therapists achieve this by working with people and communities to improve their ability to pursue careers they want, need, or aspire to, or by changing careers or environments to better support their professional participation [8].

Occupational therapy has many advantages. As a more personalized treatment than physical therapy, occupational therapy can focus on some aspects that physical therapy cannot. For osteoarthritis, occupational therapy focuses more on helping people gain independence. First of all, osteoarthritis is mainly affected by older people. And for older people, aging can mean losing independence. Family members or loved ones may worry about a fall or injury when an older person is home alone. Or they might worry about how well an older person recovers from a fall or stroke. Occupational therapists can help restore independence by working with the physical and cognitive health of older adults. Specifically, therapists can remaster hygiene tasks such as bathing, going to the bathroom, or brushing teeth to ensure that older people with osteoarthritis are safe in their daily lives [9].

Table 2. Comparison of two types of therapies

Type	Advantages	Limitations
Physical therapy	Relatively basic, cheap, and cost-effective. Professional experience and techniques. Large and mature industry chain.	It has no effect on psychological trauma after injury.
Occupational therapy	It can be applied to all kinds of people. More personalized ability to help everyone find the right treatment	Training occupational therapists take a lot of time and money, so the cost of occupational therapy is high. It takes a lot of time for the effects to become apparent.

To sum up, there is a large number of people who use physical therapy, however, only the people that have special needs or special experiences, such as athletes and soldiers, will choose occupational therapy. Besides, physical therapy is relatively basic, cheap, and cost-effective, and physical therapy has many precedents with professional experience and techniques, as shown in table 2. One researcher compared the educational costs of clinical Placements for Occupational therapy, Physical therapy, speech pathology, and audiology students. Other than speech pathology and audiology students, the sample represented 42.9% of the facilities offering occupational therapy placements and 41.4% of those offering physical therapy placements. At the same time, during a 12-month period, these facilities provided 77.3% of the total clinical hours for the occupational therapy students, and 65.1% for the physical therapy students [10]. It is obvious that training occupational therapy practitioners take

more resources and time. Therefore, physical therapy may be more suitable for ordinary people with osteoarthritis.

3. Factors that influence the rate of osteoarthritis recovery

3.1. Calcium intake

There are mainly four factors that influence the rate of osteoarthritis recovery: calcium ions intake, vitamin K intake, moisture, and amount of exercise as shown in table 3. First, calcium is an element that the body must have and needs to have a lot. Calcium helps the body conduct a variety of biological processes, the most significant of which is bone mineralization. The major component of bone is calcium, which is found in the form of calcium phosphate complexes in more than 99 percent of cases. It improves bone strength and shape while also acting as a metabolic store for intracellular and extracellular calcium. Calcium is found in the blood, extracellular fluids, muscles, and other tissues, and is involved in muscle contraction, vasoconstriction and vasodilation, nerve impulse transmission, and intracellular and extracellular communication [11]. As such an important element, calcium intake is also important. For humans, calcium intake mainly depends on the daily diet. Calcium is best obtained from foods that people consume on a daily basis, such as milk, yogurt, cheese, and calcium-fortified beverages such as almonds and soy milk. Dark green leafy vegetables, dried peas and beans, fish with bones, calcium-fortified fruit juices, and cereals are all good sources of calcium.

3.2. Vitamin K intake

Second, vitamin K is the coenzyme of carbonylated acid, assisting carboxylase to complete the carboxylation of the three R-carboxylated glutamic acid residues in the molecular structure of osteocalcin [12]. Osteocalcin is a protein hormone secreted by the osteoblast. It has played an important role in glucose homeostasis, exercise capacity, brain development, cognition, and male fertility. The carboxylated osteocalcin has a strong binding force with calcium ions and combines with hydroxyapatite to promote bone mineralization. Hydroxyapatite is a ceramic material that forms the mineral phase of bone. Vitamin K also had an effect on osteoclasts, which directly acted on pro-osteoclasts and inhibited the formation of osteoclasts. Osteoclasts are cells that live in the bone and have the function to degrade the other bone cells, mostly the dead bone cells. By inhibiting the formation of osteoclasts, the bone can grow faster and this can improve the recovery rate of osteoarthritis.

3.3. Moisture

Third, moisture also plays a very important role in the recovery of osteoarthritis. Actually, moisture is one of the main causes of arthritis. People who stay a long period of time in an area that has high humidity have a higher possibility to have arthritis. Moisture can lead to poor blood circulation in joints. This may lead to moisture accumulation and aseptic inflammation of joints, and soft tissue edema, causing swelling and pain. This can add to the release of inflammation factors to increase the level of pain of osteoarthritis. At the same time, the poor blood circulation caused by the moisture can reduce the recovery rate since the effective elements and the cells can't reach the inflammation area.

3.4. Amount of exercise

At last, a certain amount of exercise is also necessary for recovery from arthritis. Exercise can increase blood flow in inflamed areas and increase the metabolic rate for faster recovery. This will have the counter effect as the moisture. A certain amount of exercise can also help the bones maintain the same motor capacity after recovery or adapt to greater intensity of activity.

Table 3. List of the factors that can affect the recovery rate and their functions

Types	Functions	A higher amount can increase/ decrease the recovery rate
Calcium	bone mineralization, mediating muscle contraction, vasoconstriction and vasodilation, nerve impulse transmission, and intracellular and extracellular signaling	increase
Vitamin K	coenzyme of carboxylated acid, inhibition of the formation of osteoclasts	increase
Moisture	moisture accumulation and aseptic inflammation of joints, soft-tissue edema, causing swelling and pain	decrease
Amount of exercise	increase blood flow, adapt to greater intensity of activity	increase

4. Future expectations

One cell that can be used to treat osteoarthritis is the Mesenchymal stem cell (MSCS). It is a pluripotent stem cell that has all the commonalities of stem cells, such as the ability to self-renew and pluripotent differentiation. MSCS can not only contribute to tissue repair but also have immunomodulatory and anti-inflammatory effects. Mesenchymal stem cells have the properties of differentiating into chondroblasts and have anti-inflammatory and immunomodulatory effects. The cells are perfect for the treatment of osteoarthritis that requires anti-inflammatory and cartilage replacement.

Self-renewing mesenchymal stem cells can differentiate into osteoblasts, chondrocytes, adipocytes, cardiomyocytes, and vascular cells, among other mesodermal lineage cells. Mesenchymal stem cells' immunomodulatory and regenerative abilities can help to balance anabolism and catabolism in osteoarthritic joints. Despite the fact that mesenchymal stem cells have been employed for cartilage repair in a large number of cases in clinical practice, the mechanism underlying cartilage repair using mesenchymal stem cells is still unknown [13]. Injected into the joints of rat models of osteoarthritis, mesenchymal stem cells were found to significantly reduce pain and increase body weight in the model rats. This mesenchymal stem cell treatment is being studied and may one day be used as a treatment to eradicate osteoarthritis.

5. Conclusions

Osteoarthritis is arthritis that happens in the joints of the skeletal system and can happen to people from every age group, mainly in people who have ages bigger than forty years old. There are currently three types of treatments: medication, surgery, and therapy. For medication, there are Analgesics and Nonsteroidal anti-inflammatory drugs. Both of them are effective in different aspects. For surgeries, there are arthroplasty, arthrodesis, and osteotomy. Arthroplasty is best for people to have osteoarthritis since it can make the joints move freely after the surgery and reduce a lot of pain. Arthrodesis has a huge limitation and osteotomy is usually used in the protection of the normal growth of the bone. For therapies, there are physical therapy and occupational therapy. Physical therapy is better because it is a cost-effective and mature industry chain. And there are four factors that influence the rate of osteoarthritis recovery. An increase in calcium intake, vitamin K intake, and exercise can increase the recovery rate but the increase in moisture will decrease the recovery rate. At last, Mesenchymal stem cells can be seen as a future treatment for osteoarthritis and need to be researched and improved. In the future, it is still mainly to further study new therapeutic intervention methods and to conduct multi-center clinical trials to compare the advantages and disadvantages of different treatment methods, to choose a more appropriate treatment method for patients, and improve their prognosis.

References

- [1] McNeil Consumer Healthcare Division. (2019). What is Acetaminophen? Get Relief Responsibly®. Retrieved June 4, 2022.
- [2] Ohashi, N. (2020). Analgesic Effect of Acetaminophen: A Review of Known and Novel Mechanisms of Action. *Frontiers*. Retrieved June 4, 2022.
- [3] Jin, Q. H., Lee, W. G., Song, E. K., Jin, C., & Seon, J. K. (2021). Comparison of long-term survival analysis between open-wedge high tibial osteotomy and unicompartmental knee arthroplasty. *The Journal of Arthroplasty*, 36 (5), 1562 - 1567.
- [4] PharmGKB summary: ibuprofen pathways. Pharmacogenetics and genomics. 2015. Mazaleuskaya Liudmila L, Theken Katherine N, Gong Li, Thorn Caroline F, FitzGerald Garret A, Altman Russ B, and Klein Teri E.
- [5] L. Buly, Robert. (2015, February 1). Femoral Osteotomy: Anteversion, Retroversion, Surgery | HSS. Hospital for Special Surgery. Retrieved May 26, 2022.
- [6] Wikipedia contributors. (2022, May 6). Physical therapy. Wikipedia. Retrieved June 11, 2022.
- [7] Deyle, G. D., Henderson, N. E., Matekel, R. L., Ryder, M. G., Garber, M. B., & Allison, S. C. (2000). Effectiveness of manual physical therapy and exercise in osteoarthritis of the knee: a randomized, controlled trial. *Annals of internal medicine*, 132 (3), 173 - 181.
- [8] World Federation of Occupational Therapists. (2022, May 4). About Occupational Therapy. WFOT. Retrieved June 11, 2022.
- [9] NYTPS Inc. (2021, February 8). What Are the Advantages of Occupational Therapy? | Blog | NYTPS. Nytpsnyc. Retrieved June 11, 2022.
- [10] MacKinnon, J. R., & Page, G. G. (1986). An analysis and comparison of the educational costs of clinical placements for occupational therapy, physical therapy, and speech pathology and audiology students. *Journal of Allied Health*, 15 (3), 225 - 238.
- [11] Vannucci, L., Fossi, C., Quattrini, S., Guasti, L., Pampaloni, B., Gronchi, G., Giusti, F., Romagnoli, C., Cianferotti, L., Marcucci, G., & Brandi, M. L. (2018). Calcium Intake in Bone Health: A Focus on Calcium-Rich Mineral Waters. *Nutrients*, 10 (12), 1930.
- [12] M. J. Shearer, P. N. Shearer, and P. Newman, "Metabolism and cell biology of vitamin K," *Thrombosis and Haemostasis*, vol. 100, no. 10, pp. 530 – 547, 2008.
- [13] Zhang Shuang, Liu Shi, Wang Yu-feng, Lü Chan, Li Bao-ling, Wang Ping, Cong Jun, Zhu Zhi-qiang. Mesenchymal stem cells for cartilage repair in osteoarthritis[J]. *Chinese Journal of Tissue Engineering Research*, 2018, 22 (33): 5379 - 5385.