TUDAJ, Oskar, SAJEWICZ, Krzysztof, MAZUR, Aleksandra, KACZMAREK, Mikołaj, GROCHOWSKA, Wiktoria, DYLIK, Adrianna, KALISIAK, Julia, KALAS, Wiktoria, STRZAŁKOWSKA, Paulina and DULĘBA, Julia. Treatment Methods for Knee Osteoarthritis - A Literature Review. Quality in Sport. 2025;42:60948. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.42.60948
https://apcz.umk.pl/QS/article/view/60948

The journal has been awarded 20 points in the parametric evaluation by the Ministry of Higher Education and Science of Poland. This is according to the Annex to the announcement of the Minister of Higher Education and Science dated 05.01.2024, No. 32553. The journal has a Unique Identifier: 201398. Scientific disciplines assigned: Economics and Finance (Field of Social Sciences); Management and Quality Sciences (Field of Social Sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398. Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).
The authors declare that there is no conflict of interest regarding the publication of this paper.
Received: 18.05.2025. Revised: 25.06.2025. Accepted: 25.06.2025. Published: 26.06.2025.

Treatment Methods for Knee Osteoarthritis - A Literature Review

Authors

Oskar Tudaj

Samodzielny Publiczny Zakład Opieki Zdrowotnej Ministerstwa Spraw Wewnętrznych i Administracji w Poznaniu im. prof. Ludwika Bierkowskiego

https://orcid.org/0009-0003-6934-459X

Krzysztof Sajewicz

University Clinical Hospital in Poznań

https://orcid.org/0009-0007-2274-400X

Aleksandra Mazur

University Clinical Hospital in Poznań

https://orcid.org/0009-0001-5037-0080

Mikołaj Kaczmarek

Uniwersytecki Szpital Kliniczny w Poznaniu

https://orcid.org/0009-0003-8335-230X

Wiktoria Grochowska

University Clinical Hospital in Poznań

https://orcid.org/0009-0005-2681-0452

Adrianna Dylik
Poznań University of Medical Sciences
https://orcid.org/0009-0000-9931-4699
Julia Kalisiak
https://orcid.org/0009-0002-2432-0773
Wiktoria Kalas
Uniwersytet Zielonogórski
https://orcid.org/0009-0001-5051-1365
Paulina Strzałkowska
University Clinical Hospital in Poznań
https://orcid.org/0009-0000-7495-5561
Julia Dulęba
University Clinical Hospital in Poznań
https://orcid.org/0009-0009-1465-0809

Abstract

Introduction And objective:

Knee osteoarthritis (KOA) is one of the leading causes of disability worldwide. It is associated with pain and a reduced range of joint motion. As this condition affects an increasing number of patients, effective treatment strategies are needed.

The aim of the study:

This article focuses on presenting the therapeutic methods for knee osteoarthritis. Its aim is to highlight their indications, mechanisms of action and effectiveness.

Material and methods:

The PubMed database was used to gather information on knee osteoarthritis and its treatment methods. The review primarily focused on systematic reviews, meta-analyses and studies. The most commonly used search terms were 'knee osteoarthritis' and 'knee osteoarthritis treatment'."

Summary of current knowledge:

Treatment depends on the stage of the disease, the patient’s expectations, and their level of engagement. A wide range of therapeutic options for KOA is available - starting from conservative methods such as physiotherapy, through intra-articular injections and ending with surgical interventions. Many of these techniques can and should be used simultaneously to achieve the most beneficial outcome.
Conclusions:
Multidisciplinary approach combining various therapeutic methods involving specialists from different fields is often needed to achieve effective treatment. Currently, significant emphasis is being placed on research into cartilage regenerative therapies, which are seen as a promising direction for the future.

Keywords
Knee Osteoarthritis, Osteoarthritis, Treatment, Intra-articular therapy, Arthroplasty

Introduction

Osteoarthritis of the knee is a significant health issue in today's world. It is estimated that in 2020, it affected 13% of women and 10% of men over the age of 60. The total number of people suffering from this condition across all age groups is approximately 250 million [2][3][34]. This disease is expected to become increasingly prevalent in the coming years and decades due to an aging population and the growing problem of obesity [1][6][34][37]. It is characterized by damage not only to the articular cartilage and subchondral bone but also to the synovial membrane, ligaments, and muscles, making it a pathology of the entire joint [2]. It leads to chronic pain, reduced mobility, and declining quality of life. The majority of patients still do not achieve satisfactory treatment outcomes. The aim of this article is to present both currently used therapies and those that are still under development.

Pathophysiology

The pathophysiology of knee osteoarthritis (KOA) is complex and involves a combination of biochemical, biomechanical, and inflammatory factors that lead to the progressive degradation of articular cartilage, formation of osteophytes, subchondral bone sclerosis and subchondral cysts [2][6][8].

The process begins with a disruption of homeostasis within the articular cartilage, triggered by various factors such as joint injury, genetic predisposition, biomechanical disturbances, aging or obesity [7]. The inflammatory response is initiated in which catabolic factors such as cytokines (e.g., IL-8, IL-6), proteolytic enzymes and chemokines (e.g., IP-10, RANTES) outweigh anabolic factors such as anti-inflammatory cytokines and growth factors [6][7].

As a result, articular cartilage begins to degrade and loses its ability to absorb mechanical forces effectively. This leads to compensatory remodeling of the underlying subchondral bone, manifesting as sclerosis. As an effect of tissue overloading, other structural changes occur, such as the formation of osteophytes (bony outgrowths) and subchondral cysts [6][7].

Ongoing inflammation within the joint and subsequent fibrosis of the joint capsule contribute to a reduction in range of motion, increased stiffness and pain of the knee joint [7].

Stating the diagnosis

The diagnosis is established through a correlation of the patient's medical history (interview), physical examination and imaging results.

The typical clinical picture of KOA includes: morning stiffness or stiffness after periods of inactivity, pain that intensifies with physical effort and progressive loss of range of motion leading to a decreased quality of life [4].

During the physical examination, physician assesses the joint's range of motion, palpates for tenderness along the joint line, performs the patellar ballottement test to detect effusion and evaluates medial-lateral and anterior-posterior stability. It is also important to examine adjacent joints, as knee pain can often originate from hip joint pathology.

Various imaging modalities may be used for diagnostic purposes: magnetic resonance imaging (MRI), computed tomography (CT), ultrasound (US), or conventional radiography (X-ray). X-ray is most commonly used due to its relatively low cost, wide availability and high specificity. Subchondral sclerosis, osteophyte formation and joint space narrowing due to cartilage damage are the main radiographic signs of osteoarthritis [4][5]. Importantly, if the patient presents with typical symptoms and clear clinical findings, the diagnosis can be made without performing an X-ray [5]. There are several grading systems available to assess disease severity on X-rays, with the Kellgren and Lawrence (K/L) scale being the most widely used. It distinguishes four grades [43]:

Grade	Radiologic Findings
0	No radiological findings of osteoarthritis
I	Doubtful narrowing of joint space and possible osteophytic lipping
II	Definite osteophytes and possible narrowing of joint space
III	Moderate multiple osteophytes, definite narrowing of joint space, small pseudocystic areas with sclerotic walls and possible deformity of bone contour
IV	Large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour

Another useful tools are questionnaires such as WOMAC used to evaluate pain, stiffness and physical function in patients with hip and knee osteoarthritis [23]

Conservative treatment

Conservative treatment methods play a significant role in treatment of KOA. This is related to the fact that when the disease is diagnosed at an early stage, a combination of various conservative methods - such as weight reduction, physiotherapy, and physical therapy - can significantly alleviate pain, improve range of motion and functionality and slow the progression of KOA thereby delaying the need for invasive treatment [9][10][11] [12][14].

Excessive body weight is one of the main factors contributing to the onset and progression of KOA [9]. In a study conducted by Miller et al intervention group obtained an average mass reduction of 8,7% weight loss through a daily caloric deficit of 1000 kcal combined with an

exercise program performed three times a week. Patients who managed to reduce their weight by 11% achieved 35% lower WOMAC index scores. In this group, stair-climbing times and 6-minute walk distance improved by 17% [14]. Another, newer study conducted by Aaboe et al. confirmed the beneficial effects of weight loss on knee joint loading and the overall biomechanical health of the joint. The study demonstrated that a weight reduction of 10% led to clinically significant improvements in patients - a decrease in BMI of 5.1 kg/m² was associated with approximately a 30% reduction in pain. Both of these studies confirm that a weight loss of around 10% of initial body weight is the most beneficial clinically [12][14]. Moreover, for every 1 kg of weight lost, the peak knee load was reduced by 2.2 N, which shows that even small interventions can have meaningful long-term benefits [12].

A systematic review by Shahid et al. focused on identifying the most effective strategies for weight reduction in patients with KOA. Seven intervention groups were compared: diet alone (D), exercise alone (E), Mediterranean diet (M), pharmacological approach (L), psychological intervention (P), diet plus exercise (DE) and psychological intervention plus diet and exercise (PDE). All interventions resulted in significant weight loss compared to the control group. However, significant reductions in pain symptoms were observed only in the DE and PDE groups. The PDE approach proved to be the most effective in terms of improving function and reducing pain, while the DE intervention ranked highest in improving health-related quality of life (HRQoL) [13]. These findings emphasize the importance of interdisciplinary collaboration in achieving better treatment outcomes for patients with KOA [9][12][13][14].

Physiotherapy and physical therapy represent another fundamental component of KOA treatment, primarily due to their minimal side effects, relative convenience and cost-effectiveness [9]. Effective physiotherapy leads to increased quadriceps muscle strength, improved joint range of motion and a simultaneous reduction in pain symptoms. However combining conventional physiotherapy rehabilitation programs with other strategies can significantly improve the outcome. Notably, the integration of aquatic therapy has shown significantly higher satisfaction rates among older individuals compared to conventional physiotherapy alone. Another technique called Kinesio Taping, by supporting muscle function and correcting joint alignment and movement, significantly contributed to reducing pain on VAS scale (subjective measurement tool to asses the intensity of pain - from 0 to 10) increasing

the range of motion and improving hamstring flexibility — thus helping to achieve better knee extension compared to traditional physiotherapy alone [11].

Another source highlights the benefits of two physical therapy modalities: electrotherapy and laser therapy [10]:

High-frequency electrotherapy, through tissue stimulation, leads to improved circulation in the treated area, supports tissue regeneration and promotes muscle relaxation. It also has proven anti-inflammatory effects and may potentially reduce cartilage degradation. It provides stronger analgesic effects compared to low-frequency electrotherapy; however, it is also more intense in sensation, which may cause discomfort in some patients.

Long-term low-intensity laser therapy works by allowing waves of a specific wavelength to penetrate the tissues, where they are converted into energy that stimulates cellular processes and improves blood flow, thereby promoting tissue regeneration. It has been proven to reduce disability rates, decrease the use of analgesic medications and lessen pain symptoms within six months of initiation [10].

Pharmacological treatment

Pain management is a crucial component in the treatment of knee osteoarthritis. While it does not address the underlying cause of the disease, it plays a vital role in improving patient's function and reducing pain-related discomfort [8]. Oral and topical nonsteroidal anti-inflammatory drugs (NSAIDs), paracetamol (acetaminophen) and opioids represent the first-line pharmacologic options [15][18][20]. In the United States, more than half of patients suffering from osteoarthritis are prescribed NSAIDs or opioids—65% and 71%, respectively [18].

However, the widespread use of opioids requires reconsideration. According to Osani et al. opioids had only modest effects on pain relief and functional improvement with meaningful effects generally limited to the first 2–4 weeks of treatment. Over time, their efficacy

diminished, while the risk of adverse effects increased. These side effects include nausea, constipation, diarrhea, vomiting and somnolence. The authors concluded that the risk-benefit profile of opioid therapy in KOA is questionable [20].
Similar conclusions were drawn in a review and meta-analysis by Da Costa et al which emphasized that the potential harms of opioid use generally outweigh the benefits, regardless of dose [18].

In contrast, NSAIDs showed robust efficacy. Diclofenac (150 mg/day), etoricoxib (60 and 90 mg/day) and rofecoxib (25 and 50 mg/day) significantly reduced pain in 99% of treated cases. Among these, etoricoxib 60 mg/day and diclofenac 150 mg/day demonstrated the highest efficacy. Nonetheless, their use must be carefully considered due to possible gastrointestinal, cardiovascular and renal adverse events which may contraindicate treatment in patients with comorbidities [18][19].

Topical NSAIDs, such as diclofenac applied in doses of 70–81 mg/day, offer a promising alternative (Level 1A recommendation). This form provides comparable efficacy with a considerably better safety profile [17][18].

Paracetamol (acetaminophen) remains one of the most frequently used analgesics in osteoarthritis management. However, several authors have criticized its limited efficacy for this indication. Amanda O. Leopoldino's et al review indicated that acetaminophen provides only minimal analgesic benefit at doses ranging from 1.95 g to the maximum permissible dose of 4 g/day [15].

Glucosamine and chondroitin are commonly used supplements among individuals with KOA [16]. A systematic-review and meta-analysis by Simental et al. showed that both substances, when used individually, contribute to pain reduction. However, they failed to produce meaningful improvements in overall joint function as assessed by the WOMAC scale [21]. A meta-analysis of randomised controlled trials by Zhu et al. also shows that chondroitin may present a positive analgesic effect, while glucosamine appears to reduce stiffness in the knee joint. This implies that while using glucosamine and chondroitin separately might yield some

benefits, their combined use does not enhance outcomes. Further research is needed to confirm their true clinical value [16][21].

Intra-articular therapies

The treatment of knee osteoarthritis (KOA) with intra-articular injections is most commonly performed using three substances: hyaluronic acid (HA), glucocorticosteroids (GCS) and platelet-rich plasma (PRP).

Hyaluronic Acid (HA)

HA is the most frequently used substance in intra-articular KOA therapy. It is a glycosaminoglycan naturally present in the synovial membrane, synovial fluid and articular cartilage [22][23]. Administered HA is intended to restore the joint's shock-absorbing properties and improve its viscoelasticity. The study by Blicharski et al. demonstrated the efficacy of HA in patients with mild to moderate knee osteoarthritis - Kellgren-Lawrence scale Grade II-III. These patients perceived a reduction in symptoms, as determined using the WOMAC–Likert scale [23]. Similarly, Migliorini's et al. systematic review showed that HA may be effective in the short-term relief of pain symptoms - around 4 weeks post-injection - while maintaining a high safety profile [22].

Platelet-Rich Plasma (PRP)

PRP is obtained via a two-step centrifugation process of autologous plasma, resulting in a concentrate of platelets. This therapy has gained popularity in recent years due to its minimal invasiveness and relative ease of administration. PRP contains cytokines and growth factors, which exert anti-inflammatory effects and support tissue regeneration. After 6 months of therapy, PRP significantly reduced VAS and WOMAC scores, confirming its effectiveness. Notably, in the WOMAC scale, PRP performed better than oral NSAIDs. Moreover, studies have not shown a significant difference in the frequency of adverse effects compared to HA or placebo - making it a safe treatment option [24][25].

Glucocorticosteroids (GCS)

GCS exert anti-inflammatory effects and are particularly useful in patients with synovitis, where pain intensity is estimated to be up to 9.2 times higher than in patients without synovitis. This condition can be suspected in patients with a swollen, red, warm and painful joint - although this represents an advanced inflammatory stage. In early stages, physical examination alone may not be sufficient for diagnosis. Therefore, imaging methods like MRI or ultrasound may be used to better identify patients who could benefit the most from GCS therapy [27]. Systematic reviews and meta-analyses have shown that GCS contribute to significant pain reduction and functional improvement of the joint for up to 6 weeks. In the long term, a decline in their effectiveness is observed. In this situation, it is worth considering the implementation of other methods such as physiotherapy or PRP [26][28]. It is also important to avoid intra-articular GCS in patients with uncontrolled hypertension or poorly managed diabetes, as these drugs may lead to hypertension and hyperglycemia.

Surgical Treatment:

Total Knee Arthroplasty (TKA)

This is the gold standard treatment for advanced KOA. With an aging population and consequently growing number of people affected by osteoarthritis, the number of TKA procedures is increasing. Projections estimate that in 2030, up to 161,000 such procedures will be performed in Australia and up to 1.2 million in the UK in 2035. In the United States, the number is expected to reach 3.5 million in 2030. Ever-improving implants, continuously refined surgical techniques and rising patient expectations regarding quality of life have resulted in a large number of patients eager to undergo this procedure [33].

Procedure

There are many ways to perform this operation. The following aims to guide through the main steps that are common across different techniques.

Perioperatively, 40 mg of low molecular weight heparin is administered subcutaneously approximately 12 hours before the procedure and intravenous antibiotic prophylaxis is typically administered as 2g of cefazolin about 30 minutes before surgery. The procedure is most often performed under spinal anesthesia, often in combination with femoral nerve block.
The surgeon gains access to the joint cavity by incising the skin, subcutaneous tissue and fascia, followed by the joint capsule. Then the hypertrophic synovium, osteophytes, menisci and the anterior cruciate ligament – and sometimes also the posterior cruciate ligament, depending on the implants used – are removed. With the help of special cutting guides, surgeon resects parts of the femur and tibia articular surfaces, in a way that corrects the abnormal limb axis. Trial implants are then inserted into the prepared areas. The stability of the joint in the frontal plane and the range of flexion and extension are checked. Then the trial implants are replaced with the final components, once the appropriate parameters are achieved. The joint cavity is irrigated and tranexamic acid is administered to reduce postoperative bleeding. The soft tissues are then sutured in layers [35].

A review and meta-analysis by Trieu et al. shows that 84% of individuals under the age of 65 were satisfied or very satisfied with the outcomes of treatment within two years following total knee arthroplasty (TKA). A 4-point Likert scale and the VAS scale were used for assessment. Within 10 years after the procedure, between 90.2% and 93.5% of patients reported satisfaction - however, the methods of measurement for this period are not specified [33].
The systematic review by Woodland et al. indicates that in age groups 65–74 years, 75–84 years, and ≥85 years, the average satisfaction score on a 100-point scale ranged from 83.6 to 85.2 points [34].

Osteotomy and unicompartmental knee arthroplasty (UKA)

Osteotomy and unicompartmental knee arthroplasty (UKA) are therapeutic options for patients suffering from osteoarthritis affecting only one compartment of the knee. Both methods can contribute to improved joint function, pain reduction and thus delaying the need for total knee arthroplasty (TKA) [32].

UKA involves replacing only the damaged compartment of the knee joint with a prosthesis, while the unaffected compartments remain intact. Patients eligible for this procedure should meet the following criteria: angular deformity <15 degrees, flexion contracture <5 degrees, ROM >90 degrees, and good knee joint stability. In these patients, this approach allows for preservation of more bone mass and the anterior cruciate ligament compared to TKA – making it a less invasive option. UKA is associated with lower postoperative pain levels but with a smaller range of motion in the knee joint compared to high tibial osteotomy (HTO) according to Ping's et al. systematic review [36].

High tibial osteotomy (HTO**)** is a procedure aimed at offloading the damaged, typically medial, compartment of the knee joint. Proper patient selection is essential. Age under 65, mild to moderate joint degeneration ((< Grade III according to the Ahlbäck classification - (5 grade radiographic scale used to asses knee osteoarthritis)), good range of motion and absence of ligament instability are features that should characterize those qualified for this surgery [36]. In cases involving the medial compartment, the axis of the knee is corrected by eliminating varus deformity, thereby restoring a proper weight-bearing line [31][32]. The main advantage of this method is minimal interference with soft tissues and the fact that it usually does not adversely affect joint mobility and stability [31]. A systematic review by He et al. shows that treatment outcomes compared to UKA were similar in terms of Hospital for Special Surgery (HSS) scores (questionnaire focusing on patient's functionality level of pain), walking speed, patellofemoral joint degeneration and revision rates. What distinguished this method was a significantly better range of motion in the knee joint compared to UKA.
It has been shown that in patients under the age of 60 with medial compartment KOA, HTO is the most cost-effective intervention in terms of clinical improvement versus economic burden. In contrast, patients over 60 derive greater benefit from undergoing UKA [31][32].

Arthroscopy:

Arthroscopy is a minimally invasive surgical procedure in which access to the knee joint is gained through two or three small skin incisions. Procedure is conducted under camera guidance with a help of special instruments inserted to the knee joint through trocars. When operating,

surgeon can remove loose bodies, inflamed synovial membrane, suture or excise the meniscus or in certain cases fill cartilage defects [29].

However, its use in the context of treating osteoarthritis is increasingly questioned. A systematic review by Zhang et al. showed that the effectiveness of arthroscopy does not surpass that of conservative therapies such as physical therapy, intra-articular injections of hyaluronic acid (HA) or platelet-rich plasma (PRP), thus challenging its routine application [29].

A review by O'Connor et al. also demonstrated that this method has only a minimal impact on symptom relief and functional improvement in both the short and long term, when compared to patients treated conservatively [30].

Modern/Experimental Approaches:

Stem cells are a method that holds great promise. These cells, derived from various sources such as bone marrow, peripheral blood, adipose tissue or amniotic fluid, are known for their differentiation potential and for their anti-inflammatory and immunomodulatory properties [37][38]. Due to these abilities, when properly induced, they can develop into various other cell types, such as chondrocytes or osteoblasts. Therefore, they may serve in the regeneration and repair of damaged articular cartilage, which is the underlying pathology in KOA. In the meta-analysis by Huang et al., it was shown that, compared to patients treated with hyaluronic acid (HA) or glucocorticoid (GC) injections, those who received MSC therapy achieved better outcomes after 24 months in both the VAS and IKDC (International Knee Documentation Committee - a questionnaire including questions in three categories: symptoms, sports activity and knee function; scoring range: 0–100.) scores [38]. In the systematic review by Wiggers et al., it was reported that in 30% of the analyzed cases, stem cell therapy led to improvements in cartilage appearance on MRI scans - indicating regeneration. In other 50% of the cases there were no signs of further cartilage loss. Clinical outcome measures improved in 73% of the treated groups compared to controls. Patients receiving therapy showed improvements of 1.8 - 4.4 points on the VAS scale and 18 to 32 points on the KOOS (Knee injury and Osteoarthritis Outcome Score - questionnaire including questions in 5 categories: pain, symptoms, daily activities, sports and recreation and quality of life).

No serious adverse effects of this therapy were observed. Mild adverse events were reported in 30% of patients, including transient pain and mild joint swelling [37]. These results are promising, however, further studies are needed to evaluate the long-term clinical effects of this therapy [37][38].

Fibroblast Growth Factor (Sprifermin, FGF-18) is a synthetic form of human FGF-18. It binds to its specific receptor, FGFR3, on the surface of articular cartilage, leading to its regeneration [39][40]. In the review by Cao et al., it was shown that FGF-18 did not reduce cartilage loss in the medial compartment of the knee joint, however, it did reduce cartilage thinning in the lateral compartment [40]. The study by Reker et al. demonstrated that treatment with Sprifermin administered once a week for three weeks resulted in an increase in cartilage thickness throughout the entire knee joint. No significant adverse effects were observed following intra-articular administration of FGF-18 [39].

Nerve Growth Factors (NGFs) play a key role in pain signaling - particularly in KOA. Therefore, various antibodies have been developed to inhibit or block NGF - anti-NGF antibodies. By blocking NGF, they reduce the sensitivity of peripheral pain receptors and the expression of neuropeptides responsible for pain transmission. As a result, they provide excellent pain control - surpassing that offered by NSAIDs, opioids or selective COX-2 inhibitors, thereby becoming a very promising analgesic method. [41] [42].

Summary

This review presents various therapeutic methods currently used in the treatment of knee osteoarthritis. Treatment is selected based on the severity of the disease as well as the preferences and capabilities of the patients. As first-line therapy in cases of mild to moderate KOA, conservative methods are applied, including weight reduction, physiotherapy and analgesic treatment. If pain persists, intra-articular injections can be considered, such as hyaluronic acid, corticosteroids or platelet-rich plasma (PRP), with the latter demonstrating the most favorable long-term analgesic effect. When conservative and minimally invasive treatments fail, surgical interventions are introduced. In selected cases, high tibial osteotomy or unicompartmental knee arthroplasty may be appropriate. Arthroscopy, however, has not shown

significant clinical benefits for this indication. Total knee arthroplasty remains the gold standard for advanced-stage KOA. A crucial aspect of current research is the development of novel therapies, particularly those aimed at cartilage repair and regeneration. Treatments involving stem cells or growth factors such as FGF-18 offer hope for more effective and less invasive management. However, further studies are needed to evaluate their long-term efficacy.

Author's contribution:

Conceptualization: Oskar Tudaj [OT], Adrianna Dylik [AD]

Methodology: Julia Kalisiak [JK], Wiktoria Kalas [WK]

Software: n/a

Writing - rough preparation: Oskar Tudaj [OT], Krzysztof Sajewicz [KS]

Writing - review and editing: Mikołaj Kaczmarek [MK], Wiktoria Grochowska [WG]

Investigation: Adrianna Dylik [AD], Aleksandra Mazur [AM]

Resources: Paulina Strzałkowska [PS]

Data curation: Julia Dulęba [JD]

Visualization: Wiktoria Kalas [WK]

Project administration: Julia Kalisiak [JK]

Check: Krzysztof Sajewicz [KS], Paulina Strzałkowska [PS],

Formal editing: Aleksandra Mazur [AM], Julia Dulęba [JD]

Supervision: Mikołaj Kaczmarek [MK], Wiktoria Grochowska [WG]

Receiving funding: n/a

All authors have read and agreed with the published version of the manuscript.

Funding Statement:
This Research received no external funding.

Institutional Review Board Statement:
Not applicable.

Informed Constent Statement:
Not applicable.

Data Availability Statement:
Not applicable.

Acknowledgments:
Not applicable.

Conflict of Interests:
The authors of the paper declare no conflict of interest.

References

1. Moseng T, Vliet Vlieland TPM, Battista S, Beckwée D, Boyadzhieva V, Conaghan PG, Costa D, Doherty M, Finney AG, Georgiev T, Gobbo M, Kennedy N, Kjeken I, Kroon FPB, Lohmander LS, Lund H, Mallen CD, Pavelka K, Pitsillidou IA, Rayman MP, Tveter AT, Vriezekolk JE, Wiek D, Zanoli G, Østerås N. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis: 2023 update. Ann Rheum Dis. 2024;83(6):730–740. doi:10.1136/ard-2023-225041.

2. Primorac D, Molnar V, Rod E, Jeleč Ž, Čukelj F, Matišić V, Vrdoljak T, Hudetz D, Hajšok H, Borić I. Knee Osteoarthritis: A Review of Pathogenesis and State-Of-The-Art Non-Operative Therapeutic Considerations. Genes (Basel). 2020;11(8):854. doi:10.3390/genes11080854.

3. Primorac D, Molnar V, Matišić V, Hudetz D, Jeleč Ž, Rod E, Čukelj F, Vidović D, Vrdoljak T, Dobranić B, Antičević D, Borić I. Comprehensive Review of Knee Osteoarthritis Pharmacological Treatment and the Latest Professional Societies' Guidelines. Pharmaceuticals (Basel). 2021;14(3):205. doi:10.3390/ph14030205.

4. Piccolo CL, Mallio CA, Vaccarino F, Grasso RF, Beomonte Zobel B. Imaging of knee osteoarthritis: a review of multimodal diagnostic approach. Quant Imaging Med Surg. 2023;13(11):7582–7595. doi:10.21037/qims-22-1392.

5. Almhdie-Imjabbar A, Toumi H, Lespessailles E. Radiographic Biomarkers for Knee Osteoarthritis: A Narrative Review. Life (Basel). 2023;13(1):237. doi:10.3390/life13010237.

6. Coaccioli S, Sarzi-Puttini P, Zis P, Rinonapoli G, Varrassi G. Osteoarthritis: New Insight on Its Pathophysiology. J Clin Med. 2022;11(20):6013. doi:10.3390/jcm11206013.

7. Berteau JP. Knee Pain from Osteoarthritis: Pathogenesis, Risk Factors, and Recent Evidence on Physical Therapy Interventions. J Clin Med. 2022;11(12):3252. doi:10.3390/jcm11123252.

8. Lim WB, Al-Dadah O. Conservative treatment of knee osteoarthritis: A review of the literature. World J Orthop. 2022;13(3):212–229. doi:10.5312/wjo.v13.i3.212.

9. Wang W, Niu Y, Jia Q. Physical therapy as a promising treatment for osteoarthritis: A narrative review. Front Physiol. 2022;13:1011407. doi:10.3389/fphys.2022.1011407.

10. Ni X, Hu L, Zhang X, Wang Z, Yan C, Peyrodie L, Lin M, Wu X, Wang H, Hu S. Physical therapy options for knee osteoarthritis: A review. Medicine (Baltimore). 2024;103(30):e38415. doi:10.1097/MD.0000000000038415.

11. Somaiya KJ, Samal S, Boob MA. Physiotherapeutic Intervention Techniques for Knee Osteoarthritis: A Systematic Review. Cureus. 2024;16(3):e56817. doi:10.7759/cureus.56817.

12. Aaboe J, Bliddal H, Messier SP, Alkjaer T, Henriksen M. Effects of an intensive weight loss program on knee joint loading in obese patients with knee osteoarthritis. Osteoarthritis Cartilage. 2011;19(7):822–828. doi:10.1016/j.joca.2011.04.005.

13. Shahid A, Thirumaran AJ, Christensen R, Venkatesha V, Henriksen M, Bowden JL, Hunter DJ. Comparison of weight loss interventions in overweight and obese adults with knee osteoarthritis: A systematic review and network meta-analysis of randomized trials. Osteoarthritis Cartilage. 2025;33(4):399–411. doi:10.1016/j.joca.2025.01.003.

14. Miller GD, Nicklas BJ, Davis C, Loeser RF, Lenchik L, Messier SP. Intensive weight loss program improves physical function in older obese adults with knee osteoarthritis. Obesity (Silver Spring). 2006;14(7):1219–1230. doi:10.1038/oby.2006.139.

15. Leopoldino AO, Machado GC, Ferreira PH, Pinheiro MB, Day R, McLachlan AJ, Hunter DJ, Ferreira ML. Paracetamol versus placebo for knee and hip osteoarthritis. Cochrane Database Syst Rev. 2019;2019(2):CD013273. doi:10.1002/14651858.CD013273.

16. Zhu X, Sang L, Wu D, Rong J, Jiang L. Effectiveness and safety of glucosamine and chondroitin for the treatment of osteoarthritis: a meta-analysis of randomized controlled trials. J Orthop Surg Res. 2018;13:170. doi:10.1186/s13018-018-0871-5.

17. Wolff DG, Christophersen C, Brown S, et al. Topical nonsteroidal anti-inflammatory drugs in the treatment of knee osteoarthritis: a systematic review and meta-analysis. Physician Sportsmed. 2021;49(4):381–391. doi:10.1080/00913847.2021.1886573.

18. Da Costa BR, Pereira TV, Saadat P, Rudnicki M, Iskander SM, Bodmer NS, Bobos P, Gao L, Kiyomoto HD, Montezuma T, Almeida MO, Cheng PS, Hincapié CA, Hari R, Sutton AJ, Tugwell P, Hawker GA, Jüni P. Effectiveness and safety of non-steroidal anti-inflammatory drugs and opioid treatment for knee and hip osteoarthritis: network meta-analysis. BMJ. 2021;375:n2321. doi:10.1136/bmj.n2321.

19. Cioroianu GO, Florescu A, Simionescu CE, Sas TN, Tarniță DN, Rogoveanu OC. The therapeutic benefits of NSAIDs and physical therapy in knee osteoarthritis. Rom J Morphol Embryol. 2024;65(2):217–224. doi:10.47162/RJME.65.2.08.

20. Osani MC, Lohmander LS, Bannuru RR. Is there any role for opioids in the management of knee and hip osteoarthritis? Arthritis Care Res (Hoboken). 2021;73(10):1436–1445. doi:10.1002/acr.24531.

21. Simental-Mendía M, Sánchez-García A, Vilchez-Cavazos F, et al. Effect of glucosamine and chondroitin sulfate in symptomatic knee osteoarthritis: a systematic review and meta-analysis of randomized placebo-controlled trials. Rheumatol Int. 2018;38(8):1413–1428. doi:10.1007/s00296-018-4077-2.

22. Migliorini F, Maffulli N, Schäfer L, Kubach J, Betsch M, Pasurka M. Less pain with intra-articular hyaluronic acid injections for knee osteoarthritis compared to placebo: a systematic review and meta-analysis of randomised controlled trials. Pharmaceuticals (Basel). 2024 Nov 20;17(11):1557. doi:10.3390/ph17111557.

23. Blicharski T, Ławniczak P, Płaza R, Żuraw Z, Szymański M, Matuszewska E, Płaza K, Lee S, Park S. Efficacy and safety of intra-articular cross-linked sodium hyaluronate for the treatment of knee osteoarthritis: a prospective, active-controlled, randomized, parallel-group, double-blind, multicenter study. J Clin Med. 2023;12(8):2982. doi:10.3390/jcm12082982.

24. Mao H, Cheng C, Sun X, Yan Y, Zhang Q, Wang W, Guo W. Efficacy and safety of intra-articular platelet-rich plasma in osteoarthritis knee: a systematic review and meta-analysis. Biomed Res Int. 2021;2021:2191926. doi:10.1155/2021/2191926.

25. Chen P, Huang L, Ma Y, Zhang D, Zhang X, Zhou J, Ruan A, Wang Q. Intra-articular platelet-rich plasma injection for knee osteoarthritis: a summary of meta-analyses. J Orthop Surg Res. 2019 Nov 27;14(1):385. doi: 10.1186/s13018-019-1363-y.

26. Najm A, Alunno A, Gwinnutt JM, Weill C, Berenbaum F. Efficacy of intra-articular corticosteroid injections in knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Joint Bone Spine. 2021;88(4):105198. doi:10.1016/j.jbspin.2021.105198.

27. Heidari P, Heidari B, Babaei M. Efficacy and predictive factors of response to intra-articular corticosteroids in knee osteoarthritis. Reumatologia. 2020;58(6):424–435. doi:10.5114/reum.2020.102008.

28. Bensa A, Sangiorgio A, Boffa A, Salerno M, Moraca G, Filardo G. Corticosteroid injections for knee osteoarthritis offer clinical benefits similar to hyaluronic acid and lower than platelet-rich plasma: a systematic review and meta-analysis. EFORT Open Rev. 2024;9(9):883–895. doi:10.1530/EOR-23-0198.

29. Zhang Z, Hu Z, Zhao D, Huang H, Liang Y, Mao B. Arthroscopic surgery is not superior to conservative treatment in knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. BMC Musculoskelet Disord. 2024;25:712. doi:10.1186/s12891-024-07813-3.

30. O'Connor D, Johnston RV, Brignardello-Petersen R, Poolman RW, Cyril S, Vandvik PO, Buchbinder R. Arthroscopic surgery for degenerative knee disease (osteoarthritis including degenerative meniscal tears). Cochrane Database Syst Rev. 2022;2022(3):CD014328. doi:10.1002/14651858.CD014328.

31. He M, Zhong X, Li Z, Shen K, Zeng W. Progress in the treatment of knee osteoarthritis with high tibial osteotomy: a systematic review. Syst Rev. 2021;10:56. doi:10.1186/s13643-021-01601-z.

32. Zhang B, Qian H, Wu H, Yang X. Unicompartmental knee arthroplasty versus high tibial osteotomy for medial knee osteoarthritis: a systematic review and meta-analysis. J Orthop Surg (Hong Kong). 2023;31(1):10225536231162829. doi:10.1177/10225536231162829.

33. Trieu J, Gould DJ, Schilling C, Spelman T, Dowsey MM, Choong PF. Patient-reported outcomes following total knee replacement in patients <65 years of age: a systematic review and meta-analysis. J Clin Med. 2020;9(10):3150. doi:10.3390/jcm9103150.

34. Woodland N, Takla A, Estee MM, Franks A, Bhurani M, Liew S, Cicuttini FM, Wang Y. Patient-reported outcomes following total knee replacement in patients aged 65 years and over—a systematic review. J Clin Med. 2023;12(4):1613. doi:10.3390/jcm12041613.

35. Xu H, Dong J, Wang J, Gao SJ. Surgical technique of total knee arthroplasty without soft tissue balance. Orthop Surg. 2016;8(4):519–522. doi:10.1111/os.12289.

36. Ping H, Wen J, Liu Y, Li H, Wang X, Kong X, Chai W. Unicompartmental knee arthroplasty is associated with lower pain levels but inferior range of motion, compared with high tibial osteotomy: a systematic overview of meta-analyses. J Orthop Surg Res. 2022;17(1):425. doi:10.1186/s13018-022-03319-7.

37. Wiggers TGH, van der Weegen W, van der List JP, et al. Autologous stem cell therapy in knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. Br J Sports Med. 2021;55(20):1161–1169. doi:10.1136/bjsports-2021-103933.

38. Huang R, Li W, Zhao Y, Yang F, Xu M. Clinical efficacy and safety of stem cell therapy for knee osteoarthritis: A meta-analysis. Medicine (Baltimore). 2020;99(11):e19434. doi:10.1097/MD.0000000000019434

39. Reker D, Siebuhr AS, Thudium CS, Gantzel T, Ladel C, Michaelis M, Aspberg A, Berchtold MW, Karsdal MA, Gigout A, Bay-Jensen AC. Sprifermin (rhFGF18) versus vehicle induces a biphasic process of extracellular matrix remodeling in human knee OA articular cartilage ex vivo. Sci Rep. 2020;10(1):6011. doi:10.1038/s41598-020-63216-z.

40. Cao P, Li Y, Tang Y, Ding C, Hunter DJ. Pharmacotherapy for knee osteoarthritis: current and emerging therapies. Expert Opin Pharmacother. 2020;21(7):797–809. doi:10.1080/14656566.2020.1732924.

41. Wang M, Lian J, Ye M, An B. Pain mediator NGF improves chondrocyte extracellular matrix synthesis via PI3K/AKT pathway. J Orthop Surg Res. 2025;20:207. doi:10.1186/s13018-025-05503-x.

42. Cao Z, Zhou J, Long Z, Li Y, Sun J, Luo Y, Wang W. Targeting nerve growth factor, a new option for treatment of osteoarthritis: a network meta-analysis of comparative efficacy and safety with traditional drugs. Aging (Albany NY). 2020;13(1):1051–1070. doi:10.18632/aging.202232.

43. Han XA, Razak HRB, Tan HCA. The truth behind subchondral cysts in osteoarthritis of the knee. Open Orthop J. 2014;8:7–10. doi:10.2174/1874325001408010007.