DUTKA, Martyna, BERNACKI, Piotr, BERNACKI, Radosław, ZARDZEWIAŁY, Witold, ZAREMSKYI, Oleksii, BIAŁOGŁOWSKI, Konrad, SKRZYŃSKA, Klaudia, MENDYK, Krzysztof, MORDASIEWICZ, Dominika and FUSZARA, Kamil. Quality of life corrected by osteoarthritis of the hip and knee - therapeutic options for athletes. Quality in Sport. 2024;20:54011. eISSN 2450-3118.
https://dx.doi.org/10.12775/QS.2024.20.54011
https://apcz.umk.pl/QS/article/view/54011

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's 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 r. 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 interests regarding the publication of this paper.
Received: 02.08.2024. Revised: 15.08.2024. Accepted: 17.08.2024. Published: 22.08.2024.

Quality of life corrected by osteoarthritis of the hip and knee - therapeutic options for athletes

Martyna Dutka

Medical University of Lublin, al. Racławickie 1, 20-059 Lublin, Poland

martynadutka810@gmail.com

https://orcid.org/0009-0006-4747-677X

Piotr Bernacki

Medical University of Lublin, al. Racławickie 1, 20-059 Lublin, Poland

pbernacki73@gmail.com

https://orcid.org/0009-0002-9324-9632

Radosław Bernacki

Medical Center in Łańcut, ul. Paderewskiego 5, 37-100 Łańcut, Poland

rbernacki97@gmail.com

https://orcid.org/0009-0000-1554-2724

Witold Zardzewiały

1 Military Clinical Hospital in Lublin, al. Racławickie 23, 20-049 Lublin, Poland

witold.zardzewialy@gmail.com

https://orcid.org/0000-0003-4459-0535

Oleksii Zaremskyi

1 Military Clinical Hospital in Lublin, al. Racławickie 23, 20-049 Lublin, Poland

ozaremski@gmail.com

https://orcid.org/0009-0003-5111-3339

Konrad Białogłowski

University Clinical Hospital No. 1 in Lublin, ul. Stanisława Staszica 16, 20-081 Lublin, Poland

konrad.bialoglowski@gmail.com

https://orcid.org/0009-0001-1705-254X

Klaudia Skrzyńska

4th Clinical University Hospital in Lublin, ul. Kazimierza Jaczewskiego 8, 20-954 Lublin, Poland

skrzynskaklaudia1@gmail.com

https://orcid.org/0009-0004-3124-8655

Krzysztof Mendyk

Independent Public Health Care Complex in Leżajsk, ul. Leśna 22, 37-300 Leżajsk, Poland

kmendyk97@gmail.com

https://orcid.org/0009-0004-4636-8465

Dominika Mordasiewicz

Medical University of Lublin, al. Racławickie 1, 20-059 Lublin, Poland

dmordasiewicz@wp.pl
https://orcid.org/0009-0005-2633-6316

Kamil Fuszara

University Clinical Hospital No. 1 in Lublin, ul. Stanisława Staszica 16, 20-081 Lublin, Poland

kamil7197@o2.pl
https://orcid.org/0009-0003-3905-7848

Abstract

Osteoarthritis (OA) is the most common chronic joint disease that causes slow degeneration of the articular cartilage of each joint component. For years, treatments have been sought to halt the progression of OA. Modern medicine has not yet found such a cure, but it has therapies to offer that make life more comfortable for a short period of time. Oral therapies with non-steroidal anti-inflammatory drugs and paracetamol effectively relieve only minor joint pain in the early stages of OA. Hyaluronic acid (HA) and corticosteroid (GCS) delivery therapies may result in clinically significant benefits in a significant number of patients, but emerging evidence suggests that the apparent efficacy of these treatments is largely due to other factors, including the placebo effect. The paucity of high-level evidence of action and methodological limitations make it difficult to consider delivery injections with stem cell preparations as effective in treating the causes of OA. Although many promising pharmacological treatments are currently in clinical trials, the best therapeutic option for OA to date is joint alloplasty. The most common surgical access when performing hip alloplasty is the posterior access. Replacing the diseased hip joint has many benefits for the patient including pain relief, improved quality of daily life and more efficient mobility.

Keywords: osteoarthritis, osteoarthritis treatment , total hip arthroplasty

Introduction

Osteoarthritis (OA) is the most common joint disease involving all joint components, which causes chronic pain and reduces quality of life in patients by decreasing joint function [1]. The disease most commonly involves articular cartilage in joints that carry heavy loads, such as the hip, knee and shoulder. The presence of lesions in tissues such as the synovial membrane of the joint capsule, the underlying bone contributes to a more severe disease progression [2]. However, OA is clinically a highly variable disease and can be diagnosed without characteristic symptoms as well as in advanced multi-joint disease. It can be categorised into primary osteoarthritis and secondary osteoarthritis [3].

Etiology

OA can be divided according to risk factors into primary OA, which is idiopathic, and secondary osteoarthritis whose causes are iatrogenic or are due to trauma, joint infection [4].

Primary osteoarthritis is more often diagnosed, its diagnosis is less often associated with trauma and is more often influenced by the patient's age, gender, obesity, occupation as well as lifestyle.

Secondary OA is diagnosed in the case of a pre-existing joint abnormality. Predisposing conditions include single- and multi-joint injuries, infections and congenital joint abnormalities causing pathological joint mechanics and arthritis, arthritic necrosis, Paget's disease, osteoporosis, dissecting osteoarthritis, haemochromatosis, Wilson's disease, haemoglobinopathy, Marfan's syndrome or Ehlers-Danlos syndrome [3].

Pathophysiology

Osteoarthritis is currently understood as a multifactorial joint pathology caused by various inflammatory and metabolic factors that are the most common causes of joint damage.

OA is considered to be a disease involving all components of the joint including calcified cartilage, subchondral bone, capsular ligaments and joint fluid, and is not limited to degradation of articular cartilage alone.[2][5][6] Increasing evidence shows that cartilage degeneration precedes subchondral bone changes, suggesting a key role for this mechanism in the pathogenesis and progression of osteoarthritis, as well as the formation of ectopic bone and osteophytes. Subchondral bone marrow lesions (SBMLs), diagnosed by abnormal MRI signals beneath calcified cartilage, affected more than half of asymptomatic patients before 50 years of age. Their incidence appears to increase with age [5][7]. SBMLs arise from joint biomechanical abnormalities and sustained mechanical injuries that lead to cellular and biomolecular responses in response to the resulting microdamage in the subchondral layer of bone. The SBML site is characterised by a high rate of bone turnover, pain and activation of pro-inflammatory pathways, ultimately leading to increased subchondral sclerosis and increased bone mineral density. As a result, subchondral bone remodelling is now considered one of the main components of osteoarthritis, which can disrupt the integrity of the osteochondral unit and lead to increased crosstalk between cartilage and subchondral bone [5]. Clinical observations showed that, over a 24-month period, the magnitude of SBML on MRI increased in volume, particularly in the medial tibial plateau and medial condyle, which shows a strong correlation with cartilage volume loss in the respective areas of SBML in the respective bones, indicating the diagnostic value of predicting a degenerative condition within the osteochondral unit [7].

Synovitis is increasingly observed in osteoarthritis. Most patients with OA have low-grade inflammation; oxidative stress, reduced chondrocyte proliferation and extracellular matrix synthesis play major roles in the development and progression of OA [8]. In addition, synovitis promotes the production of adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and chemokines, which are responsible for histological changes in the synovial membrane, including hypertrophy and proliferation, accompanied by infiltrating mononuclear cells such as macrophages and monocytes such as T-lymphocytes and B-lymphocytes [9]. The synovitis seen in OA is dominated by macrophages, in contrast to synovitis in rheumatoid arthritis (RA) where T lymphocytes predominate [5][6]. Synovitis increases angiogenesis in the synovial membrane, which in turn accelerates inflammation. In addition, synovitis also facilitates the production of pro-inflammatory and pain neurotransmitters such as nerve growth factor and bradykinin [9].

Chondrocytes, synoviocytes and osteoblasts produce pro-inflammatory mediators such as pro-inflammatory cytokines, tumour necrosis factor (TNF), interleukin-1 beta (IL-1β), IL-6,

IL-8, IL-15, IL-17, IL-21, inflammatory mediators PGE2 , NO, adipokines (visfatin, resistin) and matrix metalloproteinases (MMP-1, MMP-3, MMP-9, MMP-13) and reactive oxygen species (ROS) are responsible for inhibiting anabolism and the release of proteolytic enzymes, contribute to the degradation of extracellular matrices and exacerbate cartilage degeneration irreversibly. Despite the presence of anti-inflammatory cytokines in OA-affected tissues such as interferon-γ (IFN-γ), IL-6, IL-10, IL-4 and TGF-β, a shift in the balance of pro- and -inflammatory cytokines towards the catabolic side can be described [5][9].

Reactive oxygen species and interdependent inflammation, is an intrinsic feature of occupied OA joints [5]. Oxidative stress, resulting from an imbalance between ROS production and the antioxidant role of chondrocytes, are the cause of chronic inflammation, cartilage degradation and chondrocyte decline. Inflammatory mediators such as interleukin-1β (IL-1β), tumour necrosis factor α (TNF-α) and interleukin-6 (IL-6) are significantly increased in joints with osteoarthritis and induce ROS production and expression of matrix-degrading proteases leading to matrix degradation and joint dysfunction. Elevated levels of ROS also lead to reduced expression of cartilage-specific genes responsible for cartilage functionality (aggrecan (ACAN) and collagen type II alpha 1 (COL2A1)) [8][10][11]. As patients age, ROS levels in chondrocytes increase, which may also be caused by mitochondrial dysfunction and reduced mitochondrial superoxide dismutase (SOD2) glutathione peroxidase (GPX) and catalase (CAT) activity, are reduced in OA, exacerbating oxidative stress. The resultant increase in ROS is oxidative damage to proteins, lipids, DNA as well as hyperoxidation inactivates peroxiredoxin (Prx) causing increased cell death. More importantly, Prx inactivation can disrupt cellular redox-regulated signalling pathways through the oxidation of protein thiols [11][12].

Conservative treatment

The most common reported symptom of osteoarthritis of the hip is pain. This symptom impairs patients' quality of life the most. Conservative treatment aims to alleviate pain and other bothersome symptoms and not affect the progression of the disease [13][14].

Pharmacological treatment

Oral non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol (acetaminophen) are the most commonly used analgesics for pain reduction in OA [13].

Paracetamol is used as a first-line analgesic, but the efficacy of this drug in OA is negligible and not superior to that of placebo [15]. Its use is due to its relative safety and the lack of effective alternatives. A recent systematic review concluded that paracetamol provides short-term minimal pain control [16].

Non-steroidal anti-inflammatory drugs (NSAIDs) are first-line drugs in the pharmacological treatment of OA. In placebo-controlled trials, NSAIDs produced greater pain reduction than placebo [6]. Topical NSAIDs used in patches or creams complement non-pharmacological treatment [15]. Topical NSAIDs show less toxicity than oral NSAIDs, but are less effective in the treatment of hip osteoarthritis, due to their deep location in the hip bones. Oral NSAIDs used chronically can cause gastrointestinal irritation, ulceration and bleeding. During chronic use of oral NSAIDs, they should be combined with proton pump inhibitors or COX-2 inhibitors [6].

Pain occurring in OA can be caused by ongoing mechanisms in the central nervous system. Duloxetine and serotonin-norepinephrine reuptake inhibitors have been used in pain of central origin. In randomised trials, the previously mentioned drugs have been shown to cause pain relief compared to placebo. Opioids are rarely used in the treatment of OA. This is due to the limited efficacy in the treatment of hip and knee osteoarthritis. Opioid analgesics also have many side effects such as constipation, drowsiness, respiratory depression and have high toxicity and potential for addiction during their use. Treatment guidelines for OA advise against the use of oral or transdermal forms of opioids with the exception of tramadol, as it is a synthetic opioid that also inhibits serotonin and norepinephrine reuptake [6][15].

Treatment with delivery injections

Patients who are unable to take oral NSAIDs, or patients for whom therapy with these drugs does not have the expected effect on pain reduction, can try intralesional injection therapy, which usually relieves pain for a few weeks. This type of therapy is particularly helpful for patients with single joint osteoarthritis. Hip joint injections are mainly performed under ultrasound guidance [6].

Non-cellular treatment options

According to the recommendations of the current guidelines for knee osteoarthritis and hip osteoarthritis, for short-term pain relief, delivery injections of glucocorticosteroids at the

lowest therapeutic dose are recommended when symptoms are refractory to treatment with oral NSAIDs. After three months, glucocorticosteroid injections have no greater effect on pain than placebo, and after one year they may show inferior results to the effect of physiotherapy. Recent data from meta-analyses of controlled trials show that even the use of multiple steroid injections has no advantage over placebo. An increase in the risk of steroid-induced articular cartilage loss and the resulting progression of degenerative changes was noted as the number of doses administered increased. No differences were found between the available glcocorticosteroid preparations in terms of their efficacy in the treatment of OA. Some studies speculate that newer forms of injectable steroids may have fewer systemic side effects than traditional steroid injections. However, steroid use is associated with altered gene expression and immunomodulation that results in inhibition of anabolic activity of chondrocytes, reduced expression of genes responsible for collagen synthesis resulting in additional joint damage and progression of OA [6][14][17].

Delivery injections of hyaluronic acid (HA) are another alternative to oral NSAID treatment. HA is a high molecular weight glycosaminoglycan that is found in cartilage and joint fluid. Intra-articular injections of HA are a common way to administer this viscous supplement, which improves joint lubrication and impact absorption. Most of the results of meta-analyses, do not show a correlation between clinical efficacy and outcomes of HA use. Meta-analyses have shown only moderate pain reduction [18][19]. According to various guidelines, the use of HA is recommended, while other guidelines do not recommend the use of HA due to the lack of data from randomised controlled trials in the countries concerned [20][21][22][23].

Cell treatment options

Intra-articular cell injection therapy in OA was designed to promote healing of damaged articular cartilage by implanting and differentiating susceptible cells into chondrocytes that build up the cartilage of affected joints. Candidate cells for this therapy may be modified chondrocytes or stem cells [24].

Platelet-rich plasma (PRP) delivery injections are the most commonly used cell therapy for the treatment of OA. PRP is a preparation of autologous blood that has been centrifuged to concentrate platelets above levels found in healthy human serum. Although this therapy is one of the best studied cell therapies for the treatment of OA, the lack of properly conducted studies and uncertainties due to the complexity of the mechanisms of action, as well as the lack of

standardisation between PRP protocols, makes it difficult to confirm the efficacy of PRP's therapeutic effect on inhibiting OA exacerbations [19][21][25]. PRP contains activated platelets, thus releasing anti-inflammatory mediators that can reduce inflammation and pain. Due to this effect, PRP is used in reducing pain in OA. The results of several meta-analyses have shown that PRP therapy is more effective than both HA therapy and placebo in reducing pain 6 and 12 months after injection [19][25][26][27][28].

Another cell therapy to offer for OA patients is injections with bone marrow concentrate (BMAC) preparations. BMAC preparations contain bone marrow stem cells, which are a heterogeneous mixture of cells that perform different functions in the joint into which they are implanted. A proportion of these cells are involved in the osteogenesis pathway and the acceleration of bone formation and regeneration, and a second proportion of stem cells from this mixture contained in BMAC are responsible for immunomodulation. BMAC contains few mesenchymal stem cells and mainly contains stem cells of haematopoietic origin, platelets as well as cytokines making the composition of the BMAC preparation similar to that of PRP [19][29][30]. The similar composition of these delivery injection preparations results in similar effects of both therapies. Despite the higher cost of BMAC therapy relative to PRP therapy, BMAC therapy is more beneficial than PRP in patients with knee OA, in patients with mild OA [29][31].

The next therapeutic option for cell therapy is adipose tissue-derived stem cell (ADSC) preparations. ADSC preparations are derived from lipoaspirate by enzymatic digestion or by mechanical treatment, which exhibit cartilage-protective effects through anti-inflammatory action. It is suspected that ADSC preparations may contain membrane proteins, cytoplasmic and nuclear proteins and extracellular matrix proteins, nucleic acids that may enhance the protective effect on articular cartilage [19][32][33]. ADSC, through its action, relieves pain and improves quality of life in OA patients 6 months after delivery injections. No significant regeneration of damaged articular cartilage defects was reported in MRI studies after 6 months. The superiority of ADSC therapy over BMAC therapy has not been demonstrated in clinical trials of cell-based treatment for OA [33][34][35].

Operative treatment

Total hip arthroplasty (THA) is the standard surgical intervention for patients with hip osteoarthritis [36]. With the use of low-friction plastics, implant survival in surgical endoprosthetic procedures has been significantly improved [37].

There have been a number of studies that have proven the efficacy of THA in relieving pain, improving quality of life and better functioning in daily life after total hip replacement [38][39].

Rear access

This is the most common method of THA in the world. Patient in side position on a traditional operating table. Using special handles, place the patient in the correct position to obtain a stable position before starting the operation. The correct positioning of the patient guarantees the operator and assistants an adequate range of movement of the operated limb during the operation. The operated limb should be sterile and freely positioned to facilitate hip dislocation.

When starting the operation, the operator makes an incision approximately 5cm from the greater ileum. The incision starts on the lateral side of the thigh at the level of the middle of the femoral shaft and then makes a proximal incision along the posterior edge of the greater ileum and then makes an arc with the blade towards the posterior superior iliac spine. The skin and subcutaneous fat should be incised to the broad fascia and the iliac tibial band. The broad fascia together with the iliopsoas muscle band is incised along the fibres of the gluteus maximus muscle. Further preparation of the deeper tissues and identification of the short external rotators of the hip joint is performed in internal rotation of the hip joint. The external rotators are then severed at their attachment to the greater ileum to visualise the posterior aspect of the hip joint capsule. The next stage of the operation is to perform a T-shaped capsulotomy. Further internal rotation together with flexion and gentle adduction at the hip joint allows it to be dislocated. If dislocation of the joint is difficult, partial or complete release of the rectus thigh muscle may be necessary especially in cases of severe hip contracture or revision.

Femoral neck osteotomies are performed using an oscillating saw. The site of the osteotomy is determined from the preoperative plan, with the minor ileum as the reference

point. The hip joint casing and other soft tissues remaining loose should also be removed and the bottom of the acetabulum worked out with a reamer.

It is a technique used in both primary hip replacement and revision surgery [40].

Summary

Modern medicine has not yet discovered a causal treatment for OA that achieves the expected therapeutic effect. Available therapies only help to treat short-term the most troublesome symptoms of OA such as pain and discomfort in the affected joint. To date, the only effective therapeutic option to cure OA is alloplasty of the affected joint. Thanks to the development of surgical techniques, this is a less invasive operation every year. Replacement of the affected joint has many benefits for the patient, including pain relief, improved quality of daily life and more efficient movement soon after surgery.

Disclosure

Author's contribution:

Conceptualization: Piotr Bernacki, Witold Zardzewiały, Radosław Bernacki

Methodology: Kamil Fuszara, Konrad Białogłowski, Klaudia Skrzyńska

Software: Krzysztof Mendyk, Oleksii Zaremskyi

Check: Martyna Dutka, Dominika Mordasiewicz

Formal Analysis: Oleksii Zaremskyi , Krzysztof Mendyk

Investigation: Klaudia Skrzyńska, Witold Zardzewiały, Kamil Fuszara

Resources: Dominika Mordasiewicz, Piotr Bernacki, Konrad Białogłowski

Data Curation: Piotr Bernacki, Radosław Bernacki, Martyna Dutka

Writing-Rough Preparation: Martyna Dutka, Radosław Bernacki

Writing-Review and Editing: Martyna Dutka, Klaudia Skrzyńska, Dominika Mordasiewicz, Radosław Bernacki, Krzysztof Mendyk, Witold Zardzewiały, Piotr Bernacki, Konrad Białogłowski, Kamil Fuszara, Oleksii Zaremskyi

Visualization: Krzysztof Mendyk, Dominika Mordasiewicz,

Supervision: Klaudia Skrzyńska, Oleksii Zaremskyi, Kamil Fuszara

Project Administration: Witold Zardzewiały, Konrad Białogłowski

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

Funding statement:

This review was not externally funded.

Statement of the institutional review board:

Not applicable.

Statement of informed consent:

Not applicable.

Statement of data availability:

Not applicable.

Conflict of interest:

The authors report no conflicts of interest

References:

1. Onoi Y, Matsumoto T, Sobajima S, Tsubosaka M, Hayashi S, Matsushita T, Iwaguro H, Kuroda R. Clinical use of autologous adipose-derived stromal vascular fraction cell injections for hip osteoarthritis. Regen Ther. 2023 Jun 15;24:94-102. doi: 10.1016/j.reth.2023.06.006. PMID: 37363753; PMCID: PMC10285449.

2. Krishnan Y, Grodzinsky AJ. Cartilage diseases. Matrix Biol. 2018 Oct;71-72:51-69. doi: 10.1016/j.matbio.2018.05.005. Epub 2018 May 24. PMID: 29803938; PMCID: PMC6146013.

3. Sen R, Hurley JA. Osteoarthritis. 2023 Feb 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 29493951.

4. Mélou C, Pellen-Mussi P, Jeanne S, Novella A, Tricot-Doleux S, Chauvel-Lebret D. Osteoarthritis of the Temporomandibular Joint: A Narrative Overview. Medicina. 2023; 59(1):8. https://doi.org/10.3390/medicina59010008

5. Coaccioli S, Sarzi-Puttini P, Zis P, Rinonapoli G, Varrassi G. Osteoarthritis: New Insight on Its Pathophysiology. Journal of Clinical Medicine. 2022; 11(20):6013. https://doi.org/10.3390/jcm11206013

6. Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. JAMA. 2021 Feb 9;325(6):568-578. doi: 10.1001/jama.2020.22171. PMID: 33560326; PMCID: PMC8225295.

7. Hu Y, Chen X, Wang S, Jing Y, Su J. Subchondral bone microenvironment in osteoarthritis and pain. Bone Res. 2021 Mar 17;9(1):20. doi: 10.1038/s41413-021-00147-z. PMID: 33731688; PMCID: PMC7969608.

8. Liu L, Zhang W, Liu T, Tan Y, Chen C, Zhao J, Geng H, Ma C. The physiological metabolite α-ketoglutarate ameliorates osteoarthritis by regulating mitophagy and oxidative stress. Redox Biol. 2023 Jun;62:102663. doi: 10.1016/j.redox.2023.102663. epub 2023 Mar 10. PMID: 36924682; PMCID: PMC10026041.

9. Han D, Fang Y, Tan X, Jiang H, Gong X, Wang X, Hong W, Tu J, Wei W. The emerging role of fibroblast-like synoviocytes-mediated synovitis in osteoarthritis: An update. J Cell Mol Med. 2020 Sep;24(17):9518-9532. doi: 10.1111/jcmm.15669. epub 2020 Jul 19. PMID: 32686306; PMCID: PMC7520283.

10. Ansari MY, Ahmad N, Haqqi TM. Oxidative stress and inflammation in osteoarthritis pathogenesis: Role of polyphenols. Biomed Pharmacother. 2020 Sep;129:110452. doi: 10.1016/j.biopha.2020.110452. Epub 2020 Jul 3. PMID: 32768946; PMCID: PMC8404686.

11. Bolduc JA, Collins JA, Loeser RF. Reactive oxygen species, aging and articular cartilage homeostasis. Free Radic Biol Med. 2019 Feb 20;132:73-82. doi: 10.1016/j.freeradbiomed.2018.08.038. epub 2018 Aug 31. PMID: 30176344; PMCID: PMC6342625.

12. Shi G, Jiang H, Yang F, Lin Z, Li M, Guo J, Liao X, Lin Y, Cai X, Li D. NIR-responsive molybdenum (Mo)-based nanoclusters enhance ROS scavenging for osteoarthritis therapy. Pharmacol Res. 2023 Jun;192:106768. doi: 10.1016/j.phrs.2023.106768. epub 2023 Apr 13. PMID: 37061147

13. Weng Q, Goh SL, Wu J, Persson MSM, Wei J, Sarmanova A, Li X, Hall M, Doherty M, Jiang T, Zeng C, Lei G, Zhang W. Comparative efficacy of exercise therapy and oral non-steroidal anti-inflammatory drugs and paracetamol for knee or hip osteoarthritis: a network meta-analysis

of randomised controlled trials. Br J Sports Med. 2023 Aug;57(15):990-996. doi: 10.1136/bjsports-2022-105898. epub 2023 Jan 2. PMID: 36593092; PMCID: PMC10423468.

14. Ossendorff R, Thimm D, Wirtz DC, Schildberg FA. Methods of Conservative Intra-Articular Treatment for Osteoarthritis of the Hip and Knee. Dtsch Arztebl Int. 2023 Sep 4;120(35-36):575-581. doi: 10.3238/arztebl.m2023.0154. PMID: 37427991; PMCID: PMC10552632.

15. Herrera-Pérez M, Valderrabano V, Godoy-Santos AL, de César Netto C, González-Martín D, Tejero S. Ankle osteoarthritis: comprehensive review and treatment algorithm proposal. EFORT Open Rev. 2022 Jul 5;7(7):448-459. doi: 10.1530/EOR-21-0117. PMID: 35900210; PMCID: PMC9297055.

16. Conaghan PG, Arden N, Avouac B, Migliore A, Rizzoli R. Safety of Paracetamol in Osteoarthritis: What Does the Literature Say? Drugs Aging. 2019 Apr;36(Suppl 1):7-14. doi: 10.1007/s40266-019-00658-9. PMID: 31073920; PMCID: PMC6509082.

17. Ferrara PE, Codazza S, Coraci D, Malerba G, Ferriero G, Ronconi G. State of art in intra-articular hip injections of different medications for osteoarthritis: a systematic review. BMC

Musculoskelet Disord. 2021 Nov 29;22(Suppl 2):997. doi: 10.1186/s12891-021-04866-6. PMID: 34844603; PMCID: PMC8630838.

18. Mao L, Wu W, Wang M, Guo J, Li H, Zhang S, Xu J, Zou J. Targeted treatment for osteoarthritis: drugs and delivery system. Drug Deliv. 2021 Dec;28(1):1861-1876. doi: 10.1080/10717544.2021.1971798. PMID: 34515606; PMCID: PMC8439249.

19. Jones IA, Togashi R, Wilson ML, Heckmann N, Vangsness CT Jr. Intra-articular treatment options for knee osteoarthritis. Nat Rev Rheumatol. 2019 Feb;15(2):77-90. doi: 10.1038/s41584-018-0123-4. PMID: 30498258; PMCID: PMC6390843.

20. Kan HS, Chan PK, Chiu KY, Yan CH, Yeung SS, Ng YL, Shiu KW, Ho T. Non-surgical treatment of knee osteoarthritis. Hong Kong Med J. 2019 Apr;25(2):127-133. doi: 10.12809/hkmj187600. Epub 2019 Mar 28. PMID: 30919810.

21. Bannuru RR, Osani MC, Vaysbrot EE, Arden NK, Bennell K, Bierma-Zeinstra SMA, Kraus VB, Lohmander LS, Abbott JH, Bhandari M, Blanco FJ, Espinosa R, Haugen IK, Lin J, Mandl LA, Moilanen E, Nakamura N, Snyder-Mackler L, Trojian T, Underwood M, McAlindon TE. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage. 2019 Nov;27(11):1578-1589. doi: 10.1016/j.joca.2019.06.011. epub 2019 Jul 3. PMID: 31278997.

22. Pendleton A, Arden N, Dougados M, Doherty M, Bannwarth B, Bijlsma JW, Cluzeau F, Cooper C, Dieppe PA, Günther KP, Hauselmann HJ, Herrero-Beaumont G, Kaklamanis PM, Leeb B, Lequesne M, Lohmander S, Mazieres B, Mola EM, Pavelka K, Serni U, Swoboda B, Verbruggen AA, Weseloh G, Zimmermann-Gorska I. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis. 2000 Dec;59(12):936-44. doi: 10.1136/ard.59.12.936. PMID: 11087696; PMCID: PMC1753053.

23. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, Callahan L, Copenhaver C, Dodge C, Felson D, Gellar K, Harvey WF, Hawker G, Herzig E, Kwoh CK, Nelson AE, Samuels J, Scanzello C, White D, Wise B, Altman RD, DiRenzo D, Fontanarosa J, Giradi G, Ishimori M, Misra D, Shah AA, Shmagel AK, Thoma LM, Turgunbaev M, Turner AS, Reston J. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. Arthritis Rheumatol. 2020 Feb;72(2):220-233. doi: 10.1002/art.41142. epub 2020 Jan 6. Erratum in: Arthritis Rheumatol. 2021 May;73(5):799. doi: 10.1002/art.41761. PMID: 31908163; PMCID: PMC10518852.

24. Im GI. Perspective on Intra-articular Injection Cell Therapy for Osteoarthritis Treatment. Tissue Eng Regen Med. 2019 Jan 23;16(4):357-363. doi: 10.1007/s13770-018-00176-6. PMID: 31413940; PMCID: PMC6675827.

25. Bennell KL, Paterson KL, Metcalf BR, Duong V, Eyles J, Kasza J, Wang Y, Cicuttini F, Buchbinder R, Forbes A, Harris A, Yu SP, Connell D, Linklater J, Wang BH, Oo WM, Hunter DJ. Effect of Intra-articular Platelet-Rich Plasma vs Placebo Injection on Pain and Medial Tibial Cartilage Volume in Patients With Knee Osteoarthritis: The RESTORE Randomized Clinical Trial. JAMA. 2021 Nov 23;326(20):2021-2030. doi: 10.1001/jama.2021.19415. PMID: 34812863; PMCID: PMC8611484.

26. Tang JZ, Nie MJ, Zhao JZ, Zhang GC, Zhang Q, Wang B. Platelet-rich plasma versus hyaluronic acid in the treatment of knee osteoarthritis: a meta-analysis. J Orthop Surg Res. 2020 Sep 11;15(1):403. doi: 10.1186/s13018-020-01919-9. PMID: 32912243; PMCID: PMC7488405.

27. 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. PMID: 31775816; PMCID: PMC6880602.

28. Everts P, Onishi K, Jayaram P, Lana JF, Mautner K. Platelet-Rich Plasma: New Performance Understandings and Therapeutic Considerations in 2020. Int J Mol Sci. 2020 Oct 21;21(20):7794. doi: 10.3390/ijms21207794. PMID: 33096812; PMCID: PMC7589810.

29. Dulic O, Rasovic P, Lalic I, Kecojevic V, Gavrilovic G, Abazovic D, Maric D, Miskulin M, Bumbasirevic M. Bone Marrow Aspirate Concentrate versus Platelet Rich Plasma or Hyaluronic Acid for the Treatment of Knee Osteoarthritis. Medicina (Kaunas). 2021 Nov 2;57(11):1193. doi: 10.3390/medicina57111193. PMID: 34833411; PMCID: PMC8623697.

30. Kim GB, Seo MS, Park WT, Lee GW. Bone Marrow Aspirate Concentrate: Its Uses in Osteoarthritis. Int J Mol Sci. 2020 May 2;21(9):3224. doi: 10.3390/ijms21093224. PMID: 32370163; PMCID: PMC7247342.

31. El-Kadiry AE, Lumbao C, Salame N, Rafei M, Shammaa R. Bone marrow aspirate concentrate versus platelet-rich plasma for treating knee osteoarthritis: a one-year non-randomized retrospective comparative study. BMC Musculoskelet Disord. 2022 Jan 3;23(1):23. doi: 10.1186/s12891-021-04910-5. PMID: 34980045; PMCID: PMC8725314.

32. Meng C, Na Y, Han C, Ren Y, Liu M, Ma P, Bai R. Exosomal miR-429 derived from adipose-derived stem cells ameliorated chondral injury in osteoarthritis via autophagy by targeting FEZ2. Int Immunopharmacol. 2023 Jul;120:110315. doi: 10.1016/j.intimp.2023.110315. epub 2023 May 27. PMID: 37245297.

33. Murata D, Fujimoto R, Nakayama K. Osteochondral Regeneration Using Adipose Tissue-Derived Mesenchymal Stem Cells. Int J Mol Sci. 2020 May 19;21(10):3589. doi: 10.3390/ijms21103589. PMID: 32438742; PMCID: PMC7279226.

34. Pintore A, Notarfrancesco D, Zara A, Oliviero A, Migliorini F, Oliva F, Maffulli N. Intra-articular injection of bone marrow aspirate concentrate (BMAC) or adipose-derived stem cells (ADSCs) for knee osteoarthritis: a prospective comparative clinical trial. J Orthop Surg Res. 2023 May 11;18(1):350. doi: 10.1186/s13018-023-03841-2. PMID: 37170296; PMCID: PMC10176826.

35. Lee WS, Kim HJ, Kim KI, Kim GB, Jin W. Intra-Articular Injection of Autologous Adipose Tissue-Derived Mesenchymal Stem Cells for the Treatment of Knee Osteoarthritis: A Phase IIb, Randomized, Placebo-Controlled Clinical Trial. Stem Cells Transl Med. 2019 Jun;8(6):504-511. doi: 10.1002/sctm.18-0122. epub 2019 Mar 5. PMID: 30835956; PMCID: PMC6525553.

36. Learmonth ID, Young C, Rorabeck C. The operation of the century: total hip replacement. Lancet. 2007 Oct 27;370(9597):1508-19. doi: 10.1016/S0140-6736(07)60457-7. PMID: 17964352.

37. Charnley J. Total hip replacement by low-friction arthroplasty. Clin Orthop Relat Res. 1970 Sep-Oct;72:7-21 PMID: 5459811.

38. Ferguson RJ, Palmer AJ, Taylor A, Porter ML, Malchau H, Glyn-Jones S. Hip replacement. Lancet. 2018 Nov 3;392(10158):1662-1671. doi: 10.1016/S0140-6736(18)31777-X. PMID: 30496081.

39. Pabinger C, Bridgens A, Berghold A, Wurzer P, Boehler N, Labek G. Quality of outcome data in total hip arthroplasty: comparison of registry data and worldwide non-registry studies from 5 decades. Hip Int. 2015 Sep-Oct;25(5):394-401. doi: 10.5301/hipint.5000239. epub 2015 Mar 20. PMID: 25837781.

40. Moretti VM, Post ZD. Surgical Approaches for Total Hip Arthroplasty. Indian J Orthop. 2017 Jul-Aug;51(4):368-376. doi: 10.4103/ortho.IJOrtho_317_16. PMID: 28790465; PMCID: PMC5525517.