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INTEGRATED STUDY MASTER'S THESIS

Treatment of Non-Traumatic Osteonecrosis of the Femoral Head in Adults

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SUMMARY

Osteonecrosis of the femoral head is a progressive and potentially disabling disorder that predominantly affects young- and middle-aged adults and may lead to femoral head collapse, secondary osteoarthritis, and the need for total hip arthroplasty. Despite various treatment options, the optimal management of non-traumatic osteonecrosis of the femoral head remains controversial due to the lack of a universally accepted treatment algorithm and heterogeneous evidence regarding treatment effectiveness.

The aim of this thesis was to evaluate and compare current treatment strategies for adult nontraumatic osteonecrosis of the femoral head, with particular consideration of the role of disease stage in guiding clinical decision-making.

A structured narrative literature review was conducted based on a systematic PubMed search. Studies published from 2010 onwards were screened according to predefined criteria. A total of 17 clinical studies were included, comprising randomized controlled trials, prospective cohort studies, and one retrospective study. Extracted data included patient characteristics, treatment modalities, and clinical and radiological outcomes such as Harris Hip Score, Visual Analogue Scale, radiographic progression, and the need for total hip arthroplasty.

The findings demonstrated considerable heterogeneity in treatment outcomes. Less invasive strategies showed inconsistent effects, with some improvement in clinical symptoms but limited impact on structural disease progression. Core decompression, the most frequently investigated joint-preserving procedure, was associated with improved clinical outcomes, particularly in early-stage disease. Biological augmentation of core decompression showed potential benefits in selected cases; however, results were inconsistent and appeared to depend on disease stage and the type of augmentation used. In advanced stages, the effectiveness of joint-preserving techniques decreased, and more invasive interventions, including structural reconstruction and arthroplasty, were associated with improved functional outcomes. Overall, treatment selection in osteonecrosis of the femoral head should primarily be guided by disease stage. Joint-preserving strategies are most appropriate in early-stage disease, whereas advanced stages often require more invasive interventions. Patient-related factors such as age, lesion characteristics, and aetiology further influence outcomes and should be considered in clinical decision-making. However, the available evidence remains limited and heterogeneous, highlighting the need for further high-quality, stage-specific research to support more individualized treatment strategies.

KEYWORDS:

Non-traumatic osteonecrosis of the femoral head, avascular necrosis, treatment, stagedependent treatment, core decompression, arthroplasty, disease staging

SANTRAUKA

Šlaunikaulio galvos osteonekrozė yra progresuojanti ir potencialiai neįgalumą sukelianti liga, dažniausiai paveikianti jaunos ir vidutinio amžiaus suaugusiuosius. Liga gali lemti šlaunikaulio galvos kolapsą, antrinę osteoartritą bei totalinės klubo sąnario artroplastikos poreikį. Nepaisant įvairių gydymo galimybių, netrauminės šlaunikaulio galvos osteonekrozės gydymas išlieka diskutuotinas dėl visuotinai priimto gydymo algoritmo trūkumo ir nevienalyčių duomenų apie gydymo efektyvumą.

Šio darbo tikslas buvo įvertinti ir palyginti dabartines suaugusiųjų netrauminės šlaunikaulio galvos osteonekrozės gydymo strategijas, ypatingą dėmesį skiriant ligos stadijos reikšmei klinikinių sprendimų priėmimo.

Buvo atlikta struktūruota naratyvinė literatūros apžvalga, paremta sisteminga PubMed duomenų bazės paieška. Į analizę buvo įtraukti nuo 2010 metų publikuoti tyrimai, atrinkti pagal iš anksto nustatytus kriterijus. Iš viso buvo įtrauktas 17 klinikinių tyrimų rinkinys, apimantis randomizuotus kontroliuojamus tyrimus, prospektyvinius kohortinius tyrimus ir vieną retrospektyvinį tyrimą. Surinkti duomenys apėmė pacientų charakteristikas, taikytus gydymo metodus bei klinikinius ir radiologinius rezultatus, tokius kaip Harris Hip Score, Visual Analogue Scale, radiologinis progresavimas ir totalinės klubo sąnario artroplastikos poreikis.

Rezultatai parodė reikšmingą gydymo rezultatų nevienalytiškumą. Mažiau invazinės gydymo strategijos pasižymėjo nevienodais rezultatais – kai kuriais atvejais buvo stebimas klinikinių simptomų pagerėjimas, tačiau poveikis struktūriniam ligos progresavimui buvo ribotas.

Šerdinė dekompresija, dažniausiai tirta sąnarį išsauganti procedūra, buvo susijusi su geresniais klinikiniais rezultatais, ypač ankstyvose ligos stadijose. Biologinė šerdinės dekompresijos augmentacija tam tikrais atvejais parodė potencialią naudą, tačiau rezultatai buvo nevienodi ir priklausė nuo ligos stadijos bei taikytos augmentacijos tipo. Pažengusiose ligos stadijose sąnarį išsaugančių metodų efektyvumas mažėjo, o invazyvesnės intervencijos, įskaitant struktūrinę rekonstrukciją ir artroplastiką, buvo susijusios su geresniais funkciniais rezultatais.

Apibendrinant galima teigti, kad gydymo pasirinkimas esant šlaunikaulio galvos osteonekrozei pirmiausia turėtų būti grindžiamas ligos stadija. Sąnarį išsaugančios strategijos yra tinkamiausios ankstyvose ligos stadijose, tuo tarpu pažengusios stadijos dažnai reikalauja invazyvesnių intervencijų. Paciento amžius, pažeidimo charakteristikos ir etiologija taip pat turi įtakos gydymo rezultatams ir turėtų būti vertinami priimant klinikinius sprendimus. Vis dėlto šiuo metu prieinami moksliniai duomenys išlieka riboti ir nevienalyčiai, todėl reikalingi tolimesni aukštos kokybės, į konkrečias ligos stadijas orientuoti tyrimai, siekiant sukurti labiau individualizuotas gydymo strategijas.

RAKTINIAI ŽODŽIAI:

Netrauminė šlaunikaulio galvos osteonekrozė, avaskulinė nekrozė, gydymas, stadijomis pagrįstas gydymas, šerdinė dekompresija, artroplastika, ligos stadijavimas

ABBREVIATIONS

ONFH = Osteonecrosis of the femoral head

ARCO = Association Research Circulation Osseous

HHS = Harris Hip Score

VAS = Visual Analogue Scale

WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

HBOT = Hyperbaric oxygen therapy

ESWT = Extracorporeal shockwave therapy

BMAC = Bone marrow aspirate concentrate

MSC = Mesenchymal stem cells

FVFG = Free vascularized fibular graft

THA = Total hip arthroplasty

SLE = Systemic lupus erythematosus

SF-36 = 36-Item Short Form Health Survey

1. INTRODUCTION

1.1 BACKGROUND AND CLINICAL RELEVANCE

Osteonecrosis of the femoral head (ONFH) is a potentially disabling orthopedic disorder that predominantly affects young- and middle-aged adults, with a higher prevalence in men than in women, and an annual incidence of 5,000 to 7,000 cases in Germany and 10,000 to 20,000 new symptomatic cases per year in the USA (1–3). Due to the relatively young age of affected patients, ONFH represents a significant clinical challenge, as it may lead to long-term functional impairment and reduced quality of life.

Osteonecrosis of the femoral head is characterized by the progressive necrosis of trabecular bone resulting from impaired blood supply to the femoral head. As the disease advances, structural weakening of the subchondral bone may lead to femoral head collapse, followed by joint incongruity and the development of secondary osteoarthritis. Clinically, patients typically present with hip pain and a reduced range of motion, with symptoms often progressing over time (3–5).

If left untreated, ONFH frequently results in irreversible joint damage requiring surgical intervention, most commonly total hip arthroplasty. Given the limited lifespan of prosthetic implants and the high functional demands of younger patients, early diagnosis and appropriate management are of particular importance (6,7).

1.2 ETIOLOGY, PATHOPHYSIOLOGY AND DISEASE PROGRESSION

Non-traumatic osteonecrosis of the femoral head is associated with a variety of underlying risk factors that may impair the vascular supply to the femoral head and contribute to the development of bone necrosis. The most commonly reported risk factors include prolonged corticosteroid use and excessive alcohol consumption, both of which have been strongly linked to the occurrence of ONFH (3,8).

Additional risk factors include smoking, obesity, and various systemic conditions such as autoimmune diseases, particularly systemic lupus erythematosus, as well as haematological disorders including sickle cell disease. These factors are thought to contribute to vascular

compromise through mechanisms such as altered lipid metabolism, increased intraosseous pressure, and impaired microcirculation (3,8–10).

In some cases, no identifiable cause can be determined, and the condition is therefore classified as idiopathic osteonecrosis. The presence of multiple risk factors in individual patients is not uncommon and may further increase the likelihood of disease development, particularly in the context of cumulative vascular impairment (3).

The pathophysiology of ONFH is complex and not yet fully understood. It is generally accepted that a disruption of the blood supply to the femoral head leads to ischemia and subsequent death of bone and bone marrow cells (3). Several mechanisms have been proposed, including intravascular coagulation, fat embolism, and increased intraosseous pressure, all of which may contribute to reduced perfusion of the femoral head (11–13). In addition, alterations in lipid metabolism and endothelial dysfunction are thought to further impair microcirculation (14,15).

On a cellular level, an imbalance between bone resorption and bone formation plays a central role in disease progression. Increased osteocyte apoptosis and reduced osteoblastic activity impair the regenerative capacity of bone, while ongoing mechanical loading of the necrotic area contributes to structural weakening of the femoral head (16).

The progression of ONFH typically follows a characteristic course. In early stages, structural integrity of the femoral head is preserved despite underlying biological alterations. As the disease advances, subchondral fractures and collapse of the femoral head may occur, leading to joint incongruity and secondary osteoarthritis. Without appropriate intervention, this process ultimately results in progressive functional impairment and the need for surgical treatment (17).

1.3 CLASSIFICATION AND STAGING SYSTEMS

The most commonly used classification systems for ONFH are the Ficat and Arlet, Steinberg (University of Pennsylvania), ARCO (Association Research Circulation Osseous), and JIC (Japanese Investigation Committee) systems. These systems are primarily based on radiographic and MRI findings, with newer systems incorporating lesion size and location to improve prognostic value (18).

These staging systems allow differentiation between early, pre-collapse stages and more advanced stages characterized by subchondral collapse and structural damage of the femoral

head. Early stages are typically defined by the absence of radiographic collapse, whereas advanced stages involve structural failure and joint incongruity (18,19).

The classification of disease stage plays a crucial role in clinical decision-making, as it directly influences the choice of treatment strategy. Joint-preserving approaches are generally considered in early stages, while more invasive procedures are typically required once structural collapse has occurred.

1.4 RATIONALE FOR TREATMENT AND EXISTING CHALLENGES

The primary aim in the management of osteonecrosis of the femoral head is to prevent or delay disease progression, preserve the native joint, and maintain function for as long as possible. However, the optimal treatment strategy remains controversial, as the effectiveness of available interventions varies depending on disease stage, lesion characteristics, and patient-related factors (20,21).

A wide range of treatment options exists, including pharmacological therapies, non-invasive physical treatments, joint-preserving surgical procedures, and arthroplasty. Despite this, no universally accepted treatment algorithm has been established, particularly for early-stage disease, where the evidence supporting conservative and adjunctive therapies remains limited (3,21).

In addition, early diagnosis of ONFH remains challenging due to nonspecific clinical symptoms and frequently normal radiographic findings in the initial stages. This may delay the initiation of appropriate treatment and negatively affect clinical outcome (17).

1.5 AIM OF THE REVIEW

The aim of this thesis is to evaluate and compare current treatment strategies for adult nontraumatic osteonecrosis of the femoral head, with particular consideration of the role of disease stage in guiding clinical decision-making.

2. MATERIAL AND METHODS

2.1 LITERATURE SELECTION STRATEGY

A comprehensive literature search was conducted in PubMed to identify literature, assessing treatment options for non-traumatic osteonecrosis of the femoral head in adults. Publications from 2010 onwards were selected and screened for predefined inclusion and exclusion criteria. Titles and abstracts were screened by the author for eligibility.

Studies including patients with traumatic osteonecrosis or individuals below the defined age threshold were excluded. The lower age threshold was set at 17 years, as several otherwise eligible studies included isolated 17-year-old patients; this minor deviation from the conventional adult threshold was not considered sufficient to justify exclusion.

A selection preference was applied toward prospective, randomized, and controlled study designs to prioritize higher levels of evidence. Nevertheless, in areas where randomized controlled trials were rare, well-designed prospective non-randomized studies and a limited number of retrospective clinical studies were also considered to provide a comprehensive overview of available treatment strategies. The search results and study selection process are summarized in Table 1. Duplicate records were removed prior to the final eligibility assessment.

Table 1 List of Databases searched for literature

Database	Search	Results	Studies included after title and abstract screening	Last search date
PubMed	((("osteonecrosis"[MeSH] OR "avascular necrosis" OR "aseptic necrosis" OR "non-traumatic osteonecrosis") AND ("femoral head" OR "hip joint") AND ("treatment" OR "therapy" OR "intervention") AND "adult"[MeSH]) NOT ("posttraumatic"[Title/Abstract] OR "traumatic fracture"[Title/Abstract]))	39	8	July 2025

	Filters: Randomized Controlled Trial, Clinical Trial, Free full text, publication date not older than 2010			
Pubmed	Identical but with the filter “full text” instead of “free full text”	120	9	July 2025

Following full text-review, a total of 17 studies were included in the final analysis. The studies included in this review are listed separately at the end of the reference section

2.2 DATA EXTRACTION AND OUTCOME PARAMETERS

The selected studies were screened for reported outcome measures to identify areas of comparability between studies. For each study, the following study characteristics were extracted, if mentioned in the study: study design, sample size, patient demographics (age and sex), main reported etiologic factors, disease stage at inclusion, inclusion and exclusion criteria, treatment modality, and follow-up duration. Reported clinical and radiological outcome measures were extracted where available. These included VAS, Harris Hip Score, WOMAC, Lequesne Index, SF-12, lesion size, vascularity parameters, radiographic progression, and need for total hip arthroplasty.

In addition, study-specific or supplementary findings not captured within the predefined outcome categories were documented when considered relevant to the overall interpretation of results. Some of the included studies reported supplementary descriptive findings, such as illustrative imaging examples or biomechanical simulation results. As these data were not derived from quantitative clinical analyses and were not directly comparable across studies, they were only considered in a limited and contextual manner and were not included in the primary synthesis of treatment outcomes.

3. RESULTS

The results are presented according to the invasiveness of the treatment modalities, ranging from pharmacological approaches to joint-preserving surgical techniques and finally

arthroplasty procedures. In studies where both treatment groups received the same baseline intervention, such as core decompression (CD), the classification was based on the additional or investigational therapy rather than the shared base procedure. This approach allows the studies to be grouped according to the therapeutic strategy under investigation and facilitates comparison between different treatment modalities.

3.1 OVERVIEW OF INCLUDED STUDIES

Among the 17 selected studies, the majority were randomized controlled trials ($n = 9$), including several double-blind and multicentred designs. Additional studies consisted of prospective non-randomized clinical trials and cohort studies ($n = 7$), as well as a single retrospective clinical study.

Sample sizes ranged from 12 to 250 hips per study, and the mean age of patients across the included studies ranged approximately from 29 to 52 years, with most study populations consisting of patients in their fourth and fifth decades of life. Across the included studies, patient populations were predominantly male. In most cohorts, approximately 60–80% of participants were male, which is consistent with the known epidemiological pattern of osteonecrosis of the femoral head showing a higher prevalence in men (22). A few studies reported a more balanced gender distribution, and in one study female patients constituted most of the participants.

The most frequently reported etiologic factors across the included studies were corticosteroid use and alcohol abuse. Several studies focused exclusively on steroid-induced osteonecrosis, while others included mixed aetiologies such as alcohol abuse, corticosteroid therapy, smoking, or idiopathic cases. Less commonly reported causes included systemic diseases such as systemic lupus erythematosus or sickle cell disease.

The most commonly reported outcome measures were the Harris Hip Score and the Visual Analog Scale, while other parameters such as WOMAC scores, radiographic progression, and the need for total hip arthroplasty were reported less consistently.

Follow-up duration varied substantially between the included studies. Several studies reported short- to medium-term follow-up periods ranging from a few weeks to 24 months, while others evaluated longer observation periods of several years. The longest follow-up reported was approximately 25 years, although most studies assessed outcomes within the first two to five years after treatment

3.2 PHARMACOLOGICAL APPROACHES

Pharmacological treatment strategies have been investigated as potential therapeutic options for early-stage osteonecrosis of the femoral head, with the aim of slowing disease progression, reducing pain and delaying structural collapse of the femoral head. These approaches primarily focus on improving microcirculation, reducing inflammation, or influencing bone metabolism in order to counteract the pathophysiological mechanisms underlying osteonecrosis (23). Several pharmacological agents have been proposed in this context, including the prostacyclin analogue Iloprost and bisphosphonates such as Alendronate. The rationale behind these treatments assumes that impaired blood supply, microvascular thrombosis, and altered bone turnover contribute to the development and progression of osteonecrosis (19). While acetylsalicylic acid aims to enhance proliferation of osteoblasts/preosteoblasts and exerts anti-inflammatory and antithrombotic mechanisms of action to help prevent disease progression (24), Bisphosphonates such as Alendronate work through a different mechanism. They inhibit the activity of osteoclasts and therefore are thought to reduced bone turnover and increased mineral density of bone (25).

The following section summarizes the reported clinical outcomes of pharmacological interventions in patients with non-traumatic osteonecrosis of the femoral head.

Four of the included studies investigated pharmacological treatment strategies, either as a standalone treatment, or their effect in combination with surgical procedures such as core decompression or multiple drilling. The investigated agents included acetylsalicylic acid and bisphosphonates such as alendronate.

One prospective cohort study with a historical control group investigated the effect of daily oral administration of 81 mg of acetylsalicylic acid (ASA) in patients with Ficat & Arlet/Steinberg stage II osteonecrosis of the femoral head. Radiographic disease progression, assessed by changes in ONFH staging on radiographs or MRI, served as the primary outcome measure. The results were compared with a historical control group from the literature that received conservative management. The authors reported a lower rate of radiographic disease progression in the acetylsalicylic acid group compared with the control cohort. In the ASAtreated group, 11 of 12 hips showed no progression of ONFH stage on radiographs or MRI at a mean follow-up of 3.7 years. The prevention of grade progression was significant compared to the control group (26).

Other studies investigated the effect of alendronate, either as adjunctive treatment to multiple drilling or in combination with daily oral calcium and vitamin. One prospective randomized control trial was conducted involving 127 hips with modified Ficat and Arlet Stage IIA, IIB, and III osteonecrosis. They compared the Harris Hip score (HHS), need for THA and time to femoral head collapse between a group receiving multiple drilling combined with alendronate (10 mg daily or 70 mg weekly for 24 weeks) and a group receiving multiple drilling alone. A significant advantage was reported for the alendronate group regarding all three outcome measures. Collapse occurred later in the alendronate group (mean 23 months) than in controls (mean 17 months). Furthermore, the study evaluated the relationship between the location of lesion, lesion size and risk factors and their effect on survival/no need for THA. In both groups, alendronate and control, central lesions showed statistical significantly better outcomes than lateral lesions. Small lesions had significantly better outcomes than medium/large lesions and steroid use and systemic lupus erythematosus were associated with higher failure rates. Alcohol use did not significantly affect outcomes. Patients were followed for a minimum of four years (27).

In another study investigating the effects of alendronate in the context of ONFH, 52 patients with 65 hips participated in a multicenter, prospective, randomized, double-blind study. The participants were divided into a control group receiving a placebo plus daily oral calcium (500 mg) and vitamin D (400 IU) and a treatment group receiving oral alendronate (70 mg) weekly for 2 years + daily oral calcium (500 mg) and vitamin D (400 IU). The patients were diagnosed with stage IIC or IIIC ONFH according to the Pennsylvania classification system. Clinical outcomes were assessed using the Harris Hip Score, the Short Form-36 health survey, radiographic progression, as well as the need for total hip arthroplasty over a period of 2 years. Alendronate therapy did not reduce THA rates or slow disease progression compared to placebo, and no functional improvement was observed (28).

Furthermore, a prospective, randomized study was conducted looking into the effect of a cocktail therapy for ONFH. The therapy consisted of extracorporeal shock wave therapy (ESWT), hyperbaric oxygen therapy (HBO) and 70 mg of oral alendronate sodium per week and was compared with a control group receiving ESWT alone. A total of 68 patients with 105 affected hips with ARCO stage I, II or III participated in said study. Both groups showed significant improvements in clinical outcome measures, including HHS, VAS, WOMAC, and SF-12, whereas no significant changes were observed regarding lesion size. No statistically significant differences between the two treatment groups were observed for the evaluated clinical outcomes. (29).

3.3 NON-INVASIVE PHYSICAL THERAPIES

Non-invasive physical therapies have been investigated as an additional option for the treatment of non-traumatic osteonecrosis of the femoral head. Among these, hyperbaric oxygen therapy (HBOT) aims to improve tissue oxygenation by increasing the amount of dissolved oxygen in the blood under elevated atmospheric pressure, thereby enhancing oxygen delivery to ischemic bone and promoting angiogenesis (30). In contrast extracorporeal shockwave therapy is thought to reduce pain and stimulate bone remodelling and neovascularization via the application of high-energy acoustic pulses. But it's also important to mention that the mechanism of action isn't understood in its entirety (31,32). The following section summarizes one study for each therapy method.

To investigate the effects of HBOT a double-blind randomized controlled study was performed. Nineteen patients with idiopathic Ficat stage II were divided into two groups who either received HBOT or just hyperbaric air for the first 6 weeks. Afterwards both groups received HBOT and the study became observational. Each group received 30 therapy sessions in these 6 weeks and a total of 90 HBO treatments in 12 months. Pain, range of motion and a stabilometry was documented throughout the treatment with the result of a significant difference in pain and range of motion after the 6 weeks. The stabilometry didn't yield any significant difference for the time of the double blind. Until the follow up period of 7 years all patients reported minimal pain with no decrease in activities of daily living. No hip arthroplasty surgeries or newly developed contralateral diseases were reported. From 9 patients who had repeated MRIs, all showed continuing improvement in radiographic appearance (30).

A three-armed prospective clinical trial including 33 patients (42 hips) with ARCO stage I–III evaluated dose-dependent effects of extracorporeal shockwave therapy. Patients received 2000, 4000, or 6000 impulses over a two-year period. Outcome parameters included pain (VAS), Harris Hip Score, stage progression, need for total hip arthroplasty, and selected serum biomarkers. Significant differences in pain and Harris Hip Score were observed between the lowest and highest dose groups at six months. Pain scores decreased over time, whereas no sustained improvement in Harris Hip Score was observed between 6 and 24 months. Total hip arthroplasty was performed in three patients (four hips) in the lowest dose group, while no procedures were required in the higher dose groups. Higher dose groups demonstrated significant changes in biomarkers related to angiogenesis, osteogenesis, and inflammation, as

well as increased perfusion parameters following treatment. However, no significant changes in infarction volume were observed across groups (32).

3.4 CORE DECOMPRESSION

A common joint-preserving surgical treatment for ONFH is core decompression, a procedure that aims at the decompression of the femoral head by reducing the intraosseous pressure, and therefore alleviating pain, improving vascularization, and facilitating the regeneration of necrotic zones. It is primarily indicated for early-stage disease as outcomes are significantly worse in more advanced stages such as stage III (1).

The first study in this chapter, compared the effects of core decompression with another invasive treatment, that of Free vascularized fibular grafting (FVFG). Twenty-seven patients with bilateral ARCO stage I to IIIB ONFH participated in this randomized control trial. Each patient's hips were randomly assigned to one of the two surgical options: one side was treated with core decompression, and the contralateral side was concurrently treated with FVFG.

Outcome measures included femoral head vascularity, ARCO stage progression, the relationship between vascularity and Harris Hip Score, and the need for total hip arthroplasty, which were assessed over a follow-up period of up to 36 months. At the final measurements, all parameters were significantly better in the fibular grafting hips compared to the core decompression, except for the need of a total hip arthroplasty (33).

Another study evaluated the outcomes of advanced core decompression, with partial comparison to conventional techniques reported in the literature. Advanced core decompression involves the use of a percutaneous expandable reamer and the refilling of the drill hole and the defect with an injectable, hard-setting, composite calcium sulphate (CaSO_4) calcium and phosphate (CaPO_4) bone graft substitute. This prospective non-randomized study included 27 patients who underwent advanced core decompression. The results were compared with preoperative data. The study group had osteonecrosis of the femoral head of up to Steinberg stage III and was followed for an average of 9.69 months. Significant improvements were observed in VAS and HHS. While 5 hips (18.5%) required THA, no progression in the remaining hips was observed on MRI. Patients with Stage IIC and higher had significant worse outcome relating to VAS and HHS compared to the other patients (34). As an additional part of the study, compression tests were performed on seven pairs of femoral cadaver bones with one femur of each pair being treated with ACD, while the

opposite side remained untreated. This was done to investigate a potential influence of ACD on bone stability. No significant difference in biomechanical stability was observed (34).

3.5 CORE DECOMPRESSION WITH BIOLOGICAL AUGMENTATION

Apart from advanced core decompression there are further augmented treatment modalities which are used together with core decompression. Many of these involve the usage of biological augmentation which refers to the application of autologous cells, such as bone marrow-derived cells or osteoblastic cells, to the necrotic area. This is done to promote osteogenesis and angiogenesis within the ischemic bone tissue and thereby support structural repair and potentially delay disease progression (1). The following section summarizes the clinical outcomes of six studies investigating cell-based augmentation strategies in the treatment of non-traumatic osteonecrosis of the femoral head.

Two randomized controlled trials investigated the outcome of core decompression with osteoblastic cells, with the difference that one study compared it to core decompression with placebo implantation (5 mL of solution without cells), while the other compared it to core decompression with bone marrow aspirate concentrate (BMAC). Both studies included patients with ARCO stage I or II and assessed VAS, radiological progression, WOMAC, and the need for total hip arthroplasty. The follow-up period was 36 months in the BMAC study and 24 months in the placebo-controlled study. Both studies reported no significant differences between the intervention and control groups (1,15). In the BMAC study, a significant improvement in VAS was observed within the treatment group when comparing pre- and post-treatment values (35).

The aforementioned application of BMAC represents a specific form of autologous bone marrow cell augmentation in combination with core decompression. Two further studies investigated the outcome of CD combined with autologous bone marrow cells compared to core decompression alone. These studies involved 19 and 18 patients, respectively; one study included patients with ARCO stage I or II, while the other included stage III as well (36,37). The study with only ARCO stage I and II patients investigated VAS, stage progression, joint symptoms (Lequesne index and WOMAC), time to failure, the size of lesions, and the need for THA. There were significantly better results in the group receiving autologous bone marrow cells in all parameters except for WOMAC and the need for THA. The volume of the

necrotic lesion decreased significantly in the bone marrow graft group compared to the control group at 24 months and approached statistical significance at 60 months ($p = 0.066$). Said study was a controlled, double-blind pilot study without randomization and had a followup time of 60 months (36). The other study was designed as a prospective, randomized study with a follow-up of 24 months. VAS, WOMAC and MRI surveillance were evaluated. The Visual Analogue Scale and the WOMAC score were both significantly better within the 2 treatment groups between pre- and post-treatment (after 24 months). Furthermore, the group receiving bone marrow injections had significantly better results in both parameters than the one receiving only core decompression. While the control group showed significant worsening on MRI, the bone marrow group had significant improvements with two patients experiencing marked improvement after 18 months. Accordingly, outcomes were significantly better in the bone marrow group compared to the control group (37).

In contrast, another study investigating autologous bone marrow concentrate included only patients with ARCO stage III osteonecrosis and therefore focused on more advanced disease stages. Said double-blind randomized controlled study involved 38 patients with 46 hips and compared a group receiving core decompression plus BMAC implantation with a control group receiving core decompression plus saline injection. VAS, WOMAC, side-effects, radiological evolution including ARCO subclassifications and the need for THA were evaluated over a period of 24 months. Overall, both groups showed significant improvements within their groups concerning VAS when comparing pre- and post-treatment values, but there were no confirmed advantages in any parameters of BMAC implantation in comparison with core decompression alone in stage III osteonecrosis (38).

In contrast to previously described approaches using bone marrow-derived cell mixtures such as BMAC, the final study related to core decompression with biological augmentation investigated the use of more specifically isolated mesenchymal stem cells. One hundred and seventeen patients who completed the study, with bilateral ARCO or Steinberg stage I or II, were followed for an average time of 25 years. Both hips had the same stage at baseline in each patient, and all cases were corticosteroid-induced. While the hip with larger necrosis received core decompression combined with autologous bone marrow-derived mesenchymal cell injection, the other side received core decompression alone. Several parameters were evaluated. At the most recent follow-up, the hips treated with core decompression combined with autologous bone marrow-derived mesenchymal cell injection showed significantly better results in VAS, HHS, vascularity, reduction in lesion size, histologic osteoneogenesis, grade

progression, time to failure (need for THA) and the general need for THA. The WOMAC score showed significant improvements in both groups but wasn't compared between them. Furthermore, in the study a younger age (less than 30 years) at time of the primary THA was associated with a significantly higher risk of revisions (39).

3.6 STRUCTURAL RECONSTRUCTION TECHNIQUES

Structural reconstruction techniques represent a further joint-preserving surgical approach for the treatment of osteonecrosis of the femoral head, particularly in more advanced stages where simple decompression procedures may be insufficient. These techniques aim to provide mechanical support to the subchondral bone, restore structural integrity of the femoral head, and prevent or delay collapse. Common approaches include vascularized or non-vascularized bone grafting as well as the use of synthetic or biomaterial-based implants (19). The following section summarizes the clinical outcomes of two studies investigating structural reconstruction techniques in the treatment of ONFH.

In the first study, 78 patients with steroid-induced osteonecrosis of the femoral head with Steinberg stage I, II or III were divided into a group receiving CD and the implantation of a biomaterial-loaded allograft threaded cage (ATC) implant and a control group receiving core decompression alone. The follow-up for this prospective blind study was 36-78 months and included assessment of the Harris-Hip-Score, the rate of progression, and femoral head collapse requiring THA in both groups (which was defined as clinical failure). While the HHS in the ATC group showed a significant improvement compared to preoperative values, no significant improvement was observed in the control group. This finding remained consistent when only non-failed hips were analysed. The clinical success rate at 36 months postoperatively was reported to be 91% in the treatment group, whereas approximately 55% of hips in the control group were classified as successful (40).

The second study aimed to compare and analyse the biomechanical repair and clinical efficacy of ONFH with the use of a metal trabecular bone reconstruction system and free vascularized fibular graft (FVFG). Therefore, 53 patients with alcohol-induced ARCO stage IIA-IIIB were treated with either a metal trabecular bone reconstruction system or FVFG. In this prospective, comparative cohort study, the treatment via a Metal trabecular bone reconstruction system showed significantly better results in HHS, Intraoperative blood loss, operation time, length of postoperative hospitalization and the SF-36 Health Survey (41). The

SF-36 measures health-related quality of life across different factors (42). Both treatment methods led to an average peak stress reduction of 46.17%, measured by a stress nephogram of the subchondral and cortical bone in the weight-bearing region of the femoral head. There were no significant between-group differences concerning VAS and postoperative complications. Furthermore, radiologically, there were more favourable findings in the metal trabecular group compared to the FVFG group, although no p-values were stated. The total clinical effective rate of young patients (20~40 years) was higher than that of older patients (41~60 years) (41).

3.7 ARTHROPLASTY PROCEDURES

Arthroplasty procedures represent the most invasive and definitive treatment option for osteonecrosis of the femoral head. They are primarily considered in advanced stages of the disease (ARCO stages III and IV) or in cases with an unfavourable prognosis due to factors such as underlying conditions, associated risk factors, lifestyle influences, or extensive structural damage of the femoral head. Although arthroplasty generally yields favourable outcomes in advanced osteonecrosis of the femoral head, implant survival and revision rates are influenced by patient-specific factors, particularly age and underlying aetiology, with younger patients often requiring revision procedures over time (1).

A retrospective clinical trial evaluated bipolar hemiarthroplasty (BHA) for the treatment of steroid-induced osteonecrosis of the femoral head. BHA is a surgical procedure that replaces only the damaged femoral head while leaving the acetabulum intact. Twenty-seven patients with 37 ARCO stage II-IV hips received BHA and were followed up for an average of approximately ten years. The Japan Orthopaedic Association (JOA) hip score was used for pre- and postoperative evaluation. It was also analysed in relation to gender, age, weight, number of joints, and necrosis stage. The JOA hip score increased from a preoperative average of 53 to 87 at final follow up. Loosening of the prosthesis was observed in five hips (13.5%) on the acetabular side, whereas no loosening occurred at the femoral component. Revision total hip arthroplasty was required in three hips (8.1%) during the study period. The reported implant survival rates, with revision THA defined as the endpoint, were 96.8% at ten years and 78.6% at fifteen years. Multiple logistic regression analysis identified preoperative age and stage of necrosis as significant factors influencing outcomes. Prosthesis loosening, which occurred only on the acetabular side, was more frequent in younger patients and in

those with more advanced stages of necrosis. When stratified by age, patients under 40 years showed a significantly higher rate of component loosening compared to older patients. Furthermore, revision rates were strongly associated with disease stage, with a rate of 3.5% in stage III and 100% in stage IV osteonecrosis (43).

4. DISCUSSION

4.1 OVERALL INTERPRETATION OF RESULTS

The present structured narrative review demonstrates that a broad spectrum of treatment strategies for non-traumatic osteonecrosis of the femoral head has been investigated, ranging from non-invasive and pharmacological approaches to joint-preserving surgical techniques and arthroplasty procedures. Across the included studies, treatment outcomes varied considerably depending on the invasiveness of the intervention, the underlying therapeutic concept, and, most importantly, the stage of disease at the time of treatment.

Less invasive treatment strategies, including pharmacological therapies and non-invasive physical interventions, showed heterogeneous effects across the included studies. While improvements in clinical parameters such as pain and function were reported in several studies, effects on structural disease progression were inconsistent, with some studies demonstrating reduced progression while others showed no significant changes. However, individual studies, such as those investigating acetylsalicylic acid, reported reduced rates of radiographic disease progression, suggesting that specific pharmacological approaches may have potential in selected patient populations.

In contrast, surgical approaches, particularly core decompression and its augmented forms, were frequently associated with improvements in clinical and radiological outcomes. Several studies suggested that the addition of biological augmentation to core decompression may enhance treatment effects compared to core decompression alone, although these benefits were not consistently observed across all patient populations, particularly in more advanced stages of the disease.

With increasing disease severity, the effectiveness of joint-preserving techniques appeared to decline. In these cases, more invasive procedures, including structural reconstruction techniques and arthroplasty, were applied and were associated with improvements in

symptom relief and functional outcomes, although at the cost of increased invasiveness and procedure-related risks.

Overall, the findings of this review indicate that treatment outcomes in osteonecrosis of the femoral head are strongly influenced by a combination of disease stage, treatment modality, and patient-specific factors, emphasizing the importance of a stage-adapted and individualized therapeutic approach.

4.2 COMPARISON OF TREATMENT STRATEGIES

When comparing the different treatment strategies investigated across the included studies, clear differences in effectiveness and therapeutic objectives become apparent.

Less invasive approaches, including pharmacological and non-invasive physical therapies, primarily aimed at symptom relief and potential slowing of disease progression. However, their overall effects were heterogeneous, and consistent evidence for a sustained influence on structural outcomes was limited.

Pharmacological treatment strategies in particular aim to influence key pathophysiological mechanisms of osteonecrosis, including impaired microcirculation, inflammation, and altered bone remodelling. With acetylsalicylic acid and bisphosphonates such as alendronate representing different pharmacological approaches targeting these processes. The results of the included studies were heterogeneous. While one study investigating acetylsalicylic acid reported a reduced rate of radiographic disease progression and a tendency towards decreased femoral head involvement, suggesting a potential benefit in selected patients, studies evaluating bisphosphonates such as alendronate showed conflicting findings. In one study, alendronate as an adjunct to core decompression was associated with delayed disease progression and improved clinical outcomes, whereas another study did not demonstrate a significant effect when alendronate was administered as a standalone therapy in combination with calcium and vitamin D.

This discrepancy may be related to differences in treatment application, study design, and patient selection. While the findings of the acetylsalicylic acid study suggest a potential benefit, the current evidence is insufficient to draw firm conclusions regarding its superiority over bisphosphonates. Further investigation of the underlying mechanisms and clinical effects of acetylsalicylic acid is therefore warranted.

These findings highlight the inconsistent effects of pharmacological interventions across studies and underline the difficulty in identifying a clearly effective pharmacological strategy for early-stage disease.

In contrast, surgical interventions, which aim to preserve the joint by reducing intraosseous pressure and improving vascularization, were generally associated with improvements in both clinical and radiological parameters. Core decompression, as the most frequently investigated joint-preserving procedure in this review, showed variable outcomes across studies when performed alone, either as a primary treatment or a control intervention.

Several studies suggested that the addition of biological augmentation, intended to promote osteogenesis and angiogenesis within the necrotic bone, may enhance the therapeutic effect of core decompression; however, these effects were not consistent, particularly in more advanced stages of the disease, indicating a possible stage-dependent benefit. Furthermore, this heterogeneity might also be related to the different forms of biological augmentation used across studies, including osteoblastic cells, autologous bone marrow cells, and bone marrow aspirate concentrate.

Corrective osteotomies represent another joint-preserving option but were not included in the analysed studies and are therefore not addressed in this comparison.

Another important methodological aspect observed across several studies is that treatment effects were often evaluated as additive to a baseline intervention, most commonly core decompression, rather than being compared to non-operative management. As a result, the reported outcomes mainly reflect the relative benefit of additional therapies rather than their absolute effectiveness. This limits the ability to determine whether the investigated interventions themselves provide a clinically meaningful effect, or whether the observed improvements are primarily attributable to the baseline procedure. In addition, not all studies consistently reported both within-group and between-group analyses. This review placed emphasis on between-group comparisons to allow a more clinically meaningful assessment of treatment effects.

Increasingly invasive treatment strategies were predominantly applied in more advanced stages of the disease. While structural reconstruction techniques aim to provide mechanical support to the subchondral bone and thereby prevent collapse, arthroplasty procedures aim to restore the joint function through joint replacement. Although these approaches were associated with improvements in certain clinical and functional parameters, the reported outcomes showed considerable heterogeneity and were based on varying assessment methods. In two studies, outcomes were assessed mainly within groups rather than through direct

comparisons. This limits the ability to draw firm conclusions regarding their relative effectiveness. One of the studies lacked the presence of a control group entirely. Furthermore, the evaluated outcome parameters differed substantially between studies, reducing comparability. Nevertheless, these approaches represent important therapeutic options in advanced disease stages, despite their increased procedural complexity and associated risks. Overall, the comparison of treatment strategies suggests that no single approach can be considered universally superior. Instead, the effectiveness of each intervention appears to depend on the stage of disease and the specific therapeutic objective, ranging from symptom control to structural preservation or joint replacement.

4.3 STAGE DEPENDENT TREATMENT CONCEPT

As stated before, the present literature suggests that the selection of the optimal treatment for non-traumatic osteonecrosis of the femoral head should be based on patient-specific factors, particularly the stage of the disease, as well as underlying risk factors. Therefore, the following section discusses the study results in relation to different disease stages and aims to identify which treatment strategies appear to be most appropriate at each stage. The goal is to outline a coherent and clinically applicable, stage-adapted treatment rationale. Since the included studies used a variety of staging systems, direct comparison between studies is limited. To address this, the results were grouped into broader categories, allowing for a more consistent interpretation of treatment effects across different classification systems.

4.3.1 EARLY-STAGE DISEASE

This section discusses, based on the included studies, therapy options for roughly ARCO, Ficat, and Steinberg stages I and II. Whilst the joint at this stage is still structurally intact (i.e., no subchondral collapse has occurred), it is already dysfunctional on a biological level (44). At this early stage, there may still be a potential for disease resolution (45). The primary aim of treatment at this stage is to prevent or delay disease progression in order to preserve structural integrity. In addition, improvement of clinical symptoms and reduction of lesion size represent important therapeutic goals.

In early-stage disease, less invasive treatment strategies, including pharmacological and noninvasive physical therapies, may be considered as initial treatment options. However, the

results across the included studies were heterogeneous, reflecting the limited and inconsistent ability of these approaches to alter the underlying disease process at this stage. While improvements in pain and functional scores were reported in several studies, consistent effects on structural disease progression were not observed.

Overall, the available evidence does not support a clearly effective pharmacological strategy for reliably preventing disease progression in early-stage osteonecrosis. Individual studies suggested potential benefits of certain pharmacological approaches; however, these findings were not consistent across all investigations. One study investigating acetylsalicylic acid reported a tendency towards decreased femoral head involvement and a reduced rate of radiographic progression compared to a historical control group, suggesting a potential benefit in selected patients (26).

In contrast, studies investigating bisphosphonates such as alendronate showed conflicting results. While one study reported delayed disease progression and improved clinical outcomes when alendronate was used as an adjunct to core decompression (27), another study did not demonstrate a significant effect when administered as a standalone pharmacological therapy in combination with calcium and vitamin D (9). These inconsistencies may be partly explained by differences in treatment application and study design, which limit the direct comparability of the results. Similarly, a study investigating a combination therapy consisting of extracorporeal shockwave therapy, hyperbaric oxygen therapy, and alendronate did not demonstrate a significant advantage over shockwave therapy alone, suggesting that combining multiple modalities does not necessarily improve outcomes in early-stage disease (29).

Pharmacological approaches may be considered as supportive treatment options; however, their ability to reliably prevent structural disease progression remains uncertain. While individual findings, such as those reported for acetylsalicylic acid, suggest a potential benefit in selected patients, the current evidence is insufficient to support their use as a primary treatment strategy.

Overall, the available evidence does not support a clearly effective pharmacological strategy for reliably preventing disease progression in early-stage osteonecrosis, which is consistent with current guidelines (20).

Similarly, non-invasive physical therapies such as hyperbaric oxygen therapy (HBOT) and extracorporeal shockwave therapy may be considered as adjunctive treatment options in earlystage disease. These approaches aim to improve tissue oxygenation and stimulate bone regeneration processes.

The available evidence suggests that these therapies may lead to improvements in clinical symptoms; however, their impact on structural disease progression remains uncertain. While HBOT showed improvements in pain and range of motion, the controlled evidence is limited, as the double-blind phase of the study was restricted to six weeks, and long-term outcomes were assessed observationally (30). Similarly, extracorporeal shockwave therapy demonstrated some effects on clinical parameters and biological markers; however, no consistent structural benefits were observed in that study. Furthermore, the absence of a control group without treatment limits the ability to assess the true effectiveness of this intervention (32).

Taken together, non-invasive physical therapies appear to contribute to symptomatic improvement in early-stage ONFH, but their ability to reliably influence structural disease progression remains uncertain, particularly based on the limited and methodologically heterogeneous evidence included in this review. However, external evidence, including systematic reviews and meta-analyses, suggests that certain modalities such as hyperbaric oxygen therapy may have a more pronounced effect on both clinical and radiological outcomes, although these should be interpreted with caution in the context of the present analysis (46).

In contrast to the previously discussed less invasive approaches, core decompression represents a commonly applied joint-preserving surgical intervention in the treatment of early-stage osteonecrosis of the femoral head. In the absence of structural collapse, this procedure aims to reduce intraosseous pressure and improve vascularization within the necrotic area, thereby providing a rationale for its use in early-stage disease.

The findings of the included studies suggest that core decompression may lead to improvements in clinical symptoms and may contribute to stabilization of disease progression in early-stage patients. However, these effects were not consistently observed across all study populations. In particular, outcomes appeared to be influenced by factors such as lesion size and location, with larger or laterally located lesions being associated with less favourable results. Furthermore, while core decompression may delay disease progression, it does not appear to reliably prevent structural deterioration in all cases, indicating that its effectiveness may be limited in certain patient subgroups.

These limitations have led to the investigation of adjunctive treatment strategies, particularly biological augmentation, with the aim of enhancing the regenerative potential of the procedure.

Several studies have therefore investigated the addition of biological augmentation to core decompression in an attempt to enhance the regenerative capacity of the necrotic bone. These

approaches, including the use of bone marrow-derived cells, bone marrow aspirate concentrate, and mesenchymal stem cells, aim to promote osteogenesis and angiogenesis within the affected area.

The majority of studies investigating these techniques were conducted in early-stage disease, primarily including patients without structural collapse. In this context, some studies suggested improved clinical and radiological outcomes compared to core decompression alone, including reductions in lesion size and delayed disease progression. However, these findings were not consistent across all investigations, as other studies did not demonstrate significant differences between augmented and non-augmented treatment groups.

This heterogeneity may be partly explained by differences in the applied cell types, treatment protocols, and study populations. In addition, most studies evaluated augmentation as an adjunct to core decompression rather than as an independent treatment, which limits the ability to determine its absolute therapeutic effect. Furthermore, not all studies compared biological augmentation to core decompression alone; some directly compared different augmentation strategies, such as osteoblastic cells and bone marrow aspirate concentrate. These comparative designs allow for an assessment of relative effectiveness between augmentation techniques but do not provide information on their benefit over core decompression itself.

Notably, one study including patients across a range of disease stages (ARCO stage I-III) reported improved outcomes following the addition of bone marrow-derived cells; however, the inclusion of mixed disease stages limits the ability to draw stage-specific conclusions. In contrast, a separate randomized controlled trial investigating bone marrow aspirate concentrate exclusively in patients with ARCO stage III did not demonstrate a significant benefit compared to core decompression alone, suggesting that the effectiveness of biological augmentation may be reduced once structural collapse has occurred.

Taken together, these findings suggest that biological augmentation may offer potential additional benefits in selected cases of early-stage disease; however, its overall effectiveness remains uncertain, and a clear advantage over core decompression alone cannot be consistently demonstrated. This supports the notion that biological augmentation may be more effective before structural collapse occurs, whereas its benefit appears limited in more advanced stages of the disease. These conclusions are in line with findings from a recent systematic review and meta-analysis involving 954 subjects (47).

Therefore, biological augmentation may be considered particularly in early-stage disease, although its routine use cannot be universally recommended yet, based on the current evidence.

Overall, these findings suggest that early-stage osteonecrosis should primarily be managed with joint-preserving strategies, with core decompression representing the central treatment option, while less invasive approaches may be considered in selected cases.

4.3.2 ADVANCED DISEASE

This section discusses, based on the included studies, therapy options for roughly ARCO, Ficat, and Steinberg stages III and IV. Whilst the joint at this stage is no longer structurally intact, as subchondral collapse has already occurred, it is associated with progressive mechanical instability and joint deterioration (44). At this stage, there is no longer a potential for disease resolution, and structural damage is typically irreversible (17). The primary aim of treatment therefore shifts from preventing disease progression to restoring joint function and alleviating symptoms. In addition, improvement of functional outcomes and prevention of further joint destruction represent central therapeutic goals (21).

Structural reconstruction techniques represent a joint-preserving surgical option in more advanced stages of osteonecrosis of the femoral head, particularly in the presence of structural compromise. These approaches aim to provide mechanical support to the subchondral bone and thereby prevent further collapse while preserving the native joint. In the included studies, these techniques primarily involved the use of biomaterial-loaded allograft implants and metal trabecular reconstruction systems, while free vascularized fibular grafting was evaluated as both a comparative standard and an established reconstruction technique with its own reported clinical and radiological outcomes.

The findings of the included studies suggest that structural reconstruction techniques may improve clinical and functional outcomes, with free vascularized fibular grafting also demonstrating improvements in clinical and functional parameters, although it appeared less effective compared to metal trabecular bone reconstruction systems in direct comparisons. In particular, the use of biomaterial-supported implants and trabecular reconstruction systems was associated with improvements in clinical scores and, in some cases, more favourable radiological outcomes. However, the reported results were heterogeneous and based on varying outcome measures, which limits comparability between studies.

It should be noted that the investigated studies included heterogeneous patient populations, spanning both pre- and post-collapse stages. As a result, the ability to draw stage-specific conclusions regarding the effectiveness of structural reconstruction techniques in advanced disease is limited.

Nevertheless, these approaches may represent a viable joint-preserving option in selected patients with early structural compromise, particularly in cases where joint replacement may be undesirable. To enable more precise stage-dependent treatment recommendations, studies focusing on more clearly defined and homogeneous disease stages would be required, which are not sufficiently represented within the studies included in this review.

Arthroplasty procedures represent the most invasive treatment option and are primarily considered in advanced stages of osteonecrosis of the femoral head, particularly in cases with extensive structural damage and secondary degenerative changes. In contrast to jointpreserving approaches, the primary aim of arthroplasty is to restore joint function and provide reliable pain relief through joint replacement (48). Total hip arthroplasty, in particular, is widely regarded as an established and effective treatment option for advanced disease, with consistently favorable clinical and functional outcomes reported in the literature (49). The findings of the included study suggest that bipolar hemiarthroplasty may lead to improvements in clinical and functional outcomes, particularly in older patients. In contrast, younger patients may be at increased risk of long-term complications and revision procedures, which should be considered when selecting this treatment option.

However, as the study population included patients across different disease stages, the ability to draw stage-specific conclusions remains limited, as does the lack of a control group. In addition, the use of arthroplasty is influenced by patient-specific factors such as age and activity level, with younger patients, in particular, facing an increased risk of revision surgery over time.

While bipolar hemiarthroplasty may represent a viable treatment option in selected patients, particularly older individuals with lower functional demands, its role should be interpreted in the context of alternative arthroplasty procedures such as total hip arthroplasty, which are widely established in the treatment of advanced disease. Furthermore, it should be noted that no studies investigating total hip arthroplasty or other arthroplasty techniques were included in this review, which limits the generalizability of these findings to arthroplasty procedures.

Overall, these findings suggest that in advanced disease stages, treatment strategies shift towards more invasive interventions. Structural reconstruction techniques represent a jointpreserving option in selected cases, while arthroplasty procedures provide a reliable solution in the presence of extensive and irreversible joint damage.

4.4 INFLUENCE OF PATIENT RELATED FACTORS

In addition to the choice of treatment strategy and disease stage, patient-related factors appear to play a significant role in determining treatment outcomes in osteonecrosis of the femoral head. These factors may influence both the progression of the disease and the effectiveness of the applied interventions.

The findings of the included studies suggest that variables such as age, underlying aetiology, lesion size and location may impact clinical and radiological outcomes. Therefore, consideration of these factors is essential for an individualized and stage-adapted treatment approach.

The predominance of male patients, with 16 out of 17 included studies including more male than female patients, reflects the known epidemiological distribution of osteonecrosis of the femoral head. A large multicentric epidemiologic study has reported a prevalence of 70.1% male patients; this male predominance in the included literature may therefore limit the generalizability of the findings to female patient populations (22).

Age appears to be an important factor influencing treatment outcomes and, therefore, treatment decision-making. There are conflicting findings regarding whether younger age represents a favourable or unfavourable factor in osteonecrosis of the femoral head. The study evaluating and comparing a metal trabecular bone reconstruction system and free vascularized fibular graft found that for both treatments, the clinical effective rate ($HHS \geq 80$) of the 20–40-year age group was statistically higher than that of the 41–60-year age group, demonstrating a potentially beneficial prognosis for younger patients. On the other hand, the study evaluating bipolar hemiarthroplasty demonstrated a significantly higher risk of component loosening and revision in patients under 40 years of age compared to patients over 40 years of age at the time of treatment.

These findings suggest that the influence of age on treatment outcomes is not uniform but may depend on the type of intervention and therefore requires further investigation. External studies also show heterogeneous results concerning the influence of age on patient outcomes (50).

The aetiology of non-traumatic osteonecrosis of the femoral head constitutes another treatment influencing factor, as different underlying causes may influence both disease progression and treatment response.

The included studies demonstrated a predominance of corticosteroid-induced and alcohol-related osteonecrosis, with several studies exclusively including patients with steroid-induced or alcohol-induced disease. Other aetiologies, such as idiopathic cases or sickle cell disease, were less frequently represented.

This uneven distribution of etiological factors may influence the interpretation of treatment outcomes, as results derived from predominantly steroid- or alcohol-induced populations may not be fully generalizable to patients with other underlying causes. Furthermore, none of the included studies directly compared treatment outcomes between different aetiological groups, which limits the ability to draw conclusions regarding aetiology-based treatment selection.

However, this aspect has been investigated in the broader literature. For example, a prospective study found significant differences in the treatment response of alcohol- and steroid-induced osteonecrosis to core decompression and bone substitute grafting, with more favourable outcomes reported in patients with alcohol-induced disease (51).

Lesion size and location appear to be important factors influencing treatment outcomes in osteonecrosis of the femoral head, particularly in the context of joint-preserving procedures. In the study investigating multiple drilling with and without alendronate, smaller lesions were associated with significantly better clinical outcomes compared to medium and large lesions. In addition, centrally located lesions demonstrated more favourable results than laterally located lesions, suggesting that lesion characteristics within the weight-bearing region may influence treatment success.

Similarly, in the study evaluating advanced core decompression, worse clinical outcomes were observed in patients with larger lesions; however, this effect was not independent of disease stage, as only stage remained a significant predictor in the overall analysis. This indicates that the influence of lesion size may be closely related to the extent of disease progression.

Taken together, these findings suggest that lesion size and location may influence treatment outcomes, with small and central lesions possibly being associated with a better prognosis, although their effect appears to be, at least partially, interrelated with disease stage and therefore should be interpreted with caution. This is also supported by the current broader literature, where lesion size and location have been identified as relevant prognostic factors (52).

Taken together, these findings highlight that patient-related factors play a relevant role in influencing treatment outcomes in osteonecrosis of the femoral head and should be carefully considered in clinical decision-making. However, the included evidence remains limited and heterogeneous, emphasizing the need for further studies to better define their impact and support more individualized treatment strategies.

4.5 METHODOLOGICAL CONSIDERATIONS AND LIMITATIONS

The interpretation of the findings of this review requires careful consideration of several methodological aspects and limitations of the included studies.

A major limitation is the considerable heterogeneity of the included studies. Differences in study design, patient populations, and treatment protocols limit the comparability of the reported results. In particular, the included studies applied different combinations of commonly used outcome parameters, including VAS, HHS, and WOMAC scores, which limit the direct comparability of clinical outcomes across studies. In addition, different staging systems were used, further complicating the interpretation of results.

Another important limitation is the variability in follow-up periods across studies, ranging from under 1 to over 10 years. Follow-up periods represent a critical factor when evaluating treatment effectiveness, particularly in a progressive disease such as osteonecrosis of the femoral head. Short follow-up durations may underestimate long-term failure rates, while longer follow-up periods are not consistently available across studies and allow for the detection of later disease progression and delayed treatment failure.

Furthermore, several studies were based on small sample sizes, with some including as few as 10 patients, and some lacked appropriate control groups, which limit the statistical power and the robustness of the reported findings. In addition, the inclusion of both prospective and retrospective study designs introduces further methodological variability and potential bias. The included studies also applied heterogeneous inclusion and exclusion criteria, which likely resulted in considerable variation in patient populations. In several studies, strict exclusion criteria may have led to the selection of more homogeneous cohorts, potentially limiting the generalizability of the reported outcomes to broader clinical populations. In particular, differences in the inclusion of patients with advanced disease stages or relevant comorbidities may have contributed to variations in reported treatment outcomes across studies.

A further limitation of this review is the heterogeneity of disease stages within the included studies. Many studies included patients across multiple stages of osteonecrosis, sometimes spanning both pre- and post-collapse disease. This limits the ability to draw precise stagespecific conclusions and complicates the development of clear stage-dependent treatment recommendations.

In studies investigating biological augmentation of core decompression, the control groups typically received core decompression alone. This allows a comparison of the additional effect of augmentation strategies; however, it does not allow conclusions about the absolute effectiveness of these interventions.

Furthermore, several studies lacked detailed subgroup analyses, for example with regard to lesion characteristics or patient-specific factors, which further limit the ability to identify predictors of treatment success. In addition, some studies were based on retrospective designs, which may introduce selection bias and limit the strength of the reported conclusions. In addition, certain treatment options, such as corrective osteotomies, were not represented in the included studies, which may limit the comprehensiveness of the evaluated treatment spectrum.

Finally, it should be noted that this review is based on a narrative approach, which inherently limits the ability to perform quantitative comparisons between studies and may introduce a degree of subjective interpretation.

4.6 CLINICAL IMPLICATIONS

The findings of this review have several implications for clinical decision-making in the management of osteonecrosis of the femoral head. Overall, the results support a stage-adapted treatment approach, in which the choice of therapy is primarily guided by the extent of structural damage and disease progression.

In early-stage disease, joint-preserving strategies should be prioritized. Core decompression appears to represent the central treatment option, particularly in patients without structural collapse. The addition of biological augmentation may provide additional benefits in selected cases; however, its routine use cannot be universally recommended based on the current evidence. Less invasive approaches, including pharmacological and non-invasive physical therapies, may contribute to symptomatic improvement but, as of now should not be relied upon as standalone strategies for preventing disease progression.

In more advanced stages of the disease, treatment strategies shift towards more invasive interventions. Structural reconstruction techniques may represent a joint-preserving option in selected patients with early structural compromise. However, in cases of extensive joint damage, arthroplasty procedures provide a reliable solution for restoring joint function and alleviating symptoms.

In addition to disease stage, patient-related factors such as age, lesion characteristics, and underlying aetiology should be taken into account when selecting the most appropriate treatment strategy. These factors may influence both treatment outcomes and long-term prognosis and therefore support the need for an individualized treatment approach. Taken together, the available evidence suggests that treatment decisions in osteonecrosis of the femoral head should be guided by disease stage, with joint-preserving strategies favoured in early-stage disease and more invasive interventions considered in advanced stages, while also taking patient-specific factors into account to optimize clinical outcomes.

In addition, clinicians should remain aware of emerging evidence, as ongoing research may further refine existing treatment strategies and contribute to the development of more effective and less invasive therapeutic options.

4.7 FUTURE PERSPECTIVES

Based on the limitations identified in this review, several areas for future research can be defined. Addressing these aspects may contribute to a more precise understanding of treatment effectiveness and support the development of more individualized and evidencebased treatment strategies for osteonecrosis of the femoral head.

Future studies should aim to reduce methodological heterogeneity by applying standardized outcome parameters and consistent staging systems, which would improve comparability across studies. In addition, longer follow-up periods are required to better assess the durability of treatment effects and long-term disease progression, especially in a chronic disease such as ONFH.

Furthermore, there is a need for well-designed prospective studies with larger and more homogeneous patient populations. In particular, studies focusing on clearly defined individual disease stages would allow for more precise stage-specific treatment recommendations. The role of patient-related factors, including age, aetiology, and lesion characteristics, should be

further investigated to better understand their influence on treatment outcomes and to support more individualized treatment approaches. In this context, comparative studies evaluating treatment responses across different aetiological subgroups would be of particular interest. In addition, future research should aim to directly compare different treatment strategies, further, including both joint-preserving and reconstructive approaches, in order to better define their relative effectiveness.

5. CONCLUSION AND SUGGESTIONS

This review aimed to evaluate and compare treatment strategies for non-traumatic osteonecrosis of the femoral head, while exploring the role of disease stage in guiding treatment decisions.

The findings suggest that treatment selection should primarily be guided by disease stage. In early-stage disease, joint-preserving strategies, particularly core decompression, represent the central treatment approach, while less invasive therapies may provide symptomatic relief but seem to have limited impact on structural disease progression. The addition of biological augmentation may offer potential benefits in selected cases, although its effectiveness remains uncertain.

In more advanced stages, treatment strategies shift towards more invasive interventions. Structural reconstruction techniques may provide a joint-preserving option in selected patients; however, in cases of extensive joint damage, arthroplasty procedures represent a reliable and well-established treatment option.

In addition to disease stage, patient-related factors such as age, lesion characteristics, and underlying aetiology should be considered when selecting the most appropriate treatment strategy, supporting the need for an individualized approach.

Overall, the available evidence highlights the importance of a stage-adapted and patientcentred treatment strategy. However, the included evidence remains limited and heterogeneous, which restricts the strength of the derived conclusions.

Future research should focus on well-designed, stage-specific studies with standardized methodologies in order to improve the comparability of results and to support more precise and evidence-based treatment recommendations.

6. REFERENCES

Note: The studies included in this review are also listed separately at the end of the reference section.

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