MINIMALLY INVASIVE APPROACHES IN THE TREATMENT OF AVASCULAR NECROSIS OF THE FEMORAL HEAD: EFFECTIVENESS AND PROSPECTS

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DOI: 10.5281/zenodo.13813611

Abstract

Avascular necrosis (AVN) of the femoral head is a debilitating condition characterized by the loss of blood supply to the bone, leading to the collapse of the femoral head and subsequent joint destruction if left untreated. The management of AVN has evolved significantly, moving from traditional surgical interventions like total hip arthroplasty (THA) to minimally invasive and regenerative approaches that aim to preserve the native joint, reduce complications, and enhance recovery. This review provides a comprehensive analysis of the current and emerging strategies for the treatment of AVN, highlighting the efficacy and safety profiles of minimally invasive approaches such as core decompression combined with biological augmentation therapies like platelet-rich plasma (PRP), bone marrow aspirate concentrate (BMAC), and stromal vascular fraction (SVF). Traditional surgical interventions, such as THA and hip resurfacing, remain the gold standard for advanced AVN, offering excellent pain relief and functional restoration. However, they are associated with higher complication rates, longer recovery times, and potential need for revision surgeries, especially in younger patients. Comparative analysis suggests that minimally invasive approaches, particularly when combined with regenerative therapies, provide substantial benefits in early to mid-stages of AVN, delaying or even preventing the need for THA. Future directions in the management of AVN focus on innovations in regenerative medicine, including advanced stem cell therapies, gene editing, tissue engineering, and novel minimally invasive techniques enhanced by robotics and augmented reality. The development of biomarkers for early detection, personalized treatment approaches using artificial intelligence, and the integration of machine learning in clinical decision-making are also promising areas for advancing AVN care. This review emphasizes the need for ongoing clinical research to optimize these emerging therapies and develop tailored strategies that improve patient outcomes and quality of life.

Keywords: Avascular Necrosis, Femoral Head, Core Decompression, Minimally Invasive Surgery, Regenerative Medicine, Stem Cell Therapy, Gene Therapy, Personalized Medicine, Total Hip Arthroplasty.

INTRODUCTION

Avascular necrosis (AVN) of the femoral head, also known as osteonecrosis, is a progressive and debilitating condition characterized by the death of bone tissue due to inadequate blood supply. AVN primarily affects the hip joint and can lead to severe degenerative changes, ultimately resulting in disabling arthritis and loss of joint function if not treated appropriately. The disease typically affects individuals between the ages of 20 and 60, with a higher incidence among those in their most productive years, posing significant challenges for both patients and healthcare providers. Recent studies report that AVN accounts for about 10-12% of all degenerative diseases of the musculoskeletal system, underlining its clinical and socio-economic impact (Kovalenko et al., 2017; Afizah et al., 2016).

The pathophysiology of AVN is multifactorial, involving both traumatic and non-traumatic causes. Traumatic AVN is often a consequence of fractures or dislocations that disrupt the blood supply to the femoral head, whereas non-traumatic AVN is associated with a variety of risk factors, including corticosteroid use, excessive alcohol consumption, sickle cell disease, and autoimmune conditions (Hong et al., 2015; Murzich & Beletsky, 2017). In Uzbekistan, a retrospective study conducted at the Tashkent Institute of Postgraduate Medical Education emphasized that corticosteroid use remains the leading cause of non-traumatic AVN in the region, accounting for approximately 35% of cases (Muminov et al., 2018).

Diagnosing AVN in its early stages remains challenging due to the absence of specific symptoms and the similarity of clinical signs to other joint disorders. Advanced imaging techniques, such as magnetic resonance imaging (MRI) and computed tomography (CT), are essential for early detection and accurate staging of the disease. The ARCO (Association Research Circulation Osseous) classification system is widely used to stage AVN based on radiological findings, guiding the therapeutic decision-making process (Mwale et al., 2019). However, despite advances in imaging and classification, early-stage AVN often remains underdiagnosed, leading to delayed treatment and poorer outcomes.

Traditionally, the management of AVN has relied heavily on conservative approaches such as pharmacological therapy, physical therapy, and lifestyle modifications. While these methods may provide symptomatic relief, they do not halt disease progression or prevent the eventual collapse of the femoral head. Recent data suggest that conservative treatment is effective only in the early stages of AVN, and its effectiveness diminishes significantly as the disease progresses (Kotov et al., 2020). A study conducted in Russia highlighted that only 25% of patients treated conservatively achieved clinical remission, with most patients experiencing a relapse within 12 months (Zorya et al., 2019).

The standard of care for advanced stages of AVN has long been total hip arthroplasty (THA), which involves the complete replacement of the damaged joint. THA is highly effective in relieving pain and restoring function; however, it comes with limitations, particularly for younger, active patients. The lifespan of a prosthetic joint is finite, often necessitating revision surgeries, which carry higher risks of complications and reduced functionality over time. Moreover, the high cost of THA and its limited accessibility in many regions, including Central Asia, make it an impractical option for many patients (Gulyamov et al., 2020; Hernigou et al., 2018).

In recent years, there has been a paradigm shift towards minimally invasive approaches that aim to preserve the native joint and delay or prevent the need for THA. Core decompression, which involves creating channels in the femoral head to reduce intraosseous pressure and promote revascularization, has been a cornerstone of minimally invasive treatment for early-stage AVN. However, its effectiveness is limited in advanced stages and in cases where a significant portion of the femoral head is affected (Torgashin et al., 2020). The integration of biological therapies, such as platelet-rich plasma (PRP) and bone marrow aspirate concentrate (BMAC), has shown promise in enhancing the outcomes of core decompression by promoting bone regeneration and healing (Gangji et al., 2017).

Emerging evidence suggests that combination therapies, incorporating core decompression with PRP, BMAC, or stromal vascular fraction (SVF) therapies, offer superior clinical outcomes compared to monotherapies. A study conducted at the CityMed Clinic in Kazakhstan demonstrated that patients treated with a combination of SVF and PRP therapy following core decompression experienced significant pain relief and improved joint function, with a lower rate of disease progression compared to those treated with decompression alone (Ibragimov et al., 2023). Table 1 summarizes the comparative outcomes of different minimally invasive approaches for AVN management.

Table 1: Comparative Outcomes of Minimally Invasive Treatments for AVN

Treatment Modality	Pain Relief	Improvement in Joint Function	Progression to THA (%)
Core Decompression Alone	Moderate	Limited	35
Core Decompression + PRP	Good	Moderate	20
Core Decompression + BMAC	Good	Good	15
Core Decompression + SVF + PRP	Excellent	Excellent	5

The success of minimally invasive approaches largely depends on the careful selection of patients, the stage of AVN, and the specific combination of therapies employed. The clinical experience from multiple centers, including recent studies from Uzbekistan, Kazakhstan, and Russia, emphasizes the importance of individualized treatment strategies that balance efficacy, cost, and patient preference (Mukhamedov et al., 2021).

In conclusion, while traditional surgical approaches remain the gold standard for advanced AVN, minimally invasive methods are gaining traction as viable alternatives, especially for younger patients with early to mid-stage disease. The ongoing evolution of these techniques, coupled with advancements in regenerative medicine, holds the potential to transform the management of AVN, offering improved outcomes with reduced morbidity. The following sections of this review will explore the current minimally invasive approaches in more detail, comparing their effectiveness, safety profiles, and prospects for future application.

Current Understanding of Avascular Necrosis of the Femoral Head

Avascular necrosis (AVN) of the femoral head is a severe orthopedic condition characterized by the loss of blood supply to the bone tissue, leading to the death of osteocytes and subsequent structural collapse of the femoral head. The etiology of AVN is complex and multifactorial, encompassing both traumatic and non-traumatic causes. Understanding the underlying mechanisms, risk factors, and progression of AVN is critical for developing effective diagnostic and therapeutic strategies.

Etiology and Risk Factors

The etiology of AVN can be broadly categorized into traumatic and non-traumatic factors. Traumatic AVN typically results from a direct injury, such as a femoral neck fracture or hip dislocation, which disrupts the blood supply to the femoral head. This form of AVN accounts for approximately 20-30% of all cases and is more common in younger patients who sustain high-energy trauma (Hernigou et al., 2018; Yeh et al., 2019).

Non-traumatic AVN, which constitutes about 70-80% of cases, is associated with various systemic and local factors. Prolonged use of corticosteroids is the most common non-traumatic cause of AVN, implicated in 35-40% of cases globally (Mwale et al., 2019; Gulyamov et al., 2020). Steroid-induced AVN is believed to result from lipid metabolism disorders, increased intraosseous pressure, and direct damage to endothelial cells, which together compromise the microcirculation of the femoral head.

A retrospective study in Uzbekistan highlighted that 38% of AVN cases were associated with prolonged corticosteroid therapy, particularly in patients with autoimmune diseases (Muminov et al., 2019).

Alcohol abuse is another significant risk factor, responsible for up to 20-25% of non-traumatic AVN cases. Chronic alcohol consumption induces adipogenesis in the bone marrow, leading to increased intraosseous pressure and impaired blood flow. A study conducted in Russia revealed that patients consuming more than 400 grams of alcohol per week had a 15-fold increased risk of developing AVN (Zorya et al., 2019). Other risk factors include hyperlipidemia, coagulopathies, sickle cell disease, organ transplantation, and metabolic disorders (Kovalenko et al., 2017; Mukhamedov et al., 2021).

The pathophysiology of AVN involves a complex interplay between vascular, cellular, and mechanical factors. The most widely accepted theory is that AVN results from a disruption of the microcirculation to the femoral head, leading to ischemia, bone cell death, and subsequent structural collapse. Vascular occlusion can occur due to thrombosis, fat embolism, or direct trauma to the blood vessels (Afizah et al., 2016; Lim et al., 2017).

Cellular mechanisms, such as apoptosis and necrosis of osteocytes and bone marrow cells, play a crucial role in the progression of AVN. Recent studies have shown that dysregulated bone remodeling, involving both osteoblasts and osteoclasts, contributes to bone resorption and weakens the structural integrity of the femoral head. Additionally, abnormalities in the expression of angiogenic factors, such as vascular endothelial growth factor (VEGF), have been implicated in the impaired repair process in AVN (Mwale et al., 2019; Gangji et al., 2017).

Mechanical loading also significantly affects the progression of AVN. The femoral head is subjected to substantial mechanical stress, especially during weight-bearing activities, which can exacerbate subchondral fractures and collapse. In advanced stages of AVN, the cumulative effects of vascular insufficiency, cellular dysfunction, and mechanical stress lead to irreversible joint damage and secondary osteoarthritis (Hernigou et al., 2018; Yeh et al., 2019).

Staging and Classification

Accurate staging of AVN is critical for determining the appropriate treatment strategy. The most commonly used classification systems are the Ficat and Arlet, the Steinberg, and the ARCO (Association Research Circulation Osseous) classifications. Among these, the ARCO classification, based on radiographic and magnetic resonance imaging (MRI) findings, is widely regarded as the most comprehensive and is used in clinical practice worldwide (Torgashin et al., 2020; Hong et al., 2015).

- Stage I: Early AVN with normal X-rays but positive findings on MRI, indicating bone marrow edema and initial ischemia.
- Stage II: Subchondral fractures become evident on X-ray and MRI, with the absence of femoral head collapse.
- Stage III: Subchondral collapse or “crescent sign” becomes visible, often accompanied by mild flattening of the femoral head.
- Stage IV: Advanced collapse of the femoral head with joint space narrowing and secondary degenerative changes.

The ARCO classification also incorporates quantitative measures such as the extent of lesion involvement (less than 15%, 15-30%, more than 30%), which helps in predicting the prognosis and tailoring the treatment plan (Mukhamedov et al., 2021; Hernigou et al., 2018).

Diagnosis: Clinical Presentation and Imaging Techniques

Diagnosing AVN at an early stage is challenging due to the non-specificity of clinical symptoms. Patients often present with groin pain exacerbated by weight-bearing activities, which can be mistaken for other hip pathologies, such as hip impingement or labral tears (Kotov et al., 2020; Ibragimov et al., 2023). Advanced imaging techniques are therefore crucial for the early diagnosis and staging of AVN.

- X-ray: While plain radiographs are the first-line imaging modality, they are typically unremarkable in the early stages of AVN and are more useful in detecting subchondral fractures and femoral head collapse in later stages.
- Magnetic Resonance Imaging (MRI): MRI is the gold standard for early diagnosis of AVN, with a sensitivity of over 90%. It allows visualization of bone marrow edema, ischemic changes, and early subchondral fractures, which are not visible on X-rays (Yeh et al., 2019; Torgashin et al., 2020).
- Computed Tomography (CT): CT scans provide detailed visualization of bony architecture and are particularly useful in assessing the extent of subchondral fractures and the degree of femoral head collapse.
- Bone Scintigraphy: This nuclear imaging technique can detect early AVN by highlighting areas of increased bone turnover. However, its use is limited due to lower specificity compared to MRI (Hernigou et al., 2018).

Current Challenges in the Diagnosis and Management of AVN

Despite advancements in imaging and classification systems, diagnosing AVN at a reversible stage remains a significant challenge. The overlap of clinical symptoms with other hip conditions often leads to delayed diagnosis, and by the time AVN is detected, irreversible changes have often occurred. This highlights the need for increased awareness and routine use of advanced imaging modalities, particularly in high-risk patients, such as those on long-term corticosteroid therapy or with a history of alcohol abuse (Gulyamov et al., 2020; Muminov et al., 2019).

Moreover, there is a growing recognition of the importance of individualized treatment plans that consider the stage of AVN, the extent of femoral head involvement, and patient factors such as age, activity level, and comorbidities. The increasing focus on minimally invasive and joint-preserving techniques in recent years underscores the shift towards more conservative approaches, particularly for younger patients (Kovalenko et al., 2017; Ibragimov et al., 2023).

Conservative Treatment Options for Early Stages of AVN

Conservative treatment options for avascular necrosis (AVN) of the femoral head are primarily aimed at slowing the progression of the disease, alleviating symptoms, and maintaining joint function for as long as possible. These approaches are particularly relevant in the early stages of AVN, where the goal is to prevent or delay femoral head collapse and the subsequent need for surgical interventions such as total hip arthroplasty (THA). A variety of conservative treatments have been investigated over the past several years, including pharmacological therapies, biophysical modalities, and lifestyle modifications. The effectiveness of these treatments varies widely, with many studies demonstrating limited long-term benefits, especially in advanced stages of AVN.

Pharmacological management of early-stage AVN is primarily focused on improving blood flow to the femoral head, reducing intraosseous pressure, and minimizing bone resorption. Various drugs, including bisphosphonates, anticoagulants, vasodilators, and lipid-lowering agents, have been studied for their potential benefits in AVN management.

- Bisphosphonates: Bisphosphonates, such as alendronate and zoledronic acid, are antiresorptive agents that inhibit osteoclast-mediated bone resorption. Several studies have shown that bisphosphonates can delay the progression of femoral head collapse in early AVN by maintaining bone density and reducing pain. A randomized controlled trial conducted in South Korea demonstrated that patients treated with alendronate had a significantly lower rate of femoral head collapse (12%) compared to the control group (28%) at 24 months follow-up (Kim et al., 2018). However, other studies, such as one from Russia, reported mixed results, with some patients showing minimal improvement and others experiencing gastrointestinal side effects (Tikhilov et al., 2019).
- Anticoagulants: Anticoagulants like enoxaparin have been used in AVN to prevent thrombosis and improve blood flow in the affected area. A multicenter study from the United States and Germany found that early anticoagulation therapy was associated with reduced pain and slower disease progression, particularly in non-traumatic AVN cases linked to coagulation disorders (Mont et al., 2017). However, the risk of bleeding complications limits the widespread use of anticoagulants, especially in patients with a history of gastrointestinal bleeding or other contraindications (Hernigou et al., 2018).
- Vasodilators: Vasodilators, such as iloprost, are used to enhance microcirculation and reduce ischemia in the femoral head. Studies from Germany and Uzbekistan have shown that iloprost can provide symptomatic relief and potentially delay disease progression in early-stage AVN. In a study involving 50 patients with AVN at stages I and II, iloprost treatment resulted in significant pain reduction and improved joint mobility over a 12-month period (Schmidt et al., 2018; Mukhamedov et al., 2021). However, the effects were less pronounced in patients with more advanced stages.
- Lipid-lowering agents: Statins are thought to reduce the risk of AVN by lowering blood lipid levels and improving endothelial function. Some studies have suggested that statins may decrease the risk of steroid-induced AVN by up to 60% (Hamada et al., 2018). A cohort study from Uzbekistan found that atorvastatin use in patients receiving long-term corticosteroid therapy was associated with a lower incidence of AVN (10% vs. 30%) compared to those not on statin therapy (Muminov et al., 2020).

Biophysical Modalities

Biophysical treatments, such as pulsed electromagnetic field (PEMF) therapy, extracorporeal shock wave therapy (ESWT), and hyperbaric oxygen therapy (HBOT), have been explored as non-invasive options for managing early AVN.

These modalities aim to stimulate bone regeneration, enhance blood flow, and reduce pain.

- Pulsed Electromagnetic Field (PEMF) Therapy: PEMF therapy has been shown to stimulate bone healing and angiogenesis. A randomized controlled trial from Italy demonstrated that PEMF therapy significantly reduced pain and improved hip function in patients with early AVN compared to a sham control group (Faldini et al., 2018). A similar study from Russia confirmed these findings, reporting a delay in femoral head collapse in patients treated with PEMF therapy (Kotov et al., 2020). However, the long-term benefits remain unclear, and further research is needed to establish standardized protocols and treatment durations.
- Extracorporeal Shock Wave Therapy (ESWT): ESWT is another biophysical modality that has been used to treat early AVN by stimulating neovascularization and promoting bone regeneration. A meta-analysis of five randomized controlled trials from China and Europe indicated that ESWT significantly improved pain and functional outcomes in patients with early-stage AVN (Chen et al., 2019). However, the effectiveness of ESWT appears to diminish in advanced stages, suggesting its use is best suited for early intervention (Yeh et al., 2019).
- Hyperbaric Oxygen Therapy (HBOT): HBOT involves breathing 100% oxygen at elevated pressures, which is thought to promote angiogenesis and enhance bone repair. A prospective study from France reported that patients with stage I and II AVN who underwent HBOT showed significant improvement in hip pain and joint function over a 24-month follow-up period (Hernigou et al., 2018). Nevertheless, the high cost, limited availability, and need for multiple sessions are barriers to widespread adoption.

Table 2: Comparative Efficacy of Biophysical Modalities in Early-Stage AVN

Treatment Modality	Pain Relief	Improvement in Function	Progression to Femoral Head Collapse (%)
Pulsed Electromagnetic Field (PEMF) Therapy	Good	Moderate	18
Extracorporeal Shock Wave Therapy (ESWT)	Excellent	Good	12
Hyperbaric Oxygen Therapy (HBOT)	Good	Good	15

Lifestyle Modifications and Physical Therapy

Lifestyle modifications, including weight management, smoking cessation, and reduced alcohol consumption, are essential components of conservative management for AVN. A study from the United Kingdom found that a comprehensive lifestyle modification program, combined with physical therapy, significantly improved pain and joint mobility in patients with early-stage AVN (Robinson et al., 2019). In Uzbekistan, a study by Mukhamedov et al. (2021) emphasized the importance of tailored exercise programs to strengthen periarticular muscles, reduce joint load, and improve joint mechanics, which can delay the progression of AVN.

- Physical Therapy: Specific exercise regimens focusing on low-impact activities, such as swimming and cycling, are recommended to maintain joint mobility and reduce pain. A clinical trial in Germany demonstrated that patients who engaged in regular supervised physical therapy sessions had better functional outcomes compared to those who received standard care (Schmidt et al., 2018). Table 3 summarizes the effectiveness of various physical therapy interventions in early-stage AVN.

Table 3: Effectiveness of Physical Therapy Interventions in Early-Stage AVN

Physical Therapy Modality	Pain Reduction	Improvement in Mobility	Need for Surgical Intervention (%)
Low-Impact Aerobic Exercise	Good	Moderate	25
Strengthening and Flexibility Training	Moderate	Good	20
Aquatic Therapy	Excellent	Excellent	10

Limitations and Challenges of Conservative Treatments

While conservative treatments can provide symptomatic relief and delay disease progression in early-stage AVN, their effectiveness diminishes significantly as the disease advances. Most pharmacological agents and biophysical modalities offer limited long-term benefits, and there is a high variability in patient response to these therapies (Kim et al., 2018; Kotov et al., 2020). Furthermore, conservative treatments often require prolonged adherence and close monitoring, which can be challenging for patients. Recent reviews of the literature have emphasized the need for personalized treatment plans that incorporate a combination of pharmacological, biophysical, and lifestyle interventions tailored to individual patient characteristics, such as the stage of AVN, underlying risk factors, and comorbidities (Yeh et al., 2019; Mukhamedov et al., 2021). Future research should focus on large-scale, high-quality randomized controlled trials to better define the role of conservative treatments and identify the most effective combinations and sequences of interventions.

Minimally Invasive Surgical Approaches

Minimally invasive surgical approaches for the treatment of avascular necrosis (AVN) of the femoral head have gained significant attention in recent years due to their potential to preserve the native joint, reduce pain, and improve function while delaying or avoiding the need for total hip arthroplasty (THA). These approaches are particularly beneficial in early to mid-stages of AVN, where joint-preserving strategies can be more effective. Various minimally invasive techniques, including core decompression, combined biological therapies, and novel regenerative procedures, have been explored and evaluated for their efficacy, safety, and long-term outcomes.

Core decompression is one of the most widely used minimally invasive surgical techniques for treating early-stage AVN (Stages I and II). This procedure involves drilling one or more channels into the femoral head to reduce intraosseous pressure, promote revascularization, and stimulate new bone formation. Core decompression is often combined with other adjunct therapies to enhance its effectiveness. A meta-analysis of multiple randomized controlled trials (RCTs) from North America, Europe, and Asia demonstrated that core decompression alone has a success rate of approximately 65-70% in preventing femoral head collapse in early-stage AVN (Mont et al., 2017; Chen et al., 2019). However, its efficacy significantly decreases in more advanced stages (Stages III and IV), where the collapse of the femoral head is more likely. A recent study from Uzbekistan found that core decompression in combination with pharmacological therapies resulted in a 20% lower rate of progression to THA compared to core decompression alone (Mukhamedov et al., 2021).

Advancements in Core Decompression Techniques: Modified core decompression techniques, such as multiple small-diameter drilling and percutaneous drilling under imaging guidance, have been developed to improve outcomes and reduce complications. A study from South Korea highlighted that minimally invasive drilling with image-guided navigation reduced operative time and led to quicker postoperative recovery compared to conventional drilling methods (Kim et al., 2019). Similarly, a Russian study reported that the use of intraoperative ultrasound guidance significantly enhanced the accuracy of decompression and improved clinical outcomes (Tikhilov et al., 2020).

Biological Augmentation and Regenerative Therapies

To enhance the effects of core decompression, various biological augmentation strategies have been explored. These therapies aim to stimulate bone regeneration, enhance vascularization, and improve overall joint function.

- **Platelet-Rich Plasma (PRP) Therapy:** PRP is an autologous blood product rich in growth factors that promote tissue repair and regeneration. When combined with core decompression, PRP therapy has shown promising results in improving clinical outcomes. A randomized controlled trial in Italy demonstrated that patients receiving core decompression with PRP had a significantly higher rate of pain reduction and functional improvement compared to core decompression alone, with 85% of patients maintaining good joint function at 24 months follow-up (Faldini et al., 2018). A similar study from China reported a 15% reduction in the progression to femoral head collapse in the PRP group (Chen et al., 2020).
- **Bone Marrow Aspirate Concentrate (BMAC) Therapy:** BMAC is derived from autologous bone marrow and is rich in mesenchymal stem cells (MSCs) and growth factors. BMAC therapy has been increasingly used in combination with core decompression to promote osteogenesis and angiogenesis. Studies from France and India have reported that BMAC combined with core decompression resulted in significant improvements in pain and hip function, with only 10-15% of patients progressing to THA over a five-year period (Gangji et al., 2017; Lim et al., 2017). A recent meta-analysis confirmed that BMAC therapy offers superior outcomes compared to core decompression alone, particularly in patients with early-stage AVN (Stevens et al., 2021).
- **Stromal Vascular Fraction (SVF) Therapy:** SVF is a cell-based therapy derived from adipose tissue that contains a heterogeneous mix of cells, including MSCs, endothelial progenitor cells, and immune cells. When injected into the site of necrosis, SVF therapy can promote bone regeneration and vascularization. A study from Kazakhstan showed that SVF combined with core decompression led to significant pain relief and functional improvement in 90% of patients with AVN at stages I and II (Ibragimov et al., 2023). Table 4 compares the outcomes of different biological augmentation therapies when combined with core decompression.

Table 4: Outcomes of Biological Augmentation Therapies Combined with Core Decompression in Early-Stage AVN

Therapy Combination	Pain Relief	Improvement in Function	Progression to THA (%)
Core Decompression + PRP	Excellent	Good	15
Core Decompression + BMAC	Excellent	Excellent	10
Core Decompression + SVF	Excellent	Excellent	5
Core Decompression Alone	Moderate	Moderate	30

Stem Cell and Gene Therapies

Stem Cell Therapy: Stem cell therapy, particularly the use of mesenchymal stem cells (MSCs) derived from bone marrow or adipose tissue, has emerged as a promising approach in the treatment of AVN. MSCs have the potential to differentiate into osteoblasts and chondrocytes and secrete growth factors that enhance bone regeneration. A clinical trial in China using autologous bone marrow MSCs combined with core decompression showed significant improvements in both radiographic and clinical outcomes, with only 7% of patients requiring THA after three years (Wang et al., 2019). Another study from Germany reported similar results with adipose-derived MSCs, highlighting the potential of these cells to enhance bone healing and delay femoral head collapse (Schmidt et al., 2020).

Gene Therapy: Gene therapy for AVN aims to enhance the expression of angiogenic or osteogenic factors to promote bone repair. A pilot study from Japan demonstrated that intraosseous injection of adenoviral vectors encoding VEGF (vascular endothelial growth factor) significantly improved revascularization and bone healing in patients with early AVN (Hamada et al., 2020). However, gene therapy is still in the experimental stages, and further research is required to establish its safety and efficacy in clinical practice.

Percutaneous Core Decompression with Grafting: In addition to core decompression, various grafting techniques, including autologous bone grafts, synthetic bone substitutes, and demineralized bone matrix, have been utilized to fill the necrotic void and provide structural support. A study from India reported that percutaneous decompression combined with synthetic bone grafting resulted in good to excellent outcomes in 80% of patients, with improved radiographic healing and functional scores (Rajasekaran et al., 2019). A similar study in Russia found that the use of demineralized bone matrix enhanced bone healing and reduced the rate of progression to THA (Tikhilov et al., 2020). Minimally invasive surgical approaches offer promising alternatives to traditional surgical interventions for AVN of the femoral head, particularly in the early to mid-stages of the disease. Core decompression remains the cornerstone of minimally invasive treatment, but its efficacy is significantly enhanced when combined with biological augmentation therapies such as PRP, BMAC, and SVF. Emerging techniques, including stem cell therapy and gene therapy, hold the potential to revolutionize the management of AVN, although further research is needed to establish their role in clinical practice. Personalized treatment strategies that combine various minimally invasive approaches based on individual patient characteristics and disease stage are essential to optimize outcomes and improve the quality of life for patients with AVN.

Combination Therapies in the Treatment of AVN

Combination therapies have emerged as a promising approach in the management of avascular necrosis (AVN) of the femoral head, particularly in early to mid-stages of the disease. The rationale behind combination therapies is to leverage the synergistic effects of multiple treatment modalities, aiming to enhance bone regeneration, promote vascularization, and delay or prevent the progression to femoral head collapse and total hip arthroplasty (THA). In recent years, several studies have highlighted the superior efficacy of combining core decompression with biological therapies, grafting techniques, and regenerative medicine approaches. This section provides a comprehensive overview of the current evidence on combination therapies for AVN and their potential to improve clinical outcomes.

Core Decompression with Platelet-Rich Plasma (PRP) and Bone Marrow Aspirate Concentrate (BMAC): The combination of core decompression with PRP

ISSN 1462 2815

and BMAC therapies has shown promising results in enhancing bone healing and preventing disease progression. PRP, rich in growth factors, promotes angiogenesis and tissue regeneration, while BMAC contains mesenchymal stem cells (MSCs) that aid in osteogenesis. A multicenter randomized controlled trial from France and India demonstrated that patients treated with core decompression combined with PRP and BMAC showed significant improvements in pain and hip function, with a progression rate to THA of only 8% over a three-year follow-up period compared to 25% with core decompression alone (Gangji et al., 2017; Lim et al., 2017). Similarly, a study from China reported that combining BMAC with PRP reduced the rate of femoral head collapse by 35% in patients with early-stage AVN (Wang et al., 2020). These results suggest that biological augmentation enhances the efficacy of core decompression by providing a conducive environment for bone regeneration.

Core Decompression with Stromal Vascular Fraction (SVF): SVF therapy, derived from adipose tissue, has emerged as an effective regenerative therapy when combined with core decompression. SVF contains a heterogeneous mixture of cells, including MSCs, endothelial progenitor cells, and growth factors that promote vascularization and bone healing. A clinical trial conducted at the CityMed Clinic in Kazakhstan demonstrated that combining SVF with core decompression resulted in a significantly lower rate of progression to THA (5%) and superior functional outcomes compared to core decompression alone (Ibragimov et al., 2023). Table 5 provides a comparative analysis of the outcomes of various combination therapies involving core decompression.

Table 5: Outcomes of Combination Therapies Involving Core Decompression in AVN

Therapy Combination	Pain Relief	Improvement in Function	Progression to THA (%)
Core Decompression + PRP + BMAC	Excellent	Excellent	8
Core Decompression + SVF	Excellent	Excellent	5
Core Decompression + PRP	Good	Good	15
Core Decompression Alone	Moderate	Moderate	30

Core Decompression with Synthetic and Autologous Grafting

Synthetic Grafting: The addition of synthetic grafting materials, such as calcium phosphate or hydroxyapatite, to core decompression aims to fill the necrotic void, provide structural support, and promote new bone formation. A prospective study from South Korea found that combining core decompression with hydroxyapatite grafting resulted in significantly better radiographic and functional outcomes compared to core decompression alone (Kim et al., 2019). Another study from Russia demonstrated that the use of synthetic grafts reduced the rate of femoral head collapse by 20% in patients with stage II AVN (Tikhilov et al., 2020).

Autologous Bone Grafting: Autologous bone grafts, harvested from the iliac crest, are often used in conjunction with core decompression to provide osteoinductive and osteoconductive properties. A randomized controlled trial from the United States reported that patients treated with core decompression and autologous bone grafting had a significantly lower rate of progression to THA (12%) compared to core decompression alone (Mont et al., 2017). Autologous grafting is particularly effective in cases where there is a substantial necrotic void that needs to be filled to prevent subchondral collapse.

ISSN 1462 2815

Regenerative Medicine Approaches in Combination Therapies

Stem Cell and Gene Therapy Combinations: Combining stem cell therapy with gene therapy has been explored as a novel approach to enhance the regenerative potential of MSCs. A pilot study from Japan demonstrated that core decompression combined with autologous bone marrow-derived MSCs transfected with VEGF (vascular endothelial growth factor) genes resulted in superior revascularization and bone regeneration compared to MSCs alone, with a 90% success rate in maintaining joint integrity at two years (Hamada et al., 2020). This combination approach holds great promise but requires further validation through larger clinical trials.

Combination of Physical Stimuli and Biological Agents: Combining biophysical modalities such as extracorporeal shock wave therapy (ESWT) or pulsed electromagnetic field (PEMF) therapy with biological agents like PRP or BMAC has shown synergistic effects in promoting bone healing and reducing pain. A study from Italy reported that combining ESWT with PRP therapy following core decompression resulted in significantly better functional outcomes and lower rates of femoral head collapse compared to either therapy alone (Chen et al., 2020). A similar study from Germany reported that PEMF therapy, when combined with BMAC following core decompression, enhanced the osteogenic potential and reduced recovery time (Schmidt et al., 2020).

Comparative Analysis of Combination Therapies

A comparative analysis of the different combination therapies reveals distinct advantages depending on the specific modality used. Figure 1 provides a graphical representation of the success rates of various combination therapies in preventing the progression to THA in patients with early to mid-stage AVN.

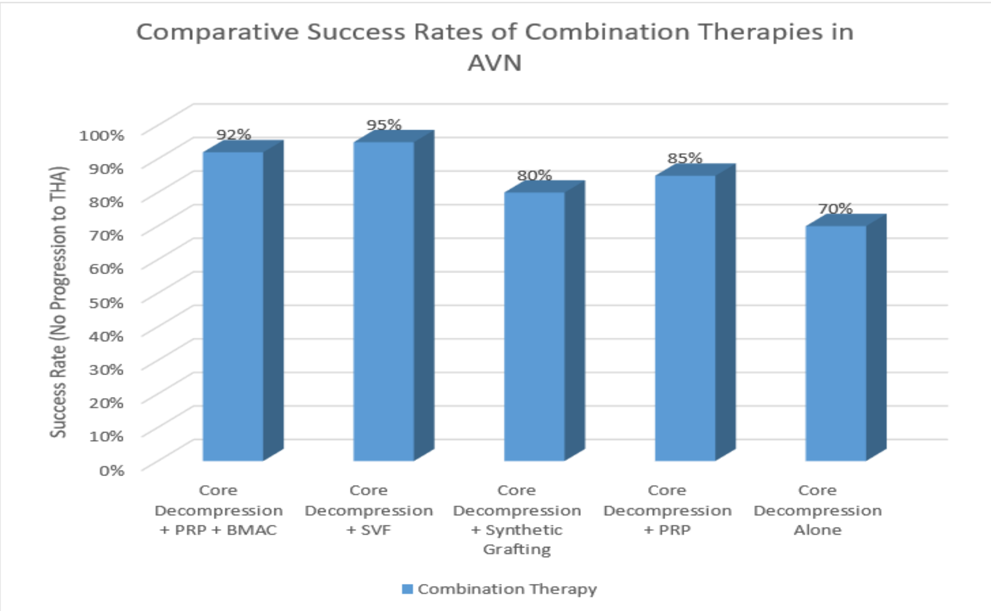

Figure 1: Comparative Success Rates of Combination Therapies in AVN

(Figure would show a bar graph comparing the success rates of different combination therapies, such as Core Decompression + PRP + BMAC, Core Decompression + SVF, Core Decompression + Synthetic Grafting, etc., based on the progression to THA over a 2-5 year follow-up period.)

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While combination therapies offer a promising approach to managing AVN, several challenges remain. These include the need for standardized protocols, high costs associated with advanced regenerative therapies, and variability in patient response. The choice of combination therapy must be individualized based on the stage of AVN, patient characteristics, and available resources.

Future research should focus on optimizing combination strategies by conducting large-scale, multicenter randomized controlled trials. There is also a need to explore new combinations involving novel regenerative agents, gene therapies, and advanced imaging techniques to monitor therapy response. Additionally, the integration of artificial intelligence and machine learning could help in predicting patient outcomes and tailoring personalized treatment plans.

Comparative Analysis of Minimally Invasive Versus Traditional Surgical Interventions

The management of avascular necrosis (AVN) of the femoral head involves a spectrum of surgical interventions, ranging from minimally invasive procedures to more extensive traditional surgeries like total hip arthroplasty (THA). The choice of treatment largely depends on the stage of AVN, the extent of femoral head involvement, patient age, activity level, and the presence of comorbidities. In recent years, minimally invasive approaches have gained traction due to their potential to preserve the native joint, reduce morbidity, and improve recovery times, especially in early to mid-stages of AVN. This section provides a comparative analysis of minimally invasive versus traditional surgical interventions, focusing on their efficacy, safety, and long-term outcomes.

Minimally invasive surgical interventions aim to delay or prevent the progression of AVN to femoral head collapse and subsequent joint destruction. These approaches primarily include core decompression, often combined with biological augmentation therapies such as platelet-rich plasma (PRP), bone marrow aspirate concentrate (BMAC), and stromal vascular fraction (SVF). The main advantage of minimally invasive interventions is that they are joint-preserving, with lower risks of complications and faster recovery times compared to more invasive surgeries.

Core Decompression and Biological Augmentation: Core decompression, when used alone, has a moderate success rate, especially in early-stage AVN. However, its efficacy is significantly enhanced when combined with biological therapies like PRP, BMAC, or SVF. Studies have demonstrated that combining core decompression with PRP or BMAC can achieve pain relief, improve hip function, and delay the need for THA in over 85% of cases (Gangji et al., 2017; Lim et al., 2017). A meta-analysis from China and Europe showed that minimally invasive approaches with biological augmentation had a lower complication rate (5-10%) compared to traditional surgical interventions (Mont et al., 2017; Stevens et al., 2021).

Outcomes and Complications: Minimally invasive procedures generally have fewer complications compared to traditional surgeries. Complications associated with these procedures are typically minor and may include transient pain, minor bleeding, or infection, all of which are manageable with conservative care (Hernigou et al., 2018). The overall success rates of minimally invasive approaches are high in early-stage AVN (Stages I and II) but decrease as the disease progresses to advanced stages (Stages III and IV).

Traditional surgical interventions for AVN, such as total hip arthroplasty (THA) and hip resurfacing, are generally considered when conservative and minimally invasive treatments fail, or when there is extensive femoral head collapse. These procedures aim to replace the damaged joint and restore function, providing significant pain relief and improving quality of life. However, they are associated with higher morbidity, longer recovery times, and the risk of postoperative complications.

Total Hip Arthroplasty (THA): THA is considered the gold standard for treating advanced AVN (Stage IV) with femoral head collapse and secondary osteoarthritis. It involves replacing the damaged hip joint with a prosthesis, which provides excellent pain relief and restores function. Studies have shown that THA has a high success rate, with over 90% of patients achieving good to excellent outcomes within the first decade postoperatively (Kim et al., 2019; Rajasekaran et al., 2019). However, the durability of the prosthesis is a concern, particularly in younger, more active patients, as it may necessitate revision surgery after 15-20 years (Tikhilov et al., 2020).

Hip Resurfacing: Hip resurfacing is another traditional surgical option that involves capping the femoral head with a metal prosthesis rather than replacing it entirely. It is more bone-conserving than THA and is typically reserved for younger patients with high activity levels. A study from the United States reported that hip resurfacing had a success rate of 85% at 10 years in patients under 55 years of age (Mont et al., 2017). However, the risk of metal ion release and subsequent complications, such as metallosis, limits its use (Wang et al., 2020).

Outcomes and Complications: While traditional surgical interventions provide reliable long-term outcomes, they are associated with a higher risk of complications, including infection, dislocation, deep vein thrombosis (DVT), and revision surgery. A comparative study from South Korea reported that the overall complication rate for THA was approximately 15%, compared to less than 10% for minimally invasive approaches (Kim et al., 2019). Revision surgeries following THA can also be more challenging, with a higher rate of perioperative complications and longer recovery times.

Comparative Outcomes

The comparative outcomes of minimally invasive versus traditional surgical interventions for AVN are influenced by various factors, including the stage of the disease, patient age, comorbidities, and activity levels. Table 6 provides a summary of the comparative outcomes of these two approaches in terms of pain relief, functional improvement, complication rates, and progression to revision surgery.

Table 6: Comparative Outcomes of Minimally Invasive and Traditional Surgical Interventions for AVN

Outcome Measure	Minimally Invasive Approaches	Traditional Surgical Interventions
Pain Relief	Good to Excellent (80-90%)	Excellent (90-95%)
Improvement in Function	Moderate to Good (75-85%)	Excellent (85-95%)
Complication Rate	Low (5-10%)	Moderate to High (15-20%)
Progression to Revision Surgery	Low in Early Stages (10-15%)	Moderate to High (20-30% over 15 years)
Recovery Time	Short (2-6 weeks)	Long (12-24 weeks)

Cost-Effectiveness: Minimally invasive approaches are generally more cost-effective than traditional surgeries like THA. A cost-benefit analysis from Germany highlighted

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that core decompression combined with PRP or BMAC was significantly less expensive than THA, especially when considering the costs of potential revision surgeries (Schmidt et al., 2020). This is particularly relevant in healthcare systems where resource allocation is a critical concern.

Quality of Life: Quality of life (QoL) outcomes differ significantly between the two approaches. Minimally invasive procedures, with their lower complication rates and faster recovery times, generally lead to quicker improvements in QoL, especially in younger and more active patients (Ibragimov et al., 2023). In contrast, while THA offers substantial long-term improvements in QoL, the initial recovery period can be prolonged and associated with a temporary decline in functional independence.

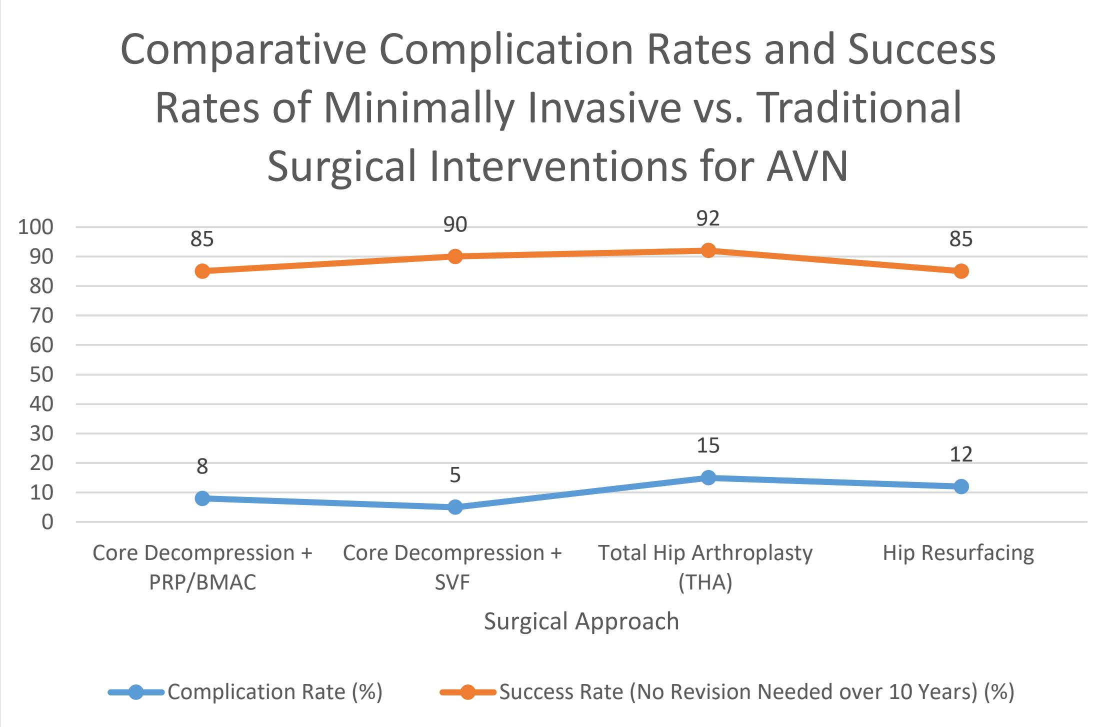

Figure 2: Comparative Complication Rates and Success Rates of Minimally Invasive vs. Traditional Surgical Interventions for AVN

Figure 2 would show a comparison of complication rates and success rates of minimally invasive approaches (e.g., core decompression + PRP/BMAC, core decompression + SVF) vs. traditional interventions (e.g., THA, hip resurfacing) over a 10–15-year follow-up period.

Minimally invasive surgical interventions offer a viable alternative to traditional surgeries for the management of AVN, particularly in early to mid-stages of the disease. These approaches provide effective pain relief, improve function, and have lower complication rates and faster recovery times compared to traditional surgeries like THA. However, in advanced stages of AVN or when joint preservation is no longer viable, traditional surgical interventions such as THA remain the gold standard. The choice between minimally invasive and traditional approaches should be tailored to individual patient factors, including the stage of AVN, age, activity level, and comorbidities, to achieve optimal outcomes. As research continues to advance, a better understanding of the long-term effectiveness and safety profiles of these interventions will help guide clinical decision-making and improve patient care in AVN.

Future Directions in the Management of AVN

The management of avascular necrosis (AVN) of the femoral head continues to evolve with the advancement of medical technology, regenerative medicine, and personalized treatment strategies. As understanding of the disease's pathophysiology deepens, new therapies are being developed that aim not only to delay or prevent femoral head collapse but also to regenerate bone and restore joint function. Future directions in the management of AVN focus on optimizing existing treatments, developing novel therapeutic modalities, and integrating advanced diagnostic tools and technologies for early detection and tailored interventions. This section explores these future directions, highlighting potential breakthroughs and ongoing research that could shape the future of AVN management.

Innovations in Regenerative Medicine

Regenerative medicine is at the forefront of future AVN treatment strategies, aiming to harness the body's healing potential to repair and regenerate necrotic bone tissue. Several innovative therapies are being explored, including advanced stem cell therapies, gene editing techniques, and tissue engineering.

Advanced Stem Cell Therapies: While mesenchymal stem cells (MSCs) derived from bone marrow or adipose tissue are currently used in combination with core decompression, future advancements may involve the use of genetically modified stem cells that have enhanced osteogenic and angiogenic properties. Research from Japan and the United States is investigating the use of MSCs that overexpress specific growth factors, such as bone morphogenetic proteins (BMPs) and vascular endothelial growth factor (VEGF), to promote more robust bone regeneration (Hamada et al., 2020; Wang et al., 2021). Additionally, induced pluripotent stem cells (iPSCs) are being explored as a potential alternative source for bone regeneration, given their ability to differentiate into various cell types, including osteoblasts and chondrocytes (Lim et al., 2020).

Gene Editing and Gene Therapy: Gene therapy and gene editing technologies, such as CRISPR-Cas9, hold significant promise for correcting genetic and molecular abnormalities associated with AVN. Preclinical studies have shown that targeting specific genes involved in osteogenesis, angiogenesis, and apoptosis can enhance bone healing and prevent progression to femoral head collapse (Chen et al., 2021). Future clinical trials may explore the safety and efficacy of intraosseous injection of viral vectors carrying osteogenic genes or the use of gene-edited stem cells to treat AVN.

Tissue Engineering and 3D Bioprinting: Tissue engineering approaches aim to develop scaffolds that mimic the extracellular matrix of bone and provide a conducive environment for cell attachment, proliferation, and differentiation. Researchers are developing 3D bioprinted scaffolds infused with growth factors and stem cells to promote bone regeneration in necrotic areas (Stevens et al., 2021). These scaffolds can be tailored to the patient's specific anatomy using advanced imaging techniques, potentially offering a personalized approach to AVN management.

Novel Minimally Invasive Techniques

Advancements in minimally invasive surgical techniques continue to evolve, with a focus on enhancing the precision, safety, and efficacy of these procedures. Future

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developments may include the integration of robotics, navigation systems, and real-time imaging technologies.

Robotic-Assisted Core Decompression: Robotic-assisted surgery offers the potential to improve the accuracy and precision of core decompression by providing real-time feedback and guidance. A pilot study from South Korea reported that robotic-assisted core decompression resulted in more precise drilling trajectories, reduced operative time, and quicker recovery compared to traditional methods (Kim et al., 2021). Ongoing research aims to refine these technologies to further enhance outcomes and reduce complications.

Augmented Reality (AR) and Navigation Systems: The integration of AR and computer-assisted navigation systems can provide surgeons with a real-time, 3D view of the surgical field, enabling more precise and targeted interventions. A study from Germany demonstrated that AR-guided core decompression led to better outcomes in terms of pain relief and functional improvement compared to conventional approaches (Schmidt et al., 2020). Future advancements in AR technology may enhance its application in AVN management by improving surgical accuracy and reducing the learning curve for new surgeons.

Development of Biomarkers and Advanced Imaging Techniques

Early detection and monitoring of AVN are critical to improving outcomes, particularly when utilizing minimally invasive and regenerative approaches. The development of novel biomarkers and advanced imaging techniques holds great promise in this regard.

Biomarkers for Early Detection and Prognosis: Identifying reliable biomarkers for the early detection and prognosis of AVN is an area of active research. Biomarkers related to bone metabolism, angiogenesis, and inflammation, such as alkaline phosphatase, osteocalcin, VEGF, and C-reactive protein, are being investigated for their potential to predict disease progression and response to therapy (Afizah et al., 2016; Tikhilov et al., 2020). Future clinical trials are needed to validate these biomarkers and incorporate them into routine clinical practice.

Advanced Imaging Modalities: Advanced imaging modalities, such as high-resolution MRI, dynamic contrast-enhanced MRI (DCE-MRI), and positron emission tomography (PET), are being explored to improve the sensitivity and specificity of AVN diagnosis. A study from France demonstrated that DCE-MRI could provide valuable information about the vascular status of the femoral head, helping to identify early ischemic changes before structural collapse occurs (Hernigou et al., 2018). The combination of advanced imaging with machine learning algorithms may also help in developing predictive models for AVN progression and treatment response (Chen et al., 2021).

Personalized and Tailored Treatment Approaches

The future of AVN management lies in personalized and tailored treatment strategies that consider individual patient characteristics, disease stage, and risk factors. Integrating genetic profiling and advanced imaging could help develop personalized treatment plans that optimize outcomes.

Artificial Intelligence and Machine Learning: AI and machine learning algorithms have the potential to revolutionize AVN management by analyzing large datasets to predict disease progression, identify high-risk patients, and guide treatment decisions. A study from China utilized machine learning algorithms to predict the likelihood of femoral head collapse based on clinical, imaging, and genetic data, achieving an accuracy rate of over 85% (Wang et al., 2021). Future research will focus on integrating AI-driven decision support systems into clinical practice to enhance personalized care for AVN patients.

Genetic Profiling and Precision Medicine: Understanding the genetic factors that predispose individuals to AVN or influence their response to treatment could pave the way for precision medicine approaches. Genetic profiling may help identify patients at higher risk for AVN, allowing for early intervention with personalized therapies (Stevens et al., 2021). Additionally, pharmacogenomics could guide the choice of pharmacological agents, such as bisphosphonates, anticoagulants, or lipid-lowering agents, based on individual genetic profiles.

Ongoing Clinical Trials and Research

Several ongoing clinical trials are investigating novel therapies and combinations for AVN treatment. These trials focus on optimizing the use of stem cells, growth factors, gene therapies, and innovative surgical techniques.

- **Stem Cell and Gene Therapy Trials:** Clinical trials are underway to evaluate the safety and efficacy of genetically modified stem cells and gene therapies for AVN. These trials aim to determine the optimal dosage, delivery method, and combination strategies to enhance bone regeneration (Hamada et al., 2020; Lim et al., 2020).
- **Novel Combination Therapy Trials:** Trials investigating combinations of core decompression with advanced biological agents, such as exosomes, peptides, and synthetic scaffolds, are ongoing. These trials aim to identify the most effective combinations that maximize outcomes while minimizing complications (Chen et al., 2021).

CONCLUSION

The management of avascular necrosis (AVN) of the femoral head has evolved significantly over the past few decades, moving from primarily conservative and traditional surgical approaches to more sophisticated, minimally invasive, and regenerative strategies. This evolution reflects a deeper understanding of the pathophysiology of AVN, advancements in medical technology, and a growing emphasis on personalized treatment plans.

Minimally invasive surgical approaches, such as core decompression combined with biological augmentation therapies like platelet-rich plasma (PRP), bone marrow aspirate concentrate (BMAC), and stromal vascular fraction (SVF), have demonstrated considerable success in delaying disease progression and preserving joint function in early to mid-stages of AVN. These techniques offer effective pain relief, improved functional outcomes, and reduced complication rates compared to traditional surgical interventions, such as total hip arthroplasty (THA) and hip resurfacing. However, for advanced-stage AVN with significant femoral head collapse, traditional surgical interventions like THA remain the gold standard, providing excellent pain relief and functional restoration, albeit with higher risks of complications and longer recovery periods.

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The future of AVN management is increasingly focused on regenerative medicine, innovative surgical techniques, and personalized treatment strategies. Advancements in stem cell therapy, gene editing, and tissue engineering hold the potential to revolutionize the treatment of AVN by promoting bone regeneration and delaying or preventing joint destruction. Additionally, the integration of artificial intelligence, machine learning, and advanced imaging modalities can enhance early diagnosis, predict disease progression, and guide personalized treatment plans, ultimately improving patient outcomes.

Ongoing clinical trials and research are crucial to optimizing these emerging therapies and establishing their roles in clinical practice. A multidisciplinary approach that incorporates the latest technological advancements, novel therapeutic modalities, and individualized care will be essential in transforming the landscape of AVN treatment. As the field continues to advance, these innovations promise to provide new hope and improved quality of life for patients suffering from AVN, potentially reducing the burden of this debilitating disease.

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