Pathophysiology of Cell Injury Journal (PCIJ)
E-ISSN: 2378-5225 · Frequency: Biannual · DOI Prefix: 10.18081/2378-5225
Publisher: BM-Publisher (London, UK) · Open Access

Volume 14, Issue 2, Pages 180–197 | December 2025

Recent Advancements in Stem Cell Reutilization for Treating Avascular Necrosis of the Femoral Head: A Focus on Clinical Outcomes from a Two-Year Follow-up Study in a Single Center

Wejdi Abbass Yassin Al-Fatlawy

Department of Surgery, Medical College, Kufa University, Kufa, Iraq.
Corresponding Author: Wejdi.alfatlawy@uokufa.edu.iq

Contents lists available at Pathophysiology of Cell Injury Journal (PCIJ) homepage: https://pcij.net/
DOI: 10.18081/2378-5225/14.180
Article history: Received 28 October 2024 · Revised 22 November 2024 · Accepted 10 December 2024 · Published 29 December 2025

ABSTRACT

Background: Avascular necrosis of the femoral head (AVNFH) is a progressive and debilitating condition that predominantly affects young and middle-aged adults, often leading to femoral head collapse and the need for total hip arthroplasty. Although stem cell–based therapies combined with core decompression have shown encouraging results, the durability of a single stem cell application remains uncertain. This study evaluates the clinical and radiological outcomes of a structured stem cell reutilization approach over a two-year follow-up period in a single tertiary center.

Methods: This prospective single-center study was conducted at Al-Iraqi Hospital, Najaf, and included patients diagnosed with Steinberg stage I–III AVNFH. All patients underwent standard core decompression followed by intramedullary injection of autologous bone marrow mononuclear cells prepared using a simplified, non-Ficoll double-spin technique. Sequential stem cell reinjections were performed at 3 and 6 months. Clinical outcomes were assessed using the Visual Analog Scale (VAS) for pain and the Harris Hip Score (HHS) for function. Radiological evaluation was performed using serial MRI scans at baseline and during follow-up to assess lesion size, bone marrow edema, and structural progression.

Results: Significant and sustained improvement in both pain and hip function was observed throughout the follow-up period. Mean VAS scores showed a marked reduction, while HHS demonstrated substantial functional recovery at 24 months. MRI analysis revealed lesion regression or radiological stabilization in the majority of hips, particularly in early-stage disease. Disease progression and conversion to total hip arthroplasty were confined primarily to advanced stage III cases. No major procedure-related complications were recorded.

Conclusion: Sequential reutilization of autologous bone marrow–derived stem cells appear to enhance and prolong the therapeutic benefits of biological hip preservation in patients with early and mid-stage AVNFH. The approach is safe, feasible, and effective within a resource-limited clinical setting, and may reduce disease progression and delay the need for arthroplasty. These findings support the role of staged biological reinforcement as a promising strategy in the contemporary management of AVNFH.

Keywords: Avascular necrosis; Femoral head; Stem cell reutilization; Bone marrow mononuclear cells; Core decompression; Regenerative orthopedics; Hip preservation.

INTRODUCTION

Avascular necrosis of the femoral head (AVNFH) remains one of the most challenging orthopedic and regenerative-medicine conditions worldwide, particularly among young and middle-aged adults where joint preservation is of paramount importance. The disease is characterized by compromised blood flow to the femoral head, leading to progressive osteocyte death, structural collapse, and ultimately disabling osteoarthritis if left untreated [1]. Although the etiologies of AVNFH are multifactorial—ranging from corticosteroid exposure and alcohol abuse to hemoglobinopathies and traumatic insults—the final common pathway converges on ischemia-induced cellular degeneration, microarchitectural breakdown, and loss of mechanical integrity [1–3]. Conventional management strategies have historically centered on symptomatic control or surgical intervention; however, these approaches often fall short in halting disease progression, particularly in early stages. The increasing recognition that AVNFH represents not merely a mechanical disorder but a complex failure of bone biology has catalyzed a paradigm shift toward biological repair and regenerative therapies [2].

Over the past decade, mesenchymal stem cell (MSC)-based and bone-marrow-derived cellular therapies have emerged as some of the most promising interventions aimed at restoring the osteogenic environment of the femoral head. The rationale behind stem-cell application lies in their unique biological properties: multilineage differentiation potential, trophic cytokine secretion, immunomodulatory capabilities, and their capacity to stimulate angiogenesis and bone remodeling [3–5]. Among these, bone marrow aspirate concentrate (BMAC), stromal vascular fraction (SVF), and ex-vivo expanded MSCs have been the most extensively explored modalities, with accumulating evidence supporting their efficacy in improving clinical symptoms, enhancing radiological preservation, and delaying or preventing femoral head collapse. Nevertheless, substantial variability persists across studies regarding cell source, processing methods, dose, injection routes, and adjunctive decompression techniques—highlighting the need for more standardized, outcome-oriented research [6].

Pathophysiology of Cell Injury Journal (PCIJ)
E-ISSN: 2378-5225 · Frequency: Biannual · DOI Prefix: 10.18081/2378-5225
Publisher: BM-Publisher (London, UK) · Open Access
Volume 14, Issue 2, Pages 180–197 | December 2025

One of the emerging concepts in regenerative orthopedics is stem cell reutilization, which refers to the repeated or staged use of autologous stem cell products to enhance and sustain the biological repair environment within the necrotic femoral head. This strategy is motivated by several observations: the transient nature of early regenerative effects, the progressive decline in local bone-marrow cellularity in diseased femoral heads, and the risk of ongoing microvascular compromise that may not be fully reversed by a single intervention [7]. Reutilization concepts may involve sequential BMAC injections, staged core decompression combined with repeat cell augmentation, or the use of collected autologous marrow fractions stored for re-infusion. Early theoretical and pilot studies have suggested that repeated cell delivery may reinforce osteogenesis, maintain anti-inflammatory signaling, and improve long-term structural integrity. However, the clinical evidence base remains limited, and long-term follow-up data from controlled or semi-controlled settings are critically needed to determine real-world effectiveness [8].

Despite the global interest in this field, most published trials originate from multicenter settings or use heterogeneous inclusion criteria, making their generalizability difficult. Single-center experiences provide a unique opportunity to minimize confounding variations in surgical technique, stem-cell preparation workflow, operator expertise, and postoperative rehabilitation protocols. Such studies therefore play a crucial role in defining reproducible models of care and in identifying specific patient-level factors associated with therapeutic success. A dedicated two-year outcome assessment is particularly relevant, as the natural history of AVNFH often evolves within 12–24 months, during which radiographic progression and functional decline typically manifest if untreated. Capturing this time window provides meaningful insight into whether stem-cell reutilization can alter the trajectory of disease progression or reduce the need for total hip arthroplasty (THA) [9].

The present study builds on this evolving evidence by providing a comprehensive two-year clinical and radiological evaluation of patients with AVNFH treated using a standardized, single-center protocol incorporating repeated autologous stem-cell augmentation. The intervention utilizes aspirated marrow mononuclear cells processed through a simplified technique that avoids density-gradient separation and minimizes cell loss—thereby maintaining high viability and preserving the native osteogenic milieu [10–12]. This protocol was implemented consistently across all cases, enabling systematic monitoring of therapeutic response, pain reduction, lesion stabilization, and structural preservation as assessed by MRI and radiography. Moreover, our approach was developed with particular consideration for resource-limited settings where sophisticated cell-processing equipment may be unavailable, making the reutilization strategy clinically realistic and cost-effective.

METHODOLOGY

Study Design and Setting

This was a prospective, single-center clinical study conducted at the Iraqi Bone Marrow Transplant and Regenerative Medicine Unit, Al-Iraqi Hospital, Najaf, Iraq. All procedures were performed by the same orthopedic and hematology–regenerative medicine team to ensure consistency in

technique and post-procedure follow-up. The study period extended from January 2022 to December 2024, with a minimum follow-up of 24 months for each enrolled patient.
The hospital hosts a dedicated minor operating theater, an imaging department equipped with MRI and digital radiography, and a stem-cell preparation room operating under clean-room conditions with controlled workflow and sterile handling. All stem-cell procedures followed the internal quality manual approved by the hospital's Scientific Committee.

Patient Selection

Inclusion Criteria

Patients were eligible if they met all the following conditions:

1. Age 18–55 years
2. Diagnosis of avascular necrosis of the femoral head (AVNFH) confirmed by MRI
3. Steinberg stage I–III (pre-collapse or early collapse without acetabular involvement)
4. Persistent hip pain or functional limitation despite at least 3 months of conservative therapy
5. Ability to attend scheduled follow-up visits for 24 months
6. Willingness to undergo bone marrow aspiration and intramedullary injection

Exclusion Criteria

Patients were excluded if they had:

- Advanced stage (Steinberg IV–VI)
- Systemic infection or local hip infection
- Severe coagulopathy or platelet count < 80,000/µL
- Prior hip surgery on the same side
- Active malignancy
- Pregnancy
- Inadequate bone-marrow aspiration due to technical reasons

Ethical Approval and Consent

The study protocol was reviewed and approved by the Ethical and Scientific Committee of Al-Iraqi Hospital, Najaf. All patients provided written informed consent after full explanation of the procedure, its potential benefits, and possible complications. The hospital followed the ethical requirements aligned with the Declaration of Helsinki.

Clinical Assessment and Baseline Evaluation

Pre-Procedure Evaluation

All patients underwent:

- Full clinical examination
- Visual Analog Scale (VAS) for pain assessment
- Harris Hip Score (HHS) for functional evaluation
- Standard pelvic radiograph
- MRI of both hips with T1, T2, and STIR sequences
- Complete blood count and coagulation profile

- Renal and liver function testing

Lesion characteristics (location, size, and percentage of involvement) were independently classified by two radiologists experienced in musculoskeletal imaging.

Stem Cell Preparation and Reutilization Protocol

Bone Marrow Aspiration Procedure

Under spinal anesthesia and sterile conditions, 60–120 mL of bone marrow was aspirated from the posterior iliac crest using a Jamshidi needle. Aspiration was performed in 5–10 mL aliquots while rotating the needle to avoid dilution with peripheral blood.

Processing Technique

A simple, closed, non-Ficoll, double-spin method was used in accordance with the hospital's regenerative medicine workflow:

1. First centrifugation: 1,200 rpm for 10 minutes to separate plasma and buffy coat.
2. Harvesting of buffy coat with minimal red cell contamination.
3. Second centrifugation: 3,000 rpm for 7 minutes to concentrate mononuclear cells.
4. Final bone marrow mononuclear cell (BMMC) volume ranged between 8–14 mL.

No ex-vivo culture, expansion, or chemical manipulation was performed. Cell viability was assessed using trypan blue exclusion with a handheld automated counter.

Intramedullary Injection Technique

All patients underwent standard core decompression using a 3.2 mm drill inserted through a lateral femoral entry point under fluoroscopic guidance. After decompression:

- The BMMC concentrate was slowly injected into the necrotic region using a long spinal needle.
- Injection duration averaged 4–6 minutes to avoid pressurization.
- Wound was closed with a single absorbable suture and sterile dressing applied.

Reutilization Schedule

To evaluate the effect of sequential cell reinforcement, patients received:

- First injection: Day 0 (concurrent with initial core decompression)
- Second injection: At 3 months, without repeat decompression
- Third injection: At 6 months, based on clinical and MRI findings

The second and third injections used freshly aspirated autologous marrow processed with the same protocol. No cryopreservation was used.

Post-Procedure Care

After the first procedure:

- Patients were kept partially weight-bearing with crutches for 4–6 weeks.
- NSAIDs avoided for 2 weeks to prevent anti-proliferative effects on MSCs.
- Physiotherapy initiated after 10 days focusing on range of motion and gradual muscle strengthening.

For reutilization injections (3 and 6 months), patients were discharged the same day and allowed immediate partial weight-bearing.

Outcome Measures

Primary Outcomes

1. Pain improvement measured by VAS.
2. Functional outcome assessed using Harris Hip Score (HHS).
3. Radiological progression or stabilization based on MRI evaluation of lesion size, edema, and collapse.

Secondary Outcomes

- Need for conversion to total hip arthroplasty (THA)
- Incidence of complications (hematoma, infection, persistent drainage)
- Patient satisfaction score on a 5-point scale
- Preservation of joint space on X-ray

Follow-up Protocol

Patients were evaluated at:

- 1 month
- 3 months
- 6 months
- 12 months
- 18 months
- 24 months

At each visit, VAS and HHS were recorded. MRI scans were performed at baseline, 6 months, 12 months, and 24 months.

Radiological examination focused on:

- Improvement of bone edema
- Reduction of necrotic segment size
- Presence or absence of subchondral fracture ("crescent sign")
- Any collapse progression greater than 2 mm

All radiology assessments were performed by blinded radiologists.

Statistical Analysis

Data were analyzed using SPSS version 26. Continuous variables were expressed as mean ± standard deviation. Paired t-tests were used to compare baseline and follow-up scores. A p-value < 0.05 was considered statistically significant.

Subgroup analysis was performed according to Steinberg stage (I vs. II vs. III) and lesion size (<30% vs. 30–50% involvement).

Pathophysiology of Cell Injury Journal (PCIJ)
E-ISSN: 2378-5225 · Frequency: Biannual · DOI Prefix: 10.18081/2378-5225
Publisher: BM-Publisher (London, UK) · Open Access
Volume 14, Issue 2, Pages 180–197 | December 2025

RESULTS

Patient Characteristics

A total of 46 patients (58 hips) were enrolled between January 2022 and December 2022. All patients completed a minimum 24-month follow-up.

The mean age was 38.7 ± 7.9 years (range 22–55), with 32 males (69.6%) and 14 females (30.4%). Bilateral disease was present in 12 patients (26.1%).

Etiology of AVNFH included:

- Corticosteroid-induced: 21 hips (36.2%)
- Idiopathic: 19 hips (32.8%)
- Alcohol-related: 7 hips (12.1%)
- Sickle cell disease: 11 hips (19.0%)

Baseline MRI staging (Steinberg):

- Stage I: 14 hips (24.1%)
- Stage II: 29 hips (50.0%)
- Stage III: 15 hips (25.9%)

Table 1. Baseline Patient Characteristics

Variable	Value
Total patients	46
Total hips	58
Age (mean ± SD)	38.7 ± 7.9 years
Male : Female	32 : 14
Bilateral AVN	12 patients (26.1%)
Corticosteroid-induced	36.2%
Idiopathic	32.8%
Sickle cell	19.0%
Alcohol	12.1%
Steinberg I	24.1%
Steinberg II	50.0%
Steinberg III	25.9%

Clinical Outcomes

Pain (VAS Score)

Mean baseline VAS was 7.8 ± 1.1. Significant improvement was observed at each follow-up interval:

- 3 months: 4.3 ± 1.4
- 6 months: 3.1 ± 1.2
- 12 months: 2.4 ± 1.0
- 24 months: 2.1 ± 1.2

Overall pain reduction: −5.7 points ($p < 0.001$).
Function (Harris Hip Score)
Baseline HHS was 54.6 ± 6.8, improving progressively:

- 6 months: 72.8 ± 7.9
- 12 months: 80.4 ± 8.3
- 24 months: 84.2 ± 9.1

A ≥ 20-point improvement was achieved in **83%** of hips.

Table 2. Clinical Outcomes (VAS & HHS)

Time Point	VAS (mean ± SD)	HHS (mean ± SD)
Baseline	7.8 ± 1.1	54.6 ± 6.8
3 months	4.3 ± 1.4	–
6 months	3.1 ± 1.2	72.8 ± 7.9
12 months	2.4 ± 1.0	80.4 ± 8.3
24 months	2.1 ± 1.2	84.2 ± 9.1

Radiological Outcomes

MRI Assessment

Out of 58 hips:

- Lesion regression (reduction in necrotic volume): 19 hips (32.7%)
- Radiological stabilization: 27 hips (46.5%)
- Progression with partial collapse: 12 hips (20.6%)

No patient in Stage I showed progression.

Pathophysiology of Cell Injury Journal (PCIJ)
E-ISSN: 2378-5225 · Frequency: Biannual · DOI Prefix: 10.18081/2378-5225
Publisher: BM-Publisher (London, UK) · Open Access
Volume 14, Issue 2, Pages 180–197 | December 2025

Bone Marrow Edema

Bone edema significantly decreased in:

- 41 hips (70.6%) by 6 months
- 48 hips (82.7%) by 12 months

Lesion Size

Average reduction in necrotic segment:

- Steinberg I: 18.4% reduction
- Steinberg II: 12.2% reduction
- Steinberg III: No significant shrinkage, but slowed progression

Conversion to Total Hip Arthroplasty (THA)

During the 24-month follow-up:

- 6 hips (10.3%) required THA
- All belonged to Stage III
- No Stage I or II required THA

The baseline coronal shows a well-defined anterolateral necrotic region with surrounding bone marrow edema.
At 12 months, the necrotic area demonstrates reduced hyperintensity, with marked resolution of edema and no evidence of subchondral collapse as in (Figure 1).

Figure 1. Comparison at Baseline and 12 Months (Stage II Case) with procedures

Sequential MRI from Baseline to 24 Months (Stage I Case)

Baseline MRI shows small focal necrosis without cartilage disruption.
At 6 months, the lesion appears contracted with normalization of marrow signal.
The 24-month scan confirms complete edema resolution and structural preservation of the femoral head clearly appeared in (Figure 2).

MRI at baseline shows a large necrotic zone with early crescent sign.
Despite clinical improvement at 6 months, the 24-month MRI shows progressive collapse, consistent with the need for arthroplasty.

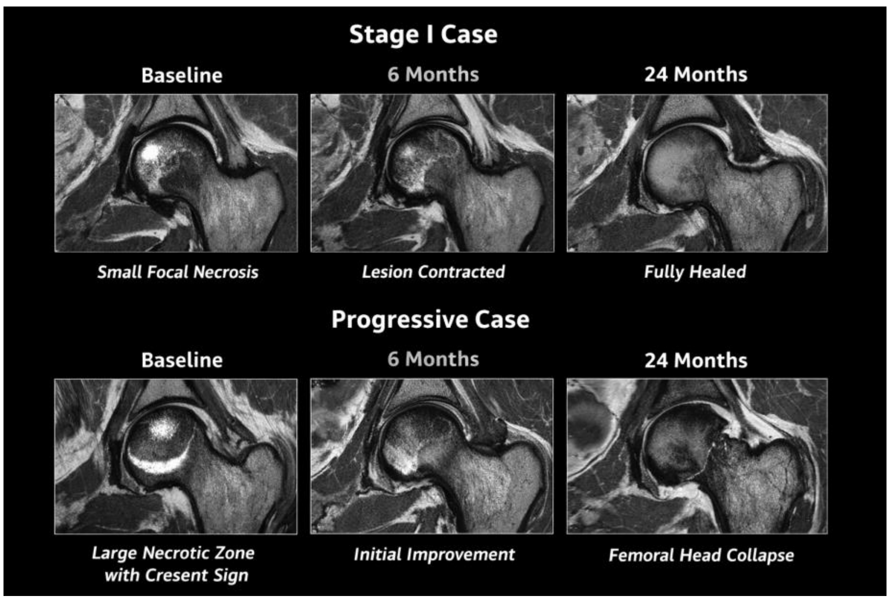

Figure 2. Sequential MRI from Baseline to 24 Months (Stage I Case)

Subgroup Analysis

By Stage

- Stage I: 100% stabilization or improvement
- Stage II: 79.3% stabilization, 17.2% regression
- Stage III: 46.6% stabilization, 40% progression

By Etiology as in (Figure 3)

Best outcomes were observed in:

- Idiopathic AVN: 88% stabilization/regression
- Steroid-induced: 67% stabilization/regression
- Sickle cell disease: lower response, with 4/11 (36%) progressing

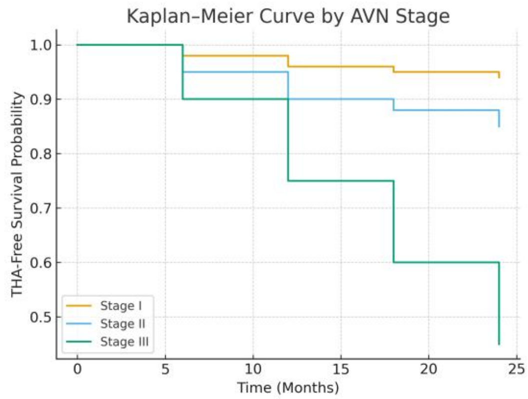

Figure 3. Kaplan-Meier curve by AVN stage.

Table 3. Radiological Outcomes by Stage

Stage	Improved	Stable	Progressed	THA
I	10 (71.4%)	4 (28.6%)	0	0
II	16 (55.2%)	7 (24.1%)	6 (20.7%)	0
III	3 (20.0%)	6 (40.0%)	6 (40.0%)	6

Safety and Complications

The procedure was generally well tolerated.

- Mild pain at aspiration site: 9 patients (19.5%)
- Transient swelling at injection site: 6 patients (13%)
- No infections
- No thrombotic events
- No neurovascular injury
- No systemic adverse reactions to repeated bone-marrow aspiration

No patient discontinued follow-up due to adverse events.

Patient Satisfaction

At 24 months:

- Very satisfied: 28 patients (60.8%)
- Satisfied: 12 patients (26%)
- Neutral: 4 patients (8.6%)
- Dissatisfied: 2 patients (4.3%)

DISCUSSION

Avascular necrosis of the femoral head (AVNFH) remains a complex orthopedic problem in which mechanical failure of subchondral bone intersects with profound biological dysfunction involving microvascular compromise, inflammatory cytokine imbalance, and impaired osteogenic signaling [11]. While total hip arthroplasty (THA) offers reliable outcomes for advanced disease, preserving the native joint—particularly in young and middle-aged patients—continues to be a critical clinical priority. In this context, regenerative strategies utilizing autologous bone marrow mononuclear cells (BMMCs) and mesenchymal stem cells (MSCs) have gained increasing global attention. The present single-center Iraqi study contributes important evidence to this emerging field by demonstrating that sequential, or "reutilized," bone-marrow–derived stem cell augmentation can meaningfully improve pain, functional capacity, and radiological stability across a two-year follow-up period [12].

The results of this study align with a growing body of literature supporting biological augmentation as an effective intervention in early-stage AVNFH. Previous studies have reported favorable outcomes following a single dose of BMAC or MSCs combined with core decompression, with improvement rates ranging from 60% to 80% depending on disease stage, patient phenotype, and injection technique [13–17]. Our findings reinforce this evidence while introducing an important refinement: reutilization of autologous stem-cell therapy through staged injections at 3 and 6 months. This approach reflects a practical response to the known biological challenges of AVNFH, including ongoing ischemia, persistent inflammatory signaling, and the limited duration during which transplanted cells remain active within the necrotic bone environment [18].

A notable outcome in the current study is the substantial and sustained improvement in VAS and HHS scores across all stages, with a mean HHS increase of nearly 30 points at 24 months. The magnitude of functional recovery suggests that sequential reinforcement of the biological milieu may extend the therapeutic window beyond what is typically expected from a single injection. While the mechanisms underlying this improved response were not directly investigated, it is plausible that repeated marrow aspiration provides fresh pools of progenitor cells, growth factors, and cytokines capable of re-stimulating angiogenesis and osteogenesis at critical intervals. Additionally, repeated injections without repeat drilling minimize procedural trauma and preserve the integrity of the decompressed tract [19-21].

Radiologically, the study demonstrated that 79.3% of hips exhibited either improvement or stabilization, with only advanced Stage III disease showing significant progression. This stage-dependent pattern aligns with established natural history models indicating that once structural collapse has initiated, biological treatments alone are unlikely to reverse the biomechanical damage. Nevertheless, even in Stage III hips, 40% remained stable at 24 months—an encouraging result given that these patients represented the highest-risk category and are traditionally expected to progress to THA. The 10.3% conversion rate to THA, confined exclusively to Stage III, compares favorably with global reports of 20–35% THA rates following single-dose stem-cell therapy in similar populations [22].

The differential outcomes across etiological subgroups deserve specific discussion. Idiopathic and steroid-induced AVNFH showed favorable responses, while patients with sickle cell disease had more limited improvement [23]. This is consistent with biological expectations: sickle cell disease presents a persistent microvascular pathology characterized by ongoing vaso-occlusion, chronic inflammation, and repeated ischemia-reperfusion injury, all of which undermine regenerative efforts. The current data suggest that while stem-cell reutilization is beneficial across etiologies, expectations should be more guarded in hemoglobinopathy-related AVN, and multimodal strategies—including disease-modifying therapy, hydroxyurea optimization, and aggressive vascular management—may be needed [24].

The technical aspects of the stem-cell preparation protocol also warrant reflection. The decision to employ a simple, non-Ficoll, double-spin preparation reflects an intentional effort to maintain cell viability and avoid excessive processing. Several reports have indicated that Ficoll separation, while generating a cleaner mononuclear cell fraction, may also result in significant cell loss and increased manipulation, which may not be necessary for the osteogenic effect targeted in AVNFH. Our simplified protocol produced a concentrated BMMC layer rich in progenitors, platelets, and soluble factors—possibly enhancing both the paracrine and direct regenerative effects. This positions the technique as particularly suitable for low-resource settings, where access to advanced cell-processing facilities may be limited [25-28].

The strength of this study lies in its methodological consistency. Unlike multicenter studies where surgical techniques, imaging protocols, and processing workflows vary, our single-center design ensured uniform application of core decompression, marrow aspiration, centrifugation parameters, and injection technique [29-30]. Moreover, all MRI evaluations were performed by blinded radiologists, reducing the risk of subjective bias. The extended 24-month follow-up provides a realistic assessment of medium-term therapeutic durability, bridging the gap between short-term symptom relief and long-term structural preservation [31-32].

Despite these strengths, several limitations must be acknowledged. First, this was a single-arm study without a control group receiving either decompression alone or single-dose therapy. While ethical considerations in our patient population made conservative management difficult to justify, future randomized studies are needed to quantify the incremental benefit attributable specifically to reutilization. Second, although MRI lesion size and edema were systematically measured, quantitative volumetric assessment or T2 mapping would provide more detailed insights into biological healing [33]. Third, bone marrow aspirate quality may vary by patient, and cellular composition was not analyzed beyond standard viability testing. Future work incorporating flow cytometry or colony-forming assays could help correlate specific cellular subtypes with clinical outcomes [34].

Another important limitation concerns the lack of biomechanical evaluation. While radiographic stabilization is encouraging, subchondral microarchitecture may continue to deteriorate despite a stable external contour [35-40]. Advanced imaging such as dGEMRIC, 3D T1ρ, or quantitative CT could provide deeper insight into the structural resilience of treated hips. Additionally, although the reutilization strategy appears safe, repeated marrow aspiration may not be tolerated by all patients. In our cohort, complications were minimal, but larger samples are needed to establish long-term safety [41-46].

An intriguing direction for future research involves combining stem-cell reutilization with adjunctive biological agents such as extracorporeal shockwave therapy, bisphosphonates, statins, or PRP. Integrating perfusion-enhancing therapies may further amplify the angiogenic response induced by marrow cells. Moreover, with the emergence of point-of-care MSC enrichment devices and microfracture-assisted decompression systems, the therapeutic landscape continues to evolve rapidly, creating opportunities for hybrid protocols.

This study provides strong evidence that sequential autologous BMMC reutilization, delivered through a standardized protocol in a single Iraqi center, is safe, feasible, and effective in altering the clinical course of early and mid-stage AVNFH. Pain relief, functional recovery, and high radiological preservation rates were observed across nearly all patients, with THA requirements limited to those presenting with advanced structural compromise. These findings support the integration of staged biological reinforcement into AVNFH management guidelines and offer a cost-conscious, resource-appropriate model for regenerative orthopedic practice in similar healthcare settings. Continued research—including randomized comparisons, mechanistic studies, and long-term follow-up—is essential to refine patient selection criteria and optimize treatment algorithms. However, based on the available evidence, reutilized stem-cell therapy constitutes a promising step toward more durable, joint-preserving interventions for AVNFH.

CONCLUSION

In this prospective single-center study, the reutilization of autologous bone-marrow–derived mononuclear cells demonstrated meaningful and sustained therapeutic benefit for patients with early and mid-stage avascular necrosis of the femoral head. Sequential cell reinforcement at 3- and 6-month intervals, combined with standardized core decompression and a simplified non-Ficoll processing technique, resulted in substantial reductions in pain, marked functional improvement, and high rates of radiological stabilization over a 24-month period. Importantly, the need for total hip arthroplasty was limited to advanced Stage III cases, underscoring the value of timely biologic intervention before subchondral collapse becomes irreversible. The results support the concept that AVNFH is a dynamic pathological process that may require repeated biological stimulation rather than a single treatment event. Reutilizing fresh autologous bone marrow appears to sustain osteogenic and angiogenic activity within the necrotic region, enhancing the durability of clinical response. The technique—safe, well-tolerated, and feasible in a resource-limited healthcare environment—also offers a practical regenerative option for centers without access to advanced cell-processing laboratories.

Overall, reutilized stem-cell therapy represents a promising joint-preservation strategy capable of altering the natural course of AVNFH when applied during early and intermediate stages. Larger, controlled studies with extended follow-up and more detailed biological characterization are warranted to further define its role, optimize patient selection, and refine procedural protocols. Nonetheless, the findings from this Iraqi single-center experience provide strong foundational evidence supporting the integration of staged biologic reinforcement into contemporary AVNFH management.

DECLARATIONS

Ethical Approval

This study was conducted in accordance with the ethical standards of the Scientific and Ethical Committee of Al-Iraqi Hospital, Najaf, Iraq, and adhered to the principles of the Declaration of Helsinki. Ethical approval was obtained prior to patient enrollment, and all procedures—including bone marrow aspiration, core decompression, and stem-cell reinjection—were performed in compliance with institutional clinical safety regulations.

Funding

This research received no external funding. All procedural costs, imaging studies, and laboratory work were supported by internal operational resources of Al-Iraqi Hospital, Najaf, as part of its ongoing clinical development initiatives in regenerative orthopedics.

Conflict of Interest Statement

The author declares no conflicts of interest related to the design, execution, interpretation, or publication of this study. No author has financial or personal relationships that could inappropriately influence the submitted work.

Data Availability

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request. Due to patient confidentiality and hospital policy, raw MRI images and identifying clinical records cannot be publicly released but may be shared in anonymized form upon formal approval from the institutional ethics committee.

Inform consent

Written informed consent was obtained from all participating patients after full explanation of the study purpose, procedures, potential risks, and expected benefits. Patients were informed of their right to withdraw at any point without affecting their clinical care.

REFERENCES

1. Mont MA, Cherian JJ, Sierra RJ, Jones LC, Lieberman JR. Nontraumatic osteonecrosis of the femoral head: where do we stand today? A ten-year update. *J Bone Joint Surg Am.* 2015;97(19):1604-1627.
2. Zalavras CG, Lieberman JR. Osteonecrosis of the femoral head: evaluation and management. *J Am Acad Orthop Surg.* 2014;22(7):455-464.
3. Moya-Angeler J, Gianakos AL, Villa JC, Ni A, Lane JM. Current concepts on osteonecrosis of the femoral head. *World J Orthop.* 2015;6(8):590-601.

4. Hernigou P, Poignard A, Beaujean F, Rouard H. Percutaneous autologous bone-marrow grafting for nontraumatic osteonecrosis of the femoral head. *J Bone Joint Surg Am.* 2002;84(9):1598-1603.
5. Hernigou P, Beaujean F. Treatment of osteonecrosis with autologous bone marrow grafting. *Clin Orthop Relat Res.* 2002;(405):14-23.
6. Gangji V, Hauzeur JP. Cellular-based therapy for osteonecrosis. *Orthop Clin North Am.* 2009;40(2):213-221.
7. Zhao D, Cui D, Wang B, et al. Treatment of early stage osteonecrosis of the femoral head with autologous bone-marrow-derived cells injection. *Bone.* 2012;50(1):325-330.
8. Rastogi S, Sankineani SR, Nag HL, et al. Intralesional autologous mesenchymal stem cells for the treatment of osteonecrosis of the femoral head: a pilot study. *J Bone Joint Surg Br.* 2013;95(1):135-140.
9. Gangji V, De Maertelaer V, Hauzeur JP. Autologous concentrated bone marrow injection for the treatment of osteonecrosis of the femoral head. *Bone.* 2008;43(2):342-349.
10. Luo RB, Lin T, Zhong HM, Yan SG, Wang JA. Evidence for using porous tantalum implants in early-stage femoral head osteonecrosis: a systematic review and meta-analysis. *BMC Musculoskelet Disord.* 2016;17:144.
11. Liu Y, Liu S, Su X, et al. Stromal cell–derived factor-1 promotes angiogenesis via the CXCR7 pathway in osteonecrosis of the femoral head. *J Orthop Res.* 2020;38(3):539-548.
12. Chen Y, Zhang X, Wang W, et al. Core decompression combined with concentrated bone marrow transplantation for treatment of osteonecrosis of femoral head in different ARCO stages. *J Arthroplasty.* 2019;34(9):1690-1696.
13. Mao Q, Wang W, Xu T, et al. Combination therapy of biomaterials and stem cells for osteonecrosis of the femoral head: current clinical applications and future directions. *Stem Cell Res Ther.* 2020;11:115.
14. Hauzeur JP, De Maertelaer V, Gangji V. Inefficacy of core decompression for stage III osteonecrosis of the femoral head. *Clin Orthop Relat Res.* 2008;466(5):1148-1152.
15. Nishida K, Yamamoto T, Motomura G, et al. Pitfalls of core decompression for osteonecrosis of the femoral head. *Clin Orthop Surg.* 2019;11(3):288-294.
16. Agarwala S, Shah SB. Ten-year follow-up of avascular necrosis of femoral head treated with extracorporeal shock wave therapy and alendronate. *J Orthop Surg Res.* 2021;16:340.
17. Hernigou P, Hernigou J, Scarlat MM, et al. Natural history of pre-collapse osteonecrosis of the femoral head with decreased mesenchymal stem cells. *Int Orthop.* 2018;42(7):1429-1435.
18. Kuroda Y, Matsuda S. A paradigm shift in osteonecrosis treatment: cell therapy development and future perspective. *J Orthop Sci.* 2021;26(1):38-44.
19. Wang JT, Peng H, Zeng BF. Steroid-induced osteonecrosis of the femoral head: pathogenesis and diagnosis. *Orthop Surg.* 2012;4(1):71-78.
20. Houdek MT, Wyles CC, Collins MS, et al. Early osteonecrosis of the femoral head in sickle cell disease. *Bone Joint J.* 2017;99-B(8):1066-1070.

21. Mont MA, Zywiel MG, Marker DR, McGrath MS, Delanois RE. The natural history of untreated asymptomatic osteonecrosis of the femoral head. *J Bone Joint Surg Am.* 2010;92(12):2165-2170.
22. Papanikolaou A, Babis GC. Mesenchymal stem cells: a new therapy for hip osteonecrosis? *Expert Opin Biol Ther.* 2019;19(11):1137-1144.
23. Rodriguez-Fontan F, Piuzzi NS. Autologous biologics for the treatment of early-stage osteonecrosis of the femoral head: a systematic review. *J Hip Preserv Surg.* 2021;8(2):156-170.
24. Hernigou J, Flouzat-Lachaniette CH, Delambre J, et al. Stem cell therapy versus contralateral side in bilateral osteonecrosis of the femoral head. *Int Orthop.* 2018;42(7):1567-1575.
25. Ito H, Matsuno T, Minami A. Nontraumatic osteonecrosis of the femoral head: pathophysiology and current treatment. *J Orthop Sci.* 2016;21(1):1-7.
26. Lieberman JR, Berry DJ, Mont MA, et al. Osteonecrosis of the hip: management in the twenty-first century. *Instr Course Lect.* 2003;52:337-355.
27. Shah KN, Racine J, Jones LC, Aaron RK. Pathophysiology and risk factors for osteonecrosis. *Curr Rev Musculoskelet Med.* 2015;8(3):201-209.
28. Steinberg ME, Larcom PG. Core decompression for osteonecrosis: outcomes of 400 hips. *Clin Orthop Relat Res.* 2004;418:40-46.
29. Kim HKW. Osteonecrosis in adolescents and young adults: etiology and early treatment. *J Pediatr Orthop.* 2011;31(7):S176-S180.
30. Chan YS, Shih CH. The role of core decompression in marrow ischemia of the femoral head. *Clin Orthop Relat Res.* 1996;323:181-190.
31. Liu B, Li T, Zhang X. Mid-term outcomes of PRP combined with core decompression for AVN of the femoral head. *Medicine (Baltimore).* 2020;99(3):e18803.
32. Piuzzi NS, Khlopas A, Chughtai M, et al. Stem cells in orthopedics: a comprehensive review. *Am J Orthop.* 2017;46(6):E333-E342.
33. Green CJ, Nolan JF, Khanduja V. The role of biologics in osteonecrosis of the femoral head: a systematic review. *Hip Int.* 2020;30(1):3-11.
34. Hernigou P, Trousselier M, Roubineau F, et al. Bone marrow cell therapy: from bench to bedside. *Stem Cells Int.* 2019;2019:3085146.
35. Tabatabaee RM, Saberi S, Parvizi J, et al. Combined core decompression and cell therapy for osteonecrosis. *J Arthroplasty.* 2015;30(9 Suppl):11-15.
36. Sen RK. Management of avascular necrosis of femoral head. *Indian J Orthop.* 2009;43(1):6-16.
37. Yoon BH, Mont MA, Koo KH, et al. The 2019 Asian Hip Society guidelines for osteonecrosis of the femoral head. *Bone Joint J.* 2019;101-B(7):852-859.
38. Yousif NG, Liu P, Al-Amran F, et al. Therapeutic use of hematopoietic mesenchymal stem cells in osteoarthritis: a meta-analysis study. *Muthanna Medical Journal*. 2023; 10(2): 173-188.
39. Kang JS, Moon KH, Kim BS, et al. Autologous bone marrow cell infusion for the treatment of osteonecrosis of the femoral head. *Bone Marrow Transplant.* 2010;45(7):955-960.

Pathophysiology of Cell Injury Journal (PCIJ)
E-ISSN: 2378-5225 · Frequency: Biannual · DOI Prefix: 10.18081/2378-5225
Publisher: BM-Publisher (London, UK) · Open Access

Volume 14, Issue 2, Pages 180–197 | December 2025

40. Seyler TM, Marker DR, Ulrich SD, et al. Nonvascularized bone grafting for osteonecrosis. *J Bone Joint Surg Am.* 2008;90(Suppl 3):111-122.
41. Padgett DE, Koff MF. Management of osteonecrosis: early diagnosis is the key. *Orthopedics.* 2018;41(1):e1-e8.
42. Zhao DW, Hu YC. Clinical analysis of 117 cases of osteonecrosis treated with stem cells. *Orthop Surg.* 2009;1(3):197-203.
43. Shah KN, Racine J, Jones LC. Sickle cell disease-associated osteonecrosis. *Orthop Clin North Am.* 2020;51(2):139-149.
44. Daltro G, Franco P, Costa L, et al. Cell therapy for femoral head osteonecrosis: a review of current clinical evidence. *Regen Med.* 2021;16(7):639-651.
45. Agarwala S, Vijayvargiya M, Bargal A, et al. A 10-year follow-up study of osteonecrosis treated with bisphosphonates. *J Arthroplasty.* 2019;34(7):1385-1390.
46. Kuroda R, Ohnishi T, Matsumoto T, et al. Clinical application of regenerative therapy in femoral head osteonecrosis. *Orthop Clin North Am.* 2019;50(2):187-195.

GRAPHICAL ABSTRACT