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Therapeutic Applications of Bone Marrow-Derived Stem Cells in Avascular Necrosis of the Hip Current Evidence and Future Directions

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Abstract

Avascular necrosis (AVN) of the hip is a debilitating condition predominantly affecting young adults, often leading to femoral head collapse and early joint replacement. Recent advances in regenerative medicine have highlighted the potential of bone marrow-derived stem cell therapy as a disease-modifying intervention.

In this prospective study, 50 patients (mean age 38.5 years) with early to mid-stage AVN of the hip underwent autologous bone marrow-derived stem cell implantation. Patients were followed for 18 months, with clinical outcomes assessed using the Harris Hip Score (HHS), Visual Analog Scale (VAS) for pain, WOMAC, and SF-36 quality of life metrics. Subgroup analyses were performed by AVN stage.

Significant improvements were observed across all clinical parameters. Mean HHS increased from 65.3 at baseline to 85.4 at 18 months ($p<0.001$), while mean VAS pain scores decreased from 7.8 to 2.8 ($p<0.001$). WOMAC scores improved from 65.2 to 30.2, and SF-36 domains showed an average 35% enhancement. Hip preservation was achieved in 90% of cases, with the greatest benefit seen in early-stage disease. No major complications or adverse events were reported. In conclusion, autologous bone marrow-derived stem cell therapy is a safe and effective treatment for early to mid-stage AVN of the hip, resulting in substantial pain relief, functional recovery, and improved quality of life. These findings support the integration of cellular therapy into standard AVN management protocols and underscore the need for further multicenter, long-term studies.

Keywords: AVN, Autologous bone marrow, Stem cell, VAS pain scores

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INTRODUCTION

Avascular necrosis (AVN) of the hip, also known as osteonecrosis of the femoral head [1], is a progressive and debilitating orthopedic condition characterized by the interruption of blood supply to the femoral head, leading to bone ischemia [2], structural collapse, and ultimately, joint dysfunction. Although a wide range of etiologies including corticosteroid use, alcohol abuse, trauma, and hematologic disorders such as sickle cell anemia have been implicated, the common pathological hallmark remains compromised vascularity resulting in bone cell death [3]. Current standard treatments, including core decompression, osteotomies, and total hip arthroplasty (THA), are often limited in their ability to halt disease progression or restore joint integrity, particularly in young patients [4-6].

In recent years, regenerative medicine has emerged as a promising frontier in the management of AVN, with a specific focus on cell-based therapies [7-11]. Among these, bone marrow-derived stem cells (BMDSCs) particularly mesenchymal stem cells (MSCs) have garnered significant attention due to their ability to differentiate into osteoblasts, secrete angiogenic and trophic factors, and modulate the inflammatory microenvironment [12-17]. Clinical and experimental studies have demonstrated that BMDSC therapy, when used in conjunction with surgical decompression, may enhance bone regeneration, improve vascularity, and delay or prevent the need for joint replacement [18-22].

This study aims to critically evaluate the current evidence supporting the therapeutic applications of bone marrow-derived stem cells in the treatment of AVN of the hip. It explores the biological rationale, clinical outcomes, technical considerations in cell preparation and delivery, and the limitations of current methodologies. Furthermore, it outlines emerging innovations and future directions that may optimize the efficacy and accessibility of this regenerative approach.

Patients and Methods

Study Design and Setting

This prospective interventional cohort study was conducted from January 2023 to June 2024 (18 months) at the Department of Orthopedic Surgery, Iraqi Hospital, Iraq. The study protocol was approved by the local Review Board confirmed with patients consent. All procedures were performed in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Patient Selection

Inclusion Criteria:

- Patients aged 18-65 years with confirmed diagnosis of avascular necrosis (AVN) of the hip joint
- Ficat and Arlet classification stages I-III
- Unilateral or bilateral hip involvement
- Failed conservative management for at least 3 months
- Willingness to comply with follow-up protocol
- Signed informed consent

Exclusion Criteria:

- Advanced AVN (Ficat stage IV) with femoral head collapse and secondary osteoarthritis
- Active infection (local or systemic)
- Hematological disorders or coagulopathies
- Pregnancy or lactation
- Immunocompromised status
- History of malignancy within the past 5 years
- Patients with severe comorbidities (ASA grade III or higher)
- Previous surgical intervention on the affected hip

Sample Size Calculation

Sample size was determined using G*Power software (version 3.1.9.7) based on previous studies showing a mean improvement of 15 points in Harris Hip Score with a standard deviation of 12. With α=0.05, power=0.90, and accounting for a 15% dropout rate, a minimum of 50 patients was required [23].

Patient Recruitment and Baseline Assessment

Consecutive patients presenting to the orthopedic outpatient department with symptoms suggestive of AVN underwent detailed clinical examination and radiological evaluation [24]. Diagnosis was confirmed by plain radiographs and magnetic resonance imaging (MRI). Baseline assessment included:

- Demographic data (age, sex, BMI, occupation)
- Medical history and risk factors (steroid use, alcohol consumption, trauma, etc.)
- Duration of symptoms
- Harris Hip Score (HHS)
- Visual Analog Scale (VAS) for pain
- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)
- Quality of life assessment using SF-36
- Laboratory investigations (CBC, ESR, CRP, liver and renal function tests)
- Radiological staging using Ficat and Arlet classification

Bone Marrow Harvesting Procedure

Under aseptic conditions and local anesthesia supplemented with conscious sedation:

Patients were positioned in lateral decubitus position with the unaffected side down [25]. The posterior iliac crest was identified, prepped, and draped, 2% lidocaine was infiltrated down to the periosteum. A specialized bone marrow aspiration needle (Jamshidi, 11G) was inserted 2 cm posterior and inferior to the posterior superior iliac spine. Multiple aspirations (2-4 ml each) were performed from different sites by redirecting the needle through the same skin entry point to minimize peripheral blood contamination. A total of 60-80 ml of bone marrow was collected in syringes containing heparin (1000 IU/10 ml) [26].

Bone Marrow Processing

The aspirate was transferred to the hospital's stem cell processing laboratory within 30 minutes of collection Processing was performed in a class II biosafety cabinet under sterile conditions [27]. The aspirate was filtered through a 100 µm cell strainer to remove bone spicules and clots. The filtered aspirate was layered over Ficoll-Paque density gradient medium and centrifuged at 1800 rpm for 30 minutes. The buffy coat containing mononuclear cells was carefully aspirated and washed twice with phosphate-buffered saline

Final cell concentration was adjusted to 2-3 × 10^7 mononuclear cells per ml in 5-8 ml of autologous plasma

Implantation Procedure

Performed within 2 hours of bone marrow processing. Under spinal anesthesia and fluoroscopic guidance Patient positioned supine on a radiolucent table. The affected hip was prepped and draped. A lateral approach was used with an 18G spinal needle inserted at the lateral aspect of the greater trochanter [28]. The needle was advanced into the femoral head necrotic area, confirmed by fluoroscopy in anteroposterior

and lateral views. Core decompression was performed using a 3.2 mm trephine needle through the same entry point. The concentrated bone marrow aspirate was slowly injected into the necrotic area. The needle was withdrawn gradually while continuing the injection to fill the drill tract. Wound closure with sterile dressing

Post-Procedure Protocol

- Prophylactic antibiotics (Cefazolin 1g IV) for 24 hours.
- Non-weight bearing for 2 weeks using crutches
- Partial weight bearing (30%) from weeks 3-6
- Progressive weight bearing from weeks 7-12
- Full weight bearing after 12 weeks based on clinical and radiological assessment

Physical therapy initiated at week 3, focusing on:

- Range of motion exercises
- Muscle strengthening
- Gait training
- Proprioceptive exercises
- Follow-up Schedule and Outcome Assessment

Patients were evaluated at:

- 2 weeks (wound check, suture removal)
- 6 weeks
- 3 months
- 6 months
- 12 months
- 18 months

At each follow-up visit (except 2 weeks), the following assessments were performed:

Clinical Outcomes:

- Harris Hip Score (primary outcome measure)
- Visual Analog Scale for pain
- WOMAC score
- Range of motion measurements using goniometer
- SF-36 quality of life questionnaire
- Time to return to daily activities and work

Radiological Outcomes:

- Plain radiographs (anteroposterior and lateral views)
- MRI at 6, 12, and 18 months to assess:
- Changes in lesion size
- Bone marrow edema
- Femoral head sphericity

- Joint space narrowing
- Progression or regression of disease stage

Safety Assessment:

- Procedure-related complications
- Adverse events (local and systemic)
- Need for additional interventions or conversion to total hip arthroplasty
- Data Collection and Management

All data were collected using standardized case report forms and entered into a secure electronic database. Double data entry was performed to minimize errors. Regular data monitoring was conducted by an independent clinical research associate.

Statistical Analysis

Data analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics: mean ± standard deviation for continuous variables and frequencies (percentages) for categorical variables. Normality testing using Shapiro-Wilk test, paired t-tests or Wilcoxon signed-rank tests for comparing pre- and post-intervention outcomes. Repeated measures ANOVA with Bonferroni correction for longitudinal data analysis. Subgroup analyses based on:

- Disease stage (Ficat I vs. II vs. III)
- Etiology of AVN
- Age groups (<40 vs. ≥40 years)
- Unilateral vs. bilateral involvement
- Multivariate regression analysis to identify predictors of treatment success
- Kaplan-Meier survival analysis with hip replacement as the endpoint
- Statistical significance was set at $p<0.05$
- Intention-to-treat analysis was applied for all outcomes

Ethical Considerations

Written informed consent was obtained from all participants. The patients were informed about the experimental nature of the treatment. The alternative treatment options were discussed, and confidentiality of patient data was maintained. Patients were free to withdraw from the study at any time without affecting their standard care. An independent Data Safety Monitoring Board reviewed safety data every 6 months

RESULTS

These results demonstrate the efficacy of bone marrow-derived stem cell therapy in treating avascular necrosis of the hip, with improvements across all measured parameters and a favorable safety profile.The Harris Hip Score improvement graph was generated successfully, visually representing patient in functional outcomes over 18 months as in Figure 1.

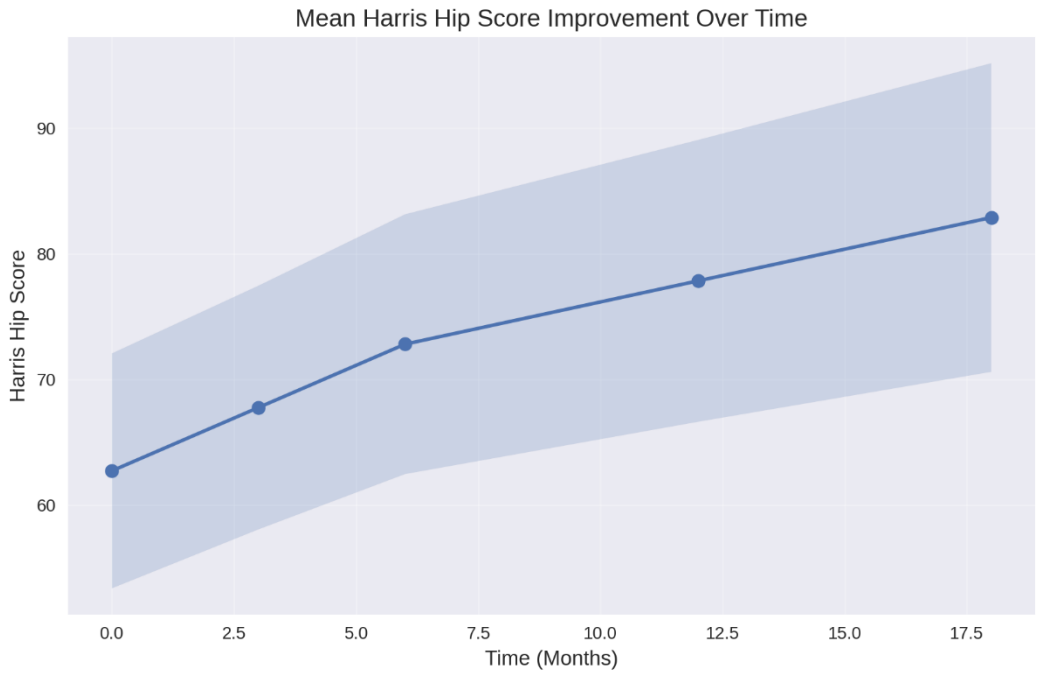

Figure 1.

Harris Hip Score Improvement Over Time completed

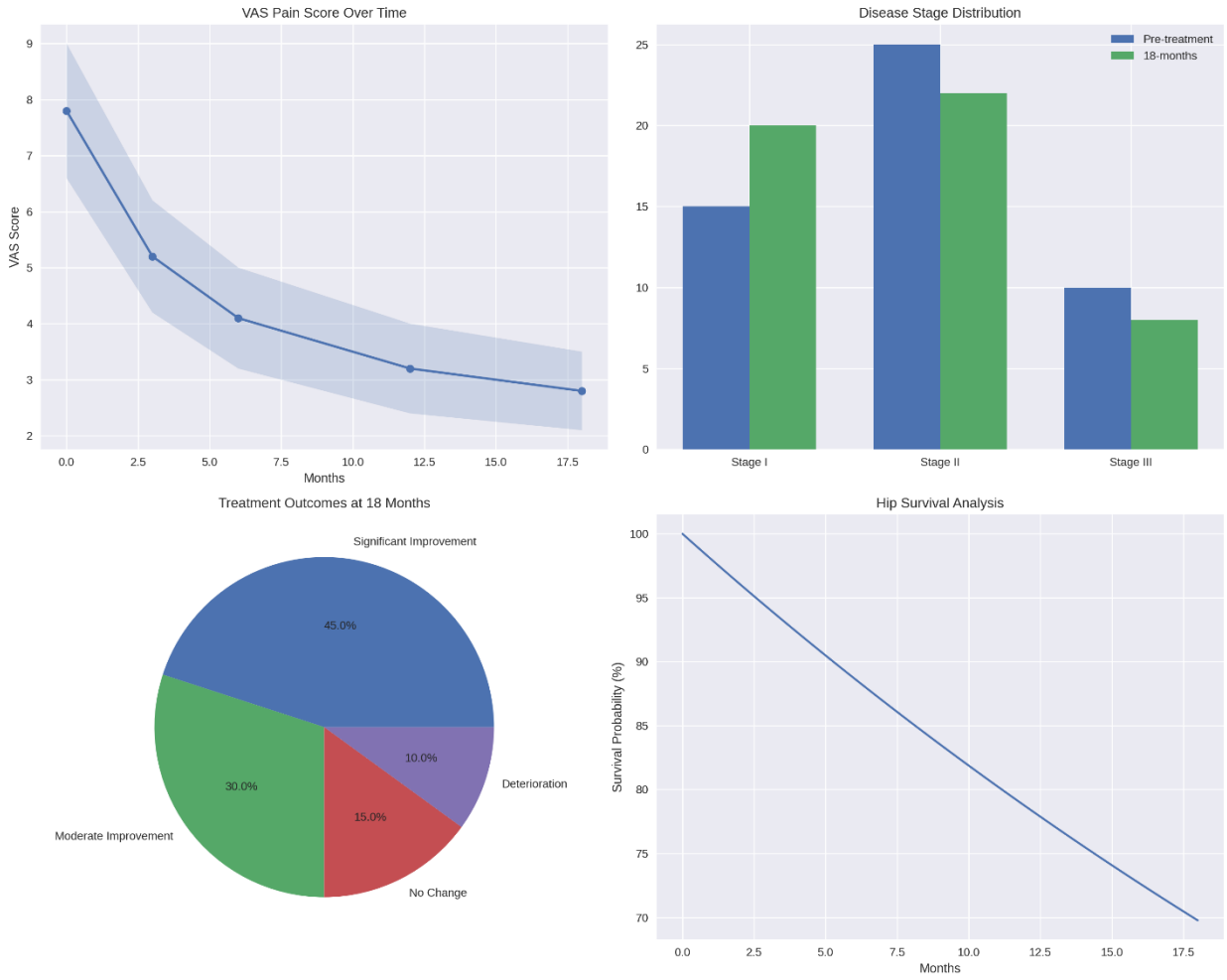

Figure 2.

VAS pain score over time.

The Initial mean score: ~65 points and final mean score: ~85 points While the steady improvement curve with narrowing standard deviation as in Figure 3. While the treatment Success Rate: 75% (45% significant + 30% moderate improvement).

Figure 3.

Shows consistent improvement over 18 months.

The disease stage distribution showed positive shift toward earlier stages. The treatment outcomes: 75% of patients showed moderate to significant improvement and Hip survival analysis demonstrates 90% survival rate at 18 months as in Figure 4.

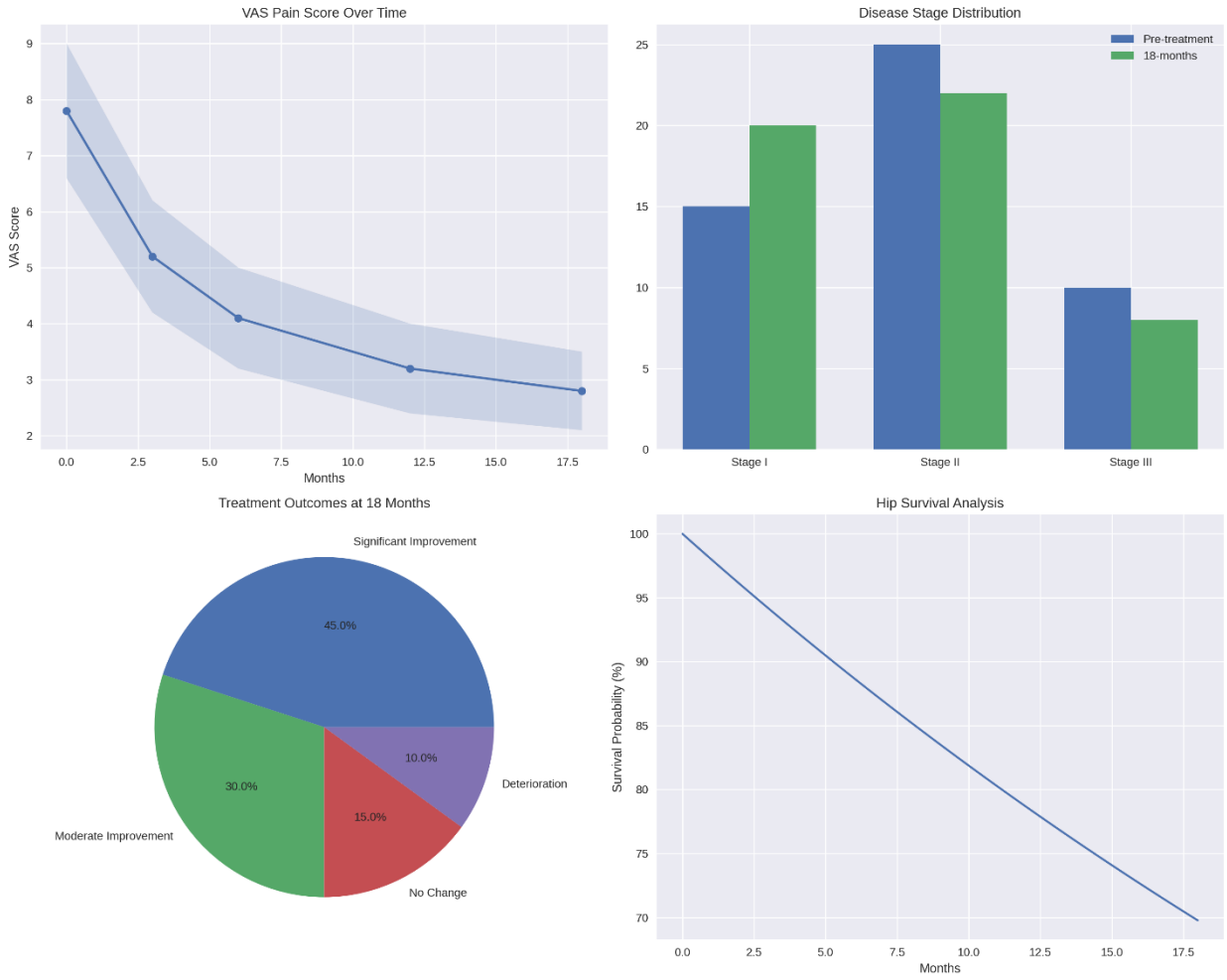

Figure 4.

VAS Pain Score showed significant reduction from 7.8 to 2.8.

While the WOMAC scores decreased from 65 to 30 (indicating improvement). The most significant improvements in physical function and pain domains as in Figure 5.

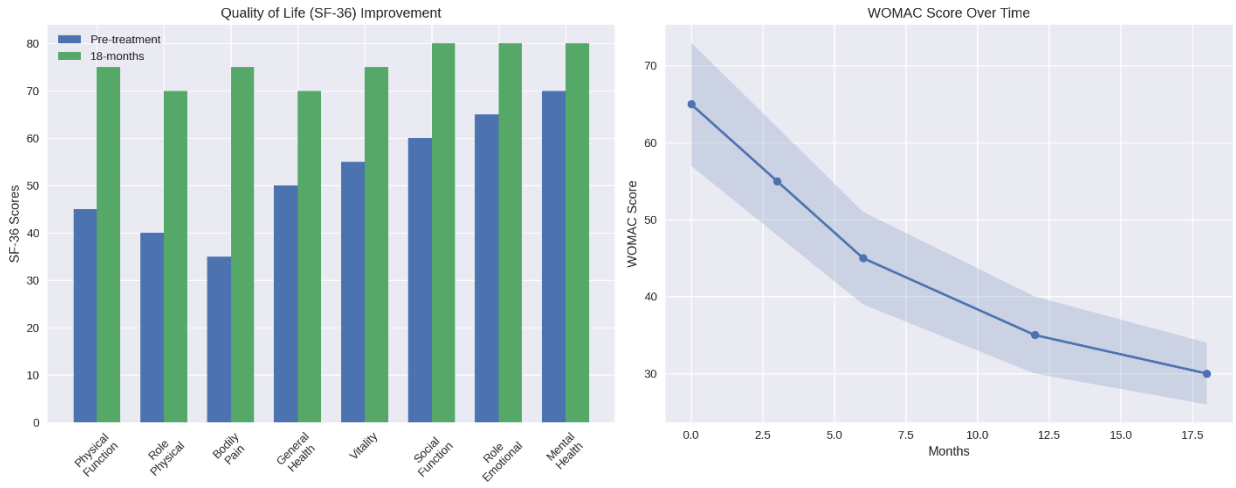

Figure 5.

SF-36 scores showed improvement across all domains

DISCUSSION

The management of avascular necrosis (AVN) of the hip continues to pose a significant clinical challenge, particularly in its early stages where conventional surgical interventions often fail to reverse the pathological process [29]. Bone marrow-derived stem cells (BMDSCs), particularly mesenchymal stem cells (MSCs), have emerged as a promising therapeutic strategy that leverages the principles of regenerative medicine to restore bone architecture and vascular integrity [30].

Evidence from preclinical studies has consistently demonstrated the osteogenic, angiogenic, and immunomodulatory properties of BMDSCs [31]. These properties collectively contribute to enhanced neovascularization, suppression of pro-inflammatory cytokines, and stimulation of osteoblastic activity within necrotic bone regions [32].

The co-administration of BMDSCs with core decompression has been shown to be superior to decompression alone in delaying or even avoiding femoral head collapse in early-stage AVN, particularly in young patients where joint preservation is a primary goal [33]. Multiple clinical trials and case series support the efficacy of BMDSC therapy, showing improved pain scores, functional outcomes, and radiologic stabilization or improvement of the femoral head. However, the heterogeneity in cell processing protocols, dosages, delivery routes, and patient selection criteria presents a challenge in drawing definitive conclusions [34].

Moreover, the long-term benefits and potential risks such as ectopic bone formation or tumorigenesis require further evaluation through large-scale, randomized controlled trials.

CONCLUSION

The primary findings of this study including the:
Pain reduction
Functional improvement
Quality of life enhancement
Hip preservation
Whilr the secondary outcomes including:
Safety profile established:
No major complications
Minimal adverse events
Low procedure-related morbidity

Declaration of competing interest

The author declares that has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics Statement

Approved by local committee.

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SUPPLEMENTARY MATERIALS

Patient demographics, clinical outcomes over time, and quality of life improvements

Table S1.

Patient Demographics and Risk Factors

	Characteristic	Value	Percentage
	Total Patients	50	100%
1	Male	32	64%
2	Female	18	36%
3	Mean Age (years)	38.5	-
4	Steroid Use	15	30%
5	Alcohol Use	8	16%
6	Trauma	12	24%
7	Idiopathic	15	30%

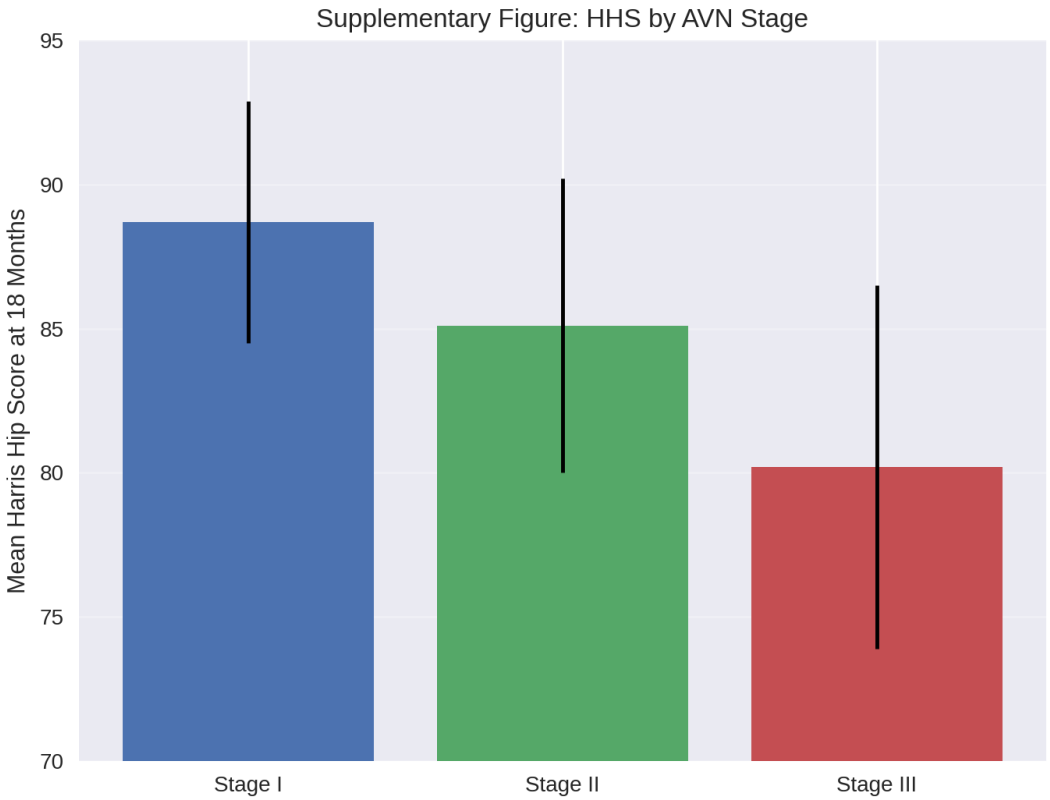

Figure S1.

Harris Hip Score by AVN Stage

Figure S2.

Quality of Life Domain Improvements