

Review Article

Clinical Guideline for Non-Surgical Treatment of Osteonecrosis of the Femoral Head (2025 Edition)

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Abstract

Background: Osteonecrosis of the femoral head (ONFH) is a prevalent and refractory condition in orthopedic clinical practice. In recent years, an increasing number of patients have been diagnosed in the early stages of the disease. Consequently, traditional surgical interventions alone can no longer satisfy current clinical needs, highlighting the urgent demand for effective non-surgical management strategies. **Objective:** This guideline aims to provide a standardized framework for the non-surgical treatment of ONFH. It focuses on how to rationally and effectively apply these methods to delay disease progression, improve hip joint function, postpone or even avoid surgery, and ultimately achieve the goal of hip preservation. **Methods:** This guideline systematically evaluates and synthesizes evidence on the application of various non-surgical treatment modalities in the prevention and management of ONFH. These modalities include general therapy, pharmacotherapy, physical therapy, traditional Chinese medicine, minimally invasive interventions, and rehabilitation. **Conclusion:** The rational and evidence-based application

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of non-surgical treatments is of great significance for patients with early-stage ONFH. By following this guideline, clinicians can develop individualized, comprehensive non-surgical regimens that effectively control risk factors, alleviate symptoms, retard the collapse of the femoral head, preserve native hip function, and improve patients' quality of life, thereby reducing the long-term need for hip arthroplasty.

Keywords

Osteonecrosis of the Femoral Head, Non-Surgical Treatment, Therapeutics, Guideline

1. Introduction

Osteonecrosis of the femoral head (ONFH) is a common and frequently occurring clinical disease that often causes hip joint pain and functional impairment, with a high disability rate. In recent years, its incidence has been increasing. Late-stage patients often require total hip arthroplasty (THA), placing a heavy burden on patients, families, and society. Therefore, at the early stage of ONFH, receiving standardized, individualized non-surgical treatment, including platelet-rich plasma (PRP), extracorporeal shock wave therapy (ESWT), ozone therapy, and cell therapy, can significantly delay disease progression, improve hip joint function, and postpone or even avoid surgery, which is of great significance to ONFH patients.

Although previously published expert consensus and clinical guidelines [1-14] on ONFH have greatly promoted the standardization of ONFH diagnosis and treatment, no comprehensive clinical guideline specifically addressing non-surgical treatment of ONFH has been identified. To further enhance clinicians' capacity for standardized ONFH management, the Society of Platelet Rich Plasma Medicine (Chinese Aging Well Association), the Society of Painology (Chinese Aging Well Association), the Shock Wave Medical Professional Committee (Chinese Research Hospital Association), and the Editorial Board of the Chinese Journal of Painology organized experts to jointly formulate this guideline, based on high-level

evidence-based literature published domestically and internationally, combined with domestic clinical experience, following multiple rounds of discussion and revision.

2. Guideline Development Methodology

The literature search period covered from database inception through June 2025. Chinese search terms included: osteonecrosis of the femoral head, avascular necrosis of the femoral head, ischemic necrosis, aseptic necrosis, etc. English search terms included: osteonecrosis of the femoral head, femoral head necrosis, avascular necrosis, aseptic necrosis, etc. Well-known domestic and international databases, including Wanfang, CNKI, PubMed, and Cochrane Library, were systematically searched. Priority was given to high-quality evidence-based literature, including systematic reviews, meta-analyses, randomized controlled trials (RCTs), case-control studies, cohort studies, expert consensus, and clinical guidelines. The GRADE (Grading of Recommendations Assessment, Development and Evaluation) system was used for evidence quality grading and recommendation strength classification (Table 1) [15-17]. After multiple rounds of discussion and online voting, this guideline was finalized.

Table 1. GRADE Evidence Quality Grading and Recommendation Strength.

Grade	Evidence Quality	Description
High (A)	Evidence Quality	Very confident that the estimate is close to the true value
Moderate (B)	Evidence Quality	Moderately confident in the estimate; it is likely close to the true value, but there is a possibility of a substantial difference
Low (C)	Evidence Quality	Limited confidence in the estimate; it may differ substantially from the true value
Very Low (D)	Evidence Quality	Very little confidence in the estimate; it is likely to differ substantially from the true value
Grade	Recommendation Strength	Description
Strong (1)	Recommendation Strength	Most patients would choose the recommended approach; most clinicians should accept it; >70% of expert panel members agree

Grade	Evidence Quality	Description
Weak (2)	Recommendation Strength	Many but not all patients would choose it; clinicians should review evidence with patients; 50–70% of panel members agree
No clear recommendation (3)	Recommendation Strength	Benefits and harms are balanced; insufficient evidence; <50% of panel members agree

GRADE = Grading of Recommendations Assessment, Development and Evaluation

3. Overview

3.1. Definition

ONFH, also known as avascular necrosis or aseptic necrosis of the femoral head, is a pathological process in which venous stasis, impaired or interrupted arterial blood supply to the femoral head leads to death of bone cells and bone marrow components, and subsequent impairment of repair processes. ONFH is a common cause of hip disability, manifesting as persistent hip pain, limited mobility, and reduced quality of life, placing a heavy burden on patients and their families [6].

3.2. Epidemiology

To date, no global epidemiological data on ONFH has been published. ONFH predominantly affects young and middle-aged adults, with peak incidence at 40–50 years of age. In China, the prevalence of non-traumatic ONFH in individuals aged 15 years and above is 0.725% [18], with an overall upward trend [7]. Prevalence is higher in males than females (1.02% vs. 0.51%) and higher in northern than southern China (0.85% vs. 0.61%) [9]. High-risk groups include individuals with alcoholism, steroid abuse, smoking [19], diabetes, and hypercoagulable states.

3.3. Classification and Etiology

ONFH is classified etiologically into traumatic ONFH and non-traumatic ONFH.

3.3.1. Traumatic ONFH

Mainly caused by direct disruption of blood supply to the femoral head due to femoral head fracture, femoral neck fracture, acetabular fracture, hip dislocation, or severe hip sprain or contusion. It predominantly affects young adults with a clear history of trauma.

3.3.2. Non-traumatic ONFH

The etiology is not fully elucidated. Common precipitating factors include long-term use of corticosteroids, chronic excessive alcohol consumption, lipid metabolism disorders, coagulation dysfunction, and decompression sickness [10, 11].

3.4. Pathogenesis

The pathophysiological mechanism of ONFH involves various factors (mechanical, chemical, etc.) that disrupt the blood circulation of the femoral head, leading to death of bone cells and bone marrow cells, impairing repair, and subsequently causing structural changes in the femoral head, resulting in hip pain and functional impairment [7]. The pathological changes of ONFH manifest as cell necrosis in the early stage, and co-existence of necrosis and repair in the middle and late stages. The main pathogenesis theories include venous outflow obstruction, arterial occlusion, fat embolism, vascular disease and intravascular coagulation, osteocyte and bone marrow fat cell necrosis, increased blood viscosity, and micro-fracture theories [1-14].

3.5. Diagnosis and Differential Diagnosis

3.5.1. Diagnostic Criteria

(1) Clinical Manifestations

ONFH typically presents as deep pain in the periarticular hip region (82% in the inguinal area, 15% in the buttock, 3% in the proximal thigh), with gradual progression. Pain is initially more prominent with weight-bearing and partially relieved by rest; in late stages it may progress to persistent rest pain. Approximately 35% of patients have referred knee pain.

(2) Imaging Examinations

MRI is the gold standard for ONFH diagnosis with a sensitivity of 99%: (i) T1WI: subchondral band-like low signal (specificity 98%), surrounding a central high-signal necrotic zone; (ii) T2WI: "double-line sign" (inner high-signal ring + outer low-signal ring), with fat-suppressed sequences showing diffuse bone marrow edema in the femoral head-neck region (indicating collapse risk); (iii) DWI sequence: elevated apparent diffusion coefficient in early ischemic areas (sensitivity 93%).

X radiography is a basic screening tool: (i) early findings include patchy sclerosis/cystic changes in the femoral head with a positive rate <30%; (ii) progressive stage shows the "crescent sign" (subchondral fracture) and femoral head deformity; (iii) late stage shows joint space narrowing and acetabular cystic changes [5].

CT is used to assess the degree of collapse. It has superior

clarity and positive rate for subchondral fractures compared to MRI and plain films. Coronal reconstruction clearly shows the subchondral fracture line, with a detection rate 40% higher than plain films. Disappearance of the "asterisk sign" and trabecular disorganization are early specific findings.

Other imaging modalities serve as supplementary tools: radionuclide tomography has relatively high sensitivity but lower specificity [20]. Digital subtraction angiography is an invasive examination and not used routinely.

(3) Other Examinations

Hip arthroscopy [21] and bone tissue biopsy (tissue obtained only during surgical procedures) may also be used.

3.5.2. Differential Diagnosis

ONFH lacks specific clinical features in its early stages and may be confused with other hip conditions, leading to misdiagnosis or missed diagnosis.

- 1) Hip osteoarthritis. More common in middle-aged and elderly patients; persistent pain with morning stiffness; radiographically characterized by joint space narrowing and osteophyte formation, whereas early ONFH has normal joint space with "crescent sign" or "double-line sign" in the necrotic zone.
- 2) Transient osteoporosis. Presents as acute hip pain with bone marrow edema; MRI shows homogeneous low signal on T1WI and homogeneous high signal on T2WI without band-like signals of necrotic foci; lesions typically resolve spontaneously within 3–12 months [22].
- 3) Bone infarction. Occurs in the diaphysis or metaphysis;

MRI shows "map-like" necrotic foci without subchondral fractures or femoral head collapse; CT may show calcification or ossification in the medullary cavity.

- 4) Hip tuberculosis. Associated with systemic symptoms such as low-grade fever and night sweats; radiographically shows joint surface destruction and cold abscess; positive PPD test and T-SPOT test.
- 5) Ankylosing spondylitis with hip involvement. Predominantly in adolescent males; HLA-B27 positive; sacroiliac joint involvement precedes hip involvement; late-stage joint ankylosis.
- 6) Pigmented villonodular synovitis. MRI shows diffuse synovial thickening with T2WI low-signal nodules; joint aspiration reveals blood-stained effusion [13].

3.6. Staging of ONFH

An ideal ONFH staging system should accurately reflect the pathological process, stage, location, extent, and degree of collapse of necrosis, and be able to guide treatment and prognosis. The ARCO (Association Research Circulation Osseous) staging system [8] and Chinese staging system [22] are widely used in clinical practice.

3.6.1. ARCO Staging

ARCO staging combines plain radiography, CT, MRI, and bone scanning to determine the location and size of necrotic areas, providing greater value in establishing diagnosis, evaluating efficacy, and prognosis (Table 2).

Table 2. ARCO Staging of ONFH (2019 Version).

Stage	Stage 1	Stage 2	Stage 3A (Early)	Stage 3B (Late)	Stage 4
Imaging	Normal X-ray/CT; abnormal bone scan or MRI	Abnormal X-ray, CT, and MRI	Subchondral fracture on X-ray or CT	Subchondral fracture on X-ray or CT	Osteoarthritis on X-ray
Examination	Bone scan, MRI	X-ray, CT, bone scan, MRI	X-ray, CT	X-ray, CT	X-ray
Description	Low-signal band in necrotic zone on MRI; cold area on bone scan; normal X-ray	Sclerosis, local osteoporosis, or cystic changes; no evidence of subchondral fracture or collapse	Subchondral fracture/partial collapse; femoral head collapse ≤2 mm	Subchondral fracture/partial collapse; femoral head collapse >2 mm	Hip osteoarthritis with joint space narrowing; acetabular changes

ARCO = Association Research Circulation Osseous

3.6.2. Chinese Staging

The Chinese staging system incorporates symptoms, signs,

and early imaging features of bone necrosis in each stage, along with assessment of necrosis volume and degree of joint involvement. Each stage is further subdivided into subtypes, making it more operationally practical (Table 3).

Table 3. Chinese Staging of ONFH.

Stage	Clinical Manifestations	Imaging	Pathological Changes
Stage I (Preclinical, no collapse) Ia: small, <15%; Ib: medium, 15–30%; Ic: large, >30%	None	MRI(+); bone scan(+); X-ray(-); CT(-)	Bone marrow tissue necrosis, osteocyte necrosis
Stage II (Early, no collapse) IIa: small, <15%; IIb: medium, 15–30%; IIc: large, >30%	None or mild	MRI(+) X-ray(±) CT(+)	Absorption of necrotic foci, tissue repair
Stage III (Intermediate, pre-collapse) IIIa: small, <15%; IIIb: medium, 15–30%; IIIc: large, >30%	Onset of pain, limping, moderate-to-severe pain, limited internal rotation	MRI T2WI shows marrow edema; CT shows subchondral fracture; X-ray shows an interruption in the outer contour of the femoral head, "crescent sign" positive	Subchondral fracture or necrotic bone fracture
Stage IV (Middle-late, collapse stage) IVa: mild <2mm; IVb: medium 2–4mm; IVc: severe >4mm	Severe pain, worsened limping, all ROM limited	X-ray shows femoral head collapse, normal joint space	Femoral head collapse
Stage V (Late, osteoarthritis)	Severe pain, all ROM severely restricted	X-ray shows flattened femoral head, narrowed joint space, acetabular cystic/sclerotic changes	Cartilage involvement, osteoarthritis

Note: ONFH refers to osteonecrosis of the femoral head. The assessment of the necrotic area is performed using MRI or CT coronal plane images, and the necrotic volume is evaluated based on the number of affected planes. In stage III, the risk of collapse is assessed by determining the proportion of the crescent sign to the length of the joint surface on frog-leg or upright X-rays. In stage IV, the degree of collapse is evaluated by measuring the depth of joint surface collapse on anteroposterior or frog-leg X-ray films. For patients who present with hip pain but show no femoral head collapse on X-ray, further MRI and CT examinations are required. The presence of bone marrow edema or subchondral bone plate fracture suggests that the necrosis has progressed to stage III. If femoral head collapse and hip pain have persisted for more than six months, significant degeneration of the articular cartilage (stage V) is indicated.

3.7. Non-Surgical Treatment of ONFH

ONFH treatment includes conservative therapy, minimally invasive therapy, and surgical therapy (Table 4). Non-surgical treatment refers to conservative and minimally invasive therapy, encompassing general treatment, medication, TCM therapy, physical therapy, minimally invasive therapy, and rehabilitation. It aims to interrupt the vicious cycle of ischemia-necrosis-collapse at an early stage, primarily through strate-

gies such as improving microcirculation (e.g., ESWT, hyperbaric oxygen), regulating bone metabolism (e.g., bisphosphonates, lipid-lowering drugs), and inhibiting apoptosis (e.g., cell therapy), thereby delaying disease progression. It is mainly indicated for early-to-middle stage ONFH patients, as well as late-stage patients who cannot or are unwilling to undergo surgery. Non-surgical treatment is an important option for hip preservation in early ONFH. Individualized treatment plans should be formulated based on the location and extent of necrosis, staging, and the patient's general condition.

Table 4. Common Treatment Methods for ONFH.

Category	Treatment Type	Representative Techniques/Drugs	Applicable Stages	Contraindications
Conservative	General Therapy	Health education, psychological therapy, self-management	All ONFH stages (combined with other modalities)	None
Conservative	Medication	Technetium [99Tc] MDP, TCM, lipid-lowering drugs, anticoagulants, osteogenic drugs	Stage I-III (early-to-middle stage); also as adjunct	See individual drug contraindications

Category	Treatment Type	Representative Techniques/Drugs	Applicable Stages	Contraindications
Conservative	TCM Therapy	Internal TCM treatment, external TCM treatment	All ONFH stages	None
Conservative	Physical Therapy	ESWT, pulsed electromagnetic field, hyperbaric oxygen	ESWT: Stage I, II; EMF/HBO as adjuncts	See individual technique contraindications
Conservative	Rehabilitation	ROM training, muscle strengthening, TCM rehabilitation	Throughout entire treatment course	None
Minimally Invasive	Minimally Invasive Intervention	PRP, cell therapy, ozone, radiofrequency	Pre-collapse Stage I–III	Active malignancy, severe immune/hematologic disorders, uncontrolled infection, organ failure
Minimally Invasive	Minimally Invasive Surgery	Core decompression (various techniques)	ARCO Stage I, II; Stage III A may be considered	Collapse >2mm, involvement >30%, unable to comply with post-op restrictions
Surgical	Hip-Preserving Surgery	Bone grafting, osteotomy, metal rod implantation	Stage I–III (early-to-middle stage)	Uncontrolled infection, coagulopathy, severe cardiopulmonary dysfunction
Surgical	Joint Replacement	Total hip replacement, hip resurfacing	Stage III–IV with severe functional loss or moderate-to-severe pain	Uncontrolled infection, coagulopathy, severe cardiopulmonary dysfunction

ONFH = osteonecrosis of the femoral head; PRP = platelet-rich plasma; ESWT = extracorporeal shock wave therapy; ARCO = Association Research Circulation Osseous

3.7.1. General Treatment

General treatment mainly includes health education [23-25], psychological therapy [26-28], and self-management [1-14, 29], and should be integrated throughout the entire ONFH treatment process (Table 5). Health education helps patients understand the causes, treatment methods, and precautions for

ONFH, emphasizing the importance of alcohol cessation, smoking cessation, blood glucose control, weight reduction, and avoidance of excessive weight-bearing. The overall mental health status of ONFH patients is generally poor, requiring targeted psychological treatment and intervention. Self-management includes lifestyle modification, protective weight-bearing, weight control, and use of assistive devices (canes, crutches, walking frames); wheelchairs are not recommended.

Table 5. Evidence Quality and Recommendation Strength for General Treatment of ONFH.

Treatment Type	Evidence Level	Recommendation Strength
Health Education [23-25]	B	1
Psychological Therapy [26-28]	B	1
Self-Management [1-14, 29]	A	1

3.7.2. Medication

Although no specific drug has been established for the prevention and treatment of ONFH, the role of pharmacotherapy in overall ONFH management continues to grow [4]. Drugs commonly used in clinical treatment of ONFH include

bisphosphonates, TCM preparations, osteogenic drugs, anti-coagulants, and lipid-lowering drugs [4]. Although common bisphosphonates such as zoledronic acid and alendronate can inhibit osteoclast formation, they do not improve ONFH outcomes [30-36]. Technetium [99Tc] methylene diphosphonate (MDP) is a China-original radiopharmaceutical that can im-

prove hip joint function in early ONFH and exert bone-protective effects [37-39]. TCM preparations are also widely applied in ONFH management [40-52]. Cervus and cucumis polypeptides injection [53-56] and levodopa-benserazide [57, 58] are used to promote bone repair and enhance osteogenic activity. Enoxaparin [59-61] is employed to improve intraosseous

microcirculation and prevent thrombus formation. Simvastatin [62-64] is administered to regulate lipid metabolism and reduce the risk of corticosteroid- or alcohol-induced osteonecrosis. Evidence Quality and Recommendation Strength for Pharmacotherapy of ONFH (Table 6).

Table 6. Evidence Quality and Recommendation Strength for Pharmacotherapy of ONFH.

Drug Category	Common Drugs	Evidence Level	Recommendation Strength
Bisphosphonates [30]	*NOT recommended: Zoledronic acid [31-35]	A	1
	*NOT recommended: Alendronate [31-36]	A	1
	Technetium [99Tc] MDP [37-39]	B	1
TCM [40-52]	Xianling Gubao Capsules [47-49]	A	1
	Tongluo Shenggu Capsules [50, 51]	B	2
	Gutouyusheng Capsules [52]	B	2
Osteogenic drugs	Cervus and Cucumis Polypeptides Injection [53-56]	A	1
	Levodopa-benserazide [57, 58]	B	3
Anticoagulants	Enoxaparin [59-61]	B	2
Lipid-lowering drugs	Simvastatin [62-64]	B	2

*High-quality evidence indicates that zoledronic acid and alendronate do not improve outcomes in ONFH patients; therefore, this guideline does NOT recommend their use for ONFH.

3.7.3. Physical Therapy

Physical therapy, as a non-invasive treatment modality, plays an important role in ONFH management. It mainly includes ESWT [2, 65-71], hyperbaric oxygen (HBO) [72-76],

and pulsed electromagnetic field (PEMF) therapy [77, 78] (Table 7). These can improve local blood circulation, promote bone tissue repair, alleviate pain, and improve quality of life. The main mechanisms of ESWT in ONFH treatment include tissue repair and remodeling, adhesion release, vasodilation and angiogenesis, analgesia and nerve terminal blockade, dense tissue lysis, and inflammation/infection control [2].

Table 7. Evidence Quality and Recommendation Strength for Physical Therapy of ONFH.

Treatment	Evidence Level	Recommendation Strength
ESWT [2, 65-71]	A	1
Hyperbaric Oxygen [72-76]	A	1
Pulsed Electromagnetic Field [77, 78]	B	2

ESWT = extracorporeal shock wave therapy

3.7.4. Traditional Chinese Medicine Treatment

TCM treatment mainly includes internal TCM therapy and

external TCM therapy. External TCM therapy primarily encompasses acupuncture [79, 80], needle-knife [81-83], and silver needle/endothemic needle therapy [84-86] (Table 8).

Table 8. Evidence Quality and Recommendation Strength for TCM Treatment of ONFH.

Treatment	Evidence Level	Recommendation Strength
Acupuncture [79, 80]	B	2
Needle-knife [81-83]	B	2
Silver needle / Endothermic needle [84-86]	B	2

3.7.5. Minimally Invasive Treatment

Image-guided PRP injection, cell therapy, core decompression (CD), ozone therapy, and radiofrequency therapy have shown great potential in the prevention and treatment of ONFH (Table 9).

(1) Platelet-Rich Plasma (PRP)

PRP is a plasma concentrate derived from the patient's own peripheral blood by centrifugation, containing a high concentration of platelets. Multiple studies have shown that PRP, used alone or in combination with other therapies, can effectively relieve pain and improve hip joint function. The main mechanisms by which PRP treats ONFH include inducing angiogenesis and promoting osteogenesis to accelerate bone healing, inhibiting inflammatory responses in necrotic foci, and preventing glucocorticoid-induced cell apoptosis [87-90].

(2) Cell Therapy

Cells can be administered via intravascular infusion, percutaneous catheter infusion, or core decompression infusion to promote bone tissue and vascular regeneration in the necrotic zone, alleviate hip symptoms, and delay ONFH progression. Cell therapy types discussed in this guideline (focused on non-surgical approaches) include local injection or infusion modalities:

- 1) Adipose tissue derivatives [91-107]: Including stromal vascular fraction (SVF), autologous fat grafting (AFG), microfat, nanofat, adipose-derived stem cells (ADSCs), preadipocytes, and extracellular matrix (ECM).
- 2) Bone marrow tissue derivatives: Including bone marrow buffy coat, bone marrow aspirate concentrate (BMAC), bone marrow-derived cell therapies (BMDCT), bone

marrow stem cells (BMSCs), bone marrow mesenchymal stem cells (BMMSCs), bone marrow mononuclear cells (BMMNCs), and bone marrow-derived exosomes.

- 3) Stem cell therapy: Mesenchymal stem cells (MSCs), induced pluripotent stem (iPS) cells, and transgenic cells. MSCs derived from bone marrow, adipose tissue, and umbilical cord have multipotent differentiation potential and paracrine functions, promoting tissue repair and anti-inflammatory effects.

(3) Core Decompression (CD) [108-111]

CD creates a decompression channel within the femoral head, breaks the intraosseous hypertension environment, facilitates new blood vessel formation, and thereby delivers more nutrients and oxygen to the ONFH area to promote bone tissue repair, delay femoral head collapse, relieve pain, and improve hip function. CD types include traditional single-port CD, small-diameter dual-channel drilling CD, multi-port fine-needle CD, and modified CD.

Main indications: (i) pre-collapse lesions (ARCO Stage 1 and 2); (ii) small to medium lesions, femoral head involvement <30% or Kerboul angle <200°; (iii) patients who cannot tolerate more extensive hip-preserving surgery.

(4) Ozone Therapy [112-114]

Studies have shown that intra-articular ozone injection, autologous ozone blood reinfusion, and ozone perfusion can alleviate hip pain, restore hip function, reduce ONFH volume, reduce bone marrow edema, and prevent premature femoral head collapse.

(5) Radiofrequency Therapy [115-117]

Pulsed radiofrequency (PRF) of hip joint branches is an alternative therapeutic approach for ONFH-related hip pain. Lumbar sympathetic nerve radiofrequency thermocoagulation is also a commonly used clinical treatment method for ONFH.

Table 9. Evidence Quality and Recommendation Strength for Minimally Invasive Treatment of ONFH.

Treatment	Subtype	Evidence Level	Recommendation Strength
PRP [87-90]	—	A	1
	SVF [96, 97]	B	1
Cell Therapy [91-107]	BMAC [98-100]	A	1
	BMMNCs [101-103]	A	2

Treatment	Subtype	Evidence Level	Recommendation Strength
	BMMSCs [98, 104-107]	A	1
Core Decompression (CD) [108-111]	—	A	1
Ozone Therapy [112-114]	—	B	1
Radiofrequency Therapy [115-117]	—	B	2

PRP = platelet-rich plasma; SVF = stromal vascular fraction; BMAC = bone marrow aspirate concentrate; BMMNCs = bone marrow mononuclear cells; BMMSCs = bone marrow mesenchymal stem cells; CD = core decompression

3.7.6. Rehabilitation

Rehabilitation is an important component of non-surgical treatment for ONFH (Table 10) [1-14, 29, 118, 119]. ONFH should be detected and treated early. Early and active hip joint functional exercise is encouraged to promote 'qi-blood' circulation, improve hip joint stability, and facilitate functional recovery. Exercise should be predominantly active, supplemented by passive movement, gradually increasing in range

and frequency based on ONFH staging. Early rehabilitation training is conducted in weight-reduced conditions with muscle strength, endurance, and ROM training, which is beneficial for maintaining and improving hip function and preventing muscular atrophy.

Main ONFH rehabilitation exercises include supine leg raises, seated hip abduction/adduction, standing leg raises, supported squats, and internal rotation-abduction exercises, performed 200 times per day divided into 3–4 sessions.

Table 10. Evidence Quality and Recommendation Strength for Rehabilitation of ONFH.

Treatment	Evidence Level	Recommendation Strength
Rehabilitation Therapy [1-14, 118, 119]	A	1

3.7.7. Combination Therapy

All of the above ONFH treatment methods have established efficacy and high safety profiles. In clinical practice, different treatment modalities are often combined to achieve better outcomes. Combination regimens include: CD+Cell Therapy (bone marrow buffy coat) [120-128], CD+BMAC [98, 99,

129], CD+BMDCT [130, 131], CD+BMSCs [132-138], CD+BMMSCs [98, 139-142], CD+PRP [88, 143-148], CD+Medication [129, 149, 150], PRP+Cell Therapy [88], PRP+Radiofrequency [151], PRP+Silver Needle [152], ESWT+BMSCs [153], ESWT+BMMSCs [154], ESWT+Medication [94, 155], and Silver Needle+Ozone [156]. Common two-modality combination protocols and their evidence levels are presented in Table 11.

Table 11. Evidence Quality and Recommendation Strength for Combination Therapy of ONFH.

Combination Regimen	Evidence Level	Recommendation Strength
CD + Cell Therapy (bone marrow buffy coat) [120-128]	B	2
CD + BMAC [98, 99, 129]	A	1
CD + BMDCT [130, 131]	A	1
CD + BMSCs [132-138]	A	1
CD + BMMSCs [98, 139-142]	A	1
CD + PRP [88, 143-148]	A	1
CD + Medication [129, 149, 150]	A	1

Combination Regimen	Evidence Level	Recommendation Strength
PRP + Cell Therapy [88]	B	2
PRP + Radiofrequency [151]	C	2
PRP + Silver Needle [152]	C	2
ESWT + BMSCs [153]	C	2
ESWT + BMMSCs [154]	B	2
ESWT + Medication [94, 155]	B	2
Silver Needle + Ozone [156]	C	2

CD = core decompression; BMAC = bone marrow aspirate concentrate; BMDCT = bone marrow-derived cell therapy; BMSCs = bone marrow stem cells; PRP = platelet-rich plasma; BMMSCs = bone marrow mesenchymal stem cells; ESWT = extracorporeal shock wave therapy

3.8. Efficacy Assessment

3.8.1. Clinical Evaluation

- 1) Hip symptom assessment: e.g., Visual Analogue Scale (VAS) for pain.
- 2) Functional assessment: e.g., Harris Hip Score, Reconstruction Hip Score (RHS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).
- 3) Gait analysis.

3.8.2. Radiological Evaluation

- 1) Plain radiography (bilateral hip AP and frog-lateral views): To assess femoral head contour collapse, joint space, and acetabular changes.
- 2) CT or MRI: To assess femoral head collapse and bone marrow edema.

4. Conclusion

With the rapid development of stem cells, 3D-printed scaffolds, gene therapy, and digital therapeutics, it is hoped that in the future, precise regeneration of necrotic zones and individualized rehabilitation will be achievable. Artificial intelligence will integrate imaging, omics, and dynamic monitoring data to predict collapse risk early and adjust treatment plans in real time, enabling more ONFH patients to recover a high quality of life while avoiding surgery. Multidisciplinary collaboration and real-world research will provide more comprehensive and individualized diagnostic and treatment plans for ONFH patients.

Abbreviations

ADSCs	Adipose-Derived Stem Cells
AFG	Autologous Fat Grafting
ARCO	Association Research Circulation Osseous

BMAC	Bone Marrow Aspirate Concentrate
BMDCT	Bone Marrow-Derived Cell Therapies
BMMNCs	Bone Marrow Mononuclear Cells
BMMSCs	Bone Marrow Mesenchymal Stem Cells
BMSCs	Bone Marrow Stem Cells
CD	Core Decompression
ECM	Extracellular Matrix
ESWT	Extracorporeal Shock Wave Therapy
GRADE	Grading of Recommendations Assessment, Development And Evaluation
iPS	Induced Pluripotent Stem
MDP	Methylene Diphosphonate
MSCs	Mesenchymal Stem Cells
ONFH	Osteonecrosis of the Femoral Head
PRP	Platelet-Rich Plasma
RCTs	Randomized Controlled Trials
RHS	Reconstruction Hip Score
SVF	Stromal Vascular Fraction
TCM	Traditional Chinese Medicine
THA	Total Hip Arthroplasty
VAS	Visual Analogue Scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

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Conflicts of Interest

All authors declare no conflicts of interest.

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