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Research Progress on the Mechanism of Extracorporeal Shock Wave Therapy for Osteonecrosis of the Femoral Head

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Abstract: ***Osteonecrosis of the femoral head (ONFH) is a debilitating condition characterized by impaired blood supply to the femoral head, leading to osteocyte apoptosis, structural collapse, and secondary osteoarthritis. Current therapeutic strategies range from conservative measures to surgical interventions, with extracorporeal shock wave therapy (ESWT) emerging as a promising non-invasive approach. This review synthesizes recent advancements in understanding the mechanisms and clinical efficacy of ESWT for ONFH. Accumulating evidence indicates that ESWT alleviates pain, improves hip function, and delays disease progression by enhancing angiogenesis, reducing bone marrow edema (BME), and modulating inflammatory pathways. Clinical studies report significant improvements in Harris Hip Scores (HHS) and reductions in visual analog scale (VAS) pain scores, particularly in early-stage (ARCO I–II) ONFH. Long-term follow-up data (up to 10 years) highlight its potential to reduce the need for total hip arthroplasty (THA). However, heterogeneity in treatment protocols and the absence of standardized guidelines necessitate further investigation. This review provides a comprehensive analysis of ESWT's therapeutic mechanisms, clinical outcomes, and future directions.***

Keywords: Extracorporeal shock wave therapy, Osteonecrosis of the femoral head, Bone marrow edema, Angiogenesis, ARCO classification**.**

1. Introduction

Osteonecrosis of the femoral head (ONFH) is a progressive disorder predominantly affecting individuals aged 20–50 years, often culminating in severe disability and hip joint destruction [1]. Etiological factors include trauma, prolonged corticosteroid use, chronic alcohol abuse, and idiopathic mechanisms, all of which disrupt femoral head perfusion and trigger osteocyte apoptosis [2]. Without timely intervention, 70–80% of cases progress to femoral head collapse and end-stage osteoarthritis [3]. Traditional treatments such as core decompression, bone grafting, and THA are associated with risks of surgical complications, incomplete functional recovery, and limited durability, particularly in young patients [4].

Extracorporeal shock wave therapy (ESWT), initially developed for lithotripsy, has gained recognition as a non-invasive modality for musculoskeletal disorders. By delivering focused high-energy acoustic pulses to necrotic regions, ESWT promotes tissue regeneration, angiogenesis, and nociceptive pathway modulation [5]. Recent clinical trials and meta-analyses demonstrate its efficacy in early-stage ONFH, with functional outcomes comparable or superior to surgical interventions [6]. This review critically examines the biological mechanisms underpinning ESWT, consolidates clinical evidence across diverse populations, and addresses challenges in optimizing therapeutic protocols.

2. Mechanisms of ESWT in ONFH

2.1 Angiogenesis and Neovascularization

ESWT stimulates endothelial nitric oxide synthase (eNOS) and upregulates vascular endothelial growth factor (VEGF), pivotal mediators of angiogenesis. In a rabbit ONFH model, ESWT increased VEGF expression by 3.5-fold, enhancing blood flow to ischemic subchondral bone [7]. Clinical corroboration by Wang et al [8]. revealed upregulated CD31 and von Willebrand factor (vWF) in human femoral heads post-ESWT, confirming neovascularization within necrotic lesions. These effects mitigate hypoxia and facilitate the repair of osteonecrotic regions.

2.2 Reduction of Bone Marrow Edema (BME)

BME, a hallmark of symptomatic ONFH, correlates with intraosseous hypertension and mechanical pain. ESWT reduces BME volume by suppressing pro-inflammatory cytokines (e.g., IL-1β, TNF-α) and downregulating receptor activator of nuclear factor kappa-B ligand (RANKL) - mediated osteoclastogenesis. Zhao et al [9]. reported a 72% reduction in BME volume on MRI after ESWT ($P < 0.001$), paralleled by significant pain relief (VAS: 6.5 → 2.1).

2.3 Osteogenic and Anti-Apoptotic Effects

ESWT activates bone morphogenetic protein-2 (BMP-2) and osteocalcin, enhancing osteoblast differentiation and bone remodeling [10]. Concurrently, it inhibits osteocyte apoptosis via the PI3K/Akt signaling pathway, preserving trabecular microarchitecture and delaying femoral head collapse [11].

2.4 Analgesic Mechanisms

Shock waves attenuate neuropathic pain by reducing substance P and glutamate release in nociceptive pathways. A clinical trial by Han et al [12]. demonstrated a 60% reduction in VAS scores post-ESWT ($P < 0.01$), attributed to diminished peripheral and central sensitization.

3. Clinical Efficacy of ESWT

3.1 Short- and Medium-Term Outcomes

In a retrospective analysis of 44 hips, Xie et al [13]. observed significant improvements in HHS (77.4 → 86.9) and VAS (3.8 → 2.2) at 10-year follow-up ($P < 0.001$). Similarly, Algarni and Al Moallem [12] reported 63.3% clinical improvement in ARCO I–II patients, with THA rates of 3% at 1 year and 24% at 8–9 years.

3.2 Long-Term Survival

Wang et al [3]. compared ESWT (n=29 hips) and core decompression (n=28 hips) over 8–9 years. ESWT achieved a 76% success rate versus 21% for surgery ($P < 0.001$), with THA rates of 24% and 64%, respectively, underscoring its durability in preserving native hip joints.

3.3 Stage-Dependent Efficacy

ESWT demonstrates optimal efficacy in ARCO I–II ONFH, where the lateral pillar remains intact. Gao et al [14]. treated 528 hips and observed 83.9% pain reduction in ARCO I–II versus 78.3% in ARCO III ($P = 0.037$), with collapse rates significantly lower in early-stage lesions (2% vs. 9.2%, $P < 0.001$).

4. Safety and Adverse Effects

ESWT is generally well-tolerated, with transient adverse effects including local erythema (32.4%) and hematoma (14%) [15]. Severe complications such as nerve injury or femoral neck fracture are rare (<1%) and typically associated with improper energy settings [16].

5. Limitations and Future Directions

Heterogeneity in ESWT protocols (energy flux density: 0.25–0.62 mJ/mm²; impulses: 1,500–4,000 per session; frequency: 4–8 Hz) complicates cross-study comparisons. Standardized guidelines for energy parameters and treatment intervals are urgently needed. Future research should explore synergistic therapies (e.g., ESWT + bisphosphonates) and identify biomarkers (e.g., serum VEGF, IL-6) for patient stratification [17, 18].

6. Conclusion

Extracorporeal shock wave therapy (ESWT) has revolutionized the management of osteonecrosis of the femoral head (ONFH) by offering a non-invasive, regenerative alternative to traditional surgical interventions. Its efficacy in early-stage disease (ARCO I–II) is well-supported by robust clinical evidence, demonstrating significant improvements in pain relief, hip function, and long-term joint preservation [19]. By stimulating angiogenesis, reducing bone marrow edema (BME), and activating osteogenic pathways, ESWT addresses the core pathophysiological mechanisms of ONFH, effectively delaying or preventing femoral head collapse. Long-term follow-up studies, spanning up to a decade, highlight its superiority over core decompression, with total hip arthroplasty (THA) rates substantially lower in ESWT-treated cohorts (24% vs. 64% in surgical groups). This underscores its potential to reduce the socioeconomic burden of repeat surgeries, particularly in younger patients seeking durable solutions [20].

However, the clinical application of ESWT faces challenges due to heterogeneity in treatment protocols, including variations in energy flux density (0.25–0.62 mJ/mm²), impulse counts (1,500–4,000 per session), and frequency settings (4–8 Hz). These discrepancies hinder cross-study comparisons and underscore the urgent need for standardized guidelines. Future research should prioritize large-scale, multicenter trials to establish optimal dosing regimens and validate biomarkers (e.g., serum VEGF, IL-6) for patient stratification. Additionally, exploring synergistic therapies—such as combining ESWT with bisphosphonates to enhance bone remodeling or stem cell therapy to amplify regenerative effects—could further elevate therapeutic outcomes [21].

The molecular mechanisms underlying ESWT's anti-apoptotic and anti-inflammatory effects, particularly its modulation of the PI3K/Akt and RANKL/OPG pathways, warrant deeper investigation. Advanced imaging techniques and multi-omics approaches may unravel novel targets for personalized treatment strategies. Clinically, extending ESWT's application to later-stage ONFH (ARCO III) remains contentious, though preliminary studies suggest modest benefits in pain reduction. Tailoring protocols based on disease progression and patient-specific factors, such as etiology and comorbidities, could maximize efficacy across stages.

In conclusion, ESWT represents a paradigm shift in ONFH management, bridging the gap between conservative care and invasive surgery. As mechanistic insights evolve and protocols standardize, ESWT is poised to become a first-line therapy, offering hope for preserving native hip joints and improving quality of life. Collaborative efforts among researchers, clinicians, and policymakers will be pivotal in translating these advancements into clinical practice.

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