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Research Progress on Extracorporeal Shock Wave Therapy for Knee Osteoarthritis: A Systematic Review

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ABSTRACT

Knee osteoarthritis (KOA) is a common chronic degenerative joint disease, primarily characterized by progressive destruction of articular cartilage, synovial inflammation, bone hyperplasia, and gradual loss of joint function. The field of osteoarthritis treatment in recent years. Starting from the basic concepts of knee osteoarthritis, this paper elucidates the physical characteristics and treatment equipment of extracorporeal shock waves, focusing on analyzing its clinical application progress and mechanisms of action in the treatment of knee osteoarthritis, while providing prospects for future research directions. Studies have shown that extracorporeal shock waves effectively relieve pain, improve joint function, and enhance patients' quality of life through multiple mechanisms including anti-inflammation, promotion of cartilage repair, and improvement of microcirculation. Extracorporeal shock wave therapy provides a new option for non-surgical treatment of knee osteoarthritis and has broad clinical application prospects.

Keywords: Extracorporeal Shock Wave; Knee Osteoarthritis; Pain; Joint Function; Research Progress

Abbreviations: KOA: Knee Osteoarthritis; ESW: Extracorporeal Shock Wave; ESWB: Extracorporeal Shock Wave Therapy; IGF-1: Insulin-Like Growth Factor-1; VAS: Visual Analog Scale; VEGF: Vascular Endothelial Growth Factor; NO: Nitric Oxide; MSCs: Mesenchymal Stem Cells; BMI: Body Mass Index; ESWT: Extracorporeal Shock Wave Therapy

Introduction

Knee osteoarthritis (KOA) is a chronic degenerative disease characterized by progressive damage to articular cartilage, synovitis, bone hyperplasia, and gradual decline in joint function [1]. The main symptoms of this disease include joint pain, morning stiffness, limited mobility, and joint deformity. These symptoms can restrict patients' daily living abilities and reduce their quality of life [2]. With the increasing aging of the global population, the incidence of knee osteoarthritis continues to rise. Epidemiological studies show that the prevalence of knee osteoarthritis in people over 60 years of age has exceeded 50%, and the incidence in women is significantly higher than that in men [3]. This may be related to the decline in estrogen levels after menopause, which weakens the protective effect on the joint. Globally, there are a huge number of patients with knee osteoarthritis, which has become one of the main causes of functional impairment and disability in middle-aged and elderly people [4]. Traditional treatments for knee osteoarthritis include drug therapy, physical therapy, and surgery, but these methods all have certain limitations. Drugs such as nonsteroidal anti-inflammatory drugs may cause side effects such as gastrointestinal discomfort and kidney damage; physical therapy has limited effects and is difficult to maintain in the long term; while surgical treatments such as joint replacement are highly invasive, have a long recovery period, are expensive, and have certain risks of complications [5]. Therefore, exploring safe and effective non-invasive treatment methods has become a key research direction in the current management of knee osteoarthritis, among which extracorporeal shock wave therapy has played an important role.

In recent years, non-invasive treatment strategies centered on extracorporeal shock wave therapy have gradually attracted attention. Studies have shown that extracorporeal shock wave therapy, as a high-energy sound wave, can be generated outside the body and transmitted to specific areas inside the body to exert its effects, producing therapeutic effects on knee osteoarthritis through multiple mechanisms [6]. Against this background, extracorporeal shock wave therapy, as a technical means that integrates acoustic principles, biological effects and precision treatment, has been gradually introduced into the field of osteoarthritis rehabilitation due to its advantages such as non-invasiveness, high safety and ease of operation [7]. For example, extracorporeal shock wave therapy can specifically improve the pain symptoms and joint function of patients with knee osteoarthritis through mechanisms such as inhibiting the expression of inflammatory factors, promoting cartilage repair and improving local microcirculation [8]. However, current research on extracorporeal shock wave therapy for knee osteoarthritis still has many limitations, such as inconsistent treatment parameters (e.g., large differences in energy density, frequency and dose), lack of standardized treatment protocols, and imperfect efficacy evaluation systems [9]. In addition, existing research still has controversies regarding the long-term effects, mechanisms of action, and individualized treatment design of extracorporeal shock wave therapy [10]. Although extracorporeal shock wave therapy can improve pain and functional impairment in patients with knee osteoarthritis, there are significant differences in treatment response among patients at different stages of the disease, requiring optimization of treatment parameters and technical pathways. In summary, the potential value of extracorporeal shock wave therapy in the management of knee osteoarthritis urgently needs to be verified through large-sample randomized controlled trials and long-term follow-up studies to provide more evidence-based intervention methods for patients with knee osteoarthritis. Based on this, this article aims to systematically analyze the research progress of extracorporeal shock wave therapy in the treatment of knee osteoarthritis in recent years, hoping to provide a theoretical basis for the development of individualized treatment protocols and to provide suggestions for future research directions.

Materials and Methods

Data Sources

Literature Search Period: 2012-2025

Search Methods: Subject heading search, Keyword search, Advanced search

Foreign Language Databases: PubMed, Web of Sciences, Cochrane Library

English Search Formula: (“Osteoarthritis, Knee”[Mesh] OR “Knee Osteoarthritis”[Title/Abstract] OR “KOA”[Title/Abstract]) AND (“Extracorporeal Shockwave Therapy”[Mesh] OR “shock wave”[Title/Abstract] OR “ESWT”[Title/Abstract]) AND (“Pain”[Mesh] OR “Joint Function”[Title/Abstract] OR “Therapy”[Title/Abstract])

Chinese Databases: CNKI, Wanfang Database, VIP Database

Chinese search terms: (“knee osteoarthritis” OR “knee joint osteoarthritis” OR “KOA”) AND (“extracorporeal shock wave therapy” OR “shockwave therapy” OR “ESWT”) AND (“pain” OR “joint function” OR “treatment”)

Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Patients with knee osteoarthritis were included in the study;
2. Extracorporeal shock wave therapy was used;
3. Assessment methods included pain scores, functional scales, and biomarkers;
4. The language was Chinese or English;
5. The study concerned the improvement of pain and function in knee osteoarthritis;
6. The article type was a clinical trial or randomized controlled trial.

Exclusion Criteria:

1. Full text unavailable;
2. Duplicate publications or studies lacking relevant outcomes;
3. Lack of clear evaluation indicators;
4. Review articles, books, documents, conference proceedings, and systematic analyses;
5. Knee osteoarthritis combined with other joint diseases;
6. Non-extracorporeal shock wave therapy.

(Figure 1)

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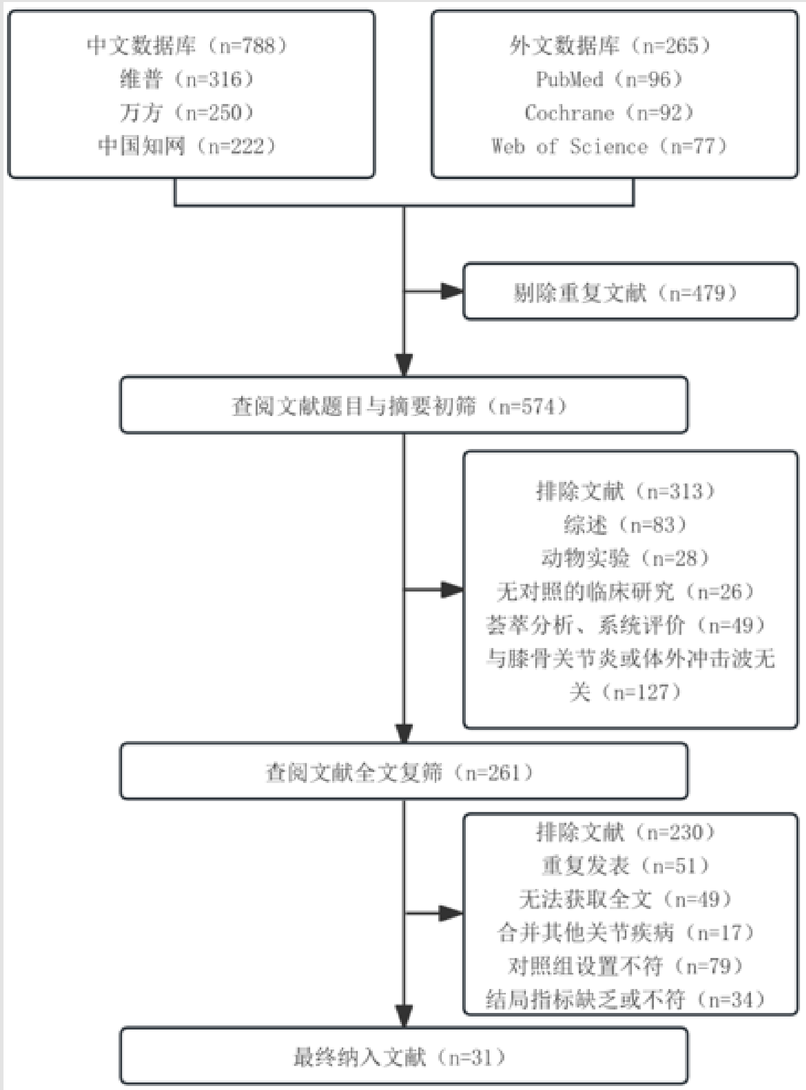

Figure 1

Overview of Knee Osteoarthritis

Concept and Epidemiology of Knee Osteoarthritis

Knee osteoarthritis (KOA) is a degenerative disease. Its main pathological changes are degeneration of articular cartilage, osteophytes at the joint margins, subchondral bone sclerosis and thickening of the joint capsule. It is one of the main causes of functional impairment and disability in middle-aged and elderly people, and it is also one of the most common joint diseases. Knee osteoarthritis not only affects articular cartilage, but also involves multiple tissue structures such as synovium, subchondral bone, ligaments, joint capsule and surrounding muscles. It is a disease that affects the entire joint [1]. Epidemiological studies show that the incidence of knee osteoarthritis is closely related to a variety of factors such as age, sex, occupation, and weight. Pasin and Karatekin's related studies show that the prevalence of knee osteoarthritis is more than 50% in people over 60 years old, and the incidence rate in women is significantly higher than that in men. This is probably because women's estrogen levels decrease after menopause, which weakens the protective effect on joints [2]. With the acceleration of population aging and the increase in the number of obese people, the incidence of knee osteoarthritis has shown an upward trend and has become a global public health problem.

Pathological Mechanisms of Knee Osteoarthritis

The core pathological change in knee osteoarthritis is the degeneration and destruction of articular cartilage. In the early stages of osteoarthritis, the cartilage surface shows fibrotic changes, the content of proteoglycans decreases, and the structure of collagen fibers is destroyed. As the condition worsens, vertical cracks appear in the cartilage, the bone tissue under the cartilage is exposed, and osteophytes form at the joint margins, causing uneven joint surfaces and joint dysfunction. Inflammation plays a significant role in the development of osteoarthritis. Studies by Liang Enlong et al. have shown that the levels of inflammatory factors such as IL-1β and TNF-α in the synovial fluid of osteoarthritis patients are significantly elevated. These factors can activate chondrocytes and synovial cells to produce proteases, accelerating the decomposition of cartilage [3]. Ma Yuhai, et al. have confirmed through clinical research that osteoarthritis is no longer considered a simple “wear and tear” disease, but an active inflammatory process involving multiple inflammatory factors and cytokines [4].

Clinical Manifestations of Knee Osteoarthritis

The main clinical manifestations of knee osteoarthritis include pain, joint stiffness, restricted movement, and joint deformity. The most common and main symptom is pain, which is characterized by worsening during activity and relief after rest. As the disease progresses, the pain gradually becomes persistent, and even nighttime pain may occur, affecting the patient’s sleep quality. Joint stiffness is another common symptom, especially when standing up after getting up in the morning or after sitting for a long time. It usually lasts for no more than 30 minutes. Xiao Zongping and Huang Tingfeng’s research showed that joint stiffness can affect patients’ normal activity ability and also reduce neuromuscular coordination [5]. As the disease progresses, patients may experience obvious joint swelling, deformity and instability, which greatly reduces their quality of life. A prospective clinical study conducted by Covelli et al. further confirmed that these symptoms do not always correspond to the degree of structural damage, suggesting the complex characteristics of clinical symptoms [6].

Traditional Treatments for Knee Osteoarthritis

Traditional treatments for knee osteoarthritis include non-pharmacological therapy, pharmacological therapy, and surgical treatment. Non-pharmacological therapy forms the foundation and involves patient education, weight management, exercise therapy, and physical therapy. The main role of pharmacological therapy is to control pain and inflammation. Commonly used drugs include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and opioids. If conservative treatment is ineffective for moderate to severe patients, surgical treatment can be chosen. Studies by Gu Bin et al. have shown that arthroscopic debridement has significant short-term efficacy, but there is controversy regarding its long-term effects [7]. For patients in the late stage, knee replacement surgery is the most effective treatment, but it is highly invasive, has a long recovery period, is expensive, and has a certain probability of complications. Zhang Zixin, et al. claimed that although there are many types of traditional treatment methods, they all have certain limitations, especially the lack of “structural improvement” therapy that can effectively block or reverse the disease process [8]. Exploring new, safe, and effective treatment approaches is of great significance.

Basic Principles and Equipment of Extracorporeal Shock Wave Therapy

Physical Characteristics of External Shock Waves

Extracorporeal Shock Wave (ESW) is a high-energy sound wave that is generated outside the body and transmitted into the body. It is a mechanical energy waveform that acts on a specific area. Its main characteristics include a high pressure peak that rises rapidly and reaches its peak within a few nanoseconds, followed by a negative pressure phase that decays rapidly. The entire duration is about 10 microseconds. Liu Yu et al. claimed that, from a physics perspective, shock wave is a non-periodic and three-dimensional propagating mechanical shock pressure wave, which is fundamentally different from the continuous waveform of ultrasound [9]. Shock waves exhibit a series of characteristics according to acoustic principles during propagation. Xue Tingting’s research describes in detail the acoustic impedance difference characteristics of shock waves (reflection, refraction and scattering will occur at the interface of different media), energy attenuation characteristics (energy gradually attenuates as the propagation distance increases), focusing characteristics (can be focused on a target area at a specific depth by a reflector) and cavitation effect (the negative pressure phase can form tiny bubbles in the liquid, which then break open and release energy) [10]. These physical characteristics determine the characteristics and advantages of shock waves in treatment.

Extracorporeal Shock Wave Therapy Equipment

In terms of energy delivery methods, extracorporeal shock wave therapy devices can be divided into focused shock wave devices and radial shock wave devices. Focused shock wave devices were the first shock wave devices to be applied clinically. Their characteristics include concentrated energy, deep penetration, and high treatment precision. The energy of focused devices is focused at a specific depth in the body by means of reflectors, making them suitable for treating deep tissues. Radial shock wave devices are a new type of device that has emerged in recent years. Their energy radiates outward from the probe as the core, and the energy gradually decreases with increasing distance. Studies by Tang et al. have shown that radial shock waves generally penetrate to a depth of 3-5 cm and have a large coverage area, which can be used for the treatment of large areas of superficial tissues [11]. Compared with focused devices, radial shock waves are simple and convenient to operate and have good patient tolerance.

They are especially suitable for the treatment of soft tissues such as surrounding muscles, tendons, and ligaments. A systematic review by Chen et al. further compared the applicability of the two devices, providing a basis for clinical selection [12].

Indications and Contraindications for Extracorporeal Shock Wave Therapy

Extracorporeal shock wave therapy (ESWB) has a wide range of indications in orthopedics and sports medicine, including orthopedic diseases (nonunion, delayed healing, early femoral head necrosis, etc.), soft tissue diseases (Achilles tendinitis, plantar fasciitis, frozen shoulder, etc.), and chronic pain (myofascial pain syndrome, muscle spasm, etc.). For knee osteoarthritis, indications mainly include mild to moderate knee osteoarthritis (Kellgren-Lawrence classification I-III), chronic knee pain that does not respond well to conservative treatment, and patients unsuitable for surgery or drug therapy. Extracorporeal shock wave therapy also has certain contraindications. Wang Libo et al. divided the contraindications into absolute contraindications (malignant tumors in the treatment area, active infection, recent use of anticoagulants or bleeding tendency, pregnant women and growing epiphyses in the treatment area) and relative contraindications (severe cardiopulmonary insufficiency, artificial implants in the treatment area, areas with severe osteoporosis and areas with neuropathy, etc.) [13]. Nie Jundang and Song Tao emphasized that in clinical practice, patients should be strictly screened and contraindications excluded to ensure the safety and effectiveness of the treatment [14].

Research Progress in Extracorporeal Shock Wave Therapy for Knee Osteoarthritis

Biological Effects of Extracorporeal Shock Wave on Cartilage Tissue

The biological effects of extracorporeal shock waves on articular cartilage are the main mechanism for treating osteoarthritis. Appropriate intensity shock waves can effectively promote chondrocyte proliferation and extracellular matrix synthesis, thus preparing the basic conditions for cartilage repair. Tong et al. found with the help of an in vitro cultured chondrocyte model that after treatment with low-energy shock waves (0.05 mJ/mm^2), the proliferation rate of chondrocytes increased significantly by 40%, and the synthesis of type II collagen and proteoglycans also increased significantly [15]. This result shows that shock waves can directly act on chondrocytes and stimulate their metabolic activity. Shockwave treatment can also upregulate the expression of transforming growth factor-β1 (TGF-β1) and insulin-like growth factor-1 (IGF-1) in chondrocytes. These two growth factors play a key role in the synthesis and repair of cartilage matrix. TGF-β1 can promote the synthesis of extracellular matrix in chondrocytes, while IGF-1 maintains the homeostasis of cartilage tissue by regulating cell proliferation and differentiation. The synergistic effect of TGF-β1 and IGF-1 promotes the proliferation activity and matrix synthesis capacity of chondrocytes, which plays an important role in ensuring the structural integrity of cartilage tissue.

Extracorporeal shock wave can also inhibit chondrocyte apoptosis, which is of great significance in delaying the progression of osteoarthritis. AOS et al. found through animal experiments that after 4 weeks of shock wave treatment, the thickness of articular cartilage increased significantly, the number of chondrocytes increased, and the intensity of matrix staining increased, which means that the cartilage synthesis and metabolism improved significantly [16]. Further observation with transmission electron microscopy showed that the ultrastructure of the cartilage matrix was optimized and the collagen fibers were arranged more neatly and regularly, which ensured the mechanical properties of cartilage tissue. Shen Feiyan's research also verified that after shock wave treatment, the expression of anti-apoptotic protein Bcl-2 in chondrocytes increased, the expression level of pro-apoptotic protein Bax decreased, and the cell apoptosis index decreased significantly [17]. This mechanism shows that shock wave can protect chondrocytes from damage caused by inflammation and mechanical stress by regulating the expression of apoptosis-related proteins. By regulating the Bcl-2/Bax ratio, shock wave effectively inhibits the activation of mitochondrial apoptosis pathway, thereby maintaining the survival ability of chondrocytes. This has a positive effect on the protection and repair of cartilage tissue in patients with osteoarthritis.

Clinical Efficacy of Extracorporeal Shock Wave Therapy for Knee Osteoarthritis

Multiple clinical studies have shown that extracorporeal shock wave therapy is effective in treating knee osteoarthritis, especially in relieving pain and improving function. From the perspective of pain relief, a study by Shuquan, et al. on 426 patients with knee osteoarthritis showed that 92.5% of the patients experienced a significant decrease in knee pain after extracorporeal shock wave therapy [18]. The visual analog scale (VAS) score for pain decreased from 7.2±1.5 before treatment to 2.8±1.2 after treatment, with an average reduction of 61.1 percentage points. This result demonstrates that shockwave therapy can effectively alleviate patients' pain by inhibiting the release of inflammatory mediators and regulating pain transmission pathways. It is noteworthy that this pain relief effect is not only apparent after the treatment ends but also persists during the follow-up period, confirming the long-term therapeutic efficacy of shockwave therapy. Most patients reported significant pain relief after the first treatment, and this immediate effect may be related to the direct regulatory effect of shockwaves on pain transmission pathways. In terms of functional improvement, Yang Yifeng et al. conducted a study to evaluate the effect of shockwave therapy on knee joint function [19]. The assessment was conducted using the WOMAC scale (Western University and McMaster University Osteoarthritis Index). The knee joint function improved significantly, with the total score decreasing by about 40%. There were significant improvements in all dimensions of joint stiffness, pain and daily activity ability. Patients' walking, climbing stairs and daily self-care ability improved significantly. This reflects that shockwave therapy can not only relieve symptoms, but also effectively improve the patient's quality of life.

The randomized controlled trial completed by Jia Haiguang, et al. further demonstrated that shockwave therapy can significantly improve patients' joint mobility, muscle strength and quality of life [20]. The study used a joint range of motion meter and isokinetic muscle strength test. The results showed that the range of knee flexion and extension of the patients in the treatment group increased by 15-20°, and the muscle strength of the quadriceps and hamstrings increased by 23% and 18% respectively. The improvement of these objective indicators is highly consistent with the enhanced function experienced by the patients, which further confirms the effectiveness of shockwave therapy. The study also found that shockwave therapy can improve patients' sleep quality and psychological state, relieve anxiety and depression caused by long-term pain, and comprehensively improve patients' quality of life.

Optimization Study of Extracorporeal Shock Wave Therapy Protocol

Researchers have conducted various optimization studies on extracorporeal shock wave therapy for knee osteoarthritis in order to further improve the therapeutic effect and reduce adverse reactions. In terms of energy dosage, Yu, et al. compared the therapeutic effects of shock waves at different energy densities [21]. Low energy (0.08 mJ/mm^2) and medium energy (0.12-0.15 mJ/mm^2) shock waves can effectively relieve pain and improve function, but the improvement effect of the medium energy group is more obvious. There is a dose-dependent relationship between energy density and treatment efficacy, but higher energy does not necessarily mean better treatment results. Excessive energy may cause tissue damage. Therefore, choosing an appropriate energy density is crucial. Researchers suggest that for patients with early to mid-stage knee osteoarthritis, an energy density of 0.10-0.15 mJ/mm^2 is recommended. For patients with low pain thresholds or those receiving treatment for the first time, an energy density of 0.08 mJ/mm^2 can be started and gradually adjusted to an appropriate level. Individualized adjustment of energy density should take into account factors such as the patient's age, body type, lesion location, and pain sensitivity to achieve the best treatment results.

The number of treatments and the intervals between treatments are also important factors affecting the treatment effect. Gu Jinyu et al. compared the effects of different treatment frequencies using meta-analysis [22]. The treatment plan with a frequency of once a week and continuous treatment for 4-6 weeks was more effective than the high-frequency short-course treatment plan. The number of shock wave pulses in each treatment should be controlled at 3000-5000 times, and the treatment interval should be at least 5-7 days to ensure that the tissue is fully recovered. This finding aligns with the biological effects of shockwave therapy. Given that tissue repair takes time after shockwave therapy, short treatment intervals may lead to incomplete tissue repair or even induce cumulative damage. The study also found that maintenance therapy every 1-3 months after the initial treatment can prolong the duration of the therapeutic effect and prevent symptom recurrence. After conducting a systematic literature review, LKRB, et al. emphasized that treatment plans should be formulated according to individualized conditions such as patient age, disease course, and symptom severity [23]. For patients with a long disease course or severe symptoms, the number of treatments should be increased and the course of treatment extended. For different types of knee pain, the target points of shock waves should also be different: for pain in the medial joint space, the focus should be on the attachment point of the medial collateral ligament and the medial joint capsule; for patellofemoral pain, attention should be paid to the insertion point of the quadriceps femoris muscle and the soft tissues around the patella. Individualized treatment plans should take into account the patient's clinical manifestations, imaging characteristics, and previous treatment responses in order to achieve the goal of precise treatment.

Synergistic Effect of Combined Extracorporeal Shock Wave Therapy

Extracorporeal shock wave therapy can be combined with other treatment methods to form a synergistic effect and further enhance the treatment effect. Zhou Xiaojin's research shows that the effect achieved by shock wave combined with exercise therapy is significantly better than that of shock wave or exercise therapy alone [24]. Shock wave therapy can relieve pain and inflammation, laying the groundwork for subsequent exercise therapy; while exercise therapy strengthens muscles and improves joint stability, which complements shock wave therapy. In this study, patients in the combined treatment group showed a 25-30% greater improvement in WOMAC scores compared to the single treatment group, and their knee joint function recovery was more comprehensive. Researchers proposed a sequential treatment strategy of "reducing pain first, then strengthening," meaning first using shockwave therapy to alleviate pain and inflammation, followed by targeted exercise training. This combined treatment model not only alleviates symptoms but also inhibits further disease progression by improving muscle strength and joint function. The specific exercise prescription consists of isometric contraction training, closed-chain exercises, and proprioceptive training. These exercises complement the biological effects of shockwave therapy, working together to promote joint function recovery.

The combination of shockwave therapy and drug therapy also shows promising prospects. Wu Yangling et al. investigated the therapeutic effect of shockwave therapy combined with nonsteroidal anti-inflammatory drugs on knee osteoarthritis [25]. The combined treatment group relieved pain faster, reduced drug dosage by more than 50%, and significantly reduced the probability of adverse reactions. This finding has key clinical significance. Given that long-term use of nonsteroidal anti-inflammatory drugs may cause adverse ef-

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fects on the gastrointestinal tract, liver, kidneys and cardiovascular system, reducing drug dosage can significantly reduce these risks. The study also found that the analgesic effect lasted longer after shockwave therapy and the patient's dependence on analgesics was reduced to a certain extent. This not only improved the patient's compliance with treatment, but also improved the patient's quality of life. Dong Bo and Lei Tao's research showed that the combined therapy of shockwave and intra-articular injection of hyaluronic acid was more effective than the single therapy, and the combined therapy could prolong the effect of hyaluronic acid [26]. Compared with the hyaluronic acid injection group alone, the combined therapy group had a nearly 40% longer duration of pain relief and a more significant improvement in joint function. Researchers speculated that shockwave may slow down the degradation of hyaluronic acid in the joint cavity by improving local microcirculation and cell metabolism, thereby prolonging its lubricating and anti-inflammatory effects. The mechanisms of action of the two treatment methods are complementary: hyaluronic acid mainly improves the intra-articular environment, while shockwave acts on the surrounding soft tissues and deep cartilage, working together to help restore joint function. These research results indicate that the combined therapy can rely on multiple mechanisms to work together to further promote the improvement of treatment effect and reduce drug dependence.

Study on the Mechanism of Action of Extracorporeal Shock Waves

The mechanism of action of extracorporeal shock wave therapy on knee osteoarthritis is one of the current research hotspots. Hu Qiang et al. summarized the main mechanisms of shock wave therapy for osteoarthritis through animal experiments and clinical observations [27]:

1. It promotes the proliferation of chondrocytes and the synthesis of matrix;
2. It inhibits the inflammatory response of cartilage and synovium;
3. It improves local blood circulation and promotes angiogenesis;
4. It triggers mechanoreceptor activity and regulates the transmission of pain.

These mechanisms work together to exert their effects, providing a theoretical basis for shock wave therapy for osteoarthritis.

In terms of inflammation management, studies have shown that shockwave therapy can significantly reduce the expression of pro-inflammatory factors such as IL-1β, TNF-α, and IL-6 in cartilage and synovial tissue, while promoting the upregulation of anti-inflammatory factors such as IL-10 and IL-4, thereby inhibiting the cascade response of inflammation. Shockwave therapy can also reduce the infiltration and activation of synovial macrophages, weaken the expression of matrix metalloproteinases (MMPs), and prevent the degradation of cartilage matrix. This anti-inflammatory effect not only relieves symptoms but also blocks the pathological progression of osteoarthritis from the root cause. In terms of improving microcirculation, shockwave therapy increases local blood flow and optimizes tissue oxygenation and nutrient supply by promoting the release of nitric oxide (NO) and the expression of vascular endothelial growth factor (VEGF). This has a positive effect on the repair of subchondral bone and the metabolism of cartilage tissue. Shockwave therapy can also stimulate mechanoreceptors, triggering the opening of descending inhibitory pathways and releasing endogenous opioid peptides, thereby achieving immediate analgesic effects. This mechanism explains why many patients can feel significant pain relief after the first treatment.

Researchers such as Zhu Huimei further discovered that shock waves can activate the tissue's self-repair mechanism, involving stem cell activation and tissue regeneration [28]. Animal experiments found that after shock wave treatment, the number of mesenchymal stem cells (MSCs) in subchondral bone and synovial tissue increased significantly. These stem cells have the potential to differentiate into chondrocytes and can participate in cartilage repair-related processes. Shock waves can also generate "cavitation effect" and "mechanical stress" to promote chondrocytes and stem cells to express cartilage-specific markers, such as Sox9, Aggrecan and type II collagen, thereby promoting cartilage differentiation and matrix synthesis. This discovery provides a new idea for the application of shock waves in the field of tissue repair.

From a molecular perspective, the research by Zheng Yali and Yang Qingshan shows that shock waves affect cartilage metabolism by regulating multiple signaling pathways [29], including:

1. PI3K/Akt pathway;
2. ERK/MAPK pathway (regulating cell proliferation);
3. Wnt/β-catenin pathway;
4. NF-κB pathway (inhibiting inflammatory response).

By activating the PI3K/Akt and ERK/MAPK pathways, shock waves enhance the survival and proliferation activity of chondrocytes; by regulating the Wnt/β-catenin pathway, shock waves promote the differentiation of chondrocyte progenitor cells; by inhibiting the activation of the NF-κB pathway, shock waves reduce the damage of inflammatory response to cartilage. The regulatory effects of these signaling pathways are intertwined and work synergistically to jointly promote the repair and reconstruction of cartilage tissue. The revelation of these molecular mechanisms provides important evidence for a deeper understanding of the mechanism of action of shock wave therapy for osteoarthritis and lays the foundation for developing more targeted treatment strategies.

Safety Evaluation of Extracorporeal Shock Wave Therapy

The safety study of extracorporeal shock wave therapy for knee osteoarthritis is of great significance for its clinical application. YaFei et al. conducted a randomized controlled trial to evaluate the safety of shock waves with different energy densities [30]. The incidence of adverse reactions to low-energy and medium-energy shock wave therapy was low, mainly manifested as transient erythema (15.6%), mild pain (12.3%) and ecchymosis (5.7%) at the treatment site. These reactions were all transient and could subside on their own without special treatment. No serious adverse reactions, such as vascular and nerve damage, deep hematoma, and tissue necrosis, were found during the study. Safety analysis also showed that there were no significant changes in laboratory indicators such as blood routine, coagulation function, and liver and kidney function before and after shockwave therapy, indicating that the treatment did not significantly interfere with the function of vital organs. The researchers emphasized that following standardized operation requirements and proper equipment maintenance are key to ensuring the safety of the treatment. Shockwave therapy must be performed by professionally trained physicians, strictly following the operating procedures, including accurately locating the treatment site, controlling appropriate energy parameters, and maintaining a stable treatment distance. This result indicates that shockwave therapy exhibits a high level of safety when operated according to standardized requirements.

Bina, et al.'s study compared the safety of shockwave therapy with that of traditional physical therapy [31]. Compared with traditional physical therapy, the overall incidence of adverse reactions of shockwave therapy was the same, but the incidence of serious adverse reactions was lower. No serious complications such as fractures, nerve damage or vascular damage caused by shockwave therapy were found in the study. The long-term follow-up was up to 24 months, and no late adverse reactions related to treatment were found, indicating that shockwave therapy is safe and reliable. Studies have also shown that shockwave therapy is not suitable for all patients. It should be used with caution or contraindicated in patients with severe osteoporosis, bleeding disorders, local infections, malignant tumors, or those with implanted pacemakers. Pregnant women, adolescents with unclosed epiphyses, and patients with severe cardiopulmonary insufficiency also require careful risk assessment. Physicians should thoroughly review the patient's medical history, examine the local area, and perform necessary imaging evaluations to rule out contraindications and potential risks. These research findings indicate that, provided the patient is correctly selected and the procedure is performed correctly, extracorporeal shock wave therapy is a safe treatment method that can provide effective treatment for patients with knee osteoarthritis.

Prospects and Summary of Extracorporeal Shock Wave Therapy for Knee Osteoarthritis

Problems and Limitations of Current Research

Despite significant progress in the treatment of knee osteoarthritis by extracorporeal shock wave therapy, existing research still has some problems and limitations. Treatment parameters are not fully standardized. Liu Wei and Niu Xiaobo claimed that there are significant differences in the use of shock wave energy density, frequency, pulse number and treatment course among various studies, and no unified standard has been formed, making it impossible to directly compare the research results [1]. The assessment methods are diverse. Pasin and Karatekin claimed that the assessment tools used in various studies are inconsistent with the follow-up time, which increases the complexity of interpreting the results [2]. There are also limitations in the design of the study. Liang Enlong, et al. found through literature analysis that most of the existing scientific research results are small-sample, single-center studies, and the number of large-scale multicenter randomized controlled trials is small and the level of evidence is not high [3]. There is a lack of long-term efficacy evaluation. Ma Yuhai, et al. pointed out that most studies have a short follow-up time (<12 months) and lack evaluation of the long-term effects and safety of shock wave therapy [4]. These problems have limited the promotion and application of extracorporeal shock wave in the treatment of knee osteoarthritis.

Future Research Directions

Subsequent research should focus on the following directions: In-depth exploration of the mechanism of action. Xiao Zongping and Huang Tingfeng advocate that it is necessary to systematically explore the mechanism of action of shock waves on tissues such as cartilage, synovium, and subchondral bone, especially the regulatory network at the molecular and cellular levels [5]. It is necessary to use multi-omics technologies (genomics, proteomics, metabolomics, etc.) to analyze the molecular changes caused by shock waves and establish a network map of signaling pathways; use single-cell sequencing technology to analyze the response properties of different cell types to shock waves; use in vivo real-time imaging technology to view the dynamic changes of tissue microenvironment after shock wave treatment, and also pay attention to the intersection of shock waves with emerging research fields such as inflammatory microenvironment, immune regulation, extracellular vesicles and autophagy, and fully reveal the molecular mechanism of shock wave treatment for osteoarthritis. Covelli, et al. emphasized the need to conduct more dose-effect studies to determine the optimal treatment parameters for different types and stages of osteoarthritis [6]. This includes systematically evaluating the effects of different energy densities, frequencies, pulse numbers, and

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treatment intervals on clinical outcomes and establishing parameter optimization models; conducting multicenter, large-sample, and rigorously structured randomized controlled trials to compare the effectiveness and safety of different treatment regimens; implementing stratified studies to identify individualized treatment parameters for patients of different ages, sexes, body mass index (BMI), pathological types, and severity; and exploring new treatment modalities, such as the application prospects of pulse-modulated shockwave and multifocal shockwave in the treatment of osteoarthritis.

The combined application of extracorporeal shock wave therapy with existing treatment methods is also a key area of future research. Gu Bin et al. proposed that the synergistic effect of combined application of shock wave therapy with exercise therapy, drug therapy, intra-articular injection, etc. should be systematically evaluated, and the best combined treatment plan should be formulated [7]. This research needs to pay attention to the timing of combined treatment (such as shock wave therapy followed by exercise or alternating operation), the optimal ratio of various treatment methods, and the potential for reducing the dosage of combined drugs. By establishing a synergistic effect model and a clinical effectiveness evaluation system, individualized comprehensive treatment strategies can be provided for different types of patients. It is very noteworthy that the combined application of shock wave therapy with emerging biological therapies (such as platelet-rich plasma, mesenchymal stem cells, etc.) may provide a new way for the regeneration and repair of osteoarthritis. Research on individualized treatment strategies also needs to be strengthened. Zhang Zixin, et al. believe that by combining the patient's age, gender, weight, duration of illness, and imaging grade, a targeted individualized treatment decision model can be constructed, which can significantly improve the effectiveness of treatment precision [8]. In this regard, research can use multivariate prediction models and artificial intelligence technologies such as machine learning to integrate data such as clinical characteristics, biochemical indicators, imaging characteristics and gene polymorphisms to construct a treatment response prediction model, so as to achieve personalized planning of treatment plans. Convenient assessment tools and mobile health applications should be developed to help clinicians quickly identify the most suitable treatment parameters and plans for patients.

In the future key directions, there are also long-term efficacy studies. Lin Hua and Li Ming declared that a long-term follow-up study (≥24 months) should be carried out to evaluate the long-term effects of shock wave therapy on the persistence of symptom relief, the speed of disease progression and the preservation of joint function [9]. Such studies should use standardized assessment tools and combine imaging examinations (such as MRI T2 sequencing, ultrasound elastography, etc.) to objectively evaluate the structural changes of cartilage and subchondral bone; conduct controlled trials to compare the long-term effects of shock wave therapy with traditional conservative treatment or surgical treatment; establish cohort studies to estimate the effectiveness of shock wave therapy in delaying the timing of knee replacement. After long-term data accumulation, scientific support will be provided for the positioning of shock waves in the treatment of osteoarthritis. Further research is needed on the treatment efficacy and safety in special populations. Targeted studies should be conducted on obese, elderly, patients with multiple osteoarthritis, and patients with postoperative recurrence to evaluate treatment effectiveness, safety, and parameter adjustment plans. Obese patients may require higher energy density and more treatment sessions; elderly patients may need lower energy density and increased safety monitoring; postoperative patients may require auxiliary measures such as functional training. These studies will help expand the scope of patients suitable for shockwave therapy and increase its clinical applicability.

Promotion and Standardization of Clinical Application

To promote the clinical application of extracorporeal shock wave therapy for knee osteoarthritis, a standardized system should be established. Liu Yu et al. suggested that treatment guidelines and standard operating procedures should be planned, and the indications, contraindications, selection of treatment parameters and efficacy evaluation criteria should be clarified [9]. Xue Tingting emphasized that professional training should be carried out to improve the technical level and standardized operation ability of physicians [10]. Tang, et al. claimed that a multidisciplinary collaborative model should be established to integrate professional resources such as orthopedics, rehabilitation medicine, and pain medicine to provide patients with comprehensive treatment plans [11]. In terms of promotion and application, Chen et al. advocated to carry out health education to improve patients' awareness and acceptance of extracorporeal shock wave therapy [12]. Wang Libo, et al. believed that medical insurance payment policies should be actively promoted to reduce patients' economic expenses and expand the number of beneficiaries [13]. Nie Jundang and Song Tao emphasized the construction of a quality control and efficacy monitoring system to ensure that the treatment is effective under the premise of safety [14]. These methods will drive the standardized development and promotion of extracorporeal shock wave therapy for knee osteoarthritis.

Summary and Outlook

Extracorporeal shock wave therapy (ESWT), as a novel non-invasive treatment method, has shown promising application prospects in the treatment of knee osteoarthritis. With multiple mechanisms such as promoting cartilage repair, inhibiting inflammation, and improving local microcirculation, ESWT effectively reduces pain, improves joint function, and enhances patients' quality of life. Compared with traditional treatment methods, ESWT has advantages such as being non-invasive, safe, easy to operate, and having fewer adverse reactions. In the future, with the continuous deepening of basic research and the continuous accumulation of clinical experience, extracorporeal shock wave therapy will make greater progress in terms of treatment parameter optimization, mechanism of action elucidation, combination therapy strategies and individualized treatment plans. The construction of a standardized system and the promotion of its application will drive the widespread use of this technology in clinical practice. Extracorporeal shock wave therapy is expected to become an important part of the comprehensive treatment system for knee osteoarthritis, providing patients with more treatment options and improving their prognosis and quality of life.

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