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Extracorporeal Shockwave Therapy as an Orthobiologic Tool for Musculoskeletal Injuries: A Narrative Review

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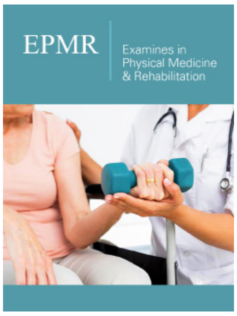

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Abstract

Since its inception with lithotripsy over 3 decades ago, Extracorporeal Shockwave Therapy (ESWT) is a globally used treatment for musculoskeletal injuries. ESWT is a non-invasive anabolic modality promoting neovascularization and angiogenesis by inducing the body's own secretion of growth factors and inflammatory mediators. Using machine-based energy via acoustic waves, ESWT facilitates bone and connective tissue metabolism and homeostasis with multiple therapeutic applications. ESWT provides analgesia via denervation and reinnervation of sensory nerves and disruption of C-Fibers. It has demonstrated safety and efficacy in a wide range of upper and lower extremity musculoskeletal conditions involving soft tissue, tendon, and bone. Given the universal increased incidence of musculoskeletal pain, physicians are seeking minimally invasive and cost-effective tools. Along with the emergence of orthobiologic injections, shockwave is gaining popularity by leveraging the body's inherent ability to self-heal. This article provides a narrative review of ESWT for chronic musculoskeletal injuries and its potential as a biologic tool.

Keywords: Shockwave therapy; Orthobiologic tool; Musculoskeletal injuries; Acoustic waves

Introduction

Extracorporeal Shockwave Therapy (ESWT) has become a more widely used primary and adjunctive treatment for several musculoskeletal injuries. It serves as a safe, noninvasive treatment with a growing body of literature supporting its efficacy in various pathologies. The aim of this narrative review is to detail its mechanisms of action and indications for use while exploring how ESWT is a machine based orthobiologic tool. The initial application of ESWT therapy began with lithotripsy (ESWL) in Germany for the fragmentation of kidney stones harnessing high energy acoustic waves. This led to the eventual use of ESWL for salivary glands, gallbladder, pancreas, and bile duct stone fragmentation. Upon further evaluation of the surrounding connective tissue and bone from ESWL, Urologists discovered incidental findings of bone regeneration. A study conducted on 26 female rabbits comparing effects on the femur and ischium following ESWT, demonstrated osteoblast stimulation following initial osteocyte damage [1]. This suggested that in addition to stone destruction, acoustic waves promoted healing in bone and connective tissue prompting further investigation into musculoskeletal applications.

Continued research on ESWT has demonstrated three primary biomechanical mechanisms for its healing properties: enhanced blood flow via neovascularization, metabolic effects on bone and connective tissue, and analgesic effects on C-fibers and sensory nerves. ESWT uses acoustic waves generated from oscillation to resonate through damaged structures. Acoustic waves penetrating through damaged tissue generate mechanotransduction, which leads to cell migration, proliferation, and differentiation [2]. This mechanism simulates mechanical loads similar to exercise, triggering metabolic effects and cell signaling. Blood flow is stimulated through the promotion of neovascularization within damaged tissue which promotes the inflammatory cascade and local healing of the damaged tissue. A study investigated the effects of ESWT treatment on ischemic muscle and discovered mechanotransduction induces release of RNA stimulating Toll-like receptor 3 (TLR3) signaling induced angiogenesis and improved blood perfusion [3]. ESWT treatment has been found to fragment calcific deposits within tendons and bone while reducing bone marrow edema. In addition, ESWT has substantial effects on Substance P and CGRP providing pain relief through the disruption of C-fibers and sensory nerves [4,5].

Methods

We conducted a review of literature related to ESWT treatment and musculoskeletal injuries. The focus of inclusion criteria for the study centered around involving ESWT treatment specifically for musculoskeletal injuries, as a significant amount of research has been published on the use of ESWT in the form of lithotripsy. Articles for this review were obtained through inclusion and exclusion criteria. Databases used include UpToDate and Medline. Due to the inability to use Mesh terms, the methodology for article selection followed the four criteria for selection: search various databases, remove duplicates, screen articles based on inclusion and exclusion criteria, and review the remaining articles. Articles were selected for screening based on their specific relevance to ESWT treatment and musculoskeletal injuries. Articles were organized by musculoskeletal pathology in the literature review section and are referenced accordingly.

True shockwave and radial pressure wave therapy

There are different types of Shockwave therapy both having their own indications in clinical practice. True shockwave includes focused and unfocused technologies. Focused Extracorporeal Shockwave Therapy (fESWT) involves a deeper point of maximum Energy Flux Density (EFD) that penetrates through skin, muscle, and bone covering a small pinpoint area. Unfocused shockwave therapy, also known as low intensity Extracorporeal Shockwave Therapy (Li-ESWT) has a deep and wide distribution of energy.

Radial Extracorporeal Shockwave Therapy (rESWT) characteristically a pressure wave and involves a superficial point of maximum EFD penetrating skin and muscle with a broader area of application [6]. There has been significantly more research and randomized control trials conducted on the efficacy of true ESWT compared to radial pressure waves. Radial ESWT has demonstrated improvement with superficial soft tissue conditions including plantar fasciitis, epicondylitis, Achilles tendinosis, and myofascial trigger points. Whereas true ESWT has been more ideal for deeper structures including bone trauma, calcifications, and chronic tendinopathies [7].

Neovascularization

ESWT has been shown to induce angiogenesis through increasing the body's secretion of growth factors and inflammatory proteins. A study conducted on the Achilles tendon of rabbits demonstrated ESWT treatment increases the levels of eNOS, VEGF, and PCNA as early as one week following administration. With eNOS and VEGF levels remaining at increased levels for 8 weeks following administration, while PCNA levels remain increased for 12 weeks before returning to normal [8]. A study conducted on mice demonstrated ESWT induces toll-like receptor 3 signaling helping mediate angiogenic response to surrounding tissue. Researchers hypothesize the induction of angiogenesis is caused by the release of cytoplasmic RNA through mechanotransduction [3].

Disruption of sensory and C-fiber nerves

ESWT treatment has short term and long-term effects for reduction of pain. ESWT creates a "wash out effect" on substance P, flooding the nervous system and distracting the body from pain. Reduction of pain with ESWT clinically can start as early as 2-5 minutes and may last for 2-4 weeks [9]. Interestingly, applying local anesthesia during treatment compromises the effect with detrimental effects on ESWT outcomes [10]. Research demonstrates the substantial involvement and role of both substance P and calcitonin gene-related peptide in pain and inflammation, especially in chronic inflammation. Studies have established a reduction in Calcitonin Gene-Related Peptide (CGRP) and substance P following ESWT application to the musculoskeletal system [11]. Substance P has been observed to be present in both unmyelinated C-fibers and A-delta fibers [4,5,12].

Literature Review

Over the past 20 years, there has been a rise in peer reviewed literature highlighting the applications of ESWT for chronic musculoskeletal conditions. Studies indicate that ESWT acts on chronic conditions through neovascularization, reducing calcium deposits and bone edema, as well as lessening pain. ESWT has shown positive results addressing common upper extremity conditions such as calcific tendinosis of the shoulder, lateral epicondylosis, carpal tunnel syndrome, greater trochanteric pain syndrome, osteonecrosis of the femoral head, patellar tendinosis, knee osteoarthritis, medial tibial stress syndrome, lower limb tendinopathies, plantar fasciitis, bone edema lesions, and non-union fractures.

Calcific tendinosis of the shoulder

Calcific tendinopathy of the rotator cuff is characterized by inflammation around deposits of calcium carbonate apatite crystals within tendon and is a common source of pain in the shoulder. Conventional treatment is conservative in nature and may involve NSAIDs, corticosteroid injections, needle barbotage, percutaneous needle tenotomy, physical therapy, and Transcutaneous Electrical Nerve Stimulation (TENS). Open vs. arthroscopic surgical procedures often yield good results at alleviating pain. Prior to moving from conservative management to a surgical procedure, ESWT can be an option for patients who wish to alleviate pain and improve overall shoulder function that may be comparable to surgical intervention. A study performed by Cacchio, et al. in 2006 followed 90 patients with radiographically diagnosed calcific tendinitis in the shoulder. In this study, rESWT was effective at dissolving calcifications at a rate that was unexpectedly better than that which was achieved with extracorporeal shockwave therapy in another study performed by Rompe et al. [13,14]. Rompe et al. [13] observed a rate of calcification disappearance of 47% and a partial disappearance of 33%; compared to the study performed by Caccio et al. [15] that yielded complete calcific disappearance in 86.6% of subjects in the treatment group and partial disappearance in 13.4% of the subjects in the treatment group. These results indicate that rESWT is an effective means of non-operatively treating pain from calcific tendinosis of the shoulder. The primary limitation of the study performed by Cacchio et al. [15] was that there was a lack of a true placebo-control group, although there were no adverse effects with an increased rate of success in the treatment group [15].

A metanalysis conducted by Wu et. al [16] investigating 14 studies with 1105 participants demonstrated Radial Shockwave Therapy (RSW), High-Energy Focused Extracorporeal Shockwave Therapy (H-FSW), and Ultrasound-Guided Needling (UGN) can successfully remove chronic calcific deposits [16]. Al-Kahir et al. [17] enrolled 45 patients with calcific shoulder tendinopathy and split patients into 3 groups: Focused shockwaves (F-SW) 1500, radial shockwaves (R-SW) 2000 and combined focused and radial shockwaves (C-SW). All three treatments demonstrated improvement in functional, clinical, and sonographic findings, but combined focused and radial ESWT was the best therapy of all three interventions [17].

Patients suffering from acute shoulder calcific tendinosis may traditionally receive Subacromial (SA) corticosteroid injections to alleviate pain prior to considering surgical management. However, ESWT is an effective tool alleviating pain in the shoulder without the long-term negative effects of repeated steroid injections. A study completed by Ioppolo et al. [18] compared the energy level of focal ESWT necessary to effectively alleviate pain in the shoulder - primarily comparing the effectiveness of 0.20mJ/mm2 and 0.10mJ/mm2. Using a VAS questionnaire that was administered prior to treatment, 3, and 6 months post-treatment, it was determined that the stronger energy level of 0.20mJ/mm2 was the most effective at alleviating pain and improving overall function [18]. The primary limitations of this study were the lack of a control group that had diagnosed calcific tendinopathy but received no ESWT treatment, as well as the small sample size.

Lateral epicondylitis

Lateral epicondylitis, also known as tennis elbow, is a common musculoskeletal injury at the elbow. The injury is most commonly chronic in nature, due to the repetitive use of extensor muscles, but can also present acutely. Current medical management for lateral epicondylitis includes physical therapy, oral and topical NSAIDs, local injections of steroid or Platelet Rich Plasma (PRP), and splinting. In comparison to traditional treatment methods, ESWT has demonstrated improvement in both grip strength and pain associated with lateral epicondylitis [19]. In an additional comparative study investigating treatment differences in ultrasound, ESWT, and kineso-taping, ESWT demonstrated the most significant decrease in Common Extensor Tendon (CET) thickness in addition to a reduction in pain and improvement in functionality/grip strength [20]. Ibrahim, et al. conducted a study investing ESWT treatment versus local corticosteroid injection in the treatment of lateral epicondylitis. 30 athletes were split into two treatment groups: ESWT and corticosteroid. Both corticosteroid injections and ESWT treatment had significant improvements in VAS pain scores, but ESWT treatment demonstrated significant improvement on long term clinical and ultrasonographic follow-up when compared to corticosteroid.

Carpal Tunnel Syndrome

Carpal Tunnel Syndrome (CTS) is the most common entrapment neuropathy, and although surgical intervention provides consistently positive outcomes, there remain complications including post-op pain, weakness, and pillar pain - which can last up to 6 weeks post-op. Plus, some patients are reluctant for surgery and prefer a non-invasive alternative with limited down time. In 2019, Chang et al. [21] studied both radial and focused ESWT on a total of 40 participants with moderate CTS to determine if ESWT could improve healing, mitigate nerve pain, and improve overall function. Both the treatment and control group received one ultrasound guided PRP injection, while the treatment group also received additional treatment with radial ESWT. The findings of this study indicated that combined PRP and rESWT had no significant difference vs the control group who received PRP alone. The researchers suggested that further studies be conducted that include multiple sessions of ESWT as opposed to one, with longer follow-up periods to verify clinical efficacy [21].

A 30 patient study conducted by Gesslbauer et al. [22] compared a control Vs a single focused ESWT treatment demonstrating a significant difference in VAS scores and hand grip strength at 3 and 12 weeks. Focused ESWT also demonstrated significant improvements in sensory nerve conduction velocity and distal motor latency of the median nerve. The authors concluded that focused ESWT is capable of being a noninvasive treatment for mild to moderate carpal tunnel syndrome [22].

Greater Trochanteric Pain Syndrome

Greater Trochanteric Pain Syndrome (GTPS), also known as lateral hip pain and trochanteric bursitis, is a chronic musculoskeletal injury of the lateral hip that can affect the lower extremity radiating to the knee. GTPS pain is associated with running, walking and standing and can be difficult to treat. Current treatment involves conservative therapy of icing, rest, and physical therapy in addition to medical management with oral/topical NSAIDs and ultrasound-guided corticosteroid and orthobiologic injections. Ramon, et al. [23] conducted a randomized control trial on 103 patients with chronic GTPS investigating the effects of f-ESWT, in addition to exercise protocol, at 1,2,3, and 6 months follow up. Outcomes were measured via Visual Analogue Pain Score (VAS), Harris Hip Score (HHS), and Lower Extremity Functional Scale (LEFS). F-ESWT with exercise demonstrated a significant improvement in VAS, HHS and LEFS scores at 2, 3, and 6 month follow up, except for LEFS score at 1 month follow up [23].

Carlisi et al. [24] investigated the effectiveness of f-ESWT in comparison to ultrasound therapy in 50 patients with GTPS. The study demonstrated that f-ESWT was more effective in reducing pain compared to ultrasound therapy, but did not demonstrate significant improvement in function [24]. A study conducted by Heaver et al. [25] investigated the effectiveness of f-ESWT treatment in comparison to ultrasound guided corticosteroid injection in 104 patients. Primary outcome measures included Visual Analogue Pain Score (VAS) with secondary outcome measures including the Harris Hip Score (HHS) and Trendelenburg test for accessing functional improvements and SF-36 for Quality of Life (QoL). The results demonstrated that f-ESWT treatment had significantly improved VAS, HHS, SF-36, and trendelenburg test scores in comparison to the injection group [25]. ESWT has shown promise as an effective, non-invasive treatment for GTPS. Further systematic reviews and larger sample size studies are needed to investigate both individual and adjunctive ESWT treatment for GTPS.

Osteonecrosis of the femoral head

Current standard treatments for osteonecrosis of the femoral head include physical therapy, NSAIDS, core decompression, bone graft, osteotomy, and ultimately total hip arthroplasty [26]. In a 2017 systematic review of ESWT in osteonecrosis of the femoral head, Zhang used data from 17 studies including 6 randomized controlled trials to propose ESWT as a viable treatment for early Osteonecrosis of the Femoral Head (ONFH). The systematic review demonstrated that ESWT is an effective conservative option which enhances motor function and reduces pain in patients with ONFH. Furthermore, MRI studies demonstrated reduced bone marrow edema, but sustained necrotic bone post ESWT [27]. In 2016 Wang studied the effectiveness of high dose versus low dose ESWT in the treatment of early hip necrosis. A total of 33 participants were exposed to 24Kv ESWT ranging from 2000-6000 impulses. The study showed that higher doses of ESWT provide better pain relief and improved neovascularization than low dose ESWT in the conservative treatment of early hip necrosis [28]. Despite the improved neovascularization in higher doses of ESWT, there were no appreciable differences in infarcted hip necrosis volume.

Patellar tendinosis

Patellar tendinosis, known as jumper's knee, is a common musculoskeletal injury primarily due to repetitive overuse with jumping and/or running. Current management of patellar tendinosis includes conservative therapy of bracing, physical therapy, rest, and icing in addition to medical management with oral/topical NSAIDs and corticosteroid and orthobiologic injections [29]. ESWT treatment has been growing in popularity as a stand-alone or adjunct treatment for chronic patellar tendinosis. A study conducted by Vulpiani et al. [30] investigated long-term effects of ESWT treatment alone on 73 sports patients with satisfactory results in 73.5% of patients and 87.5% of satisfactory results in 16 performing athletes. Patients were followed up for two years following treatment and average time for return to sport for performance athletes was 6 weeks [30]. Smith et al. [31] performed a study investigating the effectiveness in ESWT treatment in comparison to PRP treatment for chronic patellar tendinosis following failed conservative treatments. PRP and ESWT successfully reduced pain and improved function at 12 month follow up, with PRP showing improved VAS scores at 6 and 12 months [31]. A study conducted by Vetrano et al. [32] demonstrated similar findings at 6 and 12 month follow up. Both ESWT and PRP groups had improved VISA-P, VAS, and modified Blazina scale scores at 6 and 12 month follow up, with PRP having higher scores on all 3 scales at 6 and 12 months [32]. Further studies are needed investigating the synergistic effects of ESWT, PRP, and exercise treatment for chronic patellar tendinosis.

Knee osteoarthritis

Osteoarthritis (OA) is the most common joint disease in the world, with the knee most commonly implicated [33]. Current standards of treatment include physical therapy, NSAIDs, oral narcotics, bracing, intra-articular steroid or hyaluronic acid injections, orthobiologic injections, knee arthroscopy, and partial- and Total-Knee Arthroplasty (TKA) [33]. Despite the promising functionality of a TKA, up to 30% of patients report post-operative dissatisfaction in quality of life [34]. Therefore, alternatives to TKA are necessary to provide greater options for surgical candidates.

In a 2020 systematic review and meta-analysis of the efficacy and safety of ESWT in knee osteoarthritis included three Randomized Controlled Trials (RCTs) and three cohort studies. Ma et al. [35] reported significant reduction in pain at regular intervals of 4, 8, and 12 weeks after intervention. Ma et al. [35] also comments on the few adverse effects of ESWT reported as redness and swelling of the knee [35]. In a 2019 systematic and meta-regression of ESWT for knee osteoarthritis, Liao, et al. demonstrated improved pain and function 6 months after ESWT. This review of 50 trials including 4844 patients, revealed that radial and focal ESWT treatments were beneficial for addressing patients with knee osteoarthritis with high energy radial therapy having greater effect size and an improved WOMAC function index. Wang et al. [36] expands on the concept of long-term benefits of ESWT for knee osteoarthritis in a review including 8 RCTs and 1 retrospective study to reveal reduction in pain and improvement in knee function up to 12 months after ESWT treatment [36].

Despite the benefit of high-energy over low-energy ESWT, low-energy ESWT still proves superior to placebo. In 2019, Zhong analyzed the effects of low-dose ESWT in patients with knee osteoarthritis in a randomized controlled trial that included 63 participants. Participants were divided into low-dose treatment and placebo groups with four weeks of intervention. The VAS score and WOMAC pain, stiffness, and function indices were significantly improved at 5 and 12 weeks post treatment in the ESWT group compared to placebo [37]. To further analyze ESWT effects on OA based on dosage and delivery type, Liao et al. [38] performed a meta-analysis of randomized controlled trials including medium-energy, high-energy, radial, and focal shockwave therapy. In their 2022 analysis, Liao reports medium-energy focal shockwave therapy in conjunction with physical therapy as the most beneficial for pain reduction related to knee OA [38]. These studies demonstrate that ESWT can improve pain and function in patients with osteoarthritis, but the optimal dosage and delivery method has yet to be determined [36,39,40].

Medial Tibial Stress Syndrome (MTSS)

An emerging application of ESWT is in the treatment of Medial Tibial Stress Syndrome (MTSS). MTSS develops under recurrent stress and overuse often seen in athletes including military personnel. Current treatment therapies include NSAIDs, cryotherapy, corticosteroid injections, prolotherapy, and laser therapy among other treatments [41]. In a single-blind randomized control trial including 42 military cadets, participants who received ESWT with exercise therapy showed improved pain control and running endurance compared to controls. This study contrasts the findings of another randomized, sham-controlled trial including 28 participants which showed no significant difference between ESWT treatment group and ESWT sham group. Of note, the sham group received a sub-therapeutic energy level of ESWT which authors suggest may have resulted in limited therapeutic effects [42]. These early studies set the foundation for future research on the therapeutic benefit of ESWT in the management of MTSS.

Lower-limb tendinopathy

Tendinopathy affects multiple areas of the lower extremity including the connective tissue of the Achilles, tibia, patella, pes anserine, quadriceps, iliotibial tract, gluteus, and greater trochanter. Common conservative treatments range from rest, behavioral modification, physical therapy, NSAIDs, topicals and transdermal patches, steroid and orthobiologic injections for functional improvement and pain relief. Some of these treatments, however, are limited by comorbidities like obesity, kidney failure and diabetes [43]. ESWT is an emerging noninvasive tool to treat tendinopathy.

In 2018, a meta-analysis by Liao et al. [44] reviewed 29 randomized clinical trials to discuss the outcomes of ESWT for tendinopathy. A total of 873 patients received some form of ESWT ranging from low- to high-dose and radial to focal shockwave therapy to treat Achilles tibialis, and patellar tendinopathies, and other lower limb tendon dysfunctions. Liao concluded that high-dose focal shockwave treatments yielded superior results in pain and function compared to high-dose radial shockwave and low-dose radial shockwave therapy [44]. In 2017, Korakakis reviewed 15 randomized clinical trials including ESWT for Achilles tendinopathy, greater trochanteric pain syndrome, patellar tendinopathy, medial tibial stress syndrome, and proximal hamstring tendinopathy. The review found that radial ESWT can result in improved function and pain of most lower limb tendinopathies. In particular, ESWT provided better pain control for greater trochanteric pain compared to corticosteroid injections even 12 months post-intervention [45]. In 2015, Gerdesmeyer reviewed literature on ESWT for Achilles tendinopathy. It was found that ESWT is a viable treatment for chronic Achilles tendinopathy when compared to physical therapy alone or sham treatment. Furthermore, the combination of ESWT with eccentric training should be offered to patients as an alternative conservative treatment of Achilles tendinopathy. Finally, local anesthesia combined with ESWT showed reduced effectiveness compared to regional anesthesia combined with ESWT. This suggests that patient biofeedback is crucial to the success of ESWT [46].

Plantar fasciitis

Plantar fasciitis accounts for 15% of foot injuries in the general population [47]. Major risk factors for developing plantar fasciitis include increased body weight and overuse, particularly affecting athletes [47]. Current conservative measures include physical therapy, orthotic inserts, pharmacotherapy, corticosteroid and orthobiologic injections, and low dose radiotherapy [48]. ESWT provides an adjunct to the limited conservative and surgical treatment options. In 2022, Kapusta et al. [48] studied the long-term effects of ESWT on plantar fasciitis in amateur runners. A five-year follow up after ESWT intervention revealed that compared to ESWT alone, ESWT combined with laser and ultrasound therapy provided superior relief of pain frequency and intensity [48]. In meta-analysis of RCTs comparing ESWT to other therapeutic modalities including electrical muscle stimulation and cryotherapy, Sun et al. [49] found that ESWT demonstrated better pain relief in chronic plantar fasciitis. Moreover, the meta-analysis showed patients treated with ESWT compared to other therapeutic modalities had decreased return to work times and less treatment complications [49].

Sun et al. [50] conducted a meta-analysis investigating the effectiveness of ESWT treatment in treating chronic plantar fasciitis. Focused shockwave therapy demonstrated a higher success rate and greater improvement in pain for the treatment of chronic plantar fasciitis compared to sham therapy. However, larger sample sizes and systematic reviews are needed to further investigate ESWT treatment as a sole alternative treatment [50].

Bone edema and nonunion fractures

Extracorporeal shockwave therapy treatment has been shown to be effective in addressing bone edema and nonunion fractures. A study conducted by Suhr et al. [51] demonstrated the mechanical stimulations of ESWT treatment can influence cell biological changes in bone marrow stromal cells. ESWT treatment improved therapeutic performance and improved BMSC behavior demonstrating its potential to help induce healing [51].

Beling et al. [52] conducted a study investigating focused shockwave treatment for Bone Stress Injuries (BSI) in runners. The study incorporated 40 runners with majority having injury to metatarsal or posteromedial tibia and underwent ESWT treatment for 5-7 treatments. Patients received an average of 3122 pulses per session and were stratified based on location, Athlete Triad Risk Score, and injury severity. The study demonstrated that following 5±2 total ESWT sessions, most patients had significant improvement in pain with return to running at an average of 3 months. Patients with delayed and non-union BSI had a longer recovery time as expected. Studies with larger sample studies would be indicated to further investigate focused shockwave treatment for Bone Stress Injuries (BSI) [52]. Sansone et al. [53] studied 86 patients with 3 treatments of high energy ESWT treatment to the medial knee showing 86% reduction in bone marrow edema compared to 41% in control after 6 months. The study demonstrated VAS pain scores improved by 88% in ESWT versus 42% in control at 3 months and 6 months follow up. In addition to VAS pain scores, WOMAC scores improved by 65% in ESWT versus 22% control [53].

Zhao et al. [54] compared ESWT treatment with intravenous prostacyclin and bisphosphonate for the treatment of primary bone marrow syndrome in avascular necrosis of the femoral head. They demonstrated ESWT having significant improvement in VAS and WOMAC scores at 1,3 and 6 month follow ups [54]. Sansone et al. [55] treated 72 patients with 3 focused ESWT treatments to the knee demonstrating that the bone marrow lesion size corresponded with the level of patient's pain. ESWT significantly reduced bone edema and improved KOOS scores at 6 months follow up [55]. An additional study by Zghao et al. [54] on 67 patients with avascular necrosis of the femoral head showed significant improvement in bone marrow edema following focal ESWT with fluoroscopic guidance. At 3 month follow up post MRI, imaging demonstrated decreased bone edema and improved pain [54].

Discussion

With population growth and ageing, the number of people with functional limitations from musculoskeletal conditions is rapidly increasing at 1.71 billion [56]. Physicians and their patients need additional minimally invasive and evidence-based options to address pain and function. Extracorporeal Shockwave therapy (ESWT) is a promising and increasingly used modality working at the cellular level for musculoskeletal injuries. It serves as a safe, noninvasive biologic tool triggering the body's endogenous mechanisms for self-repair. Future analysis may explore shockwave's mechanotransduction properties, as cells sense and respond to acoustic mechanical loading simulating exercise. Previous studies have shown that exercise upregulates muscle Sirtuin 1 (SIRT1) gene expression and chronically increases blood enzyme concentration. Exercise increases the body's endogenous production of molecules like SIRT1 which promotes healthy ageing and longevity [57].

Conclusion

Further studies are needed to explore differences between focal and radial ESWT along with optimizing indications, protocols, frequencies, and dosing parameters. Additionally, cohort studies with larger sample sizes and follow up timelines can provide further evidence of its effectiveness and limitations. More controlled trials and outcomes data are needed exploring the potential synergistic effects of ESWT with other orthobiologic treatments like platelet rich plasma.

References

1. Graff J, Richter KD, Pastor J (1989) Effect of high-energy shock waves on bony tissue. In: Walker VR, Sutton RAL, Cameron ECB, Pak CYC, Robertson WG (Eds.), Urolithiasis. Springer, USA, pp. 997-998.
2. d'Agostino MC, Craig K, Tibalt E, Respizzi S (2015) Shock wave as biological therapeutic tool: From mechanical stimulation to recovery and healing, through mechanotransduction. Int J Surg 24: 147-153.
3. Holfeld J, Tepeköylü C, Reissig C, Lobenwein D, Scheller B, et al. (2016) Toll-like receptor 3 signalling mediates angiogenic response upon shock wave treatment of ischaemic muscle. Cardiovasc Res 109(2): 331-343.
4. Hausdorf J, Lemmens MAM, Kaplan S, Marangoz C, Milz S, et al. (2008) Extracorporeal shockwave application to the distal femur of rabbits diminishes the number of neurons immunoreactive for substance P in dorsal root ganglia L5. Brain Res 1207: 96-101.
5. Hausdorf J, Lemmens MAM, Heck KDW, Grolms N, Korr H, et al. (2008) Selective loss of unmyelinated nerve fibers after extracorporeal shockwave application to the musculoskeletal system. Neuroscience 155(1): 138-144.
6. Ryskalin L, Morucci G, Natale G, Soldani P, Gesi M (2022) Molecular mechanisms underlying the pain-relieving effects of extracorporeal shock wave therapy: A focus on fascia nociceptors. 12(5): 743.
7. Simplicio CL, Purita J, Murrell W, Santos GS, dos Santos RG, et al. (2020) Extracorporeal shock wave therapy mechanisms in musculoskeletal regenerative medicine. Journal of Clinical Orthopaedics and Trauma 11(Suppl 3): S309-S318.
8. Wang CJ, Wang FS, Yang KD, Weng LH, Hsu CC, et al. (2003) Shock wave therapy induces neovascularization at the tendon-bone junction. A study in rabbits. J Orthop Res 21(6): 984-989.
9. Chuang YC, Meng E, Chancellor M, Kuo HC (2020) Pain reduction realized with extracorporeal shock wave therapy for the treatment of symptoms associated with interstitial cystitis/bladder pain syndrome—A prospective, multicenter, randomized, double-blind, placebo-controlled study. Neurourol Urodyn 39(5): 1505-1514.
10. Klonschinski T, Ament SJ, Schlereth T, Rompe JD, Birklein F, et al. (2022) Application of local anesthesia inhibits effects of low-energy Extracorporeal Shock Wave Treatment (ESWT) on nociceptors. Pain Med 12(10): 1532-1537.
11. Ghatta S, O'Rourke ST (2006) Nitroglycerin-induced release of calcitonin gene-related peptide from sensory nerves attenuates the development of nitrate tolerance. J Cardiovasc Pharmacol 47(2): 175-181.
12. Ohtori S, Inoue G, Mannoji C, Saisu T, Takahashi K, et al. (Shock wave application to rat skin induces degeneration and reinnervation of sensory nerve fibres. Neurosci Lett 315(1-2): 57-60.
13. Rompe JD, Rumler F, Hopf C, Nafe B, Heine J (1995) Extracorporal shock wave therapy for calcifying tendinitis of the shoulder. Clin Orthop Relat Res 321: 196-201.
14. Rompe JD, Bürger R, Hopf C, Eysel P (1998) Shoulder function after extracorporal shock wave therapy for calcific tendinitis. J shoulder Elb Surg 7(5): 505-509.
15. Cacchio A, Paoloni M (2006) Effectiveness of radial shock-wave therapy for calcific tendinitis of the shoulder: single-blind, randomized clinical study. Phys Ther 86(5): 672-682.
16. Wu YC, Tsai WC, Tu YK, Yu TY (2017) Comparative effectiveness of nonoperative treatments for chronic calcific tendinitis of the shoulder: A Systematic review and network meta-analysis of randomized controlled trials. Arch Phys Med Rehabil 98(8): 1678-1692.
17. Abo Al-Khair MA, El Khouly RM, Khodair SA, Sattar Elsergany MA, Hussein MI, et al. (2021) Focused, radial and combined shock wave therapy in treatment of calcific shoulder tendinopathy. Phys Sportsmed 49(4): 480-487.
18. Ioppolo F, Tattoli M, Sante L Di, Attanasi C, Venditto T, et al. (2012) Extracorporeal shock-wave therapy for supraspinatus calcifying tendinitis: A randomized clinical trial comparing two different energy levels. Phys Ther 92(11): 1376-1385.
19. Yao G, Chen J, Duan Y, Chen X (2023) Efficacy of extracorporeal shock wave therapy for lateral epicondylitis: A systematic review and meta-analysis. Biomed Res Int 2020: 2064781.
20. Özmen T, Koparal SS, Karataş Ö, Eser F, Özkurt B, et al. (2021) Comparison of the clinical and sonographic effects of ultrasound

therapy, extracorporeal shock wave therapy, and Kinesio taping in lateral epicondylitis. Turkish J Med Sci 51(1): 76-83.

21. Chang CY, Chen LC, Chou YC, Li TY, Ho TY, et al. (2020) The effectiveness of platelet-rich plasma and radial extracorporeal shock wave compared with platelet-rich plasma in the treatment of moderate carpal tunnel syndrome. Pain Med 21(8): 1668-1675.
22. Gesslbauer C, Mickel M, Schuhfried O, Huber D, Keilani M, et al. (2021) Effectiveness of focused extracorporeal shock wave therapy in the treatment of carpal tunnel syndrome. Wien Klin Wochenschr 133(11-12): 568-577.
23. Ramon S, Russo S, Santoboni F, Lucenteforte G, Di Luise C, et al. (2020) Focused shockwave treatment for greater trochanteric pain syndrome. J Bone Jt Surg 102(15): 1305-1311.
24. Carlisi E, Cecini M, Natali G, Manzoni F, Tinelli C, et al. (2019) Focused extracorporeal shock wave therapy for greater trochanteric pain syndrome with gluteal tendinopathy: A randomized controlled trial. Clin Rehabil 33(4): 670-680.
25. Heaver C, Pinches M, Kuiper JH, Thomas G, Lewthwaite S, et al. (2023) Greater trochanteric pain syndrome: focused shockwave therapy versus an ultrasound guided injection: A randomised control trial. HIP Int 33(3): 490-499.
26. Liu N, Zheng C, Wang Q, Huang Z (2022) Treatment of nontraumatic hip osteonecrosis avascular necrosis of the femoral head. Exp Ther Med 23(5): 321.
27. Zhang Q, Liu L, Sun W, Gao F, Cheng L, et al. (2017) Extracorporeal shockwave therapy in osteonecrosis of femoral head a systematic review of now available clinical evidences. Medicine 96(4): e5897.
28. Wang CJ, Huang CC, Yip HK, Yang YJ (2016) Dosage effects of extracorporeal shockwave therapy in early hip necrosis. Int J Surg 35: 179-186.
29. Fredberg U, Bolvig L (1999) Jumper's knee. Review of the literature. Scand J Med Sci Sports 9(2): 66-73.
30. Vetrano M, d'Alessandro F, Torrisi MR, Ferretti A, Vulpiani MC, et al. (2011) Extracorporeal shock wave therapy promotes cell proliferation and collagen synthesis of primary cultured human tenocytes. Knee Surgery, Sport Traumatol Arthrosc 19(12): 2159-2168.
31. Smith J, Sellon JL (2014) Comparing PRP injections with ESWT for athletes with chronic patellar tendinopathy. Clin J Sport Med 24(1): 88-89.
32. Vetrano M, Castorina A, Vulpiani MC, Baldini R, Pavan A, et al. (2013) Platelet-rich plasma versus focused shock waves in the treatment of jumper's knee in athletes. Am J Sports Med 41(4): 795-803.
33. Jang S, Lee K, Ju JH (2021) Recent updates of diagnosis, pathophysiology, and treatment on osteoarthritis of the knee. Int J Mol Sci 22(5): 2619.
34. Canovas F, Dagneaux L (2023) Quality of life after total knee arthroplasty. Orthop Traumatol Surg Res 104(1S): S41-S46.
35. Ma H, Zhang W, Shi J, Zhou D, Wang J (2020) The efficacy and safety of extracorporeal shockwave therapy in knee osteoarthritis: A systematic review and meta-analysis. Int J Surg 75: 24-34.
36. Wang YC, Huang HT, Huang PJ, Liu ZM, Shih CL (2020) Efficacy and safety of extracorporeal shockwave therapy for treatment of knee osteoarthritis: A systematic review and meta-analysis. Pain Med 21(4): 822-835.
37. Zhong Z, Liu B, Liu G, Chen J, Li Y, et al. (2023) A Randomized controlled trial on the effects of low-dose extracorporeal shockwave therapy in patients with knee osteoarthritis. Arch Phys Med Rehabil 100(9): 1695-1702.
38. Liao CD, Huang YY, Chen HC, Liou TH, Lin CL, et al. (2022) Relative effect of extracorporeal shockwave therapy alone or in combination with noninjective treatments on pain and physical function in knee osteoarthritis: A network meta-analysis of randomized controlled trials. Biomedicines 10(2): 306.
39. Avendaño-Coy J, Comino-Suárez N, Grande-Muñoz J, Avendaño-López C, Gómez-Soriano J (2020) Extracorporeal shockwave therapy improves pain and function in subjects with knee osteoarthritis: A systematic review and meta-analysis of randomized clinical trials. Int J Surg 82: 64-75.
40. An S, Li J, Xie W, Yin N, Li Y, et al. (2020) Extracorporeal shockwave treatment in knee osteoarthritis: Therapeutic effects and possible mechanism. Biosci Rep 40(11): BSR20200926.
41. Garcia SG, Rona SR, Tinoco MCG, Rodriguez MB, Ruiz DMC, et al. (2017) Shockwave treatment for medial tibial stress syndrome in military cadets: A single-blind randomized controlled trial. Int J Surg 46: 102-109.
42. Newman P, Waddington G, Adams R (2023) Shockwave treatment for medial tibial stress syndrome: A randomized double blind sham-controlled pilot trial. J Sci Med Sport 20(3): 220-224.
43. Scott A, Purdam P (2023) Overview of the management of overuse (persistent) tendinopathy.
44. Liao C, Tsauo JY, Chen HC, Liou TH (2018) Efficacy of extracorporeal shock wave therapy for lower-limb tendinopathy: A meta-analysis of randomized controlled trials. Am J Phys Med Rehabil 97(9): 605-619.
45. Korakakis V, Whiteley R, Tzavara A, Malliaropoulos N (2018) The effectiveness of extracorporeal shockwave therapy in common lower limb conditions: A systematic review including quantification of patient-rated pain reduction. Br J Sports Med 52(6): 387-407.
46. Gerdesmeyer L, Mittermayr R, Fuerst M, Muderis MA, Thiele R, et al. (2015) Current evidence of extracorporeal shock wave therapy in chronic Achilles tendinopathy. International Journal of Surgery 24: 154-159.
47. Rhim HC, Kwon J, Park J, Borg-Stein J, Tenforde AS (2023) A systematic review of systematic reviews on the epidemiology, evaluation, and treatment of plantar fasciitis. Life 11(12): 1287.
48. Kapusta J, Domzalski M (2022) Clinical medicine long term effectiveness of ESWT in plantar fasciitis in amateur runners. J Clin Med 11(23): 6926.
49. Sun K, Zhou H, Jiang W (2020) Extracorporeal shock wave therapy versus other therapeutic methods for chronic plantar fasciitis. Foot Ankle Surg 26(1): 33-38.
50. Sun J, Gao F, Wang Y, Sun W, Jiang B, et al. (2017) Extracorporeal shock wave therapy is effective in treating chronic plantar fasciitis: A meta-analysis of RCTs. Medicine (Baltimore) 96(15): e6621.
51. Suhr F, Delhasse Y, Bungartz G, Schmidt A, Pfannkuche K, et al. (2013) Cell biological effects of mechanical stimulations generated by focused extracorporeal shock wave applications on cultured human bone marrow stromal cells. Stem Cell Res 11(2): 951-964.
52. Beling A, Saxena A, Hollander K, Tenforde AS (2023) Outcomes using focused shockwave for treatment of bone stress injury in runners. Bioengineering 10(8): 885.
53. Sansone V, Romeo P, Lavanga V (2017) Extracorporeal shock wave therapy is effective in the treatment of bone marrow edema of the medial compartment of the knee: A comparative study. Med Princ Pract 26(1): 23-29.
54. Zhao W, Gao Y, Zhang S, Liu Z, He L, et al. (2021) Extracorporeal shock wave therapy for bone marrow edema syndrome in patients with osteonecrosis of the femoral head: A retrospective cohort study. J Orthop Surg Res 16(1): 21.
55. Sansone V, Maiorano E, Pascale V, Romeo P (2019) Bone marrow lesions of the knee: Longitudinal correlation between lesion size changes and pain before and after conservative treatment by extracorporeal shockwave therapy. Eur J Phys Rehabil Med 55(2): 225-230.
56. (2023) Musculoskeletal health.
57. Juan CG, Matchett KB, Davison GW (2023) A systematic review and meta-analysis of the SIRT1 response to exercise. Sci Rep 13(1): 1-14.

