










EXTRACORPOREAL SHOCKWAVE TREATMENT FOR LOW BACK PAIN: A DESCRIPTIVE REVIEW OF THE LITERATURE

Claudio Lopes Simplicio, MD¹, Gabriel Santos, MD⁶, Gilson Tanaka Shinzato, MD²,
Guilherme Antonio Moreira de Barros, MD, PhD³, Marta Imamura, MD²,
Antonio D'Almeida Neto, MD⁴, José Fábio Santos Duarte Lana, MD⁴

¹Orthopedics – Sports Medicine – Pain Physician, Clinica Ortofisio, Araruama – RJ, Brazil

²Physiatry, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo – SP, Brazil

³Antalgic Therapy and Palliative Care, Faculdade de Medicina de Botucatu, Botucatu – SP, Brazil

⁴Physiatry, Centro de Reumatologia e Ortopedia Botafogo, Rio de Janeiro – RJ, Brazil

⁵Orthopedics – Sports Medicine – Pain Physician, Brazilian Institute of Regenerative Medicine Indaiatuba – SP, Brazil

⁶IOC - Instituto do Osso e da Cartilagem/The Bone and Cartilage Institute, Indaiatuba, SP, Brazil

Author for correspondence: Claudio Lopes Simplicio: drsimplicio@terra.com.br

Submitted: 6 June 2022. Accepted: 29 October 2022. Published: 00 XXXX 2022

Abstract

Low back pain is a common symptom in patients with chronic musculoskeletal conditions, affecting several individuals. In most cases, low back pain can often prove to be nonspecific or even multifactorial. Current treatment approach is based on surgical and noninvasive interventions, including pharmacological, psychological, physiotherapeutic, or complementary strategies. Extracorporeal shock wave therapy (ESWT) is a type of noninvasive mechanotherapy that has become popular in recent years due to its applicability in the treatment of various musculoskeletal disorders, especially in the lumbar spine of individuals with osteoporosis, sacroiliitis, and even spinal cord disorders. The objective of this manuscript is to review the scientific evidence supporting the application of this therapy in the management of low back pain, and give a brief description of the treatment techniques used in clinical settings. The articles included in this descriptive review were selected from databases using the Google Scholar tool, from which a total of 13 applicable studies matching the topic were included. Despite the need for more clinical trials, shock waves have been applied in medical health for many years with satisfactory results. Its application in the treatment of lumbar spine disorders has been shown to be advantageous in the management of pathological progression, such as the natural wear and tear process of musculoskeletal structures. In this sense, shockwave therapy may represent a viable alternative for the treatment of lumbar spine disorders; however, its therapeutic effects and mechanisms require further elucidation.

Keywords: *low back pain; shockwave therapy; regenerative medicine; orthopedics; musculoskeletal medicine*

INTRODUCTION

Low back pain is defined as pain and discomfort located between the costal margin and the inferior gluteal folds, with or without leg pain.¹ It is characterized by a variety of biophysical, psychological, and social characteristics, with negative impacts on the function and quality of life of patients.¹ In addition, it is frequently reported in physicians' offices and often does not have a specific cause.²⁻⁵ Previous studies in the literature conclude that low back pain affects about 7% of the world population,⁶ representing more than 540 million people.^{6,7} Low back pain is uncommon in the first decade of life but may occur abruptly during adolescence^{8,9} and adulthood.¹⁰

Upon diagnosis, about 60% of cases may include symptoms such as lumbosciatic pain, which may be of radicular origin in the case of herniated discs, or referred pain, typically reported in myofascial pain.¹¹ Radicular pain is characterized by discomfort arising in the limbs or trunk, triggered by ectopic activation of nociceptive afferent fibers in a spinal nerve or its roots, stimulating neuropathic mechanisms. Radicular pain is also commonly referred to as sciatica; however, this term can cause confusion as it is commonly used to refer to more than one type of pain, including referred pain.¹² Diagnosis is based primarily on clinical findings, including a history of leg pain and worsening of symptoms during sneezing or coughing.¹³

Conventional treatments include self-care or psychological, physiotherapeutic, or complementary interventions instead of relying solely on pharmacological and surgical procedures. Early pain management strategies involve thorough examination and patient education.¹⁴ Pharmacological interventions are considered when nonpharmacological approaches produce unsatisfactory results. In this case, nonsteroidal anti-inflammatory drugs (NSAIDs), for instance, may be recommended.¹⁵ Treatment with opioids is not recommended, and it should be used only as a last resource under medical supervision.¹⁴ In the literature, we identified some clinical guidelines used in the management of nonspecific low back pain, mainly in countries such as Denmark, the United States, and the United

Kingdom (Table 1). Table 1 was built according to the study published by Foster et al. in 2018.¹⁴

EXTRACORPOREAL SHOCK WAVE THERAPY

Extracorporeal shock wave therapy (ESWT) is a type of noninvasive treatment based on mechanical pulses. It has recently become a popular alternative for the management of various musculoskeletal disorders. This therapy relies on the application of transient acoustic pulses of high levels of energy and pressure, lasting for a matter of milliseconds.¹⁶ Its mechanism of action is often related to a wide variety of effects at the cellular and molecular level, promoting angiogenesis, healing, tissue regeneration, and bone remodeling.¹⁷ Furthermore, it is also associated with pain relief via the stimulation of analgesic responses.^{18,19} However, it is important to note that depending on the intensity and target tissue, shock waves may cause damage, leading to tissue necrosis, fibrosis, and infiltration of inflammatory cells.²⁰

Shockwave stimulation can be applied via focal or radial pressure waves based on their generation mechanisms. Focal waves have a wavelength of 1.5 mm, a maximum pressure of 10–100 Mpa, and a penetration depth of 5–20 cm; radial pressure shockwaves have a wavelength of 0.5–1.5 mm, a maximum pressure of 1 MPa, and a penetration depth of 2–5 cm.²¹ Focal stimulation is generated from a pressure field, which converges in a focus to specific tissues, reaching maximum pressure.²² In addition, they can be originated by three different mechanisms: electrohydraulic, electromagnetic, or piezoelectric. However, they share some similarities, such as the ability to concentrate energy in the depths of the tissues.²³ As the acoustic impedances of water and biological tissues are comparable, the use of focal waves (electrohydraulic and electromagnetic) limits reflection, facilitating the propagation of waves in the body.²¹⁻²³

Conversely, radial pressure shockwaves can be formed by two mechanisms: pneumatic or electromagnetic.²¹ Both have a pressure field that differs from the devices used for their generation, reaching maximum pressure at the source, and not deeply in

Table 1. Recommended interventions for the treatment of nonspecific low back pain.

Strategies	Acute low back pain (<6 weeks)	Persistent low back pain (>12 weeks)
Educational and self-care recommendations		
Maintenance of daily activities	First choice; incorporated into a patient's routine	First choice; incorporated into a patient's routine
Patient education	First choice; incorporated into a patient's routine	First choice; incorporated into a patient's routine
Surface heat	Second choice or adjuvant treatment	Insufficient evidence
Nonpharmacological therapies		
Exercise	Limited use	First choice; incorporated into a patient's routine
Cognitive behavioral therapy	Limited use	First choice; incorporated into a patient's routine
Spinal manipulation	Second choice or adjuvant treatment	Second choice or adjuvant treatment
Massage	Second choice or adjuvant treatment	Second choice or adjuvant treatment
Acupuncture	Second choice or adjuvant treatment	Second choice or adjuvant treatment
Yoga	Insufficient evidence	Second choice or adjuvant treatment
Stress reduction	Insufficient evidence	Second choice or adjuvant treatment
Interdisciplinary rehabilitation	Insufficient evidence	Second choice or adjuvant treatment
Pharmacological therapies		
Paracetamol	Not recommended	Not recommended
NSAIDs	Second choice or adjuvant treatment	Second choice or adjuvant treatment
Muscle relaxants	Limited use	Insufficient evidence
Selective norepinephrine reuptake inhibitors	Insufficient evidence	Second choice or adjuvant treatment
Anticonvulsants	Insufficient evidence	Insufficient evidence
Opioids	Limited use	Limited use
Systemic glucocorticoids	Not recommended	Not recommended
Interventional therapies		
Epidural glucocorticoid injection (for herniated disc with radiculopathy)	Not recommended	Limited use
Surgery		
Discectomy (for herniated discs with radiculopathy)	Insufficient evidence	Second choice or adjuvant treatment
Laminectomy (for symptomatic spinal stenosis)	Insufficient evidence	Second choice or adjuvant treatment
Spinal fusion (for nonradicular low back pain with disc degeneration)	Insufficient evidence	Insufficient evidence

NSAID, nonsteroidal anti-inflammatory drugs.

target tissues. Unlike focal waves, which are generated in water, radial pressure shockwaves originate in a device that accelerates a projectile through a tube using compressed air. The projectile is accelerated until it collides with the applicator at the end of the tube, producing a pressure wave that expands radially into the target tissue.²¹⁻²³

The application of shock wave therapy has shown promising results in the treatment of common conditions like epicondylitis, plantar fasciitis, trochanteritis, and patellar tendinitis.^{22,24} Recently, its application has been extended to the treatment of other nonorthopedic disorders, such as chronic ulcers, cardiac ischemia, and even erectile dysfunction.^{23,24} Previous studies have proposed the application of ESWT for the treatment of various spinal disorders, especially in cases of osteoporosis, sacroiliitis, and spinal cord disorders.²⁵

The objective of this manuscript is to conduct a review of the evidence that supports the application of ESWT in the management of low back pain, a common debilitating condition in adult individuals.

STUDY SELECTION

The search strategies and selection of studies were carried out using Google Scholar databases. The combination of keywords, such as “chronic low

back pain,” “inflammation,” “orthopedics,” “musculoskeletal disorders,” “regenerative medicine,” “ESWT,” and “shock wave therapy,” were used as a search strategy. Twenty-four studies were selected up to the search date, April 2022. Exclusion criteria included studies published more than 15 years ago (three studies), data collection failure (four studies), or duplicates (one study). Therefore, only 16 robust studies were deemed appropriate for this review, including randomized controlled trials, meta-analysis, case report, and retrospective study. An overview is presented in Figure 1.

APPLICATION OF ESWT IN THE TREATMENT OF LOW BACK PAIN

The application of ESWT has revealed promising results in the treatment of cervical, thoracic and lumbar spine disorders.^{25, 26-31} In the lumbar spine, therapeutic effects are often assessed using the Oswestry Disability Index (functional ability of the lumbar spine), Visual Analog Scale (pain intensity or severity), and SF-36 (quality of life improvements), as described by the studies presented in the following paragraphs.

In the literature, the efficacy of ESWT for the treatment of low back pain has been compared to standard treatments such as radiofrequency

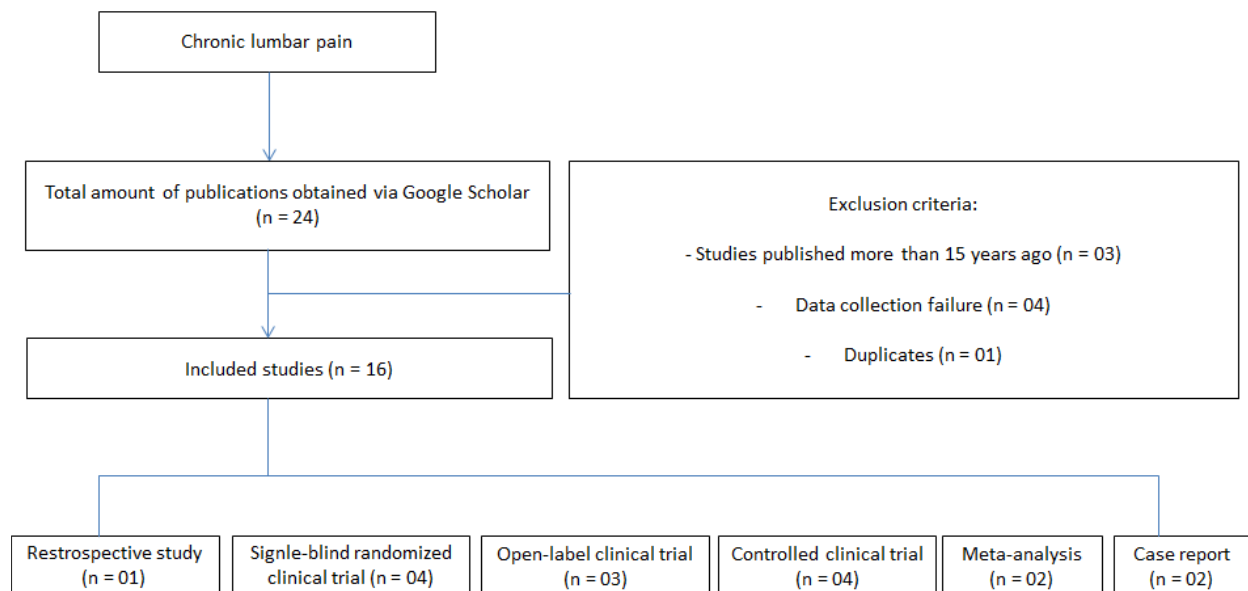


Figure 1. Eligibility criteria flowchart.

neurotomy and corticosteroid injections.²⁶ In this study, the intensity and severity of nociceptive and neuropathic pain were evaluated in a group of 62 patients. The results demonstrated that ESWT triggered more lasting results compared to the group that received corticosteroid injections. However, when compared to treatment with radiofrequency (proven to be effective in the treatment of disorders of the lumbar spine), ESWT had inferior efficacy. In general, the use of shock waves has its advantages compared to radiofrequency, since it promotes significant improvements in patient quality of life without serious side effects, such as risk of damage to neural structures.²⁶

Lee et al.²⁷ also published a study comparing the efficacy of ESWT with conservative treatments. In this study, patients were divided into two groups: Group 1 – patients who received shockwave therapy and Group 2 – patients who received conservative treatment (physiotherapy). Both groups underwent physical exercises twice a week for 6 weeks. Pain outcomes assessed by the visual analogue scale showed better results in the group that received shockwave therapy when compared to the conservative treatment group. The efficacy of ESWT in the treatment of low back pain was also demonstrated in a meta-analysis with five randomized controlled trials.²⁸ In this study, ESWT significantly reduced pain and disability in patients with low back pain, demonstrating that the therapy is effective in improving the general condition of patients, corroborating previous studies.²⁸ With regard to radial pressure shockwaves, the treatment of quadratus lumborum trigger points seems to favor the use of corticosteroids in the short term; however, in the long term, ESWT represents a more effective treatment alternative.²⁹ In addition, the application of 2000 pulses of 0.03 mJ/mm² in three sessions with 1-week intervals associated with the standard protocol of rehabilitation exercises in patients with low back pain improves pain and disability after 1 month of treatment. It also increases sensory nerve conduction amplitude after 3 months of treatment.³⁰ Furthermore, the results indicated that ESWT requires less time to exert its effects compared to standard rehabilitation exercise protocols in patients with low back pain,³⁰ reinforcing its

contribution to cell growth and angiogenesis, thus supporting previous findings.^{21,27,30}

Similarly, Walewicz and colleagues³¹ conducted a prospective, randomized, single-blind study to assess the influence of radial pressure ESWT including 52 patients with low back pain. The authors allocated the patients into two different groups: (1) patients who received the intervention of 2000 pulses of radial pressure shockwaves at 5 Hz for 7 minutes, twice a week, over 5 weeks plus stabilization training and (2) sham treatment protocol. Outcomes were assessed 1 and 3 months after the end of the interventions. The group that received ESWT had a gradual improvement in pain and disability rates in comparison to the group that received the sham treatment, making the use of radial pressure shockwaves effective in the long term.³¹

Regarding the coexistence of other disorders, the efficacy of ESWT has already been evaluated in patients with depression,³² sacroiliac joint disorders,³³ and osteoporosis.³² Given that ESWT promotes significant improvements in pain and disability relief for individuals with low back pain, Sheng and colleagues³⁴ investigated the efficacy of ESWT associated with conservative treatments in depressed individuals. To do this, 30 patients with chronic low back pain received 1000 shock waves at 2.5 Hz, with energy flow density between 0.01 and 0.16 mJ/mm², seven times per second in the regions of the quadratus lumborum muscle and the sacroiliac joint. Conservative treatments included hyperthermia, ultrasound, and transcutaneous nerve stimulation. The treatments were administered twice a week for 6 weeks and showed promising results in reduction of pain, disability, and depressive symptoms.^{34,35} When analyzing the efficacy of ESWT in sacroiliac joint disorders, Moon and colleagues³³ conducted a double-blind randomized controlled trial (considering the gold standard studies of evidence-based medicine) including 25 patients between the control and treated groups. The ESWT group received a single session of 2000 pulses at 3 Hz, with energy flux density between 0.09 and 0.25 mJ/mm² in the perpendicular region of the posterior sacroiliac line. The control group received the same treatment but without the emission of shock

waves. Pain intensity and functional outcomes were assessed at baseline, at first and fourth week of treatment. Pain indices significantly decreased in patients treated with ESWT, but there were no differences in disability and functional outcome indices.³³ As for the coexistence of osteoporosis and low back pain, waves of high and low energy levels were used in a study involving 64 postmenopausal women.³² The results suggested that low-intensity waves are better at maintaining bone mineral density after 12 months of treatment.³²

The use of ESWT was also evaluated in pathological conditions of neurogenic heterotopic ossification, in the medium³⁶ and long term.³⁷ In the medium term, the use of 4000 pulses at 3 Hz, with energy flux density between 0.056 and 0.068 mJ/mm² for 7 weeks was able to significantly reduce pain, although there was no significant change in terms of ossification size.³⁸ In the long term, low-intensity radial pressure shockwaves administered five times a week for approximately 12 months improved pain and impaired mobility and range of motion, decreasing ossification.³⁷

Despite the optimistic results, the literature remains somewhat controversial.^{39,40} Taheri et al.³⁹ published a comparative study including treatment with ESWT associated with pharmacological agents and physical exercise. In contrast to previous results, both groups (control and ESWT) had significant improvements in pain relief and disability in patients with low back pain after 3 months of treatment, including the control group.³⁹ Similar results were reported by Lange et al.⁴⁰ In this study, patients received eight sessions of radial pressure ESWT for 4 weeks, and sessions of physical therapy and analgesics twice a week. After 12 weeks, both groups had a significant improvement in pain and disability relief.⁴⁰

Despite controversial findings, there is consensus suggesting that ESWT can be considered an alternative treatment for patients with low back pain. In addition, it is a noninvasive, nonpharmacological approach that is easy to perform. ESWT not only improves musculoskeletal health but also prevents problems arising from the continuous use of medications like corticosteroids and anti-inflammatory drugs.

AUTHOR'S NOTE

Anamnesis is important for the identification of lumbar spine dysfunctions and possible causes of pain. In addition, it is useful for the assessment of joint mobility, asymmetry, painful blocks, trigger points, and taut bands. Patients receiving ESWT treatment can be placed in the following positions: lateral decubitus, ventral decubitus, pronated, or seated. The first is often used to ensure greater muscle relaxation and patient comfort. Physicians must note that ESWT application in seated elderly patients may increase risks of postural hypotension and vasovagal syncope.

As for the techniques used, we describe the sweeping technique, as illustrated by Figure 2a, and the stationary technique shown in Figure 2b. The sweeping technique involves the identification of the area of dysfunction by sliding the applicator over the lumbar region, and then the application of shockwaves in an “inverted T-shape,” dividing the spine into quadrants (vertebral body and longitudinal division). Trigger points and taut bands are commonly identified by focal or radial pressure shockwaves via the sweeping technique, aiming to evaluate the thickness and depth of each muscle group in order to select the most appropriate application depth for each region. The methods employed in the stationary technique are based on the application of shockwaves to points of dysfunction. In both, there may be a gradual increase in frequency and potency at the time of application, considering the patient’s tolerability. However, high intensities along the vertebral

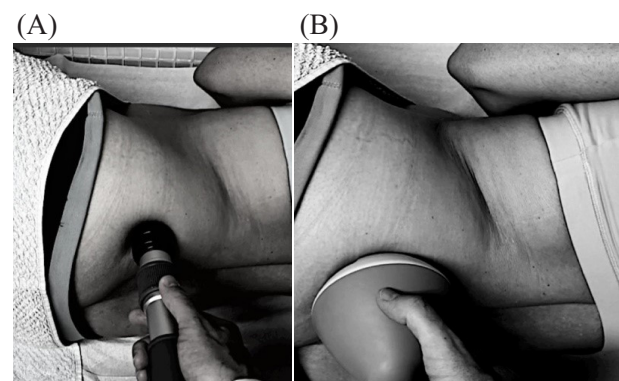


Figure 2. (A) Application of radial pressure waves. (B) Application of focal shockwaves.

axis should be avoided in the stationary technique (even with radial pressure shockwaves) due to the risk of damage to membranous structures, such as cerebrospinal fluid fistulas. In addition, patients with a history of laminectomy should be treated with caution, avoiding exposure of the spinal cord and roots to high-intensity waves.

Overall, among the treatment strategies for low back pain, the continuous scanning technique is the most efficient. The technique is used for analgesia, starting from cranial to caudal, proximal to distal, axial to peripheral, and from deep to more superficial layers. However, both techniques are important for spinal segmental sensitization,^{41–43} which is an irritated, hypersensitive, and painful vertebral ligament segment. This sensitization can be reversed with invasive procedures, such as needling and lidocaine injection in the paraspinal segment, or non-invasive, such as shock waves in the paravertebral region. When not reversed, it can compromise the effectiveness of treatment in sensitized segments.^{41–43}

In medical offices, shock waves are used in the treatment of dysfunctions in the bone marrow, deep ligaments, and muscle insertions, and it may also be applied to the myofascial layers or inflammatory areas. In addition, they are used in the treatment of low back pain, which may or may not be accompanied by sacroiliac, trochanteric, and gluteal pain. In most cases, these are related to ergonomic complications or sedentary lifestyles.⁴¹

In addition to identification and appropriate treatment, it is important to assess metabolic and autoimmune factors or the use of medications, which may hinder the clinical effectiveness of therapy. Statins, for example, cause depletion of coenzyme Q10⁴⁴ and, consequently, contribute to the formation of bone edema. Continuous administration of quinolone antibiotics can contribute to the development of tendinopathies, which are aggravated by the concomitant use of corticosteroids.^{45–48} Aromatase inhibitors in patients undergoing breast cancer treatment also perpetuate joint pain.^{49–53}

CONCLUSION

Noninvasive therapeutic modalities such as ESWT have recently gained popularity in the

treatment of musculoskeletal disorders related to the lumbar spine. Shock waves have shown promise in the treatment of numerous musculoskeletal conditions. This technique has been tested and refined in order to manage pathologies afflicting the lumbar region. In addition to being a noninvasive therapy, research suggests crucial roles in modulating biological responses associated with regulation of immune cells, faulty cells, and the synthesis of important factors for the restoration of diseased tissues. However, more robust clinical trials are warranted in order to further elucidate the long-term efficacy of this medical technique.

REFERENCES

1. Maniadakis N, Gray A. The economic burden of back pain in the UK. *Pain*. 2000;84(1):95–103. [https://doi.org/10.1016/S0304-3959\(99\)00187-6](https://doi.org/10.1016/S0304-3959(99)00187-6)
2. Hoy D, Bain C, Williams G, et al. A systematic review of the global prevalence of low back pain. *Arthritis Rheum*. 2012;64(6):2028–2037. <https://doi.org/10.1002/art.34347>
3. Kamper SJ, Henschke N, Hestbaek L, Dunn KM, Williams CM. Musculoskeletal pain in children and adolescents. *Braz J Phys Ther*. 2016;20(3):275–284. <https://doi.org/10.1590/bjpt-rbf.2014.0149>
4. Hartvigsen J, Hancock MJ, Kongsted A, et al. What low back pain is and why we need to pay attention. *Lancet*. 2018;391(10137):2356–2367. [https://doi.org/10.1016/S0140-6736\(18\)30480-X](https://doi.org/10.1016/S0140-6736(18)30480-X)
5. Hartvigsen J, Christensen K, Frederiksen H. Back pain remains a common symptom in old age: a population-based study of 4486 Danish twins aged 70–102. *Eur Spine J*. 2003;12(5):528–534. <https://doi.org/10.1007/s00586-003-0542-y>
6. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015 [published correction appears in *Lancet*. 2017 Jan 7;389(10064):e1]. *Lancet*. 2016;388(10053):1545–1602. [https://doi.org/10.1016/S0140-6736\(16\)31678-6](https://doi.org/10.1016/S0140-6736(16)31678-6)
7. Hoy DG, Smith E, Cross M, et al. Reflecting on the global burden of musculoskeletal conditions: lessons learnt from the global burden of disease 2010 study and the next steps forward. *Ann Rheum Dis*. 2015;74(1):4–7. <https://doi.org/10.1136/annrheumdis-2014-205393>

8. Calvo-Muñoz I, Gómez-Conesa A, Sánchez-Meca J. Prevalence of low back pain in children and adolescents: a meta-analysis. *BMC Pediatr.* 2013;13:14. <https://doi.org/10.1186/1471-2431-13-14>
9. Louw QA, Morris LD, Grimmer-Somers K. The prevalence of low back pain in Africa: a systematic review. *BMC Musculoskelet Disord.* 2007;8:105. <https://doi.org/10.1186/1471-2474-8-105>
10. Lemeunier N, Leboeuf-Yde C, Gagey O. The natural course of low back pain: a systematic critical literature review. *Chiropr Man Therap.* 2012;20(1):33. <https://doi.org/10.1186/2045-709X-20-3311>.
11. Konstantinou K, Dunn KM, Ogollah R, Vogel S, Hay EM; ATLAS study research team. Characteristics of patients with low back and leg pain seeking treatment in primary care: baseline results from the ATLAS cohort study. *BMC Musculoskelet Disord.* 2015;16:332. <https://doi.org/10.1186/s12891-015-0787-8>
12. Stafford MA, Peng P, Hill DA. Sciatica: a review of history, epidemiology, pathogenesis, and the role of epidural steroid injection in management. *Br J Anaesth.* 2007;99(4):461–473. <https://doi.org/10.1093/bja/aem238>
13. Verwoerd AJH, Mens J, El Barzouhi A, Peul WC, Koes BW, Verhagen AP. A diagnostic study in patients with sciatica establishing the importance of localization of worsening of pain during coughing, sneezing and straining to assess nerve root compression on MRI. *Eur Spine J.* 2016;25(5):1389–1392. <https://doi.org/10.1007/s00586-016-4393-8>
14. Foster NE, Anema JR, Cherkin D, et al. Prevention and treatment of low back pain: Evidence, challenges, and promising directions. *Lancet.* 2018;391(10137):2368–2383. [https://doi.org/10.1016/S0140-6736\(18\)30489-6](https://doi.org/10.1016/S0140-6736(18)30489-6)
15. National Guideline Centre (UK). *Low Back Pain and Sciatica in Over 16s: Assessment and Management.* London: National Institute for Health and Care Excellence (NICE); November 2016.
16. Mittermayr R, Antonic V, Hartinger J, et al. Extracorporeal shock wave therapy (ESWT) for wound healing: Technology, mechanisms, and clinical efficacy. *Wound Repair Regen.* 2012;20(4):456–465. <https://doi.org/10.1111/j.1524-475X.2012.00796.x>
17. Huang C, Holfeld J, Schaden W, Orgill D, Ogawa R. Mechanotherapy: Revisiting physical therapy and recruiting mechanobiology for a new era in medicine. *Trends Mol Med.* 2013;19(9):555–564. <https://doi.org/10.1016/j.molmed.2013.05.005>
18. Hausdorf J, Lemmens MA, Kaplan S, et al. 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.* 2008;1207:96–101. <https://doi.org/10.1016/j.brainres.2008.02.013>
19. Hausdorf J, Lemmens MA, Heck KD, et al. Selective loss of unmyelinated nerve fibers after extracorporeal shockwave application to the musculoskeletal system. *Neuroscience.* 2008;155(1):138–144. <https://doi.org/10.1016/j.neuroscience.2008.03.062>
20. Orhan Z, Cam K, Alper M, Ozturan K. The effects of extracorporeal shock waves on the rat Achilles tendon: is there a critical dose for tissue injury?. *Arch Orthop Trauma Surg.* 2004;124(9):631–635. <https://doi.org/10.1007/s00402-003-0598-5>
21. Moya D, Ramón S, Schaden W, Wang CJ, Guiloff L, Cheng JH. The role of extracorporeal shockwave treatment in musculoskeletal disorders. *J Bone Jt Surg Am Vol.* 2018;100(3):251–263. <https://doi.org/10.2106/JBJS.17.00661>
22. Wang CJ. Extracorporeal shockwave therapy in musculoskeletal disorders. *J Orthop Surg Res.* 2012;7:11. <https://doi.org/10.1186/1749-799X-7-11>
23. Holsapple JS, Cooper B, Berry SH, et al. Low Intensity Shockwave Treatment Modulates Macrophage Functions Beneficial to Healing Chronic Wounds. *Int J Mol Sci.* 2021;22(15):7844. <https://doi.org/10.3390/ijms22157844>
24. Notarnicola A, Moretti B. The biological effects of extracorporeal shock wave therapy (eswt) on tendon tissue. *Muscles Ligaments Tendons J.* 2012; 2(1):33–37.
25. Fiani B, Davati C, Griep DW, Lee J, Pennington E, Moawad CM. Enhanced Spinal Therapy: Extracorporeal Shock Wave Therapy for the Spine. *Cureus.* 2020;12(10):e11200. <https://doi.org/10.7759/cureus.11200>
26. Nedelka T, Nedelka J, Schlenker J, Hankins C, Mazanec R. Mechano-transduction effect of shockwaves in the treatment of lumbar facet joint pain: Comparative effectiveness evaluation of shockwave therapy, steroid injections and radiofrequency medial branch neurotomy. *Neuroendocrinol Lett.* 2014;35(5):393–397.
27. Lee S, Lee D, Park J. Effects of extracorporeal shockwave therapy on patients with chronic low back pain and their dynamic balance ability. *J Phys Ther Sci.* 2014;26(1):7–10. <https://doi.org/10.1589/jpts.26.7>
28. Ma J, Yan Y, Wang B, Sun W, Yue D, Wang W. Effectiveness and safety of extracorporeal shock wave treatment for low back pain a systematic review and meta-analysis of RCTs. *International Journal of Osteopathic Medicine.* Published online March 2022. <https://doi.org/10.1016/j.ijosm.2022.03.004>

29. Eftekharsadat B, Fasaie N, Gotalizadeh D, et al. Comparison of efficacy of corticosteroid injection versus extracorporeal shock wave therapy on inferior trigger points in the quadratus lumborum muscle: A randomized clinical trial. *BMC Musculoskelet Disord.* 2020;21(1):1–11. <https://doi.org/10.1186/s12891-020-03714-3>
30. Notarnicola A, Maccagnano G, Gallone MF, et al. Extracorporeal shockwave therapy versus exercise program in patients with low back pain: Short-term results of a randomised controlled trial. *J Biol Regul Homeost Agents.* 2018;32(2):385–389.
31. Walewicz K, Taradaj J, Rajfur K, et al. The effectiveness of radial extracorporeal shock wave therapy in patients with chronic low back pain: A prospective, randomized, single-blinded pilot study. *Clin Interv Aging.* 2019;14:1859–1869. <https://doi.org/10.2147/CIA.S224001>
32. Shi L, Gao F, Sun W, et al. Short-term effects of extracorporeal shock wave therapy on bone mineral density in postmenopausal osteoporotic patients. *Osteoporos Int.* 2017;28(10):2945–2953. <https://doi.org/10.1007/s00198-017-4136-7>
33. Moon YE, Seok H, Kim SH, Lee SY, Yeo JH. Extracorporeal shock wave therapy for sacroiliac joint pain: A prospective, randomized, sham-controlled short-term trial. *J Back Musculoskelet Rehabil.* 2017;30(4):779–784. <https://doi.org/10.3233/BMR-150405>
34. Sheng J, Liu S, Wang Y, Cui R, Zhang X. The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain. *Neural Plast.* 2017;2017:9724371. <https://doi.org/10.1155/2017/9724371>
35. Han H, Lee D, Lee S, Jeon C, Kim T. The effects of extracorporeal shock wave therapy on pain, disability, and depression of chronic low back pain patients. *J Phys Ther Sci.* 2015;27(2):397–399. <https://doi.org/10.1589/jpts.27.397>
36. Teasell RW, Mehta S, Aubut JL, et al. A systematic review of the therapeutic interventions for heterotopic ossification after spinal cord injury. *Spinal Cord.* 2010;48(7):512–521. <https://doi.org/10.1038/sc.2009.175>
37. Li Y, Zhu Y, Xie Z, Jiang C, Li F. Long-term radial extracorporeal shock wave therapy for neurogenic heterotopic ossification after spinal cord injury: A case report. *J Spinal Cord Med.* 2022;45(3):476–480. <https://doi.org/10.1080/10790268.2020.1760507>
38. Jeon HM, Lee WJ, Chung HS, et al. Extracorporeal shock wave therapy to treat neurogenic heterotopic ossification in a patient with spinal cord injury: A case report. *J Spinal Cord Med.* 2021;44(4):627–630. <https://doi.org/10.1080/10790268.2019.1632597>
39. Taheri P, Khosrawi S, Ramezani M. Extracorporeal Shock Wave Therapy Combined With Oral Medication and Exercise for Chronic Low Back Pain: A Randomized Controlled Trial. *Arch Phys Med Rehabil.* 2021;102(7):1294–1299. <https://doi.org/10.1016/j.apmr.2020.12.008>
40. Lange T, Deventer N, Gosheger G, et al. Effectiveness of Radial Extracorporeal Shockwave Therapy in Patients with Acute Low Back Pain-Randomized Controlled Trial. *J Clin Med.* 2021;10(23):5569. <https://doi.org/10.3390/jcm10235569>
41. Fischer AA, Imamura M. New concepts in the diagnosis and management of musculoskeletal pain. In: Lennard TA, organizador. *Pain procedures in clinical practice.* 2nd ed. Philadelphia, PA: Henley & Belfus; 2000. cap. 23. p. 213–229.
42. Fischer AA. Functional diagnosis of musculoskeletal pain by quantitative and objective methods. In: Rachlin ES, Rachlin IS, editors. *Myofascial pain and fibromyalgia. Trigger point management.* 2nd ed. St. Louis, MO: Mosby; 2002. chap. 7. p. 145–173.
43. Fischer AA, Dubo H, Young BJ, Imamura M, Cassius DA. Myofascial pain and fibromyalgia. In: O’Young BJ, Young MA, Steins SA, editors. *Physical medicine and rehabilitation secrets.* 3rd ed. Philadelphia, PA: Mosby; 2007. cap. 74. p. 369–378.
44. Barclay L. Atorvastatin decreases the coenzyme Q10 level in the blood of patients at risk for cardiovascular disease and stroke. *Arch Neurol.* 2004;61:889–892. <https://doi.org/10.1001/archneur.61.6.889>
45. Williams RJ, 3rd, Attia E, Wickiewicz TL, Hannafin JA. The effect of ciprofloxacin on tendon, paratenon, and capsular fibroblast metabolism. *Am J Sports Med.* 2000 May–Jun;28(3):364–369. <https://doi.org/10.1177/03635465000280031401>
46. Olcay E, Beytemur O, Kaleagasioglu F, Gulmez T, Mutlu Z, Olgac V. Oral toxicity of pefloxacin, norfloxacin, ofloxacin and ciprofloxacin: comparison of biomechanical and histopathological effects on Achilles tendon in rats. *J Toxicol Sci.* 2011;36(3):339–345. <https://doi.org/10.2131/jts.36.33947>
47. Kalghatgi S, Spina CS, Costello JC, Liesa M, Morones-Ramirez JR, Slomovic S, et al. Bactericidal antibiotics induce mitochondrial dysfunction and oxidative damage in Mammalian cells. *Sci Transl Med.* 2013; 5(192): 192ra85. <https://doi.org/10.1126/scitranslmed.3006055>
48. Kirchgessner T, Larbi A, Omoumi P, Malghem J, Zamali N, Manelfe J, et al. Drug-induced tendinopathy: from physiology to clinical applications.

- Joint Bone Spine. 2014;81(6):485–492. <https://doi.org/10.1016/j.jbspin.2014.03.022>
49. Morales L, Pans S, Paridaens R, Westhovens R, Timmerman D, Verhaeghe J, et al. Debilitating musculoskeletal pain and stiffness with letrozole and exemestane: associated tenosynovial changes on magnetic resonance imaging. *Breast Cancer Res Treat.* 2007;104(1):87–91. <https://doi.org/10.1007/s10549-006-9394-6>
50. Dizdar O, Ozçakar L, Malas FU, Harputluoglu H, Bulut N, Aksoy S, et al. Sonographic and electrodiagnostic evaluations in patients with aromatase inhibitor-related arthralgia. *J Clin Oncol.* 2009;27(30):4955–4960. <https://doi.org/10.1200/JCO.2008.20.5435>
51. Xepapadakis G, Ntasiou P, Koronarchis D, Koufoudakis D, Panousis D, Grosomanidis D, et al. New views on treatment of aromatase inhibitors induced arthralgia. *Breast.* 2010;19(3):249–250. <https://doi.org/10.1016/j.breast.2010.03.031>
52. Henry NL, Jacobson JA, Banerjee M, Hayden J, Smerage JB, Van Poznak C, et al. A prospective study of aromatase inhibitor-associated musculoskeletal symptoms and abnormalities on serial high-resolution wrist ultrasonography. *Cancer.* 2010;116(18):4360–4367. <https://doi.org/10.1002/cncr.25385>
53. Lintermans A, Laenen A, Van Calster B, Van Hoydonck M, Pans S, Verhaeghe J, et al. Prospective study to assess fluid accumulation and tenosynovial changes in the aromatase inhibitor-induced musculoskeletal syndrome: 2-year follow-up data. *Ann Oncol.* 2013;24(2):350–355. <https://doi.org/10.1093/annonc/mds290>