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Potential of molecular biophysical stimulation therapy in chronic musculoskeletal disorders: a narrative review

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Abstract

Current treatment of chronic musculoskeletal diseases does not give sufficient results despite the implementation of novel drugs and techniques in orthopaedics and physical therapy. For instance, osteoporosis treatment is currently mainly limited to drug application, while the goal of osteoarthritis treatment is to mitigate pain symptoms through physical therapy. The main therapeutic principle in the management of osteoporosis is not only to increase bone mass, but also to improve bone and the cartilage quality, which depends on the biomechanical balance. Therefore, there is a strong demand for advanced technologies that would safely and non-invasively accelerate cartilage regeneration and improve bone density. Ten years ago, a new state-of-the-art technology - "Molecular biophysical stimulation therapy (MBST)", specifically nuclear magnetic resonance therapy, emerged on the medical technology market and until now, it has shown successful results in the conservative treatment of musculoskeletal disorders, including back pain. The aim of this review is to provide an integrated, synthesized overview of the current evidence of efficacy of MBST for managing chronic musculoskeletal disorders.

Key Words: nuclear magnetic resonance therapy; MBST; osteoarthritis; osteoporosis; back pain.

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Nuclear Magnetic Resonance (NMR) is an umbrella term for Magnetic Resonance Imaging (MRI), Magnetic Resonance Spectroscopy (MRS), as well as for the therapeutic tool of NMR therapy, also known as Molecular Biophysical Stimulation Therapy (MBST).[1] NMR technology is used to transfer energy into the organism at the very effective proton level of the hydrogen atoms. The basic requirements for NMR are a homogeneous static basic magnetic field, the sweep field, and an additional coupled radio frequency field.[2] This signal (reflection or echo) is then used to create the image. In this way, the entire body can be penetrated without side effects. Since the human body consists of 70% - 80% of water, resonance can be optimally transferred into the body and directed to the target location of the damaged tissue in a further resonance. The physical effect of NMR stimulates proton spins in a living tissue and employs them for energy transport (intermediate energy storage via the protons of the hydrogen atomic nuclei). As a result, a measurable signal is emitted.[1,3,4] German researchers observed that patients with joint pain who underwent MRI frequently experienced relief. They discovered that the energy provided by the flow of protons promoted tissue regeneration in the surrounding area. The numerous frequencies in the MRI scanner were narrowed down to only those that have been shown to affect the surrounding tissue. In 1999, the German company MedTec Medizintechnik GmbH designed and patented the MBST device, which emits the pulsed magnetic waves that transmit energy from the movement of hydrogen atoms to injured tissue of the joints. MBST employs the same physical principle as MRI, albeit with a slightly weaker electromagnetic field than a conventional MRI scanner.[5] MBST to activates various molecular processes in organic tissue and may be a useful therapeutic method for OA.[6,7] The invention of MBST and the therapeutic equipment, which utilizes NMR for the treatment of musculoskeletal disorders such as arthritis, osteoporosis, sports injuries, and accident-related injuries, was by coincidence. Patients with joint aches reported, initially unexplained, pain relief following frequently utilized MRI exams. Doctors, biologists, and physicists have concluded that the MRI phenomenon may be responsible for this favourable effect.[8,9] Years of research led to the

invention of MBST, which was derived from the MRI and employs the same physical principle as MRI machines, but with significantly weaker electromagnetic fields and radio frequencies. The magnetic resonance frequency of MBST application ranges from 17 to 100 kHz at field strengths ranging from 0.04 to 2.35 mT.[1]
In recent years, evidence has begun to emerge on effect of MBST for management of chronic musculoskeletal diseases.[10] The aim of this narrative review is to explore and discuss the potential of Molecular Biophysical Stimulation Therapy (MBST) also known as Nuclear Magnetic Resonance Therapy in the management of chronic musculoskeletal conditions. Chronic musculoskeletal diseases, such as osteoarthritis, osteoporosis, and chronic back pain, pose significant challenges in terms of treatment and management.[5-7] Despite advancements in orthopaedics and physical therapy, current treatment methods often fail to provide satisfactory results. Therefore, there is a need for novel, safe, and non-invasive technologies that can accelerate tissue regeneration, improve bone density, and alleviate pain symptoms.

Materials and Methods

Our preliminary literature survey indicated heterogeneity between the studies in terms of conditions studies and outcome measures included. Consequently, a meta-analytical pooling of the results would be impossible at this point. Therefore, we conducted a scoping review of studies that examined the benefits of MBST for management of any chronic musculoskeletal condition. Scoping reviews provide a preliminary assessment of the available evidence and a broader overview of the existing literature, help identify gaps in existing research, and highlight areas for further investigation.[8] The literature review was conducted via the most extensive medical literature databases (Medline, PubMed, ScienceDirect, and Google Scholar) for the timeframe 1995–2022. The used search terms were: “MBST”, “magnetic resonance imaging”, “nuclear magnetic resonance therapy”. Any relevant review articles, randomized clinical trials, case reports, and case series found were included. Only articles in peer-reviewed journals, published in English language were eligible. In addition to the main research results obtained using the abovementioned databases, references of included resources were further examined and included, if suitable.

Results

In vitro evaluation of nuclear magnetic resonance therapy

The cellular response of different cell types to MBST has already been analysed. The results show that MBST does not affect apoptosis or viability of chondrocyte and osteoblast cell cultures, but rather shows a tendency of an

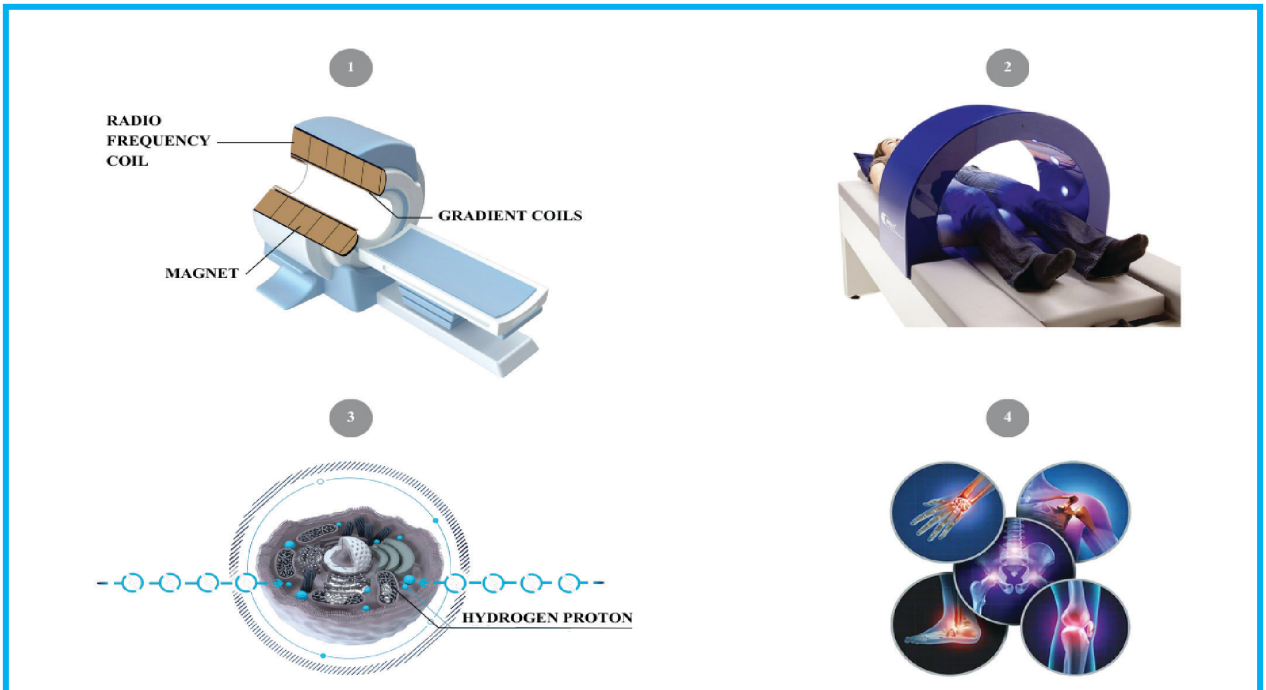

Fig 1. *The suggested key mechanism of action for MBST therapy. 1) Magnetic Field Generation: A device generates a magnetic field. 2) Target Area: The magnetic field is directed towards the target area, such as a joint affected by osteoarthritis. 3) Cellular Response: Cells in the target area, especially chondrocytes in the case of joint issues, respond to the magnetic field. The magnetic field might stimulate various cellular processes, such as cell regeneration and repair. 4) Potential Outcome: Over time, the stimulated cells might show increased activity, potentially leading to tissue repair and pain relief.*

elevated cell proliferation rate quantified by cell count.[7,11] Secondly it also counteracts IL-1β induced changes in human primary osteoarthritis chondrocytes by reducing catabolic effects, thereby decreasing inflammatory mechanisms under OA by changing NF-κB signaling.[6] MBST can also modulate IL-1β signaling events and the expression of growth factors including the miRNAs.[1] Skin fibroblasts produced less cross-linked collagen when exposed to MBST and showed changes in the expression of proteins involved in cell adhesion and movement. It was shown that MBST can also modulate the expression and the oscillation of specific core clock genes and Hif isoforms independently from the known light-induced effects.[13] New study suggests that MBST can even accelerate the regeneration of dorsal root ganglion neurons in vitro. This method promoted neuron regeneration shown by an increased cell survival, enhanced neurite network formation, and progressed neuronal differentiation status.[14] The suggested key mechanism of action for MBST therapy is presented in Figure 1.

Treatment of osteoarthritis with MBST

According to the World Health Organization (WHO), osteoarthritis (OA) is a condition that mostly affects the joints in the periphery. Globally, OA affects more than 250 million people worldwide and is one of the 50 most prevalent sequelae of diseases and traumas.[15] OA is a significant contributor to pain, disability, and a significant financial burden. There are currently no medications that can stop the structural progression of the disease.[16] Existing treatments are mostly aimed at reducing pain and maintaining joint function to enhance the quality of life.[17] Physiotherapy and occupational therapy are important aspects in the treatment of OA, while analgesia is a crucial component. Various adverse effects are associated with the available treatment options, and the efficacy of several therapies is currently under investigation. Surgery may be an option when non-pharmacological and pharmacological treatments fail to produce the desired results. Total joint replacement is regarded as the definitive treatment for OA in order to alleviate pain and restore the functionality of joints. However, surgery is linked to undesirable effects such as deep vein thrombosis and infection.[18] Up to 25% of patients with OA are not suitable candidates for joint replacement, according to studies.[19] Therefore, new non-invasive and non-pharmaceutical treatments are required. The study by Froböse investigated the effect of MBST on knee OA. This 10-week study including 14 patients measured the effectiveness of MBST. After treatment, cartilage structures grew significantly.[20] Kullich et al. evaluated the efficacy of MBST in the treatment of arthritis-related knee problems. In their six-month study with 59 patients, the effectiveness of MBST was reflected in statistically significant improvements in pain, joint stiffness, joint function, and quality of life of patients with OA.[21] Levers et al. evaluated the long-term effect of MBST on everyday activities and perceived pain in patients with OA. The study included 39 patients and evaluated the effect of MRT over a four-year period. The results showed a significant improvement in general health up to three years after the treatment.[5] The objective of the study by Kullich et al. was to demonstrate if MBST might favourably and persistently influence a variety of degenerative rheumatic conditions, particularly in the knee, hip, and ankle. This one-year trial comprised 4500 patients, of whom 2770 had knee OA. The observed improvement in pain and function lasted up to a year after treatment. In addition, the Lequesne index revealed an improvement in knee functionality and walking distance.[21]

Treatment of osteoporosis with MBST

The bone is metabolically active and continually repairing and remodelling itself. Due to structural degeneration of the bone, osteoporosis (OP) is characterized by decreased bone density and an increased risk of fractures.[11,22] The prevalence of OP and associated consequences, such as vertebral body or femoral neck fracture, would increase as a result of demographic shifts (increase in the elderly population). In addition to effective medication therapy, non-pharmaceutical therapies with minimal or no adverse effects are intriguing.[23] OP is preventable and treatable. However, it remains underdiagnosed, undertreated, and undervalued.[24] Bisphosphonates are currently the recommended pharmacological treatment for OP. The use of bisphosphonates for the treatment of OP is regarded as the first-line therapy prior to the administration of other medications. All bisphosphonates are associated with at least some extremely serious adverse effects, the most common of which being gastrointestinal and renal problems.[25] The most recent treatment for OP is RANK ligand inhibitors (RANKL), the specific antibodies against signal transduction of osteocytes.[26,27]

New studies suggest that non-invasive, nonpharmacological therapy might induce positive effects on bone cells, increase function and mobility of patients, and reduce discomfort. MBST, for instance, is an intriguing alternative therapy for increasing bone mineral density (BMD) and preventing OP. A recent study demonstrated long-term effects of MBST on BMD in OP patients. 103 patients between the ages of 45 and 89 with osteoporosis and a T-score of less than -2.5 were treated using low field NMR using a specialized NMR apparatus (MBST, MedTec, Germany) for ten consecutive days, one hour per day. From baseline to twelve months, BMD and serum osteocalcin levels significantly increased.[28] A small-scale study was conducted to determine whether MBST is an effective treatment for OP. There was a significant reduction in pain intensity and pain severity. Similarly, an increase in bone density and mineral salt content of up to 55% was observed between 22 and 52 and 120 days. The author

concludes that the magnetic resonance method for treating OP is a remarkable and extremely rapid-acting treatment method.[29]

Treatment of back pain with MBST

Chronic back pain (CBP) is a major health problem in our population. Whereas CBP may be a consequence of segmental dysfunction and muscle pain, usually associated with degenerative or post-traumatic changes in the affected part of the spine,[30] many cases are idiopathic. In many cases, treatment is only symptomatic. Regular physical activity combined with physiotherapy are usually the most suitable intervention in patients with CBP.[31,32]

The multidisciplinary rehabilitation concept was evaluated in patients with CBP. It consisted of a standardised in-patient physiotherapy programme combined with a series of treatments with 1 hour of therapy per day for 9 consecutive days in an MBST therapy system. MBST caused a sustainable improvement of the painful CBP and positive effects were evident over a period of 12 weeks. The study showed that MBST could be beneficial, easy-to-use treatment method that could be used as an additional therapy in patients with CBP. In addition, no side-effects of MBST therapy were observed in this controlled study.[33] MBST therapy has also shown consistently significant outcomes in patients with herniated discs in the lower lumbar spine. Fever sick days were taken by patients who were treated with active field utilizing the MBST.[34]

Contraindications and restrictions on use of MBST

Prior to the commencement of MBST, it is imperative to consider specific contraindications and restrictions associated with the treatment. While MBST therapy devices, under normal therapeutic conditions, do not typically pose acute or chronic health risks, the growing prevalence of active implants among patients introduces the potential for functional disorders or undesirable effects. Hence, thorough inquiry into possible contraindications is paramount before initiating the therapy.[29]

MBST therapy should be refrained from under the following conditions: implanted infusion, pain, or insulin pumps, as well as cochlear implants and other neurostimulators situated within the active treatment field. However, modern pacemakers and electrodes, specially designed to withstand magnetic fields, generally allow for MBST therapy. Similarly, the

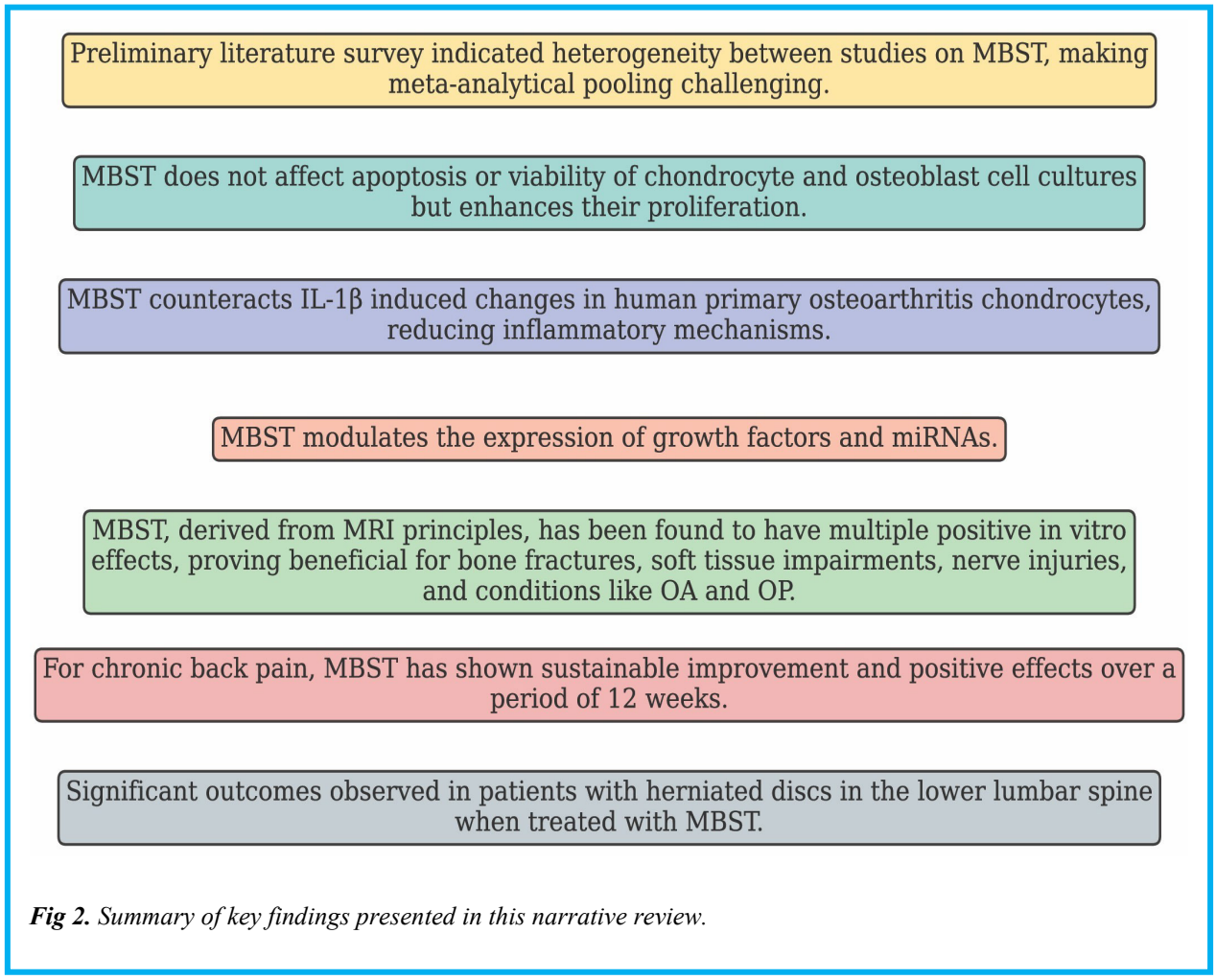

Fig 2. *Summary of key findings presented in this narrative review.*

eligibility for MBST therapy in patients with heart valve prostheses depends on the specific type and functionality of the prosthesis.[29]

In cases involving patients with pacemaker and defibrillator systems, it is essential to obtain confirmation from the implant manufacturer regarding MRI suitability. Without this confirmation, there is a risk of damage to the implants during treatment due to interactions with the therapy system's electromagnetic fields. Furthermore, patients with ferromagnetic foreign objects, such as metal shards or vascular clips, within the active treatment field are advised against undergoing MBST therapy. Pregnant women are also discouraged from MBST therapy due to insufficient research on its effects during pregnancy.[29]

For individuals with specific pre-existing conditions, including tumors in the treatment zone, leukemia, HIV infection, bacterial infection, or active rheumatic episodes, consultation with a specialist is mandatory before initiating MBST therapy. Careful evaluation, considering the benefit-risk balance, might still allow therapy in certain cases, especially if the pre-existing condition is located outside the intended treatment zone or if the potential benefits of the therapy outweigh the associated risks. It is important to note that MBST therapy does not impair the ability to drive or operate machinery. Currently, the interactions of MBST therapy with other therapeutic measures remain unknown, and there is no specific age limit for its application.[29]

Limitations

While this narrative review aims to provide an overview of the potential of Nuclear Magnetic Resonance Therapy (MBST) in the management of chronic musculoskeletal conditions (see Figure 2), it is essential to acknowledge certain limitations that may affect the interpretation of the findings. The current body of literature on MBST's therapeutic efficacy for musculoskeletal disorders, particularly osteoarthritis, osteoporosis, and chronic back pain, is still relatively limited. Many of the studies reviewed here are small-scale trials or case series, which may not provide definitive evidence of MBST's effectiveness in larger, diverse patient populations. Most of the existing research comprises non-randomized and non-controlled studies. The absence of well-designed randomized controlled trials (RCTs) makes it challenging to draw firm conclusions about the comparative effectiveness of MBST against standard treatments or placebo interventions. The studies reviewed in this narrative review also vary in terms of patient selection criteria and outcome measures. Many of the studies evaluated in this review have relatively short follow-up periods, often limited to several months. Long-term outcomes and the durability of MBST effects on musculoskeletal conditions need further investigation. The majority of the reviewed studies have been conducted on specific patient populations, and the generalizability of the findings to broader patient groups or diverse demographic backgrounds is unclear.

Future research

To overcome the limitations mentioned above and gain a more comprehensive understanding of MBST's potential in managing chronic musculoskeletal conditions, future research should encompass well-designed RCTs with adequate sample sizes, and should compare MBST with standard treatments and include long-term follow-up to assess both short-term and sustained effects. Nevertheless, taking into consideration scientific research of bone biology, and clinical experiences, it can be concluded that regardless of the mentioned limitations, and lack of prospective, long-term, double-blind, placebo-controlled studies, there is enough evidence for the acceptance of the new paradigm in the clinical approach to the musculoskeletal pathology which is based on 4P principles (preventive, predictive, personalized, participative), in which MBST- magnetic resonance therapy has an important role. Comparative effectiveness research comparing MBST with other non-invasive and pharmacological treatments would provide valuable insights into the optimal place of MBST in the treatment algorithm for specific musculoskeletal conditions. Further in-depth mechanistic studies are needed to elucidate the underlying biological processes and pathways that contribute to the therapeutic effects of MBST on musculoskeletal tissues. This knowledge would enhance our understanding of its mode of action and guide future treatment refinements. Standardization of MBST treatment protocols, including the frequency, duration, and intensity of sessions, would improve consistency across studies and facilitate comparability of results. By considering these factors, researchers and clinicians can build a more robust evidence base for MBST's role in managing chronic musculoskeletal conditions. Advancing our knowledge in these areas will inform clinical practice and contribute to evidence-based decision-making, ultimately benefiting patients suffering from musculoskeletal disorders

In concusion, new therapeutic interventions are of utmost importance in providing long-term benefits for patients with musculoskeletal disorders, such as OA, OP and CBP.

It is generally known that interventions should firstly comprise non-invasive and if possible non-pharmacological interventions, with provoking positive effects on bone cells, soft tissue, pain reduction, evolving normal joint range of motion and inducing normal function. MBST is a non-invasive procedure that was derived from the MRI and employs the same physical principle as MRI machines, but with significantly weaker electromagnetic fields and radio frequencies. It was found that MBST possess several positive in vitro effects, such as histamine-induced calcium response, activity of MAP kinases, cellular production and IL-1β reduction in ATP.

This procedure is beneficial in bone fractures, soft tissue impairments such as tendon, ligament and muscle damage or pain, while also beneficial in patients with

neurological impairments due to nerve injury and patients with OA and OP. Furthermore, clinical studies show that stimulation of the electromagnetic fields partially preserves osteoporotic bone mass, microstructures, and strength by impacting anabolic activities of the skeletal system.
To eliminate all confounding variables and limitations of the existing studies, it is necessary to undertake additional research and evaluate the long-term benefits of MBST.

List of acronyms

BMD – bone mineral density
CBP – chronic back pain
MBST - Molecular Biophysical Stimulation Therapy
OA – osteoarthritis
OP – osteoporosis
RCTs – randomized controlled trialsα

Contributions of Authors

M.Ž. and D.Š conceptualized the paper and performed the first literature review. ŽK supervised the work. All authors worked on analyzing the literature and writing the manuscript. All authors read and approved the final edited typescript.

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Conflict of Interest

The authors declare they have no conflicts of interest.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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