Double-Blind Randomized Controlled Trial Comparing Two Standardized Radial Pressure Wave Techniques Versus Pain-Site Guided Therapy in Patients With Knee Osteoarthritis: Four-Month Outcomes

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Introduction

Osteoarthritis (OA) is the most common musculoskeletal joint disorder in adults worldwide, with the knee being the most frequently affected region.[1,2,3] Knee osteoarthritis (KOA) is a chronic and progressive joint disease characterized by the loss of articular cartilage, resulting in damage to the subchondral bone, synovial structures, and surrounding soft tissues.[3,4,5] This chronic-degenerative condition is associated with a high health burden for patients and implications for healthcare systems. It is considered the leading cause of permanent disability in individuals over the age of 65, with an estimated global prevalence affecting around 365 million people.[6] In Mexico, the prevalence of KOA is 2.3% in the adult population, and within the Mexican Institute of Social Security, it ranks among the top 10 reasons for primary care visits.[3,4,5]

KOA is a multifactorial disease in which various harmful agents can initiate and perpetuate damage to the articular cartilage, subsequently triggering responses in the synovial membrane and subchondral bone. When the balance between cartilage matrix formation and degradation is disrupted—favoring degradation beyond the system's compensatory capacity—matrix breakdown ensues, ultimately leading to OA.[12] The main risk factors include age over 50 years, obesity, repetitive activities, joint instability, and malalignment.[1,3,4,5]

Extracorporeal shock wave therapy (ESWT) is a non-invasive therapeutic procedure aimed at producing analgesia and facilitating the healing of musculoskeletal conditions. There are two types of extracorporeal shock waves: focused shock waves and radial shock waves—also known as radial pressure waves—which can be generated using electrohydraulic, electromagnetic, or piezoelectric sources.[7,8] The mechanism of action involves the distribution of pressure, energy flux density, and total acoustic energy to produce microscopic interstitial and extracellular responses that promote tissue regeneration. The effects of radial pressure wave therapy (RPWT) include analgesia, protein synthesis, neovascularization, and cellular proliferation.[9,10,11,12]

ESWT for musculoskeletal disorders is considered an effective, non-invasive, and cost- and time-efficient treatment. However, there is still no standardization regarding dosage, patient positioning, or application sites for ESWT, and the current evidence regarding the definitive efficacy of RPWT in KOA remains insufficient.[8,9]

Background

The primary goal in the treatment of osteoarthritis (OA) is to relieve signs and symptoms of the disease and, if possible, slow its progression. The therapeutic spectrum ranges from general measures such as rehabilitation, orthotics, and pharmacotherapy, to surgical interventions.[2] A meta-analysis conducted by Henriksen et al. in 2016 demonstrated that the efficacy of exercise is comparable to that of oral analgesics in knee osteoarthritis (KOA).[13] In a study by Mao et al., the effectiveness of isokinetic, isometric, and isotonic exercise was compared, concluding that isotonic exercise is the best option for initial strengthening in patients with knee pain due to OA, while isokinetic exercise improves joint stability.[14]

Cho H-Y, Kim E-H, Kim J, and Yoon YW compared the application of kinesiology taping with and without tension (placebo) on the quadriceps. They found that kinesiology taping with adequate tension effectively reduces various types of pain, enhances joint mobility, and improves proprioception in patients with OA.[15] In 2020, The Knee journal published a meta-analysis on the efficacy of intra-articular injections in KOA, concluding that orthobiologic treatments alleviate symptoms by dampening the inflammatory process and have chondrogenic potential. Additionally, stromal vascular fraction injections enhance analgesic effects and functional outcomes in KOA patients for up to one year of follow-up.[16]

Extracorporeal shock wave therapy (ESWT) has become a popular non-invasive treatment modality for various musculoskeletal injuries. It is subdivided into two types: focused and radial. Radial pressure wave therapy (RPWT) reaches maximum pressure at the applicator source rather than at tissue depth. The waves are generated by accelerating a projectile via compressed air, transmitting the mechanical wave into the body through an applicator. Animal studies conducted in the 1980s showed that shock waves could alter the bone-cement interface, stimulate an osteogenic response, and enhance fracture healing.[17]

Shock wave therapy has been widely used since the 1990s to treat various musculoskeletal disorders, including long bone fractures, calcific tendinitis of the shoulder, lateral epicondylitis of the elbow, and plantar fasciitis.[12]

In recent years, RPWT has been considered and introduced as a treatment for KOA. Several studies have shown that it can accelerate meniscal healing, improve pathological changes of OA—including cartilage and subchondral bone alterations—and exert a consistent and beneficial chondroprotective effect both in early and late stages of the disease. Additionally, RPWT may reduce pain and improve functionality.[7,8,18]

A randomized controlled clinical trial was conducted in Taiwan between December 2017 and October 2019 to determine the efficacy of focused shock wave therapy

(FSWT) and RPWT in KOA. Forty-two patients with bilateral knee osteoarthritis were randomly assigned to receive three sessions of either FSWT or RPWT in a supine position with knees flexed at 90°, targeting the most tender areas (tibial plateau and femoropatellar margin), at one-week intervals. Patients were evaluated at baseline, and at 4 and 8 weeks after the final treatment. The primary outcome was the change in pain intensity measured with the visual analog scale (VAS). Secondary outcomes included the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), knee joint range of motion, and the 6-minute walk test. The study concluded that both modalities improved pain and physical function, but FSWT was more effective than RPWT.[19]

In 2012, Martha Imamura and colleagues conducted a double-blind randomized controlled trial including patients over 59 years of age with KOA who had failed at least two previous conservative treatments. The control group received sham RPWT, while the intervention group received therapeutic RPWT consisting of 2000 impulses applied to the most painful areas, with an intensity of 2.5 to 4 bars and a frequency of 8 Hz. Both groups received three sessions at one-week intervals and followed a complementary home-based physical therapy program. The outcome measures included VAS, algometry, and WOMAC. Their findings supported that RPWT produced a statistically significant improvement only in the WOMAC pain scores and some algometric measurements.[20]

The most recent study on RPWT in KOA was published by Uysal et al. and conducted between 2017 and 2018. This was a single-blind randomized controlled trial including 104 patients aged 50 to 70. Both groups received transcutaneous electrical nerve stimulation for 30 minutes, hot packs for 40 minutes, and a home exercise program for knee muscle strengthening (5 times per week for one month). One group received RPWT (2000 pulses, 10 Hz, 2.0 to 3.0 bar, once per week for three weeks), while the other received sham RPWT (2000 pulses, 10 Hz, 0.1 bar, once per week for three weeks). In both groups, patients were treated with knees flexed at 90°, applying the intervention to sensitive areas or the patellofemoral and tibiofemoral margins. Outcomes included VAS, range of motion, 20-meter walk test, WOMAC, Lequesne disability index, and isokinetic muscle performance, assessed at baseline, post-treatment, 1-month, and 3-month follow-ups. The results demonstrated that RPWT led to superior improvement in all parameters at both 1 and 3 months.[21]

It is worth noting that, based on a literature review conducted for this protocol, no studies evaluating the efficacy of RPWT in Latin American patients with KOA were identified. The present study may be the first clinical trial on RPWT conducted at the Hospital Civil de Guadalajara.

Problem Definition

KOA is one of the leading global health problems. Its management entails high costs and can result in significant disability. RPWT has been shown to be effective in controlling pain and improving function; however, scientific literature on this topic remains limited.

Research question: Is radial RPWT effective when using different application techniques in patients with chronic KOA?

Justification

KOA is a major public health concern worldwide. Its impact is such that in Mexico, KOA limits mobility in 10 out of every 100 adults over the age of 45 and is one of the leading causes of disability overall. The cost of managing KOA is high and increasing exponentially.

OA is among the ten most frequent reasons for consultation in the Physical and Rehabilitation Medicine Department of the “Fray Antonio Alcalde” Civil Hospital of Guadalajara. In 2023, gonarthrosis and other internal knee disorders were the second most prevalent condition treated at the musculoskeletal rehabilitation clinic within the same department.

Conventional treatment for KOA is often insufficient to control symptoms and prevent disability, ultimately impacting quality of life and promoting progression of degenerative changes in the articular cartilage.

RPWT is a non-surgical alternative for patients with chronic KOA. It can provide positive effects on pain and functionality in fewer sessions and less treatment time. However, scientific evidence regarding its effectiveness is limited and not yet conclusive. In addition, there is no standardized protocol regarding patient positioning or whether the application should be targeted at anatomical or painful points.

Theoretical Framework

The knee has the largest articular surface of all joints and, depending on the activity, this weight-bearing joint can support two to five times a person's body weight. The knee is the most common site of lower limb osteoarthritis, and nearly half of all adults are estimated to develop symptomatic gonarthrosis in their lifetime.

Chronic knee pain affects 25% of adults and negatively impacts daily function and quality of life, becoming one of the most common causes of disability in individuals over 65 years. OA has long been regarded as a natural part of aging, commonly referred to as "wear and tear" and classified as a degenerative joint disease. However, ongoing research has made it increasingly clear that the pathogenesis of OA is a complex and sophisticated process.

Various factors play important roles in the pathogenesis of OA, including biomechanical factors, proinflammatory mediators, and proteases. Excessive force or abnormal joint contact may trigger an innate immune response, elevating proinflammatory factors and proteases, which further exacerbate joint destruction. When proteases are activated by these inflammatory signals, they begin to hydrolyze matrix proteins in the cartilage, progressively damaging all joint components—articular cartilage, synovium, adjacent bone, menisci, and surrounding soft tissues—as OA progresses to its terminal stage.

OA pathophysiology begins with the degradation of extracellular cartilage matrix, primarily affecting type II collagen and proteoglycans. Initially, chondrocytes proliferate to attempt repair, increasing matrix synthesis, but eventually fail. They also undergo hypertrophic differentiation, expressing markers such as Runx2 and Mmp13, which further exacerbate cartilage degradation. The production of degradative enzymes such as matrix metalloproteinases and aggrecanases increases, leading to further loss of matrix components. Over time, chondrocytes undergo apoptosis, resulting in acellular zones and total cartilage loss. As the joint space narrows, bone-on-bone contact produces pain, inflammation, and osteophyte formation, culminating in significant joint dysfunction and chronic pain typical of advanced OA.

Pain in OA arises from both peripheral and central mechanisms. Nociceptors in the joint are activated by harmful stimuli, such as inflammatory mediators (bradykinins, prostaglandin E2), and transmit pain signals via peripheral nerve fibers (C and Aδ fibers). Peripheral sensitization occurs when inflammation or injury increases nociceptor excitability, causing hyperalgesia and allodynia. Nerve Growth Factor (NGF) plays a key role by enhancing nociceptor sensitivity. Central sensitization contributes to persistent pain by altering pain pathways in the central nervous system, making pain more intense and continuous. These mechanisms explain why OA pain can become resistant to conventional analgesics.

The diagnosis of KOA can be based on clinical findings such as persistent joint pain associated with use in one or a few joints, age ≥45 years, and morning stiffness ≤30 minutes. Radiographic examination may support the diagnosis and help define prognosis in symptomatic patients.

Evidence-based approaches for KOA treatment include non-pharmacological, pharmacological, and surgical modalities aimed at relieving pain, improving joint function, and modifying risk factors for disease progression. Disease-modifying therapies have not shown sufficient benefit to receive regulatory approval, though some investigational therapies appear to slow structural progression.
In recent years, RPWT has been considered and introduced in OA treatment, with studies showing that it can improve OA-related pathological changes, including those in cartilage and subchondral bone.

RPWT is a non-invasive therapeutic procedure that delivers a single acoustic pulse lasting 1 microsecond to targeted body areas, producing analgesia and promoting healing through a mechanism called mechanotransduction. This mechanotransduction travels through tissues and exerts analgesic, osteogenic, neovascular, and reparative effects. It has been proposed as the main mechanism by which RPWT induces angiogenesis and tissue regeneration at cellular and molecular levels.

Its benefits include analgesia, enhanced protein synthesis, increased vascularization, improved cell proliferation, calcification breakdown, and a protective effect on cartilage and bone.

In OA, RPWT promotes beneficial changes in cartilage and subchondral bone, stimulates chondrocyte activity, and reduces cartilage fissuring. It has anti-inflammatory effects and promotes angiogenesis, helping to relieve pain and improve motor function. RPWT also stimulates meniscal cell proliferation and extracellular matrix repair while modulating central and peripheral sensitization to reduce hypersensitivity and chronic OA-related pain.

RPWT dosing consists of several components that may influence treatment outcomes, including: Frequency (impulses per second), which affects depth and energy distribution (lower frequencies are used for deeper areas; higher for superficial). Number of pulses, with more pulses potentially improving effectiveness but also increasing side effect risks or discomfort. Power, referring to energy per pulse; higher power may be more effective for treating calcifications or dense tissues but may also be more painful. Patient positioning, which may influence effectiveness by improving target orientation and optimizing energy transmission.

Study objectives

General objective: To determine the effectiveness of radial pressure wave therapy (RPWT) using different application techniques in patients with chronic knee osteoarthritis (KOA).

Specific Objectives: 1. To evaluate whether the site of application of RPWT influences clinical outcomes in terms of pain and physical function. 2. To analyze the relationship between the radiographic severity of KOA and clinical outcomes after RPWT. 3. To determine the influence of body mass index (BMI) on clinical outcomes in patients with KOA treated with RPWT.

Materials and methods

Study design: This was a single-blind, randomized controlled trial.

Setting and population: Participants with chronic knee osteoarthritis were recruited through a digital campaign and treated at the Department of Physical Medicine and Rehabilitation of the Antiguo Hospital Civil de Guadalajara "Fray Antonio Alcalde" during the third quarter of 2024 (July–September).

Inclusion criteria: Male and female patients aged 50–80 years. Clinical diagnosis of KOA according to the American College of Rheumatology criteria. Minimum of six months of knee pain. Anteroposterior and lateral knee radiographs (within the past year).

Exclusion criteria: Previous knee surgery. Inflammatory arthropathy. Active infection. Fibromyalgia. Cancer. Severe vascular insufficiency.

Elimination criteria: Absence from one or more RPWT sessions. Voluntary withdrawal at any time for any reason.

Sampling and randomization: Patients were randomly assigned to one of three groups using a sealed opaque envelope method (also known as "paper-draw bag method"). Each envelope contained the designation of one of the three groups ("Experimental Group 1", "Experimental Group 2", or "Control Group"). This simple randomization ensured equal allocation probability and minimized selection bias.

Outcome measures: Sociodemographic data were collected using a standardized internal questionnaire. Pain intensity was assessed using the Numerical Pain Rating Scale (NPRS) at baseline, after the third treatment session, and three months post-baseline. NPRS consists of a 10 cm horizontal line where 0 represents “no pain” and 10 represents “worst imaginable pain.” Functionality was measured using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which evaluates pain (5 items), stiffness (2 items), and physical function (17 items), each scored on a 5-point Likert scale (0 = none, 4 = extreme). Higher scores indicate greater impairment. WOMAC was applied at baseline, after the third session, and three months post-treatment. Radiographic severity of KOA was assessed once using the Kellgren-Lawrence (KL) classification based on weight-bearing anteroposterior knee radiographs. The scale ranges from 0 to 4: 0 = normal; 1 = doubtful; 2 = mild; 3 = moderate; 4 = severe. Outcome evaluations will be conducted at baseline, immediately after the third RPWT session, at the two-month follow-up, and at the four-month follow-up after the first session.

Sample size calculation: The primary outcome for sample size determination was pain intensity (NPRS). Using a two-tailed α of 0.05, 80% power (β = 0.20), an expected clinically relevant effect size of 2.0, and a standard deviation of 2.1 (based on prior literature), the required sample size per group was 17 participants. Anticipating a 20% attrition rate, we adjusted the sample to 23 participants per group to preserve statistical power. Therefore, a total of 69 participants were recruited and equally distributed across the three study arms.

Intervention Groups:

- Control group: Patients received 3 weekly RPWT sessions in the supine position with the knee flexed 30°–60°. A total of 2000 shocks per session were applied at the two most painful palpated sites (based on physical examination), using a fixed frequency of 10 Hz and an intensity of 2.0 bar. At the final session, participants were trained to continue with a four-week home-based physical therapy program including superficial thermotherapy, stretching, strengthening, proprioceptive retraining, and general recommendations.

- Experimental group 1: Patients received 3 weekly RPWT sessions in the same position. A total of 2000 shocks were applied to the medial joint line using a non-fixed frequency (10 Hz) and intensity of 2.0 bar. At the final session, they were instructed to follow the same four-week home rehabilitation program as described for the control group.

- Experimental group 2: Patients received 3 weekly RPWT sessions with 2000 total shocks distributed equally over the medial (1000 shocks) and lateral (1000 shocks) joint lines. Frequency was non-fixed (10 Hz), and intensity was 2.0 bar. The same four-week home-based therapy program was prescribed after the third session.

Blinding: This study will employ a double-blind design. Both participants and the clinical evaluator responsible for conducting the physical and radiographic assessments will be blinded to the group assignments. Participants will be informed that they would receive one of three potential treatment techniques but will not be made aware of the specific approach applied to them. RPWT will be administered by a final-year resident physician in Physical Medicine and Rehabilitation who will be aware of the group allocations but will not be involved in outcome assessments. All data collection and statistical analyses will be conducted by researchers blinded to the group assignments. Furthermore, all treatment sessions will be standardized, with identical instructions, equipment setup, and clinical environments applied across the three groups to minimize performance and detection bias.

Statistical analysis plan

Software: All statistical analyses will be performed using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA).

Descriptive statistics: Descriptive statistics will be computed for all variables. Categorical variables will be reported as frequencies and percentages, while continuous variables will be reported as means and standard deviations or medians and interquartile ranges, depending on their distribution.

Normality testing: The distribution of continuous variables will be assessed using the Kolmogorov–Smirnov test.

Primary outcome: Pain intensity, assessed using the Numerical Pain Rating Scale (NPRS), is defined as the primary outcome.

Secondary outcome: Self-reported physical function, measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), is defined as the secondary outcome.

Within-group analysis: To evaluate changes over time within each treatment group (baseline, 2-month, and 4-month assessments), the following tests will be used:

- Paired-samples t-tests for normally distributed data.
- Wilcoxon signed-rank tests for non-normal distributions.
- Bonferroni correction will be applied to adjust for multiple comparisons, when appropriate.

Between-group analysis and interaction Effects: A two-way mixed-design repeated-measures ANOVA will be used to assess:

- The main effect of time.
- The main effect of the group (three levels: pain-site guided therapy, standardized medial line application, and standardized medial + lateral lines application).
- The interaction effect of time × group.

When the assumption of sphericity is violated, the Huynh–Feldt correction will be applied. Post hoc analyses will include:

- Bonferroni-adjusted pairwise comparisons for within-subject effects.
- Tukey’s Honestly Significant Difference (HSD) test for between-group comparisons.

- Homogeneous subset analyses to identify clusters of similar treatment response profiles.

Effect size and power: Partial eta squared (η^2) will be reported to estimate the effect size. Observed power ($1–\beta$) will be documented where appropriate.

Statistical significance: A two-tailed p-value of ≤ 0.05 will be considered statistically significant for all analyses.

Informed Consent Form

Title of the research project: "Effectiveness of Radial Pressure Wave Therapy Using Different Application Techniques in Patients with Chronic Knee Osteoarthritis at the Antiguo Hospital Civil de Guadalajara 'Fray Antonio Alcalde', from August to November 2024"

Principal investigators: _____. Hospital Civil de Guadalajara “Fray Antonio Alcalde”. Contact Number: +52 33 3454 9242.

Research Ethics Committee Contact number: +52 33 3942 4414

Please read this document carefully.

You are invited to participate in this research project because you meet the necessary eligibility criteria. Please read the following information to understand the nature of your participation and decide freely and informed whether you wish to participate. Feel free to ask any questions you may have.

Objective of the study: To evaluate the analgesic effects and functional improvement provided by radial pressure wave therapy in patients with knee osteoarthritis.

What does your participation involve?: This study requires your attendance at three in-person visits. During the first visit, clinical assessment scales will be administered, and you will receive the first session of radial pressure wave therapy. During the second visit, you will receive the second therapy session. During the third visit, the clinical scales will be reapplied, and you will receive the third session of therapy.

Are there any risks or inconveniences?: You may experience pain during or after the treatment, as well as bruising (ecchymosis) at the application site. These effects are generally temporary and expected to subside within a few days.

Additional considerations: This study does not require any changes to the treatment prescribed by your physician for your usual care. Any change in your treatment will be decided solely by your physician and will not be related to your participation in this study.

Do you receive any benefits from participating?: You may experience pain relief and functional improvement. You will not receive financial compensation for your participation. Investigators will be available to answer any questions about the project. Participation in this study does not imply an obligation by the research team to treat any medical condition diagnosed during the study.

Will your data remain confidential?: All information collected will be stored both in paper format and electronically. To protect your privacy, the data will be stored in a way that prevents personal identification. If study results are published, your identity will remain confidential. By signing this form, you authorize the use of your information for research purposes. Your medical records will not be made public.
However, by signing this form, you authorize access to your medical information by individuals with a legitimate reason (e.g., study monitors or ethics committees). The data from the scales administered are exclusively for research purposes. They will not be used for your medical care or diagnosis, unless you or your physician explicitly request them in writing.

What happens if you decide to withdraw?: Your participation is completely voluntary. You may agree to participate now and change your mind later. You may withdraw from the study at any time, without any consequences. Your decision will not affect your regular medical care or your right to receive any treatment you need.

Agreement to Participate

By signing this form: I confirm that I have read and understood the information presented. The study has been explained to me in a language I understand. All my questions about the study and its potential risks have been answered. Based on this information, I freely agree to participate in this research study.

Participant Consent

Name of the Participant: _____
Signature: _____

Witness 1
Name: _____
Signature: _____

Witness 2
Name: _____
Signature: _____

By signing this form, I acknowledge that I have not waived any legal rights I may have as a participant in this research study. I agree to answer any additional questionnaires required to confirm my participation in the study.

Principal Investigator

_____

Signature: _____
Date: __ /__/2024.

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