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The effect of compression by elastic bandages on pain and function in individuals with knee osteoarthritis – protocol of a randomized controlled clinical trial

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The effect of compression by elastic bandages on pain and function in individuals with knee osteoarthritis – protocol of a randomized controlled clinical trial

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ABSTRACT

Introduction: Although compression is used to control pain in KOA, this clinical application is poorly supported and there is a lack of scientific evidence to support its clinical use. As a low-cost and accessible protocol, compression by elastic bands could be a non-pharmacological intervention to reduce pain and improve physical function in individuals with KOA. The aim of this paper is to evaluate the effects of compression on pain and function of individuals with knee osteoarthritis (KOA). **Methods and Analysis:** A randomized controlled clinical trial will be carried out. Individuals with KOA (n=90; both sexes; between 40 and 75 years old) will be allocated into three groups (n=30/group): Compression (compression by elastic bandage on the affected knee, once a day for 20 min, on 4 consecutive days); Sham (same protocol, but the elastic band is placed around the affected knee without compression); and Control (no intervention). The individuals of the three groups will be evaluated one day before the first intervention; one day after the last intervention; and at the 12th and 24th weeks after the end of interventions. Pain intensity by Visual Analog Scale (VAS) will be the main outcome. The secondary variables are physical function assessed by the Western Ontario & McMaster Universities Osteoarthritis (WOMAC) questionnaire and physical tests (step test; 30s sit and stand test; 40m accelerated walk test). Global Rating of Change Scale (GRC) will also be applied to quantify the volunteer's perceived change. **Ethics and dissemination:** The project was approved by the Human Research Ethics Committee of the Federal University of São Carlos, São Paulo, Brazil (3.955.692). Results will be published in peer-reviewed journals.

Trial registration number: NCT04724902.

Keywords: Osteoarthritis; compression; pain, knee; physiotherapy.

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Strengths and limitations of this study

- The study is conducted by well-established reporting guidelines. The methodology was designed to minimize the potential for bias in including hidden information treatment allocation and blinding of the evaluator and biostatistician therapist.
- The study will evaluate the subjective and objective result's physical function measures.
- The therapist delivering the therapies and the patients cannot be blinded.

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INTRODUCTION

KOA represents an average cost of US$ 15,000/year per user, is radiographically present in 30% of individuals over 45 years old and symptomatic in at least half of these cases.[1] Characterized as chronic and progressive, it is one of the main causes of musculoskeletal pain and functional disability.[2–5] Among the treatment options,[6–8] a combination of pharmacological interventions (paracetamol; non-steroidal anti-inflammatory drugs; and topical agents),[9,10] and non-pharmacological (patient education; weight reduction, when necessary; physical exercise and physical therapy) is recommended.[10,11]

Even knowing that physical exercises make up the basic treatment of KOA, pain management is important for the initiation and adherence of treatment.[12,13] Among the non-drug alternatives, the use of knee brace is common in this population.[14,15] Although compression is used to control pain in KOA,[16] for example in the use of these knee braces[14,15] and associated with the application of physical agents,[17] a review showed that its effect is moderate and low for pain relief and improvement of function, respectively, in individuals with KOA.[16] Thus, despite compression being recommended and widely used, this clinical application is poorly supported, due to the scarcity and heterogeneity of protocols,[14,15,18] and there is still a lack of scientific evidence to support its clinical use.[15,16,19]

The possible mechanism of action of compression in pain relief can be explained by the floodgate theory,[20] according to which pain can be modulated by the stimulation of tactile receptors in the skin.[20–22] In addition, aspects such as improved proprioception may be present and promote beneficial functional effects, such as better stability during movements.[23,24] In this context, compression may be a low-cost, easy-to-apply alternative for pain control and functional improvement in this population.[14,15]

This study presents the design of a randomized study, whose objective is to analyze the effect of compression on pain and function of individuals with KOA. Our hypothesis is that compression will be effective in reducing pain and improving function in these individuals.

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MATERIALS AND METHODS

This study protocol was designed following the guidelines recommended by the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT);[25] Template for Intervention Description and Replication (TIDieR);[26] and the OARSI recommendations for clinical trials with KOA patients.[27] The randomized trial will be reported following the guidelines of the Consolidated Standards of reporting Trials (CONSORT) for non-pharmacological studies.[28]

Study design and setting

The study consists of a non-probabilistic, convenience and intentional single-centre randomized controlled clinical trial. Four evaluations will be performed, two immediately before and after the application of the therapy, and two follow- up evaluations at 12 and 24 weeks. The evaluation and intervention periods are shown in **Figure 1**. All evaluations will be carried out by a "blind" evaluator without information about the identification of the group to which the volunteer belongs. The procedures will always be carried out at the same times for each volunteer, during the intervention and evaluation days, so that the same time interval between interventions and evaluations is respected. All participants will be instructed not to start any other treatment during the study period. In addition, they will receive a diary describing the possible drugs used (name, dosage, frequency and route of administration) during the study period.

Participants

Volunteers will be recruited from public announcements and waiting lists from local and regional physiotherapy, rehabilitation, orthopedics, and rheumatology outpatient clinics, as well as from an existing list of volunteers diagnosed with KOA, available in our laboratory. In this project, 90 volunteers of both sexes, aged between 40 and 7 years, with a diagnosis of KOA according to the clinical and radiographic criteria of the American College of Rheumatology will participate.[29,30] The subjects will perform a radiographic examination of both knees, with views in profile, anteroposterior

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and axial. The screening of volunteers will be carried out by a physical therapist specialized in the subject and with experience in the evaluation of individuals with KOA.

Individuals included in the study must present signs of OA in at least one of the compartments of the knee joint (tibiofemoral and/or patellofemoral joint);[31] grade 2 or 3, according to *Kellgren & Lawrence criteria* in the radiographic examination of KOA,[32] and a minimum score of 04 cm on the Visual Analogue Scale (VAS, total of 10 cm).[27] Individuals who present at least one of the following criteria will be excluded: regular practice of moderate or intense physical activity for more than 45 min per week;[33] having started physical activity or performed any physical therapy treatment in the previous 3 months; use of corticosteroid injection in the knee (prior 6 months);[34] previous knee or hip surgeries;[35] and/or any clinical restriction that makes it impossible for them to participate in the proposed evaluations or intervention (cardiorespiratory, neurological, musculoskeletal, vascular changes, and/or the presence of skin lesions from the application of the bandage).

Interventions

The compression intervention protocol is based on a previously accepted methodology developed in our research laboratory.[17] To standardize the level of compression presented, a previous reliability study was carried out (n=10), with the aid of a pressure gauge (Stabilizer ® - *Chattanooga Group*), positioned on the knee, between the patient's skin and the elastic bandage. The manometer was inflated to a value of 40mmHg, the value indicated by the manufacturer as the pressure at rest of the pneumatic bag,[36] and then we started to wrap the knee with the bandage. The number of turns that the tensioned elastic bandage allowed to wrap the knee was collected to reach the indicated compression range (30 mmHg $\leq x \geq$ 60 mmHg),[37–40] and if necessary, more than one band could be used. It was also evaluated what level of compression the *Sham group* would receive with the untensioned bandage. In both groups, the circumference of the knees was collected at three points (popliteal fossa, 10 cm above and 10 cm below) and the number of turns with the bandage.

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This first step was performed in a test-retest format, with an interval of seven days, so that it was possible to calculate the level of intra - evaluator reliability, which indicated a Kappa coefficient[41] of 0.625, considered a substantive agreement.[42] From the reliability study, it was possible to calculate the average number of turns that must be performed both in the *Compression group* and in the *Sham group* so that the compression level is maintained in the stipulated range. In the *Compression group*, all patients used a bandage, with a mean of 5.7 wraps (ranging from 5 to 7 wraps) and a maintained pressure level of 48 mmHg (ranging from 46 to 52 mmHg). In the Sham group, all of them also used a bandage, with an average of 4 wraps (ranging from 3 to 5 wraps) and the pressure level maintained at 00 mmHg.

Compression Protocol

To apply compression, the volunteer must remain in the supine position on a stretcher, with both lower limbs extended and relaxed. The intervention in the *Compression group* will be performed with elastic bandages (*Selecta* ® 13cm x160 cm, composed of 45% cotton, 20% elastodiene and 27% polyamide) covering the entire surface of the knee, positioned considering anatomical aspects: covering the femoral condyles and the anterior tuberosity of the tibia – **Figure 2**). The bandage will wrap the knee from distal (tibial tuberosity) to proximal (femoral condyles), respecting the blood flow of venous return. The level of compression was defined in accordance with recommendations in the literature on interventions for compression in lymphedema and venous disorders and should be maintained between 30 mmHg and 60 mmHg.[37–40] Variations within the stipulated minimum and maximum values may be interfered according to the volunteer's self-report, which must indicate a moderate, comfortable, and pain-free level of compression. The occurrence of any sign of venous stasis (redness and/or edema) may also indicate the need for a reduction in the level of compression or interruption of the procedure. The intervention will be performed for 20 minutes, once a day, on 4 consecutive days (**Figure 1**).[17,19,43–45]

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Sham Protocol

The Sham group will receive the same procedure performed in the compression group; however, the bandage will not be tensioned, that is, it will only gently involve the knee joint with KOA.

Control Protocol

The *Control group* will be composed of individuals with KOA, who will not receive any type of intervention[46] and will carry out the evaluations at the same time intervals as the other groups. They will be instructed to not start another treatment during their participation in the project.

Outcome measurements

Assessments will be performed by a physical therapist blinded to the allocation of each volunteer. Pain is the primary variable of the study and will be assessed using the VAS[47,48] and the WOMAC pain domain.[49,50] As secondary variables, the domains of rigidity and physical dysfunction of the WOMAC[49,50] questionnaire - physical stiffness and dysfunction scales, as well as functional physical tests: Sit and stand test - 30 seconds;[17,51] Step test; 40 meters (4x10m) accelerated walk test.[51] GRC scale will also be applied to quantify the volunteer's perceived change in overall status.[54] The detailed description of the instruments for evaluating the variables, as well as the evaluation moments, is described in **Table 1.**

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TABLE

Table 1. Description of assessment instruments.

Variables	Instructions	Scores	Reference values	Evaluation moment
Visual Analog Scale	The scale will be visually available to the individual so that he can classify the average pain intensity for the last week,[47] and before and after each functional physical test.	The scale will vary from 0 to 10 cm, with 0 being the complete absence of pain, and 10 being the maximum intensity of pain.[52]	A reduction of 1.75 cm will be considered a DMCI.[58]	Initial, final and follow - up assessments of 12 and 24 weeks.
Western Ontario & McMaster Universities Osteoarthritis questionnaire	Self-report questionnaire designed to assess problems experienced by individuals with lower limb OA in the last 72 hours. The questionary contains 24 questions, which comprise three domains: pain, stiffness, and physical function.[49,59]	The score for the items is expressed through the *Likert scale*, classified as: none = 0, low = 25, moderate = 50, severe = 75 and very severe = 100. Higher scores indicate greater levels of pain, stiffness, and physical dysfunction.[50]	A reduction of 8.74 points in the pain domain, from baseline, will be considered a DMCI.[60] For the other domains, the 12% improvement will be considered a DMCI.[60]	Initial, final and follow - up assessments of 12 and 24 weeks.
Chair sit-up test 30 seconds	The test will be performed using an armless chair, with a seat height of approximately 43 cm from the floor. The participant will sit in the chair, with a straight back, feet apart, shoulder-width apart and resting on the floor at an angle slightly behind the line of the knees. The arms should remain crossed against the chest and to help with balance, one foot may remain slightly in front of the other. [17]	The test will last 30 seconds and in this time the number of complete cycles that the individual performs will be counted, that is, how many times he or she moves from sitting to standing and sits down again.	The increase of 2 complete cycles will be considered a DMCI.[52]	Initial, final and follow - up assessments of 12 and 24 weeks.

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Step test	The individual will be positioned in front of the stairs, and by voice command will be guided to go up the 9 steps and go down soon after, returning to the starting point, and thus, the test will end.[52,53]. Each step will be 20 cm high, and it will be allowed to use the handrail as a safety instrument.	The score will be calculated from the time, in seconds, in which the volunteer completes the test.[52]	A minimum detectable difference (MDD) will be considered a reduction of 5.5 seconds in the test execution.[53]	Initial, final and follow - up assessments of 12 and 24 weeks.
40m accelerated walk test (4x10m)	Participants will be asked to walk as quickly, safely, without running, 10m from one cone, then turn around in a second cone, return and repeat the process until the 40-meter mark.[53]	The test score will be based on the gait speed performed by the individual, and the higher the speed, the better the result. [53] The speed will be obtained through the data of distance traveled (40 meters) and the time, in seconds, required to complete the course.[52]	An increase of 0.2 m/s will be considered a DMCI.[52]	Initial, final and follow - up assessments of 12 and 24 weeks.
Global Rating of Change	Its use has been recommended for the outcome of chronic pain, mainly in clinical trials aiming at better applicability of the results in clinical practice. It is used to quantify the patient's improvement or worsening over time, according to the patient's perception. The volunteer will be asked to assess their current health status, associated with knee pain, compared to the pre - intervention period.[54]	It consists of an analog numerical scale, which quantifies the patient's self-perception of improvement after the application of an intervention. The scale has a total of 15 points, and ranges from -7 (much worse) to +7 (much better).[54]	For this variable, an increase of 2 points will be considered a DMCI[54]. In addition, studies have indicated that, considering the Least Important Difference (MDI), variations of 1 to 3 points may indicate small changes, 4 or 5 as moderate changes and 6 or 7 as large.[61]	Final assessment and follow up of 12 and 24 weeks.

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Randomization

The individuals included in the study will be stratified by sex and randomly divided, using the digital tool (*www.randomization.com*). Three groups will be randomized, with 30 individuals each: *Compression*; *Sham*; and *Control*. To avoid selection bias, the secret allocation method will be adopted using an opaque, non-translucent and sealed envelope.[27] Furthermore, the group to which the individual belongs will only be revealed immediately before the intervention. After completion of the evaluations, individuals from the three groups will be referred to face-to-face training (if available) and will receive a booklet with consisting of therapeutic exercises recommended for the treatment of KOA.

Sample size

The sample size was preliminarily calculated using the G*Power *software* (version 3.1.3; University of Trier, Germany).[55] Two calculations were performed, the first considering pain (assessed by VAS) and the second, function (assessed by WOMAC questionnaire). The calculation was based on the application of an *F -test* for the difference between three independent means (three groups). The effect size considered for this calculation, based on a previous study,[17] was d=0.45 for EVA, d=0.39 for WOMAC, which after conversion represent respectively f=0.225 and f=0.195).[56] The f effect sizes are between small and moderate and coincide with the range of classification for the values of d presented. The significance level was 5% and the power was 95%. The calculations indicated a total of 54 subjects by the VAS and 72 subjects by the WOMAC questionnaire. The calculation to be considered will be the one referring to the WOMAC questionnaire, with 24 individuals per group, making a total of 72 individuals. Considering a possible dropout rate of 20%[17], 29 participants should be allocated to each

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group, but to facilitate calculations and randomization, 30 participants will be allocated per group (n=90).

Data management and statistical analysis

The registration of the data collected in the evaluations will be carried out through digital forms (*Google Forms)* and automatically stored in an electronic database in the Cloud (*Google Drive*), protected by a password, to ensure the security of data and participants. After completing the collections, the data will be analyzed by a "blind" biostatistician, without information on the identification of the groups, using the SPSS 24.0 software (SPSS Inc, Chicago, IL).

The independent variables of interest in the study are group (*Compression, Sham* and *Control*) and time [pre- intervention (assessment 1) and post-intervention (assessments 2, 3 and 4)]. The dependent variables are VAS (pain intensity), WOMAC (total score), Step test (seconds), 30-second sit-to-stand test (number of repetitions), and 40 m accelerated walk test (speed in m/s). Data distribution, or normality, will be tested by the *Kolmogorov - Smirnov test* and, according to the result, parametric or non-parametric tests will be used.

Initially, descriptive analyzes will be performed, using measures of central tendency and dispersion: mean and standard deviation when following a normal distribution, and the median, minimum and maximum, when distribution is not normal. For normal data, *two-way ANOVA* with mixed design will be the parametric test chosen for comparison between the means of the dependent variables, considering the two factors simultaneously, one from repeated measurements (pre - and post-intervention, and *follow up* at 12 and 24 weeks) and another with independent samples (Compression, *Sham* and *Control*). If significant differences are found, multiple comparison tests (post-Hoc) will

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be performed to assess the differences. For distribution of non-normal data, the possible reasons for non-normality will be verified, analysis of possible correction and then, non-parametric tests can be applied, using both repeated (time) and non-repeated (groups) comparisons with Bonferroni adjustments or similar.

For all variables, a confidence level of 95% will be determined and a significance level of 5% will be considered statistically significant. Added to that, the difference between the groups will be compared to the MDCI values defined for each variable. When MDCI values are not available, *Cohen's d* coefficient will be calculated (effect size: > 0.8 large, close to 0.5 moderate and ≤ 0.2 small).[57] Finally, to preserve the benefit of randomization, allowing the balanced distribution of prognostic factors in the compared groups and, consequently, the observed effect, an analysis by intention to treat will be adopted through the expectation maximization imputation method.[17,57]

Ethics and dissemination

The project was initially submitted to the Human Research Ethics Committee of the Federal University of São Carlos, São Paulo, Brazil (Plataforma Brasil), approved under number 3.955.692, and later, it was submitted to the clinical trials registry (*www.clinicaltrials.gov*), approved with the identification: NCT04724902. Then, the study activities will be carried out. Volunteers will receive a verbal and written explanation of the objectives and methodology of the study, and those who agree to participate will sign an informed consent form (Supplemental Material). Participants are free to withdraw from the study at any time, without prejudice to future treatment. Results will be presented at scientific meetings and published in peer-reviewed journals. All publications and presentations related to the study will be authorized and reviewed by the study investigators.

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Discussion

Currently, KOA is one of the main causes of musculoskeletal pain and functional disability.[2–5] It is known that patients with osteoarthritis have high health costs,[14,18] and therefore effective and low-cost interventions are important.[15] It is already established by high quality evidence that physical exercise improves pain levels and physical function in individuals with KOA.[10,12,13] However, adherence to these protocols tends to reduce over time due to barriers such as worsening of pain and fear of movement.[12,13] Adherence, therefore, is an important factor for the maintenance of these exercises in the long term.[12,13] Thus, using techniques that allow pain control can be effective to ensure greater motivation to and adherence to physical exercise in the long term.

Compression using elastic bandages or soft orthoses are low-cost and easy-to-apply alternatives, making them widely accessible to the population with some knee disorder.[14,15] Although compression is used to control pain in KOA,[16] this is the first study that seeks to understand the isolated effect of compression on pain and physical function. To minimize the blinding limitation of the interventional therapist and volunteers - blinding made impossible by the physical nature of the intervention and ethical issues -[62] we used subjective[49,50] and objective[17,51] outcome measures of physical function by blinded assessment therapists, and leading to research in accordance with well-established reporting guidelines.[26-28] We believe that the results of this study will contribute new scientific evidence on the effects of compression on pain and control of function in KOA and may incorporate the treatment package for pain management in individuals with KOA.

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Authors contributions

Study concept and design: A.V.F., L.O.D, F.A.S. and T.F.S.

Therapeutic interventions: A.V.F.

Data collection: J.P.M.P. and H.J.A.S.

Statistical design: A.V.F. and F.A.S.

Drafting the manuscript: A.V.F.

Critical revision of the manuscript: A.V.F, L.O.D, J.P.M.P., H.J.A.S., F.A.S. and T.F.S.

Obtained funding: A.V.F., J.P.M.P and T.F.S.

Administrative, technical, or material support: A.V.F., J.P.M.P. and T.F.S.

Study supervision: T.F.S.

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Role of the funder/ sponsor

The funding agencies had no role in design and conduct of the study; acquisition, management, analysis, and interpretation of data; writing of the manuscript; or the decision to submit the manuscript for publication, and do not own ultimate authority over any of these activities.

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Competing interests/ Conflict of Interest

None declared.

Patients and public involvement

The patients and public were not involved in the planning, design, conduct, reporting or dissemination of this study.

Patient consent for publication

Obtained.

Data availability statement

All data collected during the trial will be compiled electronically. Requests for data or any form of analysis should be directed to angelicaferrari@estudante.ufscar.br or tania@ufscar.br. Requesters will be asked to sign a data access agreement. Our host institution does not yet have a platform for collecting, managing, and disseminating research data. However, as soon as the Research Electronic Data Capture (REDCap) platform is acquired by the institution, the project data will also be transferred and stored in this system. Any changes made to the protocol will be reported to the research ethics committee via its national website: http://plataformabrasil.saude.gov.br/. Changes will also be included in the clinical trial registry (https://clinical-trials.gov/).

Trial status

The trial is currently recruiting and is expected to complete (including follow-up testing) by December 2022. Data collection has not yet exceeded 50% of the total data stipulated in this protocol.

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FIGURE LEGENDS

Figure 1. Study design.

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Assessments: pain intensity (VAS); physical functionality questionnaire (WOMAC); Change perception scale global (GRC) and tests in occupation physics (Test of step, test in to sit and rise gives chair in 30 seconds, 40 brisk walk test meters).

Interventions: *Compression* (elastic bandage with compression) and *Sham* (elastic bandage without compression) groups.

Figure 2. Positioning of the volunteer with an elastic bandage.

(A) During application of the elastic bandage without compression. (B) After application of the elastic bandage without compression. (C) During application of the elastic bandage with compression. (D) After application of the elastic bandage with compression.

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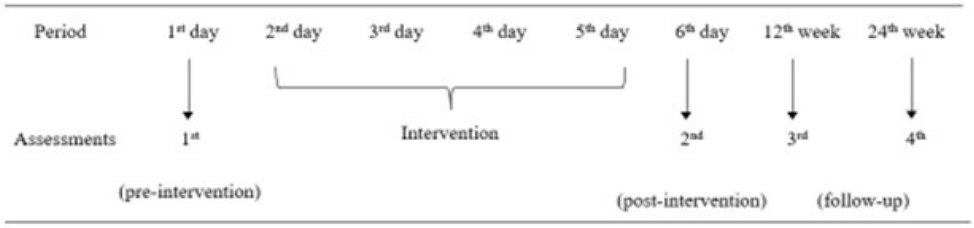

Figure 1 - Study design.
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166x41mm (96 x 96 DPI)

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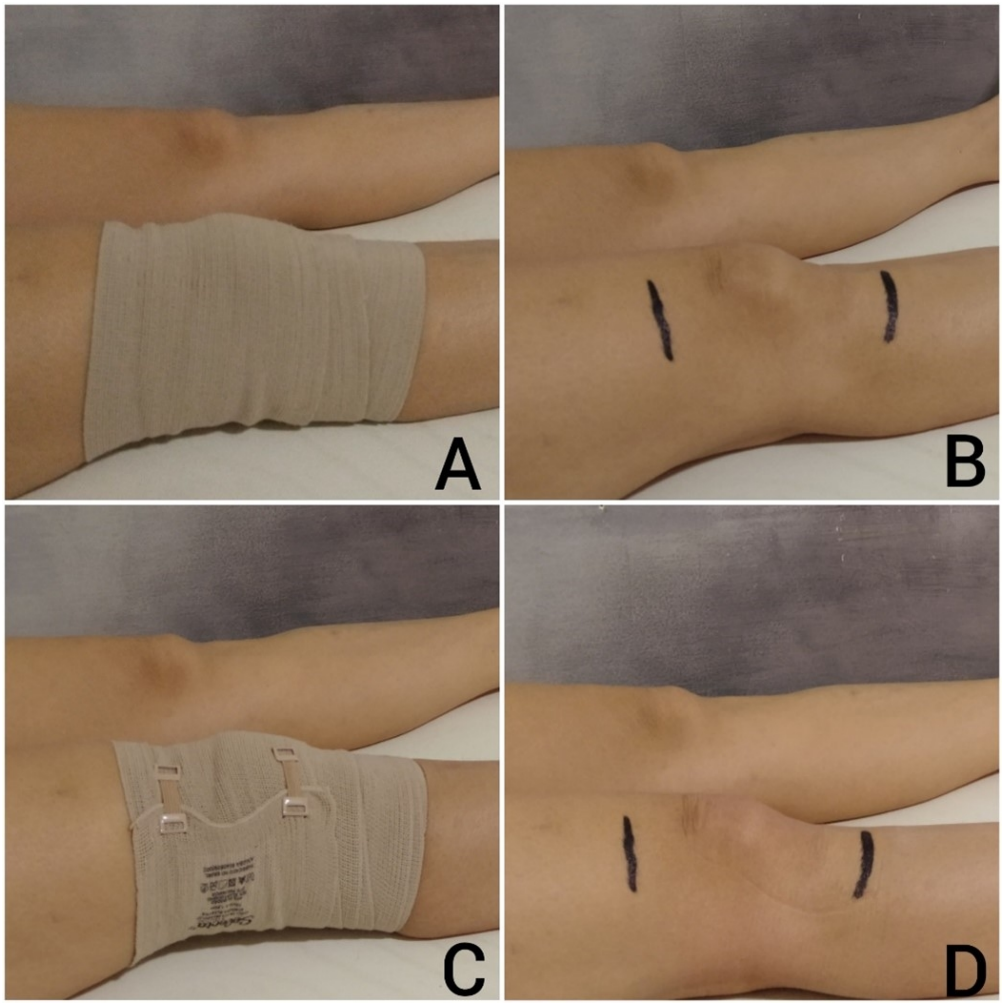

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(A) During application of the elastic bandage without compression. (B) After application of the elastic bandage without compression. (C) During application of the elastic bandage with compression. (D) After application of the elastic bandage with compression.

121x121mm (220 x 220 DPI)

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FREE AND CLARIFIED CONSENT TERM

(CNS Resolution 466/2012)

You are being invited to participate in the research **"The *effect of compression by elastic bandages on pain and function in individuals with knee osteoarthritis – randomized controlled clinical trial*"**, developed at the Laboratory of Muscular Plasticity, by student Angélica Viana Ferrari, from the Postgraduate Program in Physiotherapy at the Federal University of São Carlos (UFSCAR), under the guidance of Prof. Dr Tania de Fátima Salvini.

The objective of this study will be to evaluate the effect of applying local compression to the knee, using elastic bandages (bands), on pain and function of individuals with knee osteoarthritis (arthrosis). This work may contribute with new scientific evidence for the physiotherapeutic treatment of the individual with knee pain due to osteoarthritis.

You were selected as a volunteer in this research because you are between 40 and 75 years old, have a grade 2 or 3 diagnosis of knee osteoarthritis (KOA) in the radiographic examination, pain intensity with a score of 04 cm on the Visual Analog Scale (VAS 0 to 10 cm). They were also selected for not performing more than 45 minutes of physical activity with moderate or intense intensity per week, not having undergone physical therapy treatment in the 3 months prior to the project, not having performed corticosteroid infiltration in the knee (6 months prior to the project), and/or previous knee or hip surgeries; and/or any clinical restriction that makes it impossible for them to participate in the proposed evaluations or intervention (cardiorespiratory, neurological, musculoskeletal, vascular alterations, and/or the presence of lesions on the skin of the bandage application). The effect of compression by elastic bandages on pain, analgesic consumption, and functionality in individuals with knee osteoarthritis. The intervention will be carried out in a controlled environment of the School Health Unit - USE, of the Federal University of São Carlos (UFSCar) - individual care room - guided and supervised by a previously trained therapist. Data collection will be performed on 4 different days (evaluation one day *before, immediately at the end of the intervention program, and 12 and 24 weeks after the end of the program)*. On these occasions, a specific questionnaire will be applied to assess physical function in the KOA (Western *Ontario & McMaster universities Osteoarthritis)*, Visual Analog Scale (VAS) to measure pain, scale for perception of change (Global Rating of Change), and functional tests (sitting down and rising from a chair in 30 seconds, going up and down stairs and fast walking test in 40 meters).

Your **participation is voluntary,** that is, at any time you can withdraw from participating and withdraw your consent, and your refusal will not affect your relationship with the researcher or the institution where the study is conducted. There will be no form of remuneration for participating in the experiment and the data obtained will be the exclusive property of the researchers and they may be disclosed in any way at their discretion. You will not incur any cost or financial compensation for participating in the study. However, all transportation and food expenses arising from your participation in the research, when applicable, will be reimbursed on the day of collection. You will be entitled to compensation for any type of damage resulting from your participation in the research.

If you accept to participate in the study, all your answers and results will be treated anonymously and confidentially, that is, at no time will your name be disclosed at any stage of the study. When it is necessary to exemplify a certain situation, your privacy will be ensured. The collected data may be disclosed in events, magazines and/or scientific works, but always in a way to preserve your identity.

After passing the inclusion and exclusion criteria, you will be selected, via lottery, to participate in one of three groups: a Compression group, which will receive standard treatment; or a Sham group, which will receive the simulated treatment; or a Control group, which will be forwarded to the waiting list. In

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addition, you will receive a diary to record any possible use of oral or topical drug treatment (name of drug, dosage and frequency of use).

After completing the evaluations, participants in the Sham and Control groups may receive the same treatment provided to the Compression group, if they so choose. In addition, they will remain on our list of volunteers for future studies at OAJ. At the end of the study, regardless of the group that participated, you will receive face-to -face training, consisting of therapeutic exercises recommended by the scientific literature for the treatment of KOA, as well as a booklet with the proposed exercises, prepared by our group of research, so that you can also perform the exercises without supervision. Thus, by accepting to participate in the study, you declare that you are aware that you are equally likely to be drawn into one of the three groups mentioned. But that, regardless of the group, will have guaranteed access to the proposed treatment and also to the treatment with greater scientific evidence for KOA.

The procedures of this study are not invasive. The risks of your participation are low, and there may be discomfort when answering any question in the questionnaire that evokes feelings, memories and/or unpleasant emotions. If this occurs, you will be given time, if necessary, to compose yourself in a private and safe environment. It may also present a risk of falling from its own height, and/or fatigue and muscle fatigue, respectively during and after the physical tests. To minimize symptoms, you can take breaks between tests, and even choose to immediately suspend your participation in the study. In addition, you will be accompanied by a physical therapist throughout the period of assessment and intervention, and the researchers themselves are responsible for first aid or any type of physical therapy assessment as a result of physical damage. If more serious damage is found, the researchers are responsible for accompanying her to a doctor for adequate treatment.

The benefits of this study for you will be a detailed assessment of your state of health and functionality, related to Osteoarthritis (arthrosis) of the knee. In addition, you will receive face-to-face training, consisting of therapeutic exercises recommended by the scientific literature for the treatment of KOA, as well as a booklet with the proposed exercises, prepared by our research group, so that you can also perform the exercises at home, without supervision.

This work can directly contribute to the improvement of the treatment of patients with knee pain due to osteoarthritis, expanding knowledge about physical therapy treatment, clinical reasoning and the relationship of symptoms and dysfunctions found in this population.

You will receive a copy of this term, initialed on all pages by you and the researcher, with the telephone number and address of the main researcher. You can clear your doubts about the project and your participation now or at any time.

I Declare that I have received in writing, read, and understood the objectives, risks and benefits of my participation in the research, and I am willing to voluntarily participate in this work. The researcher informed me that the project was approved under registration XXXXX by *the Ethics Committee for Research on Human Beings* of UFSCar, which works at the Dean of Research at the Federal University of São Carlos, located at Rodovia Washington Luiz, Km. 235 - PO Box 676 - CEP 13.565-905 - São Carlos/SP – Brazil. Phone (16) 3351-8028. Electronic address: cephumanos@ufscar.br.

São Carlos,____de_____de 20___.

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Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

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Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

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		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	11
Protocol version	#3	Date and version identifier	n/a
Funding	#4	Sources and types of financial, material, and other support	19
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	18

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Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	11
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	1
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	1
Objectives	#7	Specific objectives or hypotheses	1
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	2
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	2
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will	6

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		perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	5
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	5
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	5
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8

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Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	11
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	n/a
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	9
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	9

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Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	9
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	7
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	11
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	11

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Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	11
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	11
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	25
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

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The effect of compression by elastic bandages on pain and function in individuals with knee osteoarthritis – protocol of a randomized controlled clinical trial

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The effect of compression by elastic bandages on pain and function in individuals with knee osteoarthritis – protocol of a randomized controlled clinical trial

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ABSTRACT

Introduction: Although compression is used to control pain in knee osteoarthritis (KOA), its clinical application is poorly supported, and there is a lack of scientific evidence to support its clinical use. As a low-cost and accessible protocol, compression using elastic bands could be a non-pharmacological intervention to reduce pain and improve physical function in individuals with KOA. This study aims to evaluate the effects of compression on pain and function in individuals with KOA.

Methods and analysis: A randomised controlled clinical trial will be conducted. Individuals with KOA (n=90; both sexes; between 40 and 75 years old) will be allocated into three groups (n=30/group): compression (compression by the elastic bandage on the affected knee, once a day for 20 min, on 4 consecutive days); sham (same protocol, but the elastic band is placed around the affected knee without compression), and control (no intervention). The individuals in the three groups will be evaluated 1 day before the first intervention, 1 day after the last intervention, and at the 12th and 24th weeks after the end of the intervention. Pain intensity by the visual analogue scale and pain scale from Western Ontario & McMaster Universities Osteoarthritis Index (WOMAC) will be the primary outcomes. The secondary variables will be physical function assessed by the WOMAC questionnaire and physical tests (step test; 30 s sit and stand test; 40 m accelerated walk test). The Global Rating of Change Scale will also be applied to quantify the volunteers' perceived change.

Ethics and dissemination: The project was approved by the Human Research Ethics Committee of the Federal University of São Carlos, São Paulo, Brazil (3.955.692). The results will be published in peer-reviewed journals.

Trial registration number: NCT04724902.

Keywords: Osteoarthritis; compression; pain, knee; physiotherapy.

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Strengths and limitations of this study

- The study will be conducted according to well-established reporting guidelines. The methodology was designed to minimise the potential for bias, including hidden information treatment allocation and blinding of the evaluator and biostatistician therapist.
- This study will assess physical function using both objective and subjective tools. Thus, in addition to the test performance, the patient's self-perception of improvement will be considered.
- The therapist delivering the therapies and the patients cannot be blinded.

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INTRODUCTION

Knee osteoarthritis (KOA), representing an average cost of US$ 15,000/year per user, is radiographically present in 30% of individuals over 45 years old and symptomatic in at least half of these cases.[1] It is characterised as chronic and progressive and is one of the main causes of musculoskeletal pain and functional disability [2–5]. Among the treatment options,[6–8] a combination of pharmacological (paracetamol, nonsteroidal anti-inflammatory drugs, and topical agents)[9,10] and non-pharmacological interventions (patient education; weight reduction, when necessary; physical exercise, and physical therapy) is recommended.[10,11]

Even though physical exercises constitute the basic treatment of KOA, pain management is important for initiating and adhering to treatment.[12,13] Among the non-drug alternatives, the use of a knee brace is common in this population.[14,15] Although compression is used to control pain in KOA,[16] for example, the use of knee braces[14,15] and associated with the application of physical agents,[17] a review showed that its effect is moderate and low for pain relief and improvement of function, respectively, in individuals with KOA.[16] Thus, despite compression being recommended and widely used, its clinical application is poorly supported because of the scarcity and heterogeneity of protocols,[14,15,18] and there is still a lack of scientific evidence to support its clinical use.[15,16,19]

The floodgate theory can explain the possible mechanism of action of compression in pain relief,[20] according to which pain can be modulated by the stimulation of tactile receptors in the skin.[20–22] In addition, aspects such as improved proprioception may be present and promote beneficial functional effects, such as better stability during movement.[23,24] In this context, compression may be a low-cost and easy-to-apply alternative for pain control and functional improvement in people with KOA.[14,15]

This study presents the design of a randomised study whose objective is to analyse the effect of compression on the pain and function of individuals with KOA. Our hypothesis is that compression will effectively reduce pain and improve function in these individuals.

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MATERIALS AND METHODS

Patients and public involvement

The patients and the general public were not involved in the planning, designing, conducting, reporting, or dissemination of this study.

Study design and setting

The study consists of a non-probabilistic, convenient, and intentional single centre randomised controlled clinical trial. This study was designed and will be conducted according to the guidelines recommended by Template for Intervention Description and Replication (TIDieR),[25] the OARSI recommendations for clinical trials with KOA patients,[26] and in accordance with the recommendations outlined in the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT).[27] Randomised trials will be reported following the guidelines of the Consolidated Standards of Reporting Trials (CONSORT) for non-pharmacological studies.[28] Four evaluations will be performed: two immediately before and after the application of the therapy and two follow-up evaluations at 12 and 24 weeks. The evaluation and intervention periods are shown in **Figure 1**. A "blind" evaluator will carry out all evaluations without information about the identification of the group to which the volunteer belongs. The procedures will always be carried out simultaneously for each volunteer during the intervention and evaluation days so that the same time interval between interventions and evaluations is respected. All participants will be instructed not to start any other treatment during the study period. In addition, they will receive a diary describing the drugs that will be used (name, dosage, frequency, and route of administration) during the study period.

Participants

Volunteers will be recruited from public announcements and waiting lists from local and regional physiotherapy, rehabilitation, orthopaedics, and rheumatology outpatient clinics, as well as from an existing list of volunteers diagnosed with KOA available in our laboratory. In this project,

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90 volunteers of both sexes, aged between 40 and 75 years,[29,30] diagnosed with KOA according to the clinical and radiographic criteria of the American College of Rheumatology will participate.[31,32] The subjects will undergo a radiographic examination of both knees, with profile, anteroposterior, and axial views. Volunteer screening will be carried out by a physical therapist specialising in the subject and with experience in evaluating individuals with KOA.

Individuals who will be included in the study are required to present with signs of OA in at least one of the compartments of the knee joint (tibiofemoral and/or patellofemoral joint);[33] grade 2 or 3, according to *the Kellgren & Lawrence criteria* in the radiographic examination of KOA,[34] and a minimum score of 4 cm on the visual analogue scale (VAS, total of 10 cm).[26] In the case of bilateral KOA, only the knee with the highest level of symptoms will be randomised as long as it meets the inclusion criteria. In addition, individuals who present with at least one of the following criteria will be excluded: regular practice of moderate or intense physical activity for more than 45 min per week;[35] have started physical activity or performing any physical therapy treatment in the previous 3 months; use of corticosteroid injection in the knee (6 months prior);[36] previous knee or hip surgeries;[37] and/or any clinical restriction that makes it impossible for them to participate in the proposed evaluations or intervention (cardiorespiratory, neurological, musculoskeletal, vascular changes, and/or the presence of skin lesions from the application of the bandage).

Interventions

The compression intervention protocol is based on a previously accepted methodology that was developed in our laboratory.[17] To standardise the level of compression presented, a previous reliability study was performed (n=10) with the aid of a pressure gauge (Stabilizer ® - *Chattanooga Group*) positioned on the knee between the patient's skin and the elastic bandage. The manometer was inflated to a value of 40 mmHg, the value indicated by the manufacturer as the pressure at rest of the pneumatic bag,[38] and the knee was then wrapped with the bandage. The number of turns of the tensioned elastic bandage required to wrap the knee to reach the indicated compression range (30

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mmHg ≤ x ≥ 60 mmHg) was noted,[39–42] and, if necessary, more than one band could be used. The level of compression that the *sham group* would receive with the untensioned bandage was also evaluated. In both groups, the circumference of the knees was measured at three points (popliteal fossa, 10 cm above and 10 cm below) and the number of turns with the bandage.

This first step was performed in a test-retest format, with an interval of 7 days, so that it was possible to calculate the level of intra-evaluator reliability, which indicated a Kappa coefficient[43] of 0.625, considered a substantive agreement.[44] From the reliability study, it was possible to calculate the average number of turns to be performed in both the *compression and sham groups* so that the compression level was maintained within the stipulated range. In the *compression group*, all patients used a bandage, with a mean of 5.7 wraps (range, 5–7 wraps) and a maintained pressure level of 48 mmHg (range, 46–52 mmHg). In the *sham group*, all of them also used a bandage with an average of 4 wraps (range, 3–5 wraps), and the pressure level was maintained at 0 mmHg.

Compression Protocol

To apply compression, the volunteer must remain in the supine position on a stretcher with both lower limbs extended and relaxed. The intervention in the *compression group* will be performed with elastic bandages (*Selecta* ® 13 cm x160 cm, composed of 45% cotton, 20% elastodiene, and 27% polyamide) covering the entire surface of the knee, positioned considering anatomical aspects: covering the femoral condyles and anterior tuberosity of the tibia (**Figure 2**). The bandage will wrap the knee from distal (tibial tuberosity) to proximal (femoral condyles), respecting the blood flow of venous return and without restricting blood flow. The level of compression was defined following recommendations in the literature on interventions for compression in lymphedema and venous disorders and should be maintained between 30–60 mmHg.[39–42] Variations within the stipulated minimum and maximum values may be changed according to the volunteers' self-report, indicating a moderate, comfortable, and pain-free level of compression. The occurrence of any sign of venous stasis (redness and/or oedema) may also indicate the need for a reduction in the level of compression

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or interruption of the procedure. The intervention will be performed for 20 min, once a day, for 4 consecutive days (**Figure 1**).[17,19,45–47]

Sham Protocol

The *sham group* will receive the same procedure performed in the compression group; however, the bandage will not be tensioned, that is, it will only gently wrap the knee joint with KOA.

Control Protocol

The *control group* will be composed of individuals with KOA who will not receive any type of intervention[48] and will undergo the evaluations at the same time intervals as the other groups. In addition, they will be instructed not to start another treatment during their participation in the project.

Outcome measurements

Assessments will be performed by a physical therapist who will be blinded to the allocation of each volunteer. Pain is the primary variable of the study and will be assessed using the VAS[49,50] and WOMAC pain domain.[51,52] As secondary variables, the domains of rigidity and physical dysfunction of the WOMAC[51,52] questionnaire—physical stiffness and dysfunction scales, as well as functional physical tests: sit and stand test, 30 s;[17,53] step test; 40 m (4 × 10 m)) accelerated walk test.[53] The Global Rating of Change Scale will also be applied to quantify the volunteers' perceived change in overall status.[54] A detailed description of the instruments for evaluating the variables, as well as the evaluation moments, is presented in **Table 1.**

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TABLE

Table 1. Description of assessment instruments.

Variables	Instructions	Scores	Reference values	Evaluation moment
Visual Analog Scale	The scale will be visually available to the individual so that he can classify the average pain intensity for the last week,[49] and before and after each functional physical test.	The scale will vary from 0 to 10 cm, with 0 being the complete absence of pain, and 10 being the maximum intensity of pain.[55]	A reduction of 1.75 cm will be considered a DMCI.[56]	Initial, final and follow - up assessments of 12 and 24 weeks.
Western Ontario & McMaster Universities Osteoarthritis questionnaire	Self-report questionnaire designed to assess problems experienced by individuals with lower limb OA in the last 72 hours. The questionary contains 24 questions, which comprise three domains: pain, stiffness, and physical function.[51,57]	The score for the items is expressed through the *Likert scale*, classified as: none = 0, low = 25, moderate = 50, severe = 75 and very severe = 100. Higher scores indicate greater levels of pain, stiffness, and physical dysfunction.[52]	A reduction of 8.74 points in the pain domain, from baseline, will be considered a DMCI.[58] For the other domains, the 12% improvement will be considered a DMCI.[58]	Initial, final and follow - up assessments of 12 and 24 weeks.
Chair sit-up test 30 seconds	The test will be performed using an armless chair, with a seat height of approximately 43 cm from the floor. The participant will sit in the chair, with a straight back, feet apart, shoulder-width apart and resting on the floor at an angle slightly behind the line of the knees. The arms should remain crossed against the chest and to help with balance, one foot may remain slightly in front of the other. [17]	The test will last 30 seconds and in this time the number of complete cycles that the individual performs will be counted, that is, how many times he or she moves from sitting to standing and sits down again.	The increase of 2 complete cycles will be considered a DMCI.[55]	Initial, final and follow - up assessments of 12 and 24 weeks.

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Step test	The individual will be positioned in front of the stairs, and by voice command will be guided to go up the 9 steps and go down soon after, returning to the starting point, and thus, the test will end.[55,59]. Each step will be 20 cm high, and it will be allowed to use the handrail as a safety instrument.	The score will be calculated from the time, in seconds, in which the volunteer completes the test.[55]	A minimum detectable difference (MDD) will be considered a reduction of 5.5 seconds in the test execution.[59]	Initial, final and follow - up assessments of 12 and 24 weeks.
40m accelerated walk test (4x10m)	Participants will be asked to walk as quickly, safely, without running, 10m from one cone, then turn around in a second cone, return and repeat the process until the 40-meter mark.[59]	The test score will be based on the gait speed performed by the individual, and the higher the speed, the better the result. [59] The speed will be obtained through the data of distance traveled (40 meters) and the time, in seconds, required to complete the course.[55]	An increase of 0.2 m/s will be considered a DMCI.[55]	Initial, final and follow - up assessments of 12 and 24 weeks.
Global Rating of Change	Its use has been recommended for the outcome of chronic pain, mainly in clinical trials aiming at better applicability of the results in clinical practice. It is used to quantify the patient's improvement or worsening over time, according to the patient's perception. The volunteer will be asked to assess their current health status, associated with knee pain, compared to the pre - intervention period.[54]	It consists of an analog numerical scale, which quantifies the patient's self-perception of improvement after the application of an intervention. The scale has a total of 15 points, and ranges from -7 (much worse) to +7 (much better).[54]	For this variable, an increase of 2 points will be considered a DMCI[54]. In addition, studies have indicated that, considering the Least Important Difference (MDI), variations of 1 to 3 points may indicate small changes, 4 or 5 as moderate changes and 6 or 7 as large.[60]	Final assessment and follow up of 12 and 24 weeks.

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Randomisation

Individuals included in the study will be stratified by sex and randomly divided using a digital tool (www.randomization.com). Three groups will be randomised with 30 individuals each: *compression*, *sham*, and *control*. The secret allocation method will be adopted to avoid selection bias using an opaque, non-translucent, and sealed envelope.[26] Furthermore, the group to which an individual belongs will only be revealed immediately before the intervention. After the completion of the evaluations, individuals from the three groups will be referred to face-to-face training (if available) and will receive a booklet consisting of therapeutic exercises recommended for the treatment of KOA.

Sample size

The sample size was preliminarily calculated using the G*Power software (version 3.1.3; University of Trier, Germany).[61] Two calculations were performed: pain (assessed using the VAS) and function (assessed using the WOMAC questionnaire). The calculation was based on the application of an *F-test* for the difference between the three independent means (three groups). The effect size considered for this calculation, based on a previous study,[17] were d=0.45 for EVA and d=0.39 for WOMAC, which after conversion represented f=0.225 and f=0.195, respectively.[62] The f effect sizes were between small and moderate and coincided with the range of classification for the values of d presented. The significance level was set at 5%, and the power was 95%. The calculations indicated a total of 54 participants using the VAS and 72 participants using the WOMAC questionnaire. The calculation to be considered will be based on the WOMAC questionnaire, with 24 individuals per group, making a total of 72 individuals. Considering a possible dropout rate of 20%[17], 29 participants should be allocated to each

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group; however, to facilitate calculations and randomisation, 30 participants will be allocated to each group (n=90).

Data management and statistical analysis

The registration of the data collected in the evaluations will be carried out through digital forms (*Google Forms)* and automatically stored in an electronic database in the Cloud (*Google Drive*), protected by a password, to ensure the security of data and participants. After completing the collections, the data will be analysed by a "blind" biostatistician, without information on the identification of the groups, using SPSS software (version 24.0; SPSS Inc., Chicago, IL).

The independent variables of interest in the study are the group (*compression, sham,* and *control*) and time (pre-intervention [assessment 1] and post-intervention [assessments 2, 3, and 4]). The dependent variables are the VAS (pain intensity), WOMAC (total score), step test (seconds), 30-second sit-to-stand test (number of repetitions), and 40 m accelerated walk test (speed in m/s). In addition, data distribution, or normality, will be tested using the *Kolmogorov - Smirnov test,* and according to the results, parametric or non-parametric tests will be used.

Initially, descriptive analyses will be performed using measures of central tendency and dispersion: mean and standard deviation when following a normal distribution and the median, minimum, and maximum when the distribution is not normal. For normal data, *two-way ANOVA* with a mixed design will be the parametric test chosen for comparison between the means of the dependent variables, considering the two factors simultaneously, one from repeated measurements (pre- and post-intervention, and *follow-up* at 12 and 24 weeks) and another with independent samples (*compression*, *sham,* and *control*). If significant differences were found, multiple comparison tests (post-hoc) were

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performed to assess the differences. For the distribution of non-normal data, the possible reasons for non-normality will be verified, analysis of possible correction, and then non-parametric tests can be applied, using both repeated (time) and non-repeated (groups) comparisons with Bonferroni adjustments or similar.

A confidence level of 95% will be determined for all variables, and a significance level of 5% will be considered statistically significant. In addition, the differences between the groups will be compared to the MDCI (minimal clinically important difference) values defined for each variable. When MDCI values are not available, *Cohen's d* coefficient will be calculated (effect size: > 0.8, large; close to 0.5, moderate; and ≤ 0.2, small).[63] Finally, to preserve the benefit of randomisation, allowing the balanced distribution of prognostic factors in the compared groups and, consequently, the observed effect, an analysis by intention-to-treat will be adopted through the expectation maximisation imputation method.[17,63]

Ethics and dissemination

The project was initially submitted to the Human Research Ethics Committee of the Federal University of São Carlos, São Paulo, Brazil (Plataforma Brasil), approved under number 3.955.692, and later submitted to the clinical trials registry (*www.clinicaltrials.gov*), approved with the identification: NCT04724902. Subsequently, the study activities will be conducted. Volunteers will receive a verbal and written explanation of the objectives and methodology of the study, and those who agree to participate will be required to provide written informed consent (Supplementary Material). The participants are free to withdraw from the study at any time without prejudice toward future treatment. The results will be presented at scientific meetings and

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will be published in peer-reviewed journals. All publications and presentations related to this study will be authorised and reviewed by the study investigators.

Discussion

Currently, KOA is one of the main causes of musculoskeletal pain and functional disability [2–5] It is known that patients with osteoarthritis have high health costs.[14,18] Therefore, effective and low-cost interventions are important.[15] High-quality evidence has already established that physical exercise improves pain levels and physical function in individuals with KOA.[10,12,13] However, adherence to these protocols tends to reduce over time due to barriers such as worsening pain and fear of movement.[12,13] Therefore, adherence is an important factor for the continuation of these exercises in the long term.[12,13] Thus, using techniques that allow pain control can effectively ensure greater motivation to and adherence to physical exercise in the long term.

In 2009, the estimated US spending on total knee joint replacement surgery was $28.5 billion, and healthcare costs for osteoarthritis patients were approximately $2,600 per year.[3,18] Compression using elastic bandages or soft orthoses is a low-cost and easy-to-apply alternative and is widely accessible to the population with knee disorders.[14,15] Although compression is used to control pain in KOA,[16] to the best of our knowledge, this is the first study that seeks to understand the isolated effect of compression on pain and physical function.

The possible mechanism of action of compression by elastic bandages in relieving pain can be explained by the theory of the gates of Melzack and Wall,[20] according to which pain can be modulated by the stimulation of tactile receptors in the skin. According to the authors, a tactile stimulus, such as compression, is identified by mechanoreceptors in the skin and conducted to the spinal cord through myelinated Aβ-type afferent fibres.[20]

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In contrast, painful stimuli from nociceptors are conducted in the spinal cord by unmyelinated fibres of type C.[20–22] In this way, the proportion of tactile impulses that would reach the spinal cord would be higher because of the stimulation that is taking place and its higher conduction velocity In this way, the proportion of tactile impulses that would reach the spinal cord would be higher, because of the stimulation that is taking place and its higher conduction velocity. Faced with the competition for simultaneous stimuli (tactile and painful), there would be a modulation of the conduction of nociceptive impulses and a reduction in the central perception of pain.[20,21,64] In addition, aspects such as improved proprioception may be present and promote beneficial functional effects, such as better stability during movement.[16,23,24]

To minimise the blinding limitation of the interventional therapist and volunteers - blinding made impossible by the physical nature of the intervention and ethical issues- we used subjective[51,52] and objective[10,53] outcome measures of physical function by blinded assessment therapists, leading to research in accordance with well -[65] established reporting guidelines.[26-28] We believe that the results of this study will contribute new scientific evidence on the effects of compression on pain and control of function in KOA and may incorporate the treatment package for pain management in individuals with KOA.

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Authors contributions

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Role of the funder/ sponsor

The funding agencies had no role in design and conduct of the study; acquisition, management, analysis, and interpretation of data; writing of the manuscript; or the decision to submit the manuscript for publication, and do not own ultimate authority over any of these activities.

Competing interests/ Conflict of Interest

None declared.

Patient consent for publication

Obtained.

Data availability statement

All data collected during the trial will be compiled electronically. Requests for data or any form of analysis should be directed to angelicaferrari@estudante.ufscar.br or tania@ufscar.br. Requesters will be asked to sign a data access agreement. Our host institution does not yet have a platform for collecting, managing, and disseminating research data. However, as soon as the Research Electronic Data Capture (REDCap)

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platform is acquired by the institution, the project data will also be transferred and stored in this system. Any changes made to the protocol will be reported to the research ethics committee via its national website: http://plataformabrasil.saude.gov.br/. Changes will also be included in the clinical trial registry (https://clinical-trials.gov/).

Trial status

The trial is currently recruiting and is expected to complete (including follow-up testing) by December 2022. Data collection has not yet exceeded 50% of the total data stipulated in this protocol.

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WORD COUNTER MANUSCRIPT: 3975

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FIGURE LEGENDS

Figure 1. Study design.

Assessments: pain intensity (VAS); physical functionality questionnaire (WOMAC); Change perception scale global (GRC) and tests in occupation physics (Test of step, test in to sit and rise gives chair in 30 seconds, 40 brisk walk test meters).

Interventions: *Compression* (elastic bandage with compression) and *Sham* (elastic bandage without compression) groups.

Figure 2. Positioning of the volunteer with an elastic bandage.

(A) During application of the elastic bandage without compression. (B) After application of the elastic bandage without compression. (C) During application of the elastic bandage with compression. (D) After application of the elastic bandage with compression.

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*Note: The person depicted are not patient and were taken with the participants knowledge.

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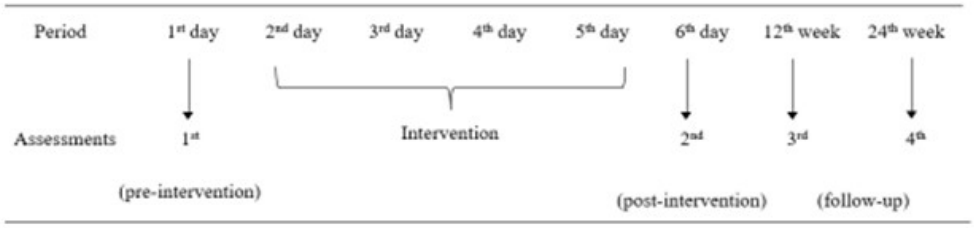

Figure 1 - Study design.
Assessments: pain intensity (VAS); physical functionality questionnaire (WOMAC); Change perception scale global (GRC) and tests in occupation physics (Test of step, test in to sit and rise gives chair in 30 seconds, 40 brisk walk test meters).
Interventions: Compression (elastic bandage with compression) and Sham (elastic bandage without compression) groups.

166x41mm (96 x 96 DPI)

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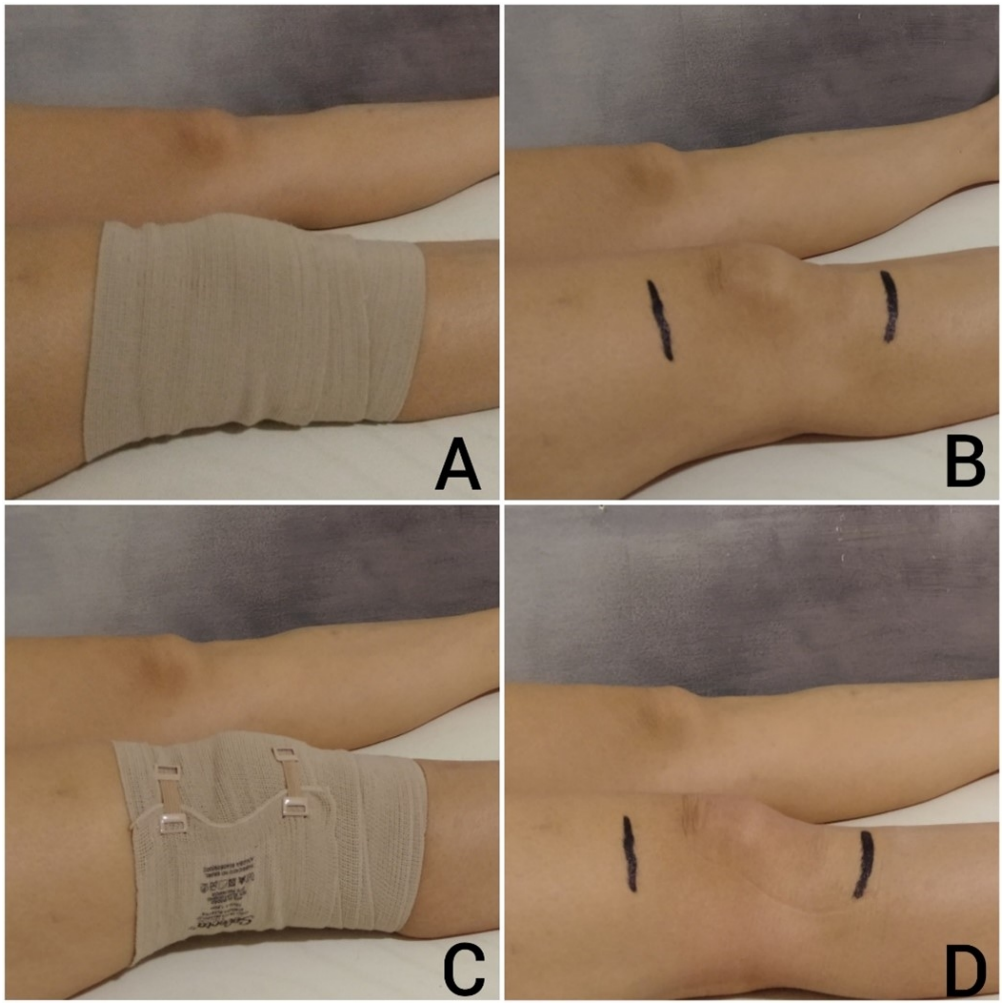

Figure 2. Positioning of the volunteer with an elastic bandage.(A) During application of the elastic bandage without compression. (B) After application of the elastic bandage without compression. (C) During application of the elastic bandage with compression. (D) After application of the elastic bandage with compression.
*Note: The person depicted are not patient and were taken with the participants knowledge.

121x121mm (220 x 220 DPI)

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FREE AND CLARIFIED CONSENT TERM

(CNS Resolution 466/2012)

You are being invited to participate in the research **"The *effect of compression by elastic bandages on pain and function in individuals with knee osteoarthritis – randomized controlled clinical trial*"**, developed at the Laboratory of Muscular Plasticity, by student Angélica Viana Ferrari, from the Postgraduate Program in Physiotherapy at the Federal University of São Carlos (UFSCAR), under the guidance of Prof. Dr Tania de Fátima Salvini.

The objective of this study will be to evaluate the effect of applying local compression to the knee, using elastic bandages (bands), on pain and function of individuals with knee osteoarthritis (arthrosis). This work may contribute with new scientific evidence for the physiotherapeutic treatment of the individual with knee pain due to osteoarthritis.

You were selected as a volunteer in this research because you are between 40 and 75 years old, have a grade 2 or 3 diagnosis of knee osteoarthritis (KOA) in the radiographic examination, pain intensity with a score of 04 cm on the Visual Analog Scale (VAS 0 to 10 cm). They were also selected for not performing more than 45 minutes of physical activity with moderate or intense intensity per week, not having undergone physical therapy treatment in the 3 months prior to the project, not having performed corticosteroid infiltration in the knee (6 months prior to the project), and/or previous knee or hip surgeries; and/or any clinical restriction that makes it impossible for them to participate in the proposed evaluations or intervention (cardiorespiratory, neurological, musculoskeletal, vascular alterations, and/or the presence of lesions on the skin of the bandage application). The effect of compression by elastic bandages on pain, analgesic consumption, and functionality in individuals with knee osteoarthritis. The intervention will be carried out in a controlled environment of the School Health Unit - USE, of the Federal University of São Carlos (UFSCar) - individual care room - guided and supervised by a previously trained therapist. Data collection will be performed on 4 different days (evaluation one day *before, immediately at the end of the intervention program, and 12 and 24 weeks after the end of the program)*. On these occasions, a specific questionnaire will be applied to assess physical function in the KOA (Western *Ontario & McMaster universities Osteoarthritis)*, Visual Analog Scale (VAS) to measure pain, scale for perception of change (Global Rating of Change), and functional tests (sitting down and rising from a chair in 30 seconds, going up and down stairs and fast walking test in 40 meters).

Your **participation is voluntary,** that is, at any time you can withdraw from participating and withdraw your consent, and your refusal will not affect your relationship with the researcher or the institution where the study is conducted. There will be no form of remuneration for participating in the experiment and the data obtained will be the exclusive property of the researchers and they may be disclosed in any way at their discretion. You will not incur any cost or financial compensation for participating in the study. However, all transportation and food expenses arising from your participation in the research, when applicable, will be reimbursed on the day of collection. You will be entitled to compensation for any type of damage resulting from your participation in the research.

If you accept to participate in the study, all your answers and results will be treated anonymously and confidentially, that is, at no time will your name be disclosed at any stage of the study. When it is necessary to exemplify a certain situation, your privacy will be ensured. The collected data may be disclosed in events, magazines and/or scientific works, but always in a way to preserve your identity.

After passing the inclusion and exclusion criteria, you will be selected, via lottery, to participate in one of three groups: a Compression group, which will receive standard treatment; or a Sham group, which will receive the simulated treatment; or a Control group, which will be forwarded to the waiting list. In

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addition, you will receive a diary to record any possible use of oral or topical drug treatment (name of drug, dosage and frequency of use).

After completing the evaluations, participants in the Sham and Control groups may receive the same treatment provided to the Compression group, if they so choose. In addition, they will remain on our list of volunteers for future studies at OAJ. At the end of the study, regardless of the group that participated, you will receive face-to -face training, consisting of therapeutic exercises recommended by the scientific literature for the treatment of KOA, as well as a booklet with the proposed exercises, prepared by our group of research, so that you can also perform the exercises without supervision. Thus, by accepting to participate in the study, you declare that you are aware that you are equally likely to be drawn into one of the three groups mentioned. But that, regardless of the group, will have guaranteed access to the proposed treatment and also to the treatment with greater scientific evidence for KOA.

The procedures of this study are not invasive. The risks of your participation are low, and there may be discomfort when answering any question in the questionnaire that evokes feelings, memories and/or unpleasant emotions. If this occurs, you will be given time, if necessary, to compose yourself in a private and safe environment. It may also present a risk of falling from its own height, and/or fatigue and muscle fatigue, respectively during and after the physical tests. To minimize symptoms, you can take breaks between tests, and even choose to immediately suspend your participation in the study. In addition, you will be accompanied by a physical therapist throughout the period of assessment and intervention, and the researchers themselves are responsible for first aid or any type of physical therapy assessment as a result of physical damage. If more serious damage is found, the researchers are responsible for accompanying her to a doctor for adequate treatment.

The benefits of this study for you will be a detailed assessment of your state of health and functionality, related to Osteoarthritis (arthrosis) of the knee. In addition, you will receive face-to-face training, consisting of therapeutic exercises recommended by the scientific literature for the treatment of KOA, as well as a booklet with the proposed exercises, prepared by our research group, so that you can also perform the exercises at home, without supervision.

This work can directly contribute to the improvement of the treatment of patients with knee pain due to osteoarthritis, expanding knowledge about physical therapy treatment, clinical reasoning and the relationship of symptoms and dysfunctions found in this population.

You will receive a copy of this term, initialed on all pages by you and the researcher, with the telephone number and address of the main researcher. You can clear your doubts about the project and your participation now or at any time.

I Declare that I have received in writing, read, and understood the objectives, risks and benefits of my participation in the research, and I am willing to voluntarily participate in this work. The researcher informed me that the project was approved under registration XXXXX by *the Ethics Committee for Research on Human Beings* of UFSCar, which works at the Dean of Research at the Federal University of São Carlos, located at Rodovia Washington Luiz, Km. 235 - PO Box 676 - CEP 13.565-905 - São Carlos/SP – Brazil. Phone (16) 3351-8028. Electronic address: cephumanos@ufscar.br.

São Carlos,____de_____de 20___.

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Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	11
Protocol version	#3	Date and version identifier	n/a
Funding	#4	Sources and types of financial, material, and other support	19
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	18

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Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	19
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	11
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	1
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	1
Objectives	#7	Specific objectives or hypotheses	1
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	2
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	2
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will	6

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		perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	5
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	6
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	5
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	5
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8

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Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	9
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	5
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	11
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	n/a
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	9
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	9

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Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	10
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	9
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	7
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	11
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	11
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	11

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Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	19
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	11
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	11
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	25
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

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