Effectiveness of therapeutic ultrasound in the treatment of pain and return to function in knee osteoarthritis - an integrative review

Efetividade do ultrassom terapêutico no tratamento da dor e retorno da função na osteoartrite de joelho - uma revisão integrativa

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RESUMO
Introdução: A osteoartrite (OA) é um distúrbio articular bastante comum em nossa sociedade e sua incidência aumenta com o avançar da idade. Embora possa afetar várias articulações do nosso corpo, as alterações mais evidentes são observadas em grandes articulações de carga. A abordagem terapêutica da OA visa reduzir a sintomatologia dolorosa, diminuir os níveis de rigidez, melhorar a mobilidade e a qualidade de vida. Dentre as opções terapêuticas não farmacológicas temos a terapia com ultrassom (US) que promove um aquecimento profundo nos tecidos e cujo tópico carece de mais evidências científicas que comprovem sua eficácia no alívio da dor em pacientes com OA de joelho. Objetivo: Este trabalho visa descrever os efeitos e a eficácia do ultrassom terapeêutico (UST) no tratamento da dor e função na osteoartrose primária de joelhos. Métodos: Foi realizado uma busca sistemática nas bases de dados PubMed, LILACS, CENTRAL, SCIELO e PEDro por ensaios clínicos randomizados e quasi-

randomizados, publicados nos últimos 10 anos. As palavras-chave utilizadas foram Ultrassom, Terapia por Ultrassom, Dor, Joelho, Articulação do Joelho, Osteoartrite do Joelho. Resultados: Seis estudos, que avaliaram ao todo 561 paciente foram selecionados. Alguns estudos demonstraram que não houve diferença significativa entre os grupos US contínuo e US pulsado no alívio da dor e melhora da função. O US quando usado como coadjuvante terapêutico resultou em melhora da dor. Conclusão: Os trabalhos selecionados sugerem que aplicações de US combinado principalmente com exercícios são eficazes no alivio de dor e melhora da funcionalidade de pacientes com osteoartrite de joelho.

Palavras-chave: ultrassom, joelho, reabilitação, osteartrite do joelho .

ABSTRACT
Introduction: Osteoarthritis (OA) is a very common joint disorder in our society and its incidence increases with advancing age. Although it can affect several joints in our body, the most obvious changes are seen in large load joints. The therapeutic approach to OA aims to reduce painful symptoms, decrease stiffness levels, improve mobility and quality of life. Among the non-pharmacological therapeutic options we have ultrasound therapy (US) that promotes deep heating in the tissues and that little evidence shows that it is capable of reducing pain in patients with knee OA. Aim: This paper aims to describe the effects and efficacy of UST in the treatment of pain and function in primary knee osteoarthritis. Methods: A systematic search was performed in the PubMed, LILACS, CENTRAL, SCIELO and PEDro databases for randomized and quasi-randomized clinical trials, published in the last 10 years. The keywords used were 'Ultrasound', 'Ultrasound Therapy', 'Pain', 'Knee', 'Knee Joint', 'Knee Osteoarthritis'. Results: Six studies, including 561 patients, were selected. Some studies have shown that there was no significant difference between the continuous and pulsed US groups in pain relief and function improvement. The US when used as a therapeutic adjuvant showed good results. Conclusion: Selected studies suggest that US applications combined mainly with exercise are effective in relieving pain and improving the functionality of patients with knee osteoarthritis.

Keywords: ultrasound, knee, rehabilitation, knee ostearthritis.

1 INTRODUCTION

Osteoarthritis (OA) is a degenerative condition of the cartilaginous tissue that mostly affects large load joints such as the knees, hips and shoulders (1). Affected patients usually experience significant pain, functional deficits in activities of daily living, leading to a loss of productivity and worsening quality of life (2–4).

The OA is characterized by focal areas of loss of articular cartilage in synovial joints, accompanied by bone changes at the subchondral level, formation of osteophytes in the joint margins, thickening of the joint capsule and mild synovitis (5).

The main objectives of osteoarthritis treatment are to return the patient to the desired level of activity and participation and to prevent chronic complaints and recurrences. The fact that there are many types of treatment for osteoarthritis leads us to believe that no single approach has been able to demonstrate its superiority. The evidence shows that the effectiveness

of some interventions is supported for pain control (for example, exercises) (6–10). Inseri mais uma referencia que é inclusive da Clinics. Os corpos editoriais veem com bons olhos citações da própria revista.

Although many conservative treatment modalities are available for the management of mild to moderate OA, therapeutic ultrasound (UST) is one of many modalities commonly used for musculoskeletal disorders by health professionals, such as physical therapists, osteopaths, chiropractors and sports therapists and can be used as part of a general rehabilitation program (11–13).

Therapeutic ultrasound consists of high frequency sound vibrations that can be pulsed or continuous (14). Pulsed ultrasound (USP) produces non-thermal effects and is generally recommended for acute pain and inflammation while continuous ultrasound (USC) generates thermal effects and is recommended in chronic phases of inflammation (15,16). Ultrasonic sound waves penetrate deep into the tissue, enough to increase collagen elasticity, a fact that can be useful in the early stages of a flexibility program (17).

A complementary technique in the use of ultrasound (US) is called sonophoresis, it uses ultrasound as a physical intensifier for the systemic delivery of drugs, and some studies have shown to effectively deliver various types of drugs, regardless of their electrical characteristics (18,19).

However, the effectiveness of ultrasound for musculoskeletal problems remains controversial. Previous systematic reviews of the effects of ultrasound therapy for different musculoskeletal disorders have found that there are few studies and some controversial on this topic and that there is a lack of evidence on its usefulness in the treatment of degenerative rheumatic disorders and myofascial pain (5,13,20).

The literature on comparing different modes of US therapy in the knee with OA and placebo-controlled trials is scarce. The aim of this review was to examine and compare the effects and efficacy of UST in the treatment of pain and function in primary knee osteoarthrosis.

2 METHODS

Only randomized controlled trials (RCTs) published in any language, that evaluated the use of TUS as a treatment in people with knee OA for inclusion in this systematic review were considered. We only included studies with more than one day's follow-up.

Studies that recruited and analyzed adult patients with clinically and/or radiologically confirmed primary osteoarthritis were included. We excluded studies of postoperative patients

and individuals in which a specific cause for osteoarthritic condition was determined (eg, fracture, malignancy).

We included all RCTs that used any type of continuous or pulsed therapeutic ultrasound, studies comparing ultrasound (alone or in combination with exercise) with placebo or other interventions for OA. We excluded studies with sonophoresis with other therapeutic modalities; those in which the ultrasound was part of a treatment package and it was not possible to determine the effectiveness of the ultrasound alone; for example, we did not include a study that compared aerobic exercises + exercises at home with warm compress + ultrasound + TENS (transcutaneous electrical nerve stimulation), but we did include a study comparing an ultrasound exercise program to the same non-ultrasound exercise program.

The main results were pain and function, as currently recommended for osteoarthritis trials (21,22). In the selection of studies, there was a restriction on the year of publication for the last 10 years and there was no restriction on the language.

We searched CENTRAL's electronic databases through the Cochrane Library (http://mrw.interscience.wiley.com/cochrane/), MEDLINE and LILACS through the BVS platform (https://bvsalud.org/), SCIELO through EBSCOhost (http://eds.b.ebscohost.com) and evidence database in physiotherapy (PEDro).

To search for evidence, the subject descriptors in the DECs - Health Sciences Descriptors were used, which are: ‘Ultrasound’, ‘Ultrasound Therapy’, ‘Pain’, ‘Knee’, ‘Knee Joint’, ‘Knee Osteoarthritis’ in portuguese, english and spanish combined with the Boolean operators OR and AND (Appendix 1) and to elaborate the search strategy P.I.C.O (Problem - Intervention - Control - Outcome).

At the end of the searches in each database, the identified articles whose titles and/or abstracts contained indications that they were consistent with the objective of the present study were pre-selected and obtained in full. Then, such articles were evaluated in order to select those that fit the inclusion criteria established for this review.

3 RESULTS

Of the 4428 articles initially identified through the researched databases, 670 were removed for careful evaluation, 652 of which were excluded by the analysis of abstracts. Eighteen full texts were evaluated for eligibility, of which 07 were excluded for not meeting the inclusion criteria (Figure 01). A total of ten studies from different countries were included, with four randomized controlled trials, two quasi-randomized controlled trials and four studies not reporting the randomization method.

The studies investigated 561 patients of these, 538 received effective ultrasonic therapy (non-placebo) in isolation or adjuvant to other therapeutic resources (exercise, low-power laser, neuromuscular electrostimulation)

Table 01 shows all the studies included in this review

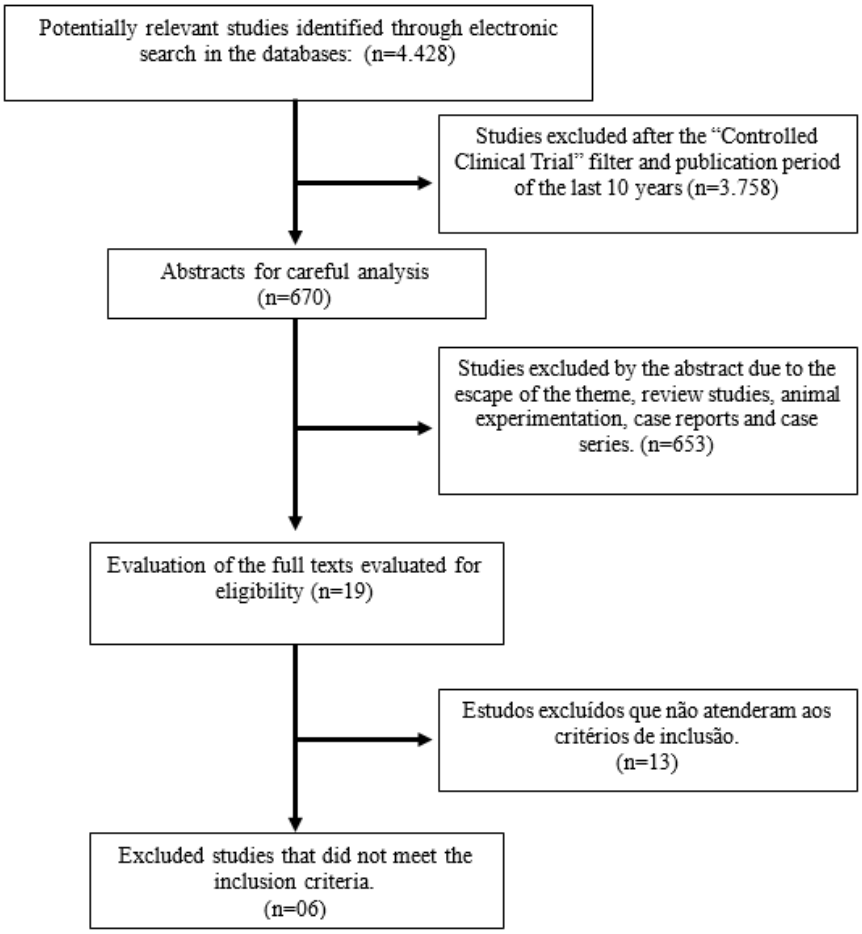


Figure 01- Search and selection of studies for systematic review according to PRISMA

Table 01 – Summary of the studies included in this review.

AUTHOR (YEAR) COUNTRY	OBJECTIVE	SAMPLE INTERVENTION	VARIABLES	OUTCOMES
ALFREDO; JUNIOR; CASAROTTO (2020) Brazil	Compare the effects of USC and USP, associated with strengthening exercises	G1: USC for 1 month. (n = 20) G2: USP for 1 month (n = 20) G3: USC for 2 months (n = 20) G4: USP for 2 months (n = 20) G5: Exercise sessions for eight weeks (n = 20) All patients in the groups who received ultrasound performed exercises in the second month of treatment. The sessions took place three times a week	Pain (VAS) Function and Activity Level (Lequesne - WOMAC) ROM Muscle strength Mobility (Timed Up and Go test)	The authors suggests that prolonged applications of continuous ultrasound combined with exercise have been shown to be more effective in providing pain relief, improving mobility, functionality and activity in individuals with knee osteoarthritis.
BOYACI et al. (2013) Turkey	To compare the effectiveness of Sonophoresis, Short-wave diathermy (SWD), and ultrasound (US) in knee osteoarthritis	G1: Sonophoresis (n = 33) G2: US (n = 33) G3: SWD (n = 35) Before each intervention, 20 minutes of hot compresses were performed. There were 10 interventions distributed 05 days a week for 02 weeks.	Pain (VAS) Function and Activity Level (WOMAC) Mobility (walking time 15m)	The authors found that pain, 15 m walking time and WOMAC parameters improved with all three types of deep warm-up. However, there was no significant difference between the three modalities in terms of effectiveness.

Table 01(continuation) – Summary of the studies included in this review.

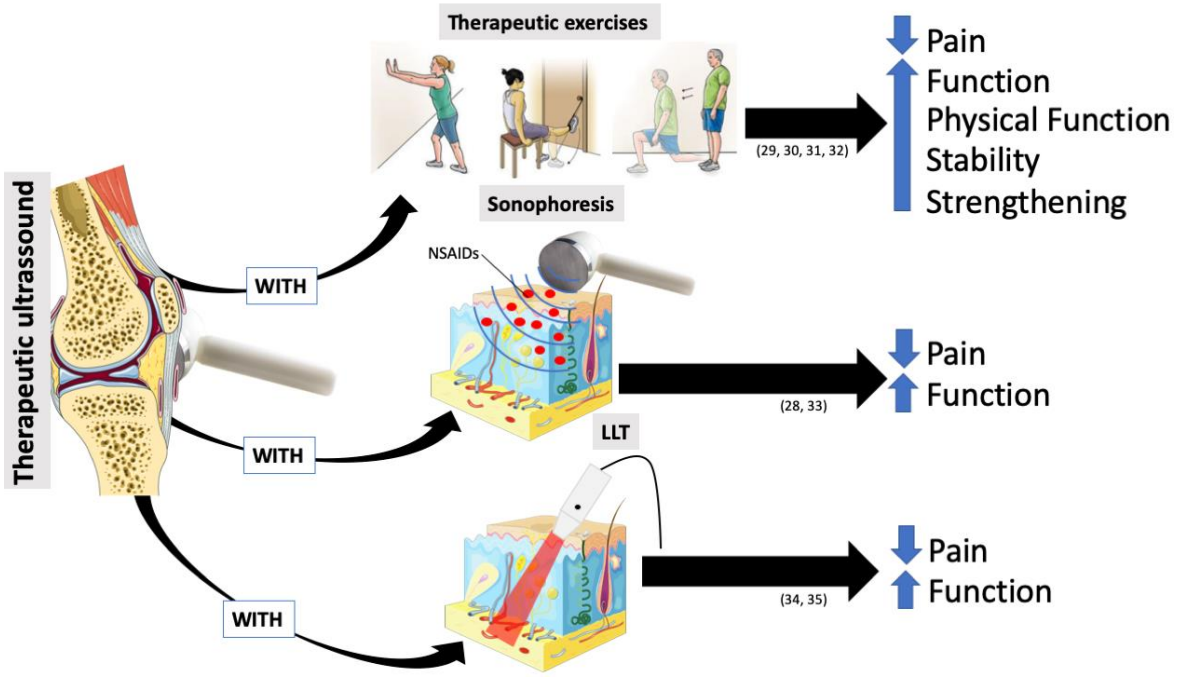
AUTHOR (YEAR) COUNTRY	OBJECTIVE	SAMPLE INTERVENTION	VARIABLES	OUTCOMES
DEVRIMSEL; METIN; SERDAROGLU BEYAZAL (2014) Turkey	To determine the effects of TUS and neuromuscular electrical stimulation (NMES) on muscle architecture and functional capacity in patients with knee osteoarthritis.	G1 = NMES + hot compress + exercises. (n = 30) G2 = UST + hot compress + exercises (n = 29) 5x week for 03 weeks	Pain (VAS) Function (WOMAC) Mobility (15m walk test) Muscular architecture	The 2 groups showed significant improvement in all outcome measures before and after treatment There was a significant improvement in pain, stiffness score and WOMAC physical function for the G2 group compared to the G1 group. The NMES group exhibited more increases in the values of muscle thickness and fascicle length when compared to the ultrasound therapy group. They observed that ultrasound therapy seems to be an effective treatment in reducing pain and improving functional capacity and that the application of NMES has more effects on muscle architecture.
YILDIZ et al (2015) Turkey	Investigate the effectiveness of UST in primary knee osteoarthritis.	G1: USC (n = 30) G2: USP (n = 30) G3: US Placebo (n = 30) All patients received an exercise program at home	Pain (VAS) ROM Function (Lequesne) Quality of life	The increase in knee ROM was similar in both ultrasound groups, while the change in the placebo group was not statistically significant. EVA scores and Lequesne scores from the placebo group in the second month were significantly higher than the scores from both ultrasound groups. Significant improvement in terms of pain, function and quality of life scales were seen in both ultrasound groups compared to the placebo group. No statistically significant difference was found in terms of effectiveness between continuous and pulsed ultrasound.

Table 01(continuation) – Summary of the studies included in this review.

AUTHOR (YEAR) COUNTRY	OBJECTIVE	SAMPLE INTERVENTION	VARIABLES	OUTCOMES
LUKSURAPAN; BOONHONG, (2013) Thailand	To compare the effects of sonophoresis with piroxicam and UST in patients with mild to moderate degree of symptomatic knee OA.	G1: Phonophoresis (n = 23) G2: UST (n = 23)	Pain(VAS) Function (WOMAC)	Function (WOMAC) The EVA and WOMAC scores improved significantly after treatment in both groups. The G1 group tended to show more significant effects than the G2 group, both in reducing the EVA score and improving the WOMAC score, although it didn't reach the level of statistical significance.
MASCARIN, et al. (2012) Brasil	Investigate the effects of kinesiotherapy, electrotherapy and UST on functional capacity	G1: Kinesiotherapy (n = 16) G2: Electrostimulation with TENS (n = 12) G3: UST (n = 10)	Pain (VAS) ADM Function (WOMAC) Mobility (6-minute walk test)	Groups G1 and G3 showed significantly longer 6-minute walk test distances compared to their respective pre-intervention values. All treatments were effective in reducing pain and improving the WOMAC index, with no statistically significant difference between them.

LABEL:
UST: Ultrasound Therapy
USC: Continuos Ultrassound
USP: Pulsed Ultrasound
VAS: Visual Analogic Scale
W/cm^2: Watts per square centimeter
WOMAC: *Western Ontario e o McMaster Universities Osteoarthritis*

Figure 02 - main findings regarding combined therapies with ust in the treatment of knee osteoarthritis. legend: nsaids (non-steroidal anti-inflammatories), llt (low level lasertherapy).



4 DISCUSSION

Osteoarthritis treatment aims to reduce joint pain and stiffness, preserve and improve joint mobility, reduce limitations, increase quality of life and educate patients about their condition.

In order to avoid or minimize undesirable gastrointestinal and cardiac side effects generated by pharmacological agents, the use of physical modalities is used as a therapeutic option.

In 2010, the Osteoarthritis Research Society International recommended that optimal management of OA requires a combination of pharmacological agents and non-pharmacological modalities, including physical therapy, but does not specifically mention therapeutic ultrasound as an adjunct treatment (23).

In this review and also in the older literature, it is noticed that several authors have researched the efficacy of therapeutic US and it is still inconclusive on the effects on knee OA (24–26).

Welch et al (27) conducted a clinical trial in which they compared therapeutic US with placebo and they concluded that therapeutic US appears to have no benefit over placebo or short wave diathermy for patients with knee OA. In an updated review by Rutjes et al. (5) their results

suggested that therapeutic US may be beneficial for patients with knee OA and that it is also reported by Boyaci (28) (Table1).

After searching the databases, we identified potential articles, then screened, elected and included 06 recent studies. It was possible to verify that the publications are quite heterogeneous as to the characteristics of the ultrasonic device, the population, the stage of OA, the form of therapeutic application of the US and low methodological quality of the included trials, which leads us to limited conclusions about the therapeutic action of the US in osteoarthritis.

The main results found in table 01 by Ulus et al (29), Devrimsel; Metin; Serdaroglu-Beyazal (30), Yildiz et al (31) and Alfredo; Junior; Casarotto (32) reported that ultrasonic therapy should be applied frequently in patients with knee osteoarthritis in conjunction with exercise programs aimed at relieving pain, improving physical function, stability, strengthening and general cardiovascular fitness (Figure 02).

Good results were reported in the publications by Boyaci et al (28) and Luksurapan and Boonhong et al (33) when they used the US as a sonophoresis technique or compared it with the UST. The use of topical non-steroidal anti-inflammatory drugs (NSAIDs) is a therapeutic option in patients with symptomatic knee OA who are at a high risk of adverse events from oral NSAIDs (Figure 02). The skin is a perfect barrier to the administration of transcutaneous drugs. The use of US as a facilitator in the penetration of drugs as proposed in sonophoresis has been an increasing option for those professionals who treat musculoskeletal pain.

Despite the frequent use of sonophoresis by physical therapists, the lack of good scientific evidence permeates doubts regarding the effectiveness of the treatment, especially in knee OA. The results presented by Boyaci et al (28) and Luksurapan and Boonhong et al (33) (Table 01) suggest that sonophoresis is slightly more effective than UST for reducing pain and improving function in patients with symptomatic knee OA (Figure 02).

Throughout the preparation of this review, we found publications that associated UST with Low Power Laser (LPL). The use of LBP in combination or not with UST are generally safe, non-ionizing radiation (in the case of Laser) ideal for use in daily clinical practice with cost-benefit, portability and adherence to treatment by the patient.

In the study presented by Raymundo et al (34) and Paolillo et al (35) report that LPL together with therapeutic US reduces pain and increases functional autonomy in individuals with knee OA, this can be justified because LPL has the capacity to promote an increase in beta-endorphin (36) while therapeutic US has antinociceptive effects (37,38).

Individuals with OA often have muscle weakness in the lower limbs that are associated and worsen with physical inactivity, more severe joint degeneration, greater pain and

symptomatic disease progression (39). The low mobility of the limb leads to the production of a continuous reflex inhibition known as arthrogenic muscle inhibition and consequent reduction in stimulation of the muscle efferent motor neuron. According to Devrimsel, Metin, Serdaroglu-Beyazal (30) ultrasound therapy can promote a reverse effect on the inhibition of the arthrogenic muscle and the excitability of the motoneuron pool could be facilitated and, in addition, when using electrical stimulation, it could contribute increased muscle strength, changes in system structure and fib composition muscle and capillary. Causes muscle atrophy to improve due to prolonged immobilization.

Zhang et al (40) corroborating Yildz et al (31) demonstrated that therapeutic US is an effective treatment to reduce pain and improve physical function in patients with knee osteoarthritis. However, Cakir et al (41) reported that the US did not provide additional benefit in improving pain and functions beyond physical training. (Table 01)

We believe that patients with chronic inflammatory conditions and absence of joint edema, continuous ultrasound showed slightly superior results compared to pulsed US (33,38,42) corroborating the findings of Draper et al (43) and Tascioglu et al (26).

5 FINAL CONSIDERATIONS

Most of the assessments included in this review differ. Pulsed ultrasound can lead to a small decrease in pain and an improvement in functionality in osteoarthritis, but the certainty of the evidence is still low.

We can infer that pulsed ultrasound is a widely used therapy, but with limited results, which implies a significant amount of time to attend the necessary sessions, so the balance between costs and benefits is not favorable.

Although the effect observed on pain is statistically significant in most of the selected articles, the magnitude of the effect was quite divergent. The functionality indexes analyzed by the authors (Lequesne and WOMAC, mainly) showed good results in the vast majority of the analyzed papers.

The results of this work provide us with more evidence that patients with knee OA can obtain significant benefits by associating US with other procedures such as kinesiotherapy (exercises), short wave diathermy, neuromuscular electrostimulation or even LBP.

In terms of safety, the adverse effects were not described in any of the studies included in this review, therefore, we can consider the US as a safe resource with good adherence by professionals and patients. New reviews, especially if they can obtain additional information from existing studies, need to be carried out and can provide more reliable results.

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APENDICE 1- Estratégias de Busca nas bases de dados

LILACS – MEDLINE via Bireme (BVS)

(MH:Joelho OR Knee OR Rodilla OR A01.378.610.450 OR MH:"Articulação do Joelho" OR "Knee Joint" OR "Articulación de la Rodilla" OR A02.835.583.475 OR MH: "Osteoartrite do Joelho" OR "Osteoarthritis, Knee" OR "Osteoartritis de la Rodilla" OR MH: "Artrose de Joelho" OR "Artrose do Joelho" OR Gonartrose OR "Osteoartrite de Joelho" OR C05.550.114.606.500 OR C05.799.613.500 OR MH:Dor OR Pain OR Dolor OR "Sofrimento Físico" OR C23.888.592.612 OR F02.830.816.444 OR G11.561.790.444 OR MH:Dor OR Pain OR Dolor OR "Sofrimento Físico" OR C23.888.592.612 OR F02.830.816.444 OR G11.561.790.444) AND (MH:Ultrassom OR Ultrasonics OR Ultrasonido OR H01.671.031.849 OR "Terapia por Ultrassom" OR "Ultrasonic Therapy" OR "Terapia por Ultrasonidonados" OR E02.565.280.945)

Base de Dados PEDro

Search Field	Search Terms
Abstract & Title	Ultrasound Osteoarthritis
Therapy	- No selection -
Problem	- No selection -
Body Part	Lower leg or knee
Subdiscipline	- No selection -
Method	Clinical Trial
When searching	Match all search terms (AND)