

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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Is pulsed ultrasound an alternative for osteoarthritis?

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Abstract

INTRODUCTION

Many osteoarthritis patients persist symptomatic despite nonsurgical treatment. Pulsed ultrasound might be a viable alternative for such cases, but its real clinical relevance remains unclear.

METHODS

A literature review was conducted in Epistemonikos, the largest database for systematic reviews in health that compiles multiple sources, including MEDLINE, EMBASE, and Cochrane, among others. Relevant data were extracted, and information from the primary studies was reanalyzed. A subsequent meta-analysis was conducted, and summary of findings tables were constructed using the GRADE methodology.

RESULTS AND CONCLUSIONS

Six systematic reviews including eight randomized trials were identified. In conclusion, it is not clear whether pulsed ultrasound improves functionality, and it might slightly decrease pain but the certainty of the evidence is low.

Problem

Osteoarthritis is a highly prevalent disease worldwide and a frequent cause of medical consultation for both, primary care and specialists. The persistence of pain despite nonsurgical treatment is one reason for such consults, and no clearly established alternatives exist for pain management.

Pulsed ultrasound corresponds to the use of sound waves in order to relieve pain or disability. For this purpose, it can direct the beam with a transducer over the area to be treated and it is interrupted in the form of pulsations, allowing higher intensities in order to have a greater effect.

There is no precise information about side effects of the use of therapeutic ultrasound, possibly because they do not exist, or they are very infrequent and related to the use in supra physiological intensities.

Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary

studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a

summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- Pulsed ultrasound could lead to a small decrease in pain in osteoarthritis, but the certainty of the evidence is low.
- It is not clear if the use of pulsed ultrasound produces an improvement in functionality in patients with osteoarthritis, because the certainty of the evidence is very low.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found six systematic reviews [1],[2],[3],[4],[5],[6] including eight studies overall, corresponding to randomized controlled trials [7],[8],[9],[10],[11],[12],[13],[14].
What types of patients were included*	All of the trials focused on osteoarthritis of the knee. Average body mass index (BMI) ranged between 28.75 and 32.2 in four trials [7],[8],[11],[14] and four did not report it [9],[10],[12],[13]. Average age of the participants ranged between 57 and 65 years in the different trials. The proportion of women was between 33 and 100% in the different trials.
What types of interventions were included*	All of the trials used pulsed ultrasound. One trial used ultrasound with a frequency of 1 MHz and potency of 1.5 W/cm ² in sessions of twelve minutes each, for two weeks (10 sessions in total) [7]. One trial used ultrasound with a frequency of 1 MHz and potency of 1.5 W/cm ² in sessions of fifteen minutes each, for eight weeks (24 sessions in total) [9]. One trial used ultrasound with a frequency of 1 MHz and potency of 2.5 W/cm ² in sessions of fifteen minutes each, three times a week for eight weeks (24 sessions in total) [10]. One trial used ultrasound with a frequency of 1 MHz and potency of 0.2 W/cm ² in sessions of nine and a half minutes each, for eight weeks (24 sessions in total) [11]. One trial used ultrasound with a frequency of 2.5 MHz in sessions of fifteen minutes each, for eight weeks (24 sessions in total) [13]. One trial used ultrasound with a frequency of 1 MHz and potency of 2 W/cm ² in sessions of five minutes each, for two weeks (10 sessions in total) [14]. Two trials did not describe the frequency or the power of the pulsed ultrasound, or the amount of sessions or the duration of them [8],[12]. Two trials associated isokinetic exercises to the pulsed ultrasound [9],[10]. Four trials compared against placebo or standard therapy [10],[11],[12],[13]. Four trials compared against placebo and against continued wave ultrasound [7],[8],[9],[14].
What types of outcomes were measured	The outcomes, as classified in the identified systematic reviews, were as follows: effect on the intensity of pain (analyzed as a decrease or improvement) according to visual analogue scale; knee osteoarthritis severity index established by Lequesne; and sub-scale of physical functionality established by the Western Ontario and McMaster Universities Arthritis Index (WOMAC). The average follow-up of the trials was 16 weeks with a range between 2 and 52 weeks.

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

Summary of Findings

The information on the effects of pulsed ultrasound was based on three randomized trials that included 200 patients [8],[9],[10]. The remaining trials were not included in the meta-analysis as none of the identified systematic reviews extracted sufficient trial data. The three evaluated trials reported improvement in pain measured with visual analogue scale, and functionality by Lequesne knee osteoarthritis severity index. The summary of findings is as follows:

- Pulsed ultrasound could lead to a small decrease in pain in osteoarthritis, but the certainty of the evidence is low.
- It is not clear if the use of pulsed ultrasound produces an improvement in functionality in patients with osteoarthritis, because the certainty of the evidence is very low.

Pulsed ultrasound for osteoarthritis				
Patients	Individuals with osteoarthritis			
Intervention	Pulsed ultrasound			
Comparison	Placebo			
Outcomes	Absolute Effect***		Relative Effect (95% CI)	Certainty of Evidence (GRADE)
	WITHOUT Pulsed ultrasound	WITH Pulsed ultrasound		
	Difference: patients in 1000			
Pain* (0 to 10 points)	2.45 points reduction	3.96 points reduction	--	⊕⊕○○ Low ¹
	MD: 1.51 (Margin of error: 1.08 to 1.93)			
Functionality** (0 to 24 points)	3.11 points increase	4.88 points increase	--	⊕○○○ Very low ²
	MD: 1.77 (Margin of error: 1.33 to 2.21)			
Margin of error = 95% Confidence Interval. RR: Relative Risk. MD: Mean difference GRADE: Grading of Evidence according to the GRADE Working Group. *Pain: Evaluated with visual analogue scale, that consists on a straight line with numbers from zero to ten, were the patient choose a point that represents with the amount of pain that he feels (0 = no pain, 10 = worst pain imaginable). **Functionality: evaluated with Lequesne index, that consists on a list of 11 questions grouped in 3 sections: pain/discomfort, maximum distance walked y daily life activities. Each section has a minimum score of 0 and maximum of 8. The sum of the sections leads to a score equivalent to the Lequesne index and its interpretation is: 0 means no disability, 1-4 low, 5-7 moderate, 8-10 severe, 11-13 very severe, and 14 or more extremely severe. ***The risks WITHOUT pulsed ultrasound were based on risks of the control groups in the studies. The risk WITH pulsed ultrasound (and the respective margin of error) was calculated from the relative effect (and respective margin of error). ¹ We downgraded the certainty of the evidence in two levels: one for serious risk of bias according to what was reported by the reviews, and one level for inconsistency (I ² of 57%). ² We downgraded the certainty of the evidence in three levels: one for serious risk of bias according to what was reported by the reviews, and two levels for inconsistency (I ² = 85%).				

Visit the following link to access the interactive version of this table ([Interactive Summary of Findings - iSoF](#))

About the certainty of the evidence (GRADE)*
⊕⊕⊕⊕ High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.
⊕⊕⊕○ Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate
⊕⊕○○ Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.
⊕○○○ Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.
*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'. † Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- While the intention of this summary was to include osteoarthritis in general, considering all of the possible affected joints, the trials that were found focused specifically on osteoarthritis of the knee.
- In absence of direct evidence for other joints, we believe that extrapolating the conclusions of this summary could lead to error since the effect of ultrasound depends on the target tissue, and there are other joints deeper (surrounded by more soft tissue) such as hip and shoulder, in which we could assume a lower intensity of ultrasound and therefore a lesser effect.
- It is important to emphasize that different primary studies evaluating pulsatile ultrasound used different frequencies and intensities, with different application times and total treatment duration. It is not possible with the existing data to make judgments about the effectiveness of some specific type of pulsatile wave ultrasound.

About the outcomes included in this summary

- The outcomes included in this summary are those considered critical for decision-making by the authors of this summary. Furthermore, we conducted a search of the Core Outcome Measures in Effectiveness Trials (COMET) Initiative, finding one relevant article [15] that indicated, through a consensus, the following as the most relevant outcomes: joint pain, functionality, quality of life in relation to health, work situation, mortality, reoperation, hospital readmission, and overall satisfaction with the results of the treatment.

Balance between benefits and risks, and certainty of the evidence

- Although the observed effect over pain is statistically significant, the magnitude of the effect was below the minimally important difference reported in the literature [16]. In the case of functionality by Lequesne index, according to the literature [17] the difference presented in the meta-analysis would be clinically significant, but the certainty of the evidence is very low.
- In terms of safety, adverse effects have not been described in any of the trials included in this summary, therefore we expanded the search to ultrasound in general. One study described the intention of monitoring the incidence of adverse events associated to the use of continued wave ultrasound and reported absence of major complications [18]. Another study reported absence of adverse events during and after the application of continued wave ultrasound [19].

Resource considerations

- Although pulsed ultrasound is a widely available therapy and at a cost generally accessible to the majority of the population, it implies a significant amount of time to attend the multiple sessions that are needed.
- Considering the scarce benefit reported, even when the existing evidence shows no adverse effects, the balance between costs and benefits is not favorable.

What would patients and their doctors think about this intervention

- Faced with the evidence presented in this summary, most patients and clinicians should lean against the use of this intervention.
- However, without clearly effective therapeutic alternatives, variation could exist in the clinical decisions made by patients and individual clinicians.

Differences between this summary and other sources

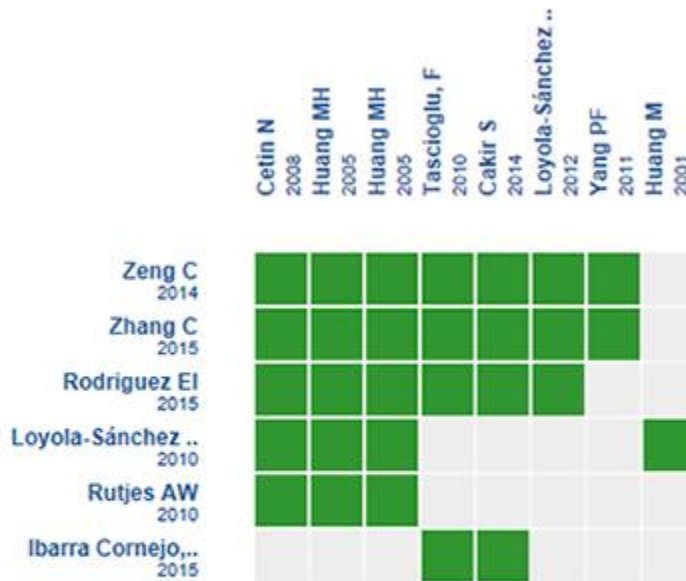
- The reviews included in this summary differ among each other. One review [1] concluded pulsed ultrasound would be better than placebo on pain reduction and functionality improvement, without associated adverse effects. Another review [2] reported pulsed ultrasound could be beneficial in decreasing pain, but it mentions treatment duration as a limitation because it must be defined patient by patient. Four reviews [3],[4],[5],[7] concluded ultrasound could be beneficial in decreasing pain and improving functionality in patients with knee osteoarthritis, but given that the available evidence has methodological limitations and is difficult to compare, new studies of better quality are required. Finally, another review [6] determines ultrasound is ineffective for decreasing pain in knee osteoarthritis because the evidence has low certainty or it is controversial.
- The conclusions of this summary agree with the main international guidelines for osteoarthritis: The Osteoarthritis Research Society International (OARSI) [20] indicates it is uncertain whether therapeutic ultrasound for the treatment of knee osteoarthritis is useful and it is not recommended for the treatment of knee osteoarthritis or multiple joints. The American Academy of Orthopedic Surgeons (AAOS) [21] concludes that given the inconsistency of the findings for multiple physical therapies, including therapeutic ultrasound, they cannot make a recommendation in favor or against its use in patients with symptomatic knee osteoarthritis.

Could this evidence change in the future?

- The probability that the conclusions of this summary change with future trials is high, due to the low and very low certainty of the existing evidence.
- We identify at least four ongoing trials [22],[23],[24],[25] in the International Clinical Trials Registry Platform of the World Health Organization, which could provide relevant information.
- New reviews, especially if they manage to obtain additional information from existing trials, could provide more reliable results. However, we did not identify ongoing reviews in the PROSPERO database.

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question.

Rows represent systematic reviews, and columns show primary studies.

The boxes in green correspond to studies included in the respective revisions.

The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version**: [Pulsed ultrasound versus placebo for osteoarthritis](#)

Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated

notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly

format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here

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Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

Potential conflicts of interest

The authors do not have relevant interests to declare.

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