The Effect of Photobiomodulation on Pain Management and Functionality in Knee Osteoarthritis: A Systematic Review Protocol

O Efeito da Fotobiomodulação no Manejo da Dor e da Funcionalidade na Osteoartrite do Joelho: Protocolo de Revisão Sistemática
El Efecto de la Fotobiomodulación en el Manejo del Dolor y la Funcionalidad en la Osteoartritis de Rodilla: Un Protocolo de Revisión Sistemática

RESUMO
Objetivo: Este protocolo de revisão sistemática visa analisar o efeito da fotobiomodulação no manejo da dor e funcionalidade em pacientes com osteoartrite de joelho. **Método:** Registrado na PROSPERO e seguindo as diretrizes PRISMA, incluirá ensaios clínicos randomizados que utilizem fotobiomodulação em pacientes com osteoartrite de joelho. A busca será realizada nas bases MEDLINE, COCHRANE, EMBASE, AMED, SCOPUS e PEDRO. A seleção e extração dos dados serão feitas por dois revisores independentes, com um terceiro para resolver discordâncias. O risco de viés será avaliado pela escala PEDro. A síntese dos dados incluirá meta-análise com modelos de efeitos aleatórios e avaliação da qualidade da evidência pelo sistema GRADE. **Conclusão:** Esta revisão fornecerá uma visão abrangente sobre a eficácia da fotobiomodulação no manejo da dor e melhora da funcionalidade em pacientes com osteoartrite de joelho, contribuindo para a prática clínica baseada em evidências.
DESCRITORES: Osteoartrite de joelho; Fotobiomodulação; Dor; Funcionalidade; Revisão sistemática.

ABSTRACT
Objective: This systematic review protocol aims to analyze the effect of photobiomodulation on pain management and functionality in patients with knee osteoarthritis. **Method:** Registered in PROSPERO and following PRISMA guidelines, it will include randomized clinical trials using photobiomodulation in patients with knee osteoarthritis. The search will be conducted in MEDLINE, COCHRANE, EMBASE, AMED, SCOPUS, and PEDRO databases. The selection and extraction of data will be carried out by two independent reviewers, with a third to resolve any discrepancies. The risk of bias will be assessed using the PEDro scale. The data synthesis will include meta-analysis with random effects models and evaluation of the quality of evidence using the GRADE system. **Conclusion:** This review will provide a comprehensive overview of the effectiveness of photobiomodulation in managing pain and improving functionality in patients with knee osteoarthritis, contributing to evidence-based clinical practice.
DESCRIPTORS: Knee osteoarthritis; Photobiomodulation; Pain; Functionality; Systematic review.

RESUMEN
Objetivo: Este protocolo de revisión sistemática tiene como objetivo analizar el efecto de la fotobiomodulación en el manejo del dolor y la funcionalidad en pacientes con osteoartritis de rodilla. **Método:** Registrado en PROSPERO y siguiendo las directrices PRISMA, incluirá ensayos clínicos aleatorizados que utilicen fotobiomodulación en pacientes con osteoartritis de rodilla. La búsqueda se realizará en las bases MEDLINE, COCHRANE, EMBASE, AMED, SCOPUS y PEDRO. La selección y extracción de los datos serán realizadas por dos revisores independientes, con un tercero para resolver discrepancias. El riesgo de sesgo será evaluado mediante la escala PEDro. La síntesis de los datos incluirá un meta-análisis con modelos de efectos aleatorios y una evaluación de la calidad de la evidencia mediante el sistema GRADE. **Conclusión:** Esta revisión proporcionará una visión global de la eficacia de la fotobiomodulación en el manejo del dolor y la mejora de la funcionalidad en pacientes con osteoartritis de rodilla, contribuyendo a la práctica clínica basada en evidencias.
DESCRIPTORES: Osteoartritis de rodilla; Fotobiomodulación; Dolor; Funcionalidad; Revisión sistemática.

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INTRODUCTION

Osteoarthritis (OA) is a prevalent degenerative and chronic disease that impacts health systems and has multiple socioeconomic effects [1,2]. According to the American College of Rheumatology, knee osteoarthritis can be diagnosed clinically based on the following symptoms: knee crepitus, joint stiffness lasting at least 30 minutes, functional changes, joint pain and the presence of osteophytes detected by imaging tests [3,4,5]. The number of patients with Osteoarthritis of the Knee (OAJ) increases exponentially from the fourth decade of life onwards, and the condition is more common in women [6,7].

Osteoarthritis is commonly defined as an inflammatory joint process, changes in bone structure, cartilage degradation and biochemical changes that impair joint congruence. These physiological changes can result in osteochondral lesions, which decrease arthrokinetics and stiffen the joint, increasing its vulnerability to microfractures and, ultimately, the development of osteophytes. In addition, there may be changes in the growth of synovial fluid, as well as metabolic and enzymatic alterations that result in structural changes in the osteochondral region [8,9].

Among the physiotherapeutic treatments used, neuromuscular training is categorized as moderate evidence, while supervised exercise and pain education stand out as strong evidence. However, the following are categorized as limited evidence: photobiomodulation (low-intensity laser), transcutaneous electrical stimulation, percutaneous electrical nerve stimulation/pulsed electromagnetic field therapy, manual therapy, massage, acupuncture and extracorporeal shockwave therapy. The management of pain and functionality has made use of photobiomodulation [10,11,12,13,14].

Musculoskeletal tissue is the main target of this therapeutic modality, which involves the interaction of light with various biological tissues within a therapeutic window of 600-1000 nm. When applied within the appropriate spectrum and dose response parameters, photobiomodulation treatments for OAJ can have a substantial impact on the clinical status of patients with knee osteoarthritis, reducing pain and improving physical disability.

A preliminary search of databases such as PROSPERO, Medline, EMBASE, SCOPUS and Google Scholar's gray literature did not identify any published systematic reviews on the specific effect of photobiomodulation on pain management and functionality in patients with knee osteoarthritis. However, an initial search using Health Sciences Descriptors (DeCS) indicated the existence of relevant studies that met the inclusion criteria. Thus, this systematic review protocol aims to analyze the effect of photobiomodulation on pain management and functionality in patients with knee osteoarthritis.

METHOD

The protocol was registered with

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PROSPERO (CRD42025647979), and the review will be reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15].

Eligibility criteria

This review will include randomized clinical trials investigating people with knee osteoarthritis of both sexes and any age. The intervention of interest will be any method of photobiomodulation. To investigate the possible specific effects of photobiomodulation, the intervention of interest will be contrasted with control (i.e. placebo, no intervention, waiting list or simulation). Comparisons between photobiomodulation techniques and any other active intervention, as well as the other active intervention on its own, will be considered to determine whether photobiomodulation techniques increase the estimated effects of the other active intervention.

The outcomes of interest will be pain intensity and functionality. In addition to validated questionnaires (KOOS or WOMAC) or functional tests, any valid tool for measuring pain intensity will be considered, such as the Visual Analog Scale (VAS) or Numerical Rating Scales (NRS).

The following will be excluded: observational studies; articles written in languages other than English; case series and individual case studies; non-randomized clinical trials; secondary analysis of qualitative data (e.g. systematic reviews); individuals with knee pain or anterior cruciate ligament injuries who have not been diagnosed with osteoarthritis; research examining the experiences of individuals who have undergone additional interventions (such as knee replacement surgery); research examining experiences with perioperative knee replacement care; research examining opinions on the choice to go ahead with a complete knee replacement.

Sources of information

The review will include the following databases and sources: MEDLINE, COCHRANE, EMBASE, AMED, SCOPUS and PEDRO. These sources were chosen to ensure the comprehensiveness and relevance of studies in the area.

Search strategy

A search strategy based on the acronym PEO (Population, Exposure, Outcomes) was developed to identify relevant keywords and locate articles in databases and grey literature. The strategy aims to locate original studies published from the beginning of the database to the present, in any language. If necessary, a professional translator will be used to translate the studies into English. The P component refers to the study population (people with knee osteoarthritis), E corresponds to the exposer (photobiomodulation) and O represents the outcome (pain and functionality). Boolean operators will be used to combine the key terms: the "OR" operator will be used to connect terms from the same PEO category, and the "AND" operator will be used to connect terms from different categories.

TABLE 1: Search strategy

Population:	"Knee Osteoarthritis"[Mesh] OR "Osteoarthritis, Knee" OR "Knee Osteoarthritides" OR "Osteoarthritides, Knee" OR "Osteoarthritis Of Knee" OR "Knee, Osteoarthritis Of" OR "Knees, Osteoarthritis Of" OR "Osteoarthritis Of Knees"
Exposition:	"Photobiomodulation"[Mesh] OR "Low-Level Light Therapy"[Mesh] OR "Photobiomodulation Therapy" OR "Low Level Laser Therapy" OR "LLLT" OR "Low-Level Laser Therapy" OR "Low Level Light Therapy" OR "Laser Therapy, Low-Level" OR "Light Therapy, Low-Level"
Outcome:	"Pain"[Mesh] OR "Pain Measurement"[Mesh] OR "Pain Management"[Mesh] OR "Functionality" OR "Functional Performance" OR "Physical Function" OR "Disability Evaluation"[Mesh] OR "Recovery of Function"[Mesh]

In the first stage of creating the search strategy, MeSH phrases were used to identify the most relevant terms, with PubMed being the first database searched. A detailed search strategy was developed for PubMed, using MeSH terms to index relevant publications.

TABLE 2: Medline (Pubmed) database search strategy

MEDLINE (PubMed):	((("Knee Osteoarthritis"[Mesh] OR "Osteoarthritis, Knee" OR "Knee Osteoarthritides" OR "Osteoarthritides, Knee" OR "Osteoarthritis Of Knee" OR "Knee, Osteoarthritis Of" OR "Knees, Osteoarthritis Of" OR "Osteoarthritis Of Knees")) AND ("Photobiomodulation"[Mesh] OR "Low-Level Light Therapy"[Mesh] OR "Photobiomodulation Therapy" OR "Low Level Laser Therapy" OR "LLLT" OR "Low-Level Laser Therapy" OR "Low Level Light Therapy" OR "Laser Therapy, Low-Level" OR "Light Therapy, Low-Level")) AND ("Pain"[Mesh] OR "Pain Measurement"[Mesh] OR "Pain Management"[Mesh] OR "Functionality" OR "Functional Performance" OR "Physical Function" OR "Disability Evaluation"[Mesh] OR "Recovery of Function"[Mesh])

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Selection process

Duplicate citations will be eliminated after collection and entry into Rayyan (Qatar Computing Research Institute, Doha, Qatar). Two independent reviewers will examine titles, abstracts and keywords against the inclusion criteria (population, exposure and outcomes). Studies will be classified as "yes" (meets criteria), "maybe" (uncertain) or "no" (does not meet criteria). Discrepancies will be resolved by consensus or by a third reviewer. Reasons for exclusion will be documented at all stages (title/abstract screening and full text selection). To ensure consistency, a preliminary review of a subset of studies will be carried out, and procedures will be adjusted as necessary. Two emails will be sent to authors to request additional information, if necessary. The selection process will be recorded in a PRISMA flowchart [15].

Data collection process

Two independent reviewers will extract data using a customized spreadsheet. Data will include study characteristics (authors, year, country, design), participant characteristics (age, gender, function, sample size) and associated risk factors (excessive workload, lack of institutional support, among others). Secondary outcomes such as mental health impacts, absenteeism, job turnover, reduced performance and overall quality of life will also be collected. The authors of the articles will be contacted twice to obtain missing information. After 30 days, discrepancies or missing information will be noted in the evaluation report.

Item data

All research outcomes will be listed and defined, including methods for deciding which outcomes to collect. Additional variables, such as participant characteristics, interventions and funding sources, will also be listed. Assumptions for dealing with missing or unclear information will be described.

Risk assessment

The risk of bias will be assessed by two independent reviewers using the PEDro scale from 0 to 10. According to this scale, higher scores will represent higher methodological quality. Discrepancies will be resolved by a third reviewer. Where available, we will use the scores already in the PEDRO database.

Measures of effect

For each outcome, weighted or standardized mean differences (for continuous data) and relative risk or odds ratios (for dichotomous data) will be used.

Synthesis method

Random effects models (DerSimonian and Laird technique) will be used in a meta-analysis once the data has been transformed, if possible, to a common scale. In the forest plots, mean differences (MD) and 95% CIs will be shown. The estimates will be shown as standardized mean differences (SMDs) if converting the data to a common scale is not feasible. By comparing the estimated effect sizes and 95% CIs with the Minimum Clinically Significant Difference (MCSD) of the outcome of interest or, in the absence of MCSD, the Minimum Detectable Change (MDC), the clinical relevance of the treatments of interest will be assessed. Two points on a scale of 0-10 will be the DMCS considered for pain intensity.

Where feasible, statistical meta-analysis using Stata v. 17 (Stata Corp LLC, Texas, USA) will be used to group studies offering the same outcome measures. If all studies assess the same outcome using the same instrument, weighted mean differences will be used for continuous data, and relative risk and odds ratios will be used to characterize effect sizes for dichotomous data. When using several instruments to assess the same outcome, standardized mean differences will be employed. The results will be explained using the appropriate units (e.g. functional assessment scales, range of motion in degrees or pain intensity ratings). Standard χ^2 and I^2 tests will be used to assess heterogeneity, and confidence intervals will be calculated for all effect sizes.

The statistical analysis will use a random effects model to account for variation between studies. To assess publication bias, funnel plots will display the results and effect estimates in relation to the sample size. If sufficient information is available, subgroup studies evaluating the effects of photobiomodulation on various degrees of knee osteoarthritis, pain thresholds and functional outcomes will be carried out. Initially, only studies without methodological problems will be included in sensitivity analyses; later, all research, including those with limitations, will be included.

Key factors of photobiomodulation (such as wavelength, power density, dosage and application site) and their impact on pain relief and functional improvement in patients with knee osteoarthritis will be highlighted in the narrative presentation of the results, which will be supported by tables and figures.

Assessment of reported bias and evaluation of confidence level

The GRADE system (Grading of Recommendations, Assessment, Development, and Evaluations) (16)will be used by two impartial reviewers to assess the quality of the available evidence. A third reviewer or consensus will resolve any disputes. Evidence can range from high to very low quality, according to the four-level GRADE system; low levels suggest that the estimated effects are likely to change in future high-quality trials. For each of the following problems, the evidence in this review will be downgraded from its initial high quality: substantial risk of bias when more than 25% of the sub-

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jects analyzed come from trials with a high risk of bias (i.e. PEDro scores below 7 out of 10) and serious imprecision when the sample analyzed is less than 400. When $I^2 > 50\%$, visual examination of forest plots, or when combination is not feasible, serious discrepancy will be taken into account. When combining data from at least 10 trials in a single meta-analysis, we will use Egger's test and visual examination of funnel plots to assess publication bias, using an $\alpha = 0.1$.

CONCLUSION

This systematic review will provide a comprehensive overview of the effectiveness of photobiomodulation in managing pain and improving functionality in patients with knee osteoarthritis. The results will contribute to evidence-based clinical practice by identifying optimal treatment parameters and factors that may influence therapeutic response. In addition, this review could guide future research in the area, highlighting gaps in current knowledge and suggesting directions for new studies.

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