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RESEARCH ARTICLE

APPLICATION OF THERAPEUTIC ULTRASOUND IN KNEE OSTEOARTHRITIS: AN INTEGRATIVE REVIEW OF RANDOMIZED CONTROLLED TRIALS

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Therapeutic ultrasound, Knee osteoarthritis, Physical therapy, Phonophoresis, Randomized controlled trial.

Abstract

Knee osteoarthritis is a leading cause of pain and disability, and therapeutic ultrasound is a widely used electrophysical agent for its conservative manThis integrative review searched PubMed, SciELO, Google Scholar and PEDro for randomized controlled trials published between 2020 and 2026 on continuous, low-intensity pulsed (LIPUS), phonophoretic and focused therapeutic ultrasound in men and women aged 20 to 70 years with knee osteoarthritis; the earliest eligible trial was published in 2022, with most published between 2024 and 2026. Two additional randomized crossover trials conducted in healthy volunteers were analyzed separately, as mechanistic rather than clinical evidence.Pain reduction and functional improvement (WOMAC, Lequesne index) were the most frequently reported outcomes, and combining ultrasound with therapeutic exercise produced greater gains than ultrasound alone. However, most included trials administered ultrasound as part of multimodal protocols, which limits conclusions about its independent effect; parameter heterogeneity and the absence of a formal risk-of-bias assessment further constrain the strength of the evidence.

Introduction:-

Knee osteoarthritis (OA) is a degenerative and progressive joint disease characterized by deterioration of the hyaline cartilage, subchondral bone remodeling, and low-grade synovial inflammation, resulting in pain, stiffness, reduced range of motion, and functional impairment. It is one of the leading causes of musculoskeletal disability among middle-aged and older adults, with substantial socioeconomic impact arising from work absenteeism, healthcare utilization, and the eventual need for total knee arthroplasty. Among the electrophysical agents used in musculoskeletal physical therapy, therapeutic ultrasound (TUS) holds a historically prominent position, being applied in both continuous and pulsed modes for analgesic, anti-inflammatory, and tissue-repair purposes. Over the

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past decades, the development of variants such as low-intensity pulsed ultrasound (LIPUS), phonophoresis (the use of ultrasound to enhance transdermal drug delivery), and, more recently, low-intensity focused ultrasound for neuromodulation has expanded the range of investigated applications of this technology in knee osteoarthritis, although several of these applications remain at an early, exploratory stage of clinical investigation (ABED et al., 2024; ILFELD et al., 2025). Recent studies have also explored combining ultrasound with other physical therapy interventions, such as therapeutic exercise and extracorporeal shockwave therapy, seeking synergistic effects on pain and joint function (YANG et al., 2025; KHADOUR; KHADOUR; ALHARBI, 2025).

Despite its widespread use, the literature on the effectiveness of therapeutic ultrasound in knee osteoarthritis is still marked by considerable methodological heterogeneity regarding application parameters (frequency, intensity, duty cycle, exposure time), whether or not it is combined with other interventions (exercise, electrotherapy, laser therapy, shockwave therapy), and the outcome instruments used (ATAN et al., 2024; CP et al., 2024; SHARMA et al., 2025). This dispersion hinders the derivation of uniform clinical recommendations and justifies periodic reviews that update the evidence landscape, particularly given the growing output of randomized controlled trials in recent years.
Beyond the analgesic and functional effects classically attributed to therapeutic ultrasound, recent mechanistic investigations have demonstrated its impact on the biomechanical properties of periarticular tissues, such as the stiffness and gliding of the infrapatellar fat pad, a structure implicated in anterior knee pain (IKEDA et al., 2024; IKEDA et al., 2026), as well as on inflammatory biochemical markers in the synovial fluid when combined with other physical modalities (KHADOUR; KHADOUR; ALHARBI, 2025). These findings reinforce the biological plausibility of the observed clinical effects and justify a systematic update of the evidence on this topic.

This integrative review was designed to address the following guiding question: what is the effectiveness of therapeutic ultrasound, across its different modalities, on pain and function outcomes in men and women aged 20 to 70 years with knee osteoarthritis, according to randomized controlled trials published between 2020 and 2026?

Objective:-

To synthesize and critically analyze the evidence available from randomized controlled trials, published between 2020 and 2026, on the application of therapeutic ultrasound — in its continuous, low-intensity pulsed, phonophoretic, and focused modalities — in the conservative management of knee osteoarthritis in adults aged 20 to 70 years, identifying application protocols, assessed outcomes, observed clinical effects, and methodological gaps in the current literature.

Methodology:-

Study design:-

This is an integrative literature review, a method that allows the incorporation of studies with different designs to provide a broad understanding of the phenomenon under investigation, following the following steps: (1) identification of the research question; (2) definition of inclusion and exclusion criteria and literature search; (3) categorization of studies; (4) evaluation of the included studies; (5) interpretation of results; and (6) synthesis of knowledge.

PICO strategy:-

To structure the research question and guide the search strategy, the PICO framework was adopted, a strategy widely used in health literature reviews to break down the clinical question into its constituent elements:
P (Population): men and women aged 20 to 70 years with a clinical and/or radiographic diagnosis of knee osteoarthritis;
I (Intervention): application of therapeutic ultrasound, in its continuous, low-intensity pulsed (LIPUS), phonophoretic, or low-intensity focused modalities, alone or combined with other physical therapy interventions;
C (Comparison): no intervention, sham procedure, placebo, or other isolated therapeutic modalities (therapeutic exercise, laser therapy, extracorporeal shockwave therapy, among others);
O (Outcomes): pain reduction (Visual Analogue Scale – VAS, Numerical Rating Scale – NRS, algometry) and functional improvement (WOMAC, Lequesne index, range of motion, gait parameters), in addition to secondary biomechanical and biochemical outcomes, when available.
To these four elements, the study design (S) was added as a complementary component, restricted to randomized controlled trials, forming the PICOS strategy that underpinned both the construction of the search terms and the eligibility criteria detailed below.

Search strategy:-
The search was conducted in the PubMed/MEDLINE, SciELO, Google Scholar, and PEDro (Physiotherapy Evidence Database) databases, using English and Portuguese descriptors combined with Boolean operators AND/OR, with parentheses grouping the OR terms to avoid ambiguity in operator precedence: ("therapeutic ultrasound" OR "low-intensity pulsed ultrasound" OR "phonophoresis" OR "focused ultrasound") AND ("knee osteoarthritis" OR "knee OA") AND ("randomized controlled trial" OR randomized OR randomised), and their Portuguese equivalents (e.g., "ultrassom terapêutico", "osteoartrite de joelho", "ensaio clínico randomizado"). In the PEDro database, priority was given to the "clinical trial" design filter and to searching the body part/structure "knee" combined with the term "ultrasound".

Eligibility criteria:-
Studies were included if they met the following criteria: (a) randomized controlled trial design; (b) publication between January 2020 and 2026 — eligible studies retained for the primary clinical synthesis span from 2022 to 2026; (c) sample composed of men and women aged 20 to 70 years with a clinical and/or radiographic diagnosis of knee osteoarthritis; (d) use of therapeutic ultrasound (continuous, pulsed, phonophoretic, or focused) as the intervention under evaluation, whether isolated or combined with another resource; (e) assessment of pain and/or function outcomes. Studies were excluded from the primary clinical synthesis if their samples fell exclusively outside the established age range, as well as systematic reviews, preclinical studies, research protocols without published results, and studies in which ultrasound use was restricted to diagnostic purposes or guidance for invasive procedures (e.g., ultrasound-guided genicular nerve blocks), since these do not represent a therapeutic application of the resource. Two randomized crossover trials conducted exclusively in healthy volunteers (IKEDA et al., 2024; IKEDA et al., 2026) did not meet criterion (c) and were therefore analyzed separately as mechanistic/experimental evidence, not pooled with the clinical evidence on patients with knee osteoarthritis. Likewise, one identified trial applied ultrasound only for baseline characterization rather than as the therapeutic intervention under evaluation (KAMAL et al., 2025); as this study did not meet criterion (d), it is reported separately, outside the primary synthesis of therapeutic-ultrasound evidence.

Data extraction and synthesis:-
From the selected studies, the following information was extracted: authorship and year of publication, design and sample size, characteristics of the ultrasound intervention (physical parameters, association with other techniques, treatment frequency and duration), outcome instruments used (Visual Analogue Scale – VAS, Western Ontario and McMaster Universities Osteoarthritis Index – WOMAC, Lequesne index, among others), and main findings. The methodological quality of each included randomized controlled trial was additionally assessed using the Cochrane Risk of Bias tool for randomized trials (RoB 2), covering the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting; the resulting overall judgment for each study (predominantly "some concerns," driven mainly by unblinded participants where masking was not feasible given the intervention, and by incompletely reported allocation concealment) is presented in Table 1; two studies (Yang et al., 2025; Sharma et al., 2025) are marked "unclear" because full-text access to their methods sections was restricted. Data were organized into a summary table (Table 1) and analyzed narratively, grouping studies by the type of ultrasound modality employed and, within each modality, distinguishing whether ultrasound was tested in isolation or as one component of a multimodal protocol, so that gains attributable to adjunct interventions are not presented as evidence of an independent ultrasound effect.

Results:-
The database search and study-selection process is summarized in the PRISMA 2020 flow diagram (Figure 1). Across the combined identification and verification searches, 15 unique studies met the eligibility criteria and were retained: 12 were included in the primary clinical synthesis, 2 were retained as mechanistic evidence from healthy volunteers (not pooled with the clinical evidence), and 1 was excluded from the primary synthesis because ultrasound was not the therapeutic intervention under evaluation. For a defined verification search of PubMed/MEDLINE, SciELO/Google Scholar and PEDro, 26 records were identified, 4 duplicates were removed, 22 unique records were screened, 13 were excluded at the title/abstract stage (5 systematic/narrative reviews, 5 preclinical/animal/in vitro studies, 1 wrong population, 2 outside the 2020–2026 window), 9 were assessed in full text, and 1 was excluded at that stage (Jo et al., 2022, a single-arm study without a comparator group, and therefore not a randomized controlled trial); the remaining 8 were included, of which 3 (Khadour et al., 2025; Yang et al., 2025; Ilfeld et al., 2025) overlapped with studies already retained from an earlier search and 5 (Fayez et al., 2022; Jia et al., 2022; Samaan et al., 2022; Karakaş et al., 2020; Kitano et al., 2023) were newly added. The search identified a set of randomized controlled trials published between 2022 and 2026 that met the eligibility criteria for

the primary clinical synthesis, encompassing different modalities of therapeutic ultrasound applied to knee osteoarthritis: conventional continuous ultrasound used as part of multimodal physical therapy protocols, low-intensity pulsed ultrasound (LIPUS), drug phonophoresis, and low-intensity focused ultrasound for neuromodulation. Two additional randomized crossover trials conducted in healthy volunteers, and one trial in which ultrasound was not the therapeutic intervention under evaluation, are reported separately (see "Mechanistic studies in healthy participants" and the note on Kamal et al., 2025, below) and were not pooled with the clinical evidence. Table 1 summarizes the main characteristics, methodological quality, and findings of the included studies, grouped by ultrasound modality.

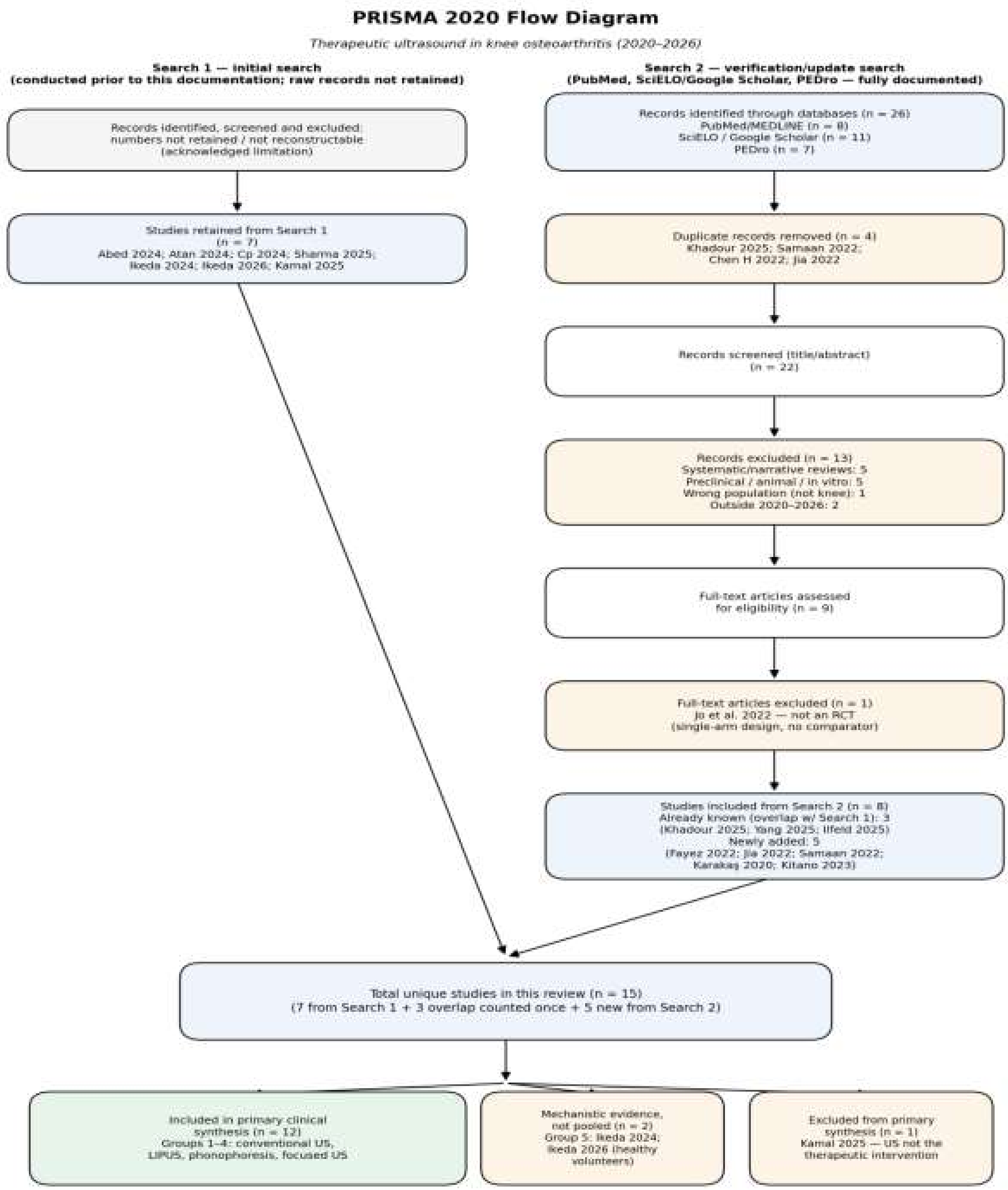

Figure 1 – PRISMA 2020 flow diagram of study identification, screening and inclusion.

Table 1 – Summary of randomized controlled trials on therapeutic ultrasound in knee osteoarthritis (2022–2026), classified by evidence group, with risk-of-bias assessment

Group	Author/ Year	Design and sample	OA severity	Ultrasound intervention & comparator	Duration	Main outcomes	Risk of bias (RoB 2)	DOI
Group 3 – Phonophoresis (includes a conventional-US comparison arm)	Abed et al. (2024)	RCT, n=78 (100 screened, 15 ineligible, 7 declined); randomization via online generator; allocation concealed (sealed opaque envelopes)	Mild-to-moderate	Metformin 1.2% phonophoresis + exercise vs. phonophoresis alone vs. conventional therapeutic US (neutral gel), 3x/week	4 weeks	All groups improved on VAS, WOMAC and ROM; exercise-combined group superior to the other conditions ($p<0.05$)	Some concerns – single-blind (patients blinded; outcome assessor NOT blinded, acknowledged by authors as a limitation)	https://doi.org/10.1186/s13018-024-05120-0
Group 2 – LIPUS	Yang et al. (2025)	RCT, n=90 (30/group)	Not reported	LIPUS alone vs. aerobic exercise (AE) vs. LIPUS+AE. Primary outcome: gait parameters (stride speed/length, distance); secondary: NRS pain (not VAS) and Lequesne index	12 weeks	LIPUS+AE superior to LIPUS or AE alone in pain (NRS), Lequesne index and gait parameters	Unclear – randomization/blinding not reported in the available sources	https://doi.org/10.1097/MD.0000000000043343
Group 2 – LIPUS (combined with shockwave therapy)	Khadour; Khadour; Alharbi (2025)	RCT, n=220 (110/group); 236 screened, 16 excluded (8 ineligible, 3 refused, 5 lost); computer-generated block randomization; allocation concealed (opaque sequential envelopes, prepared by an uninvolved person)	K-L grade I–III	LIPUS 1 MHz/0.5 W/cm² (20-min daily) + shockwave therapy (LESWT) vs. shockwave therapy alone (R-ESWT)	5 weeks (5x/week)	LESWT superior in clinical effectiveness, WOMAC, VAS, ROM; reduced IL-1β, TNF-α, MMP-3	Some concerns – outcome assessors blinded, but patients not blinded (inherent to the intervention type)	https://doi.org/10.1186/s13018-025-06384-w
Group 2	Samaan	RCT, patients	K-L	High-intensity laser	Asses	Both groups	Some	https://doi.org/1

– LIPUS (compared with high-intensity laser therapy)	et al. (2022)	with knee OA, K-L grade 2–3, under 65 years old	grade 2–3	therapy (HILT) + exercise vs. LIPUS + exercise	sed post-treatment and at 12-week follow-up	improved significantly in VAS, WOMAC and Lequesne index (pain $p<0.001$, function $p<0.012$); no significant difference between HILT and LIPUS groups on any outcome	concerns – random allocation and concealment confirmed (PEDro 8/10), but patients and therapists not blinded	0.1111/1756-185X.14361
Group 2 – LIPUS (targeting the infrapatellar fat pad)	Kitano et al. (2023)	RCT, double-blind, sham-controlled, n=26 (13/group); registered UMIN000038501; age significantly higher in LIPUS group (63.5±8.6y) vs. sham group (56.5±7.5y), $p<0.05$	K-L grade II (100% both groups)	LIPUS (3 MHz, 120 mW/cm², 20 min) applied to the infrapatellar fat pad + home exercise vs. sham LIPUS + home exercise, 2x/week	5 weeks (10 sessions)	LIPUS group showed significantly greater reduction in patellar tendon-tibial angle (IFP swelling marker, $p<0.01$), VAS pain ($p<0.01$), Kujala score ($p<0.01$) and knee-extension ROM ($p<0.05$) vs. exercise-only group; no significant differences in WOMAC, muscle strength, TUG or two-step test	Some concerns – randomization and double-blinding well described, but unadjusted baseline age imbalance between groups and small sample size (n=13/group)	https://doi.org/10.1589/jpts.35.163
Group 4 – Focused ultrasound / neuromodulation (pilot feasibility)	Ilfeld et al. (2025)	Pilot RCT, 3 arms (0 W sham / 18 W / 27 W), allocation ratio 1:2:2; both participants and outcome assessors masked	Not reported	Low-intensity focused ultrasound (neuromodulation) targeting knee structures vs. sham	[AUTHOR: verify]	Feasibility study; potential analgesic effect via reversible nerve conduction block, no relevant adverse events	Some concerns – randomization and double masking adequately described, but small pilot	https://doi.org/10.1002/jum.16706

							sample limits precision	
Group 3 – Phonophoresis	Sharma et al. (2025)	Partially randomised patient-preference RCT: 108/116 randomized, 8 allocated to HILT by patient preference; 109 analyzed (57 HILT/52 IGP); registered NCT04320914	K-L grades I–IV	Ibuprofen gel phonophoresis (IGP, 8 min) vs. high-intensity laser therapy (HILT, 15 min) + home exercise 3x/week	3 weeks	HILT significantly superior to IGP on WOMAC (pain, stiffness, physical function, total) and most SF-36 domains (physical function, role-physical, energy/fatigue, social functioning, pain, general health) after adjusting for baseline differences (Quade's ANCOVA); no group difference in SF-36 role-emotional or emotional well-being	Some concerns – partially randomised patient-preference design (8/116 not randomized); outcome-assessor blinding not reported; baseline imbalances present but adjusted for via ANCOVA	https://doi.org/10.1007/s10103-025-04613-6
Group 1 – Conventional US as a component of a multimodal protocol	Atan et al. (2024)	Single-blinded RCT, n=30 women, registered NCT05319964	Moderate-to-severe (advanced)	Therapeutic US + TENS + hot pack in all groups; anti-gravity treadmill vs. traditional treadmill vs. control	8 weeks	Anti-gravity group showed greater pain reduction and functional improvement; traditional treadmill reduced femoral cartilage thickness	Some concerns – single-blind design; randomization method and allocation concealment not accessible (paywalled)	https://doi.org/10.1007/s11845-024-03836-w
Group 1 – Convent	Cp et al. (2024)	RCT, n=30; randomization by lottery	Grade IV (Kellgre	Conventional physiotherapy (US 1.5 W/cm², 7 min +	4 weeks	Both improved LEFS scores; adding	Some concerns –	https://doi.org/10.1038/s41598-024-67511-x

ional US as a component of a multimodal protocol		method (SPSS) via an independent researcher; outcome assessor blinded, no dropouts	n-Lawrence)	isometric strengthening) vs. same baseline treatment + shockwave therapy		shockwave therapy increased the gain (81.9% vs. 48.1%)	assessor blinded, patients not blinded; allocation concealment not described	
Group 1 – Conventional US as a component of a multimodal protocol	Fayez et al. (2022)	RCT, n=80 (20/group), 4 arms; randomization via online generator by an independent researcher; registered NCT05151432	Moderate (unilateral)	Pulsed US (1 MHz, 1 W/cm², 20% duty cycle, ~9.5 min) + exercise vs. PEMF + exercise vs. US+PEMF+exercise vs. sham US+sham PEMF+exercise, 3x/week	4 weeks	US+PEMF+exercise group showed the largest gains in VAS, WOMAC, ROM, TUG and 10-m walk test vs. all other groups ($p<0.001$)	Some concerns – randomization/allocation by an independent researcher described; blinding of outcome assessors not reported	https://doi.org/10.53730/ijhs.v6nS5.10926
Group 1 – Conventional US as a component of a multimodal protocol	Jia et al. (2022)	RCT, n=114 (57/group), observer-blinded; opaque sequential randomization envelopes prepared by an uninvolved person; registered ChiCTR2000032735	Mild-to-moderate (authors note the sample was relatively young)	Focused LIPUS (0.6 MHz, 20% duty cycle, 20 min/day) vs. pulsed shortwave diathermy (PSWD), both plus standard daily-care advice	12 days (with follow-up to 24 weeks)	FLIPUS superior to PSWD in WOMAC, NRS, ROM, TUG and GRC scores at 12 days, sustained through 24-week follow-up; no adverse events in either group	Some concerns – observer-blinded only (patient blinding not feasible given the devices); intention-to-treat analysis used	https://doi.org/10.1038/s41598-022-17291-z
Group 1 – Conventional US as a compon	Karakaş et al. (2020)	RCT, double-blind, sham-controlled, n=96 randomized (48/group), 75	K-L grade ≤3	Pulsed US (1 MHz, 1 W/cm², pulsed ratio 1:4, 10 min) vs. sham US, 3x/week, all + home exercise	8 weeks (12-week follow-up)	Both groups improved significantly in pain and function ($p<0.001$); no significant	Some concerns – double-blind, registere	https://doi.org/10.1177/0269215520942953

ent of a multimodal protocol		completed (39/36); ages 45–75; ACR criteria; registered NCT03705039				difference between active and sham US on pain, function, femoral cartilage or synovial sac thickness	d trial; exact allocation-concealment method not accessible (paywalled)	
Group 5 – Mechanistic study in healthy volunteers (does not meet the knee-OA population criterion)	Ikeda et al. (2024)	Crossover RCT, single-blind (sham-controlled), n=24, healthy	N/A (healthy volunteers)	HICUS 1 MHz/2.5 W/cm², 100% duty cycle, 5 min, over the infrapatellar fat pad, vs. sham (applied on 2 separate days)	Single session (acute crossover)	Reduced stiffness and improved fat pad gliding at 10° of flexion, effect sustained for 15 min	Some concerns – single-blind (not double-blind as originally stated); randomized, sham-controlled	https://doi.org/10.1016/j.ultrasmedbio.2024.09.006
Group 5 – Mechanistic study in healthy volunteers (does not meet the knee-OA population criterion)	Ikeda et al. (2026)	Crossover RCT, single-blind (sham-controlled, same research group/protocol as Ikeda 2024), n=20, healthy	N/A (healthy volunteers)	HICUS combined with active knee exercise, same protocol as the previous study, vs. sham	Single session (acute crossover)	Exercise + HICUS enhanced the reduction in fat pad stiffness across different flexion angles	Some concerns – blinding level presumed single-blind by analogy with the companion 2024 study from the same research group and protocol, as the 2026 paper's own methods section was not accessible for	https://doi.org/10.1016/j.jbiomech.2026.113191

							independent confirmation	
Excluded from primary synthesis – ultrasound was not the therapeutic intervention evaluated	Kamal et al. (2025)	RCT, n=130 randomized (160 screened), 112 completed (58 SG/62 CG); randomization by an independent physician; NO blinding of participants or assessors (explicitly acknowledged by the authors as a limitation)	K-L grades I–IV (mostly I–III)	Therapeutic US (part of a conventional electrotherapy/TENS /laser protocol) used only for baseline quadriceps-thickness characterization, not as the evaluated intervention; comprehensive program with gait training vs. conventional program	2-week intervention (10 sessions), reassessed at 6 weeks	Gait training showed superior functional gains; ultrasound was used only for baseline characterization and did not inform the intervention	Not applicable (US not evaluated as a therapeutic intervention); other domains: high risk (no blinding of participants or assessors, per the authors' own statement)	https://doi.org/10.3390/medicina61122118

Source: prepared by the author (2026), based on data retrieved from PubMed and from the original publications.

Note: studies are classified into five evidence groups — (1) conventional therapeutic ultrasound as a component of a multimodal protocol, (2) LIPUS, (3) phonophoresis, (4) focused ultrasound/neuromodulation, and (5) mechanistic studies in healthy volunteers — plus a separate note for Kamal et al. (2025), which was excluded from the primary clinical synthesis because ultrasound was not the therapeutic intervention evaluated. Risk-of-bias ratings (RoB 2, overall judgment) were derived from the original publications where methodological detail was available (open-access sources); for Yang et al. (2025) and Sharma et al. (2025), full-text access was restricted and the rating is marked "Unclear" pending the authors' own reading of the complete methods. Abbreviations: AE, aerobic exercise; ChiCTR, Chinese Clinical Trial Registry; DOI, digital object identifier; GRC, Global Rating of Change scale; HICUS, high-intensity continuous ultrasound; HILT, high-intensity laser therapy; IGP, ibuprofen gel phonophoresis; IL-1β, interleukin-1 beta; K-L, Kellgren-Lawrence grade; LEFS, Lower Extremity Functional Scale; LESWT, LIPUS-augmented extracorporeal shockwave therapy; LIPUS, low-intensity pulsed ultrasound; MMP-3, matrix metalloproteinase-3; N/A, not applicable; NCT, National Clinical Trial (ClinicalTrials.gov registration number); NRS, Numerical Rating Scale; OA, osteoarthritis; PEMF, pulsed electromagnetic field; PSWD, pulsed shortwave diathermy; RCT, randomized controlled trial; R-ESWT, radial extracorporeal shockwave therapy; RoB 2, Cochrane risk-of-bias tool for randomized trials, version 2; ROM, range of motion; SF-36, 36-Item Short Form Health Survey; SG/CG, study group/control group; TENS, transcutaneous electrical nerve stimulation; TNF-α, tumor necrosis factor alpha; TUG, Timed Up and Go test; US, (therapeutic) ultrasound; VAS, Visual Analogue Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Therapeutic ultrasound as a component of multimodal rehabilitation:-

In several studies, continuous therapeutic ultrasound appeared as a baseline component of conventional physical therapy protocols, generally combined with electrotherapy (TENS), superficial thermotherapy, and kinesiotherapy, serving as a comparator or standard treatment against more recent interventions. Atan et al. (2024) compared anti-gravity treadmill training with traditional treadmill training, both combined with hot packs, TENS, and therapeutic ultrasound, observing a significant reduction in pain in both the intervention and control groups, with a more pronounced functional improvement in the anti-gravity treadmill group, whereas traditional treadmill training was associated with reduced femoral cartilage thickness. Similarly, Cp et al. (2024) used therapeutic ultrasound as part of conventional physiotherapy in patients with grade IV osteoarthritis, finding significant functional improvement in both the conventional physiotherapy group alone and the group that additionally received extracorporeal shockwave therapy, with a greater gain in the latter. Fayez et al. (2022) combined pulsed ultrasound with pulsed electromagnetic field therapy and exercise in patients with moderate knee osteoarthritis, finding that the triple-combination group achieved the largest improvements in pain, range of motion and functional mobility. Jia et al. (2022) compared focused low-intensity pulsed ultrasound with pulsed shortwave diathermy, both alongside standard daily-care advice, and found that focused ultrasound produced greater and more sustained improvements in pain and function through 24 weeks of follow-up. In contrast, Karakaş et al. (2020), in a double-blind, sham-controlled trial, found no additional benefit of active pulsed ultrasound over sham ultrasound on pain, function, femoral cartilage or synovial sac thickness, despite both groups improving from baseline — a negative finding that illustrates the heterogeneity of results within this evidence group.

Low-intensity pulsed ultrasound (LIPUS):-

LIPUS was investigated both alone and in combination with aerobic exercise or extracorporeal shockwave therapy. Yang et al. (2025) demonstrated that combining LIPUS with aerobic exercise produced greater gains in pain, Lequesne index, and gait kinematic parameters compared with each intervention alone, suggesting a synergistic effect between the electrophysical agent and voluntary mechanical stimulation. Khadour, Khadour, and Alharbi (2025) compared LIPUS combined with radial extracorporeal shockwave therapy (LESWT) with shockwave therapy alone, finding a higher clinical effectiveness rate in the combined group, accompanied by a more pronounced reduction in synovial fluid inflammatory markers (interleukin-1β, tumor necrosis factor-α, and metalloproteinase-3), which provides evidence of a biochemical mechanism underlying the observed clinical effect. Samaan et al. (2022) compared LIPUS plus exercise with high-intensity laser therapy plus exercise and found both groups improved significantly in pain and function, with no significant difference between the two modalities, suggesting comparable short- and mid-term effectiveness. Kitano et al. (2023), targeting LIPUS specifically at the infrapatellar fat pad in patients with knee osteoarthritis, found significantly greater improvements in pain, knee extension range of motion and the Kujala functional score compared with exercise alone, alongside a reduction in an ultrasonographic marker of fat-pad swelling; however, the LIPUS and control groups differed significantly in baseline age, an imbalance the authors themselves flagged as a limitation.

Phonophoresis:-

Phonophoresis, a technique that uses ultrasound to deliver drugs transdermally, was evaluated in two relevant studies. Abed et al. (2024) compared metformin phonophoresis combined with therapeutic exercise, phonophoresis alone, and conventional therapeutic ultrasound (neutral gel), finding significant improvement in all groups after four weeks, but with statistically significant superiority in the group that combined phonophoresis with exercise across all assessed outcomes (pain, range of motion, and function). Sharma et al. (2025) compared ibuprofen gel phonophoresis with Class IV high-intensity laser therapy in a population living in mountainous terrain, finding significant within-group improvement in both arms, with high-intensity laser therapy showing a significantly larger adjusted treatment effect than phonophoresis on most pain and functional domains; notably, 8 of the 116 participants were allocated to the laser group by patient preference rather than randomization.

Low-intensity focused ultrasound (neuromodulation):-

A more recent line of investigation concerns the use of low-intensity focused ultrasound as a non-invasive neuromodulation technique, with the potential for reversible blockade of peripheral nerve conduction, analogous to a local anesthetic block. Ilfeld et al. (2025) conducted a randomized, masked, sham-controlled pilot study aimed at assessing the feasibility and safety of this technique in patients with knee osteoarthritis pain, with no relevant complications reported, indicating that this is an emerging line of research that still requires larger-scale efficacy trials.

Mechanistic studies in healthy participants:-

Two studies conducted by Ikeda et al. (2024; 2026), although carried out in healthy volunteers rather than specifically in patients with knee osteoarthritis, were considered relevant for understanding the biomechanical mechanisms of therapeutic ultrasound, as they demonstrated that high-intensity continuous ultrasound (HICUS), alone or combined with active knee exercise, reduces stiffness and improves gliding of the infrapatellar fat pad, a structure frequently implicated in anterior knee pain and potentially relevant to the pathophysiology of osteoarthritis.

Discussion:-

The synthesis of the included studies suggests that some ultrasound-based interventions may provide additional improvements in pain and function in patients with knee osteoarthritis when incorporated into multimodal rehabilitation programs; however, because most included trials administered ultrasound alongside exercise, TENS, hot packs, laser therapy, or shockwave therapy, the independent clinical efficacy of therapeutic ultrasound itself cannot be established from this body of evidence. A recurring finding stands out: combining ultrasound with active interventions — particularly therapeutic exercise — produced greater gains than isolated application in the studies that tested this comparison (ABED et al., 2024; YANG et al., 2025), which is consistent with international osteoarthritis management guidelines that position therapeutic exercise as a first-line intervention and electrophysical agents as adjuncts. This pattern should be interpreted as evidence for ultrasound as an adjunct to active rehabilitation, not as evidence of a stand-alone therapeutic effect.

Within the LIPUS modality specifically, however, the evidence is not uniformly positive. While Khadour, Khadour, and Alharbi (2025), Yang et al. (2025), Samaan et al. (2022), Kitano et al. (2023) and Jia et al. (2022) reported significant benefits of LIPUS — whether combined with shockwave therapy, aerobic exercise, or targeted at a specific tissue such as the infrapatellar fat pad — Karakaş et al. (2020), in a double-blind, sham-controlled trial using a broadly comparable pulsed ultrasound protocol, found no additional benefit of active ultrasound over sham on pain, function, femoral cartilage, or synovial sac thickness, despite both groups improving from baseline. This divergence indicates that “LIPUS” should not be treated as a therapeutically homogeneous category: target tissue, intensity, treatment duration, and, critically, the presence of a genuine sham comparator appear to influence whether a treatment effect is detected, and the negative finding of Karakaş et al. (2020) tempers the otherwise favorable picture drawn from the remaining LIPUS trials.

From the standpoint of mechanisms of action, the findings by Khadour, Khadour, and Alharbi (2025) regarding the reduction of synovial inflammatory markers after LIPUS combined with shockwave therapy, as well as the biomechanical studies by Ikeda et al. (2024; 2026) on the reduction of infrapatellar fat pad stiffness, provide biological plausibility that therapeutic ultrasound may act not only through symptomatic modulation but also through interference with inflammatory processes and the mechanical properties of periarticular tissues. It should be emphasized that the Ikeda et al. studies were conducted in healthy volunteers rather than patients with knee osteoarthritis and used acute, single-session protocols; they therefore support biological plausibility but do not, by themselves, establish clinical efficacy in the target population, and were not included in the primary clinical synthesis of this review.

The emergence of low-intensity focused ultrasound as a neuromodulation strategy (ILFELD et al., 2025) broadens the rationale for ultrasound use beyond its classic thermal and mechanical effects, bringing it closer to non-invasive interventional techniques for chronic joint pain control. However, as the only available study is a pilot, sham-controlled feasibility trial, its results establish safety and feasibility rather than clinical efficacy; larger, adequately powered efficacy trials are needed before conclusions about analgesic benefit can be drawn. Adverse events and tolerability were inconsistently reported across the included trials: only Ilfeld et al. (2025) explicitly reported the absence of relevant adverse events, while most other studies did not describe safety outcomes in detail; future trials should systematically report adverse events and tolerability for each ultrasound modality.

Among the limitations identified in the analyzed literature, the following stand out: (a) substantial heterogeneity in the physical parameters of ultrasound application (frequency, intensity, duty cycle, exposure time), which hinders direct comparison between studies and the definition of an optimal protocol; (b) a predominance of small samples and single-center designs, limiting the generalizability of findings; (c) variability in the outcome instruments used, although the Visual Analogue Scale and WOMAC are the most recurrent; (d) a scarcity of studies isolating the specific effect of therapeutic ultrasound without simultaneous association with other interventions, hindering causal attribution of the observed effects; (e) sample age ranges not always matching the 20-to-70-year range adopted in this review, with a predominance of middle-aged and older participants, reflecting the epidemiological profile of knee osteoarthritis; (f) the risk-of-bias assessment (RoB 2) of the included trials was completed for most studies using methodological detail available in the original publications, yielding predominantly "some concerns" ratings driven by a lack of participant and/or outcome-assessor blinding (inherent to several of the compared physical interventions) and by incomplete allocation-concealment reporting; two studies (Yang et al., 2025; Sharma et al.,

2025) could not be fully assessed because full-text access was restricted, and their RoB 2 rating remains "unclear" until their complete methods sections can be consulted; and (g) the study-selection process is fully documented by a PRISMA 2020 flow diagram (Figure 1) for a defined verification search of PubMed/MEDLINE, SciELO/Google Scholar and PEDro (26 records identified, 22 screened after de-duplication, 9 assessed in full text, 8 included); however, the identification and screening counts for an earlier search that contributed seven of the twelve primarily-synthesized studies (Abed et al., 2024; Atan et al., 2024; Cp et al., 2024; Sharma et al., 2025; and the two Ikeda mechanistic studies and Kamal et al., 2025) were not retained and could not be reconstructed retrospectively, so the flow diagram cannot report a single fully auditable trail for the review as a whole — a transparency gap that should be corrected, ideally by re-running and documenting that search, before submission.

Additionally, it was observed that a considerable share of recent scientific output on “ultrasound” and knee osteoarthritis refers to the use of ultrasound as an imaging tool to guide invasive procedures (genicular nerve blocks, chemical neurolysis, intra-articular injections), rather than as an electrophysical therapeutic resource per se. Such studies were deliberately excluded from this review, as they did not correspond to the proposed object of investigation, although their frequency in the literature signals a trend toward shifting the clinical use of ultrasound from direct therapeutic application toward guidance for minimally invasive interventions.

Conclusion:-

Current evidence from randomized controlled trials published between 2022 and 2026 suggests that some ultrasound-based interventions — including continuous, low-intensity pulsed, and phonophoretic modalities — may provide additional improvements in pain and function when incorporated into multimodal rehabilitation programs for adults aged 20 to 70 years with knee osteoarthritis, particularly when combined with therapeutic exercise. However, because most of these trials administered ultrasound as part of multimodal protocols and did not include an ultrasound-only comparison arm, the independent clinical efficacy of therapeutic ultrasound remains uncertain; this uncertainty is compounded by substantial parameter heterogeneity, small sample sizes, and an incomplete risk-of-bias assessment of the included trials. Low-intensity focused ultrasound is an emerging neuromodulation strategy for which only pilot feasibility data are currently available, and its clinical efficacy has not yet been established. Future clinical trials should isolate the specific effect of therapeutic ultrasound through dedicated ultrasound-only comparison arms, standardize application parameters, use comparable outcome instruments, and report a formal risk-of-bias assessment, in order to support more robust clinical recommendations for physical therapy practice.

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