Systematic Review



Efficacy of Ultrasound-Guided Pulsed Radiofrequency in the Management of Pain **Caused by Knee Osteoarthritis: A Systematic Review and Meta-Analysis**

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Background: Knee osteoarthritis (KOA) is a prevalent degenerative disease that leads to significant disability among elderly individuals. Ultrasound-quided pulsed radiofrequency (UG-PRF) has been shown to be a nonpharmacological, less invasive alternative to other treatment methods for reducing severe chronic joint pain.

Objective: To establish whether using UG-PRF to manage KOA pain improves short-term and long-term clinical outcomes for patients with that condition.

Study Design: A systematic review and meta-analysis.

Methods: Within PubMed, MEDLINE, Embase, and the Cochrane Library, a comprehensive search of relevant studies published from those databases' inception through July 11, 2024, was conducted. Studies assessing the effectiveness of UG-PRF in KOA patients were selected based on predefined inclusion criteria that required the exclusive use of UG for PRF delivery. Data extraction and synthesis utilized a random-effects model to analyze outcomes related to pain reduction and physical function improvement. We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to appraise the robustness of the evidence.

Results: A total of 658 records were identified, with 8 studies involving 688 patients included in the meta-analysis. UG-PRF was associated with significant reductions in visual analog scale (VAS) scores at one month (MD = -14.40; 95% CI [-19.61, -9.19]; P < 0.01; GRADE: high), 3 months (MD = -7.83; 95% CI [-10.38, -5.27]; P < 0.01; GRADE: high), 6 months (MD = -5.64; 95% CI [-7.62, -3.66]; P < 0.01; GRADE: high), and 12 months after treatment (MD = -1.08; 95% CI [-1.94, -0.23]; P < 0.01; GRADE: moderate), and those results all exhibited substantial heterogeneity (I^2 > 90%; P < 0.01). Similarly, secondary outcomes were associated with significant improvements in WOMAC scores at one month (MD = -20.71; 95% CI [-27.43, -13.99]; P < 0.01; GRADE: high) and 3 months after treatment (MD = -22.09; 95% CI [-31.33, -12.84]; P < 0.01; GRADE: high), with high heterogeneity ($I^2 = 77\%$ at one month, 89% at 3 months; P < 0.01). Sensitivity analysis confirmed the robustness of results, except for the VAS at 12 months. Subgroup analysis indicated no significant differences across treatment targets (P > 0.05). Publication bias was suggested for VAS outcomes at one and 6 months, yet fail-safe analysis (N = 86 required to nullify the 12-month effect) and trim-and-fill methods maintained the significance of the findings.

Limitations: Incomplete reporting of WOMAC scores constrain the robustness of the study's conclusions, particularly as far long-term efficacy as is concerned. Additionally, the current study's limited data on nerve regeneration mechanisms after pulsed radiofrequency ablation (RFA) restricts a comprehensive understanding of the factors that contribute to pain recurrence at the 12-month

Conclusions: UG-PRF effectively reduces KOA pain and improves function in the short term, with significant benefits observed up to 6 months after treatment. However, the analgesic effects diminish by 12 months, highlighting the need for further research into the long-term efficacy and underlying mechanisms of this technique. The meta-analysis supports the clinical application of UG-PRF as a safe, minimally invasive option for managing KOA pain in adults aged \geq 40 years (mean 62.1 \pm 9.4 years), though sustained pain relief may require additional interventions.

Key words: Knee osteoarthritis, ultrasound guided, pulsed radiofrequency, visual analog scale, meta-analysis, systematic review

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nee osteoarthritis (KOA), a highly prevalent degenerative joint disorder, imposes substantial socioeconomic and clinical burdens on aging populations, with radiographic prevalence exceeding 37% in adults over 60 years of age, while 33% of patients endure chronic pain and 25% develop activity-limiting disability (1,2). These functional and psychosocial consequences manifest further as reduced independence in instrumental activities of daily living (IADLs), progressive mobility impairment, and diminished psychosocial well-being, driven primarily by persistent pain-related sleep disturbances and social isolation. As the global population ages, optimizing KOA management has emerged as a public health imperative to mitigate the condition's multidimensional impact on individual quality of life and health care system sustainability (3,4).

Recent studies have demonstrated growing interest in the application of ultrasound-guided pulsed radiofrequency (UG-PRF) for managing KOA, with research efforts concentrated on elucidating the neuroanatomy of genicular nerves, refining patient selection criteria, and assessing the relative efficacy and safety of PRF compared to conventional treatments (5). Sam et al recently synthesized evidence on PRF's modulation of nociceptive signaling, immune activity, and synaptic plasticity, providing a critical foundation for understanding PRF's clinical effects[6]. Advancements in RFA (radiofrequency ablation) techniques, including cooled RF (CRF) and PRF, have been explored to enhance therapeutic outcomes, with randomized controlled trials indicating that genicular nerve RFA (GNRFA) may outperform intra-articular steroid injections, viscosupplementation, and oral analgesics in pain reduction and functional improvement (7,8). Meta-analyses have corroborated the effectiveness of RFA in decreasing pain and enhancing knee function over extended periods (8). Additionally, innovative approaches such as cooled RFA (CRFA), which induces larger local neuronal damage, and PRF, which offers a minimally neurodestructive alternative to other techniques, have gained traction in clinical

practice (9,10). However, despite these advancements, there is a paucity of research evaluating the long-term outcomes of PRF (11,12). These gaps highlight the need for comprehensive analyses to determine the short- and long-term effectiveness and safety of PRF techniques in the management of KOA.

For those reasons, we designed our study to undertake a systematic review and meta-analysis to establish whether using UG-PRF as a treatment for KOA pain could improve short- and long-term clinical outcomes.

METHODS

Protocol and Registration

This systematic review and meta-analysis was conducted in strict adherence to the guidelines described in the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2020 (13) (PRISMA-P) (Supplemental Material). The research is duly registered with the International Prospective Registry of Systematic Reviews (PROSPERO) and bears the registration number CRD42024626581. No amendments were made to the information provided at registration or in the protocol. No specific funding was received for this study. The review was conducted independently without financial or nonfinancial support from any external organization. The authors declare no competing interests related to this systematic review and meta-analysis.

Search Strategy

The search for relevant studies was conducted across multiple databases: PubMed, MEDLINE, Embase, and the Cochrane Library, with a search deadline of July 11, 2024. No language restrictions were applied, and only studies published in English were included. Two experienced reviewers (Lai and Luo), who had a rich history of identifying pertinent studies, crafted the search strategy meticulously. The search strategy included terms such as "ultrasound-guided pulsed radiofrequency," "PRF," "saphenous nerve," "sciatic nerve," and "genicular nerve." Mesh terms used and

the number of results retrieved from each database are illustrated in the annex (Suppl. Table 1). For a more comprehensive approach, both authors also scrutinized the reference sections of relevant articles to identify additional potential studies for consideration.

Selection Criteria

Studies were included if they met the following criteria: (1) the effectiveness of PRFA was assessed; (2) the study focused on the use of UG-PRF to target the genicular nerves or intra-articular regions in patients with KOA; (3) the study measured pain levels on the Visual Analog Scale (VAS), Numeric Rating Scale (NRS-11), or Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC); (4) a physical function outcome score was used to assess patients' physical function; and (5) the article was published in English. Papers were excluded if they were: (1) studies that employed non-UG techniques or traditional RFA; (2) animal or cadaver studies; (3) editorials or letters to the editor; (4) reviews or metanalyses; (5) conference abstracts; or (6) studies that did not report outcomes on VAS, NRS-11, or WOMAC scores.

The selection of studies for inclusion was carried out in 2 stages. The first was abstract and title selection; the second was full text selection. Abstract and title selection was performed by reviewers Lai and Luo, who worked collaboratively to screen the initial records. Full text selection was performed independently by Lai. Duplicate studies were identified and removed using the clinical scientific research platform EndNote™ version X10 (Clarivate). Any disagreements during the selection process were resolved by the third reviewer, Liu. The characteristics of the included studies were extracted, including each study's country of origin, population characteristics (such as age and gender), follow-up duration, and relevant clinical outcomes (e.g., pain reduction and physical function improvement).

Data Analysis

The data extraction and processing were conducted by the aforementioned 2 reviewers, Lai and Luo, who reviewed and extracted the relevant data from the included studies independently. The data extraction process encompassed a variety of study characteristics, including country of origin, population, gender distribution, follow-up time, mean age, intervention types, RFA methods, intervention parameters, treatment targets, baseline pain scores, and the scoring methods used for outcomes. The work was performed collaboratively, with discrepancies resolved by a third

reviewer, Liu. The detailed information for each study was organized systematically to ensure accuracy and consistency across all studies included in the analysis.

Risk-of-Bias Assessment of Included Studies

The risk of bias for each study was assessed using the Cochrane Risk of Bias tool. The reviews were performed by 2 independent assessors (Lai and Luo), with discrepancies resolved by Liu. Additionally, publication bias was evaluated using funnel plots, and Egger's test was applied to determine whether asymmetry existed. If publication bias was suspected, the trim-and-fill method was used to adjust for missing studies.

Treatment Effect Assessment

The primary outcome measure pre-specified in this meta-analysis was the VAS score, while the secondary outcome encompassed the WOMAC score. Improvements in WOMAC scores encompassed reductions in pain during weight-bearing activities (e.g., walking), decreased morning stiffness, and enhanced capacity for daily tasks such as rising from a seated position. These outcomes were selected based on their relevance to assessing the effectiveness of interventions in managing osteoarthritis and related conditions. To evaluate the robustness of the evidence, the online iteration of GRADEpro GDT software (www.gradepro.org) was deployed; evidence strength was stratified as high, moderate, low, or very low (14,15).

Heterogeneity Assessment

Heterogeneity was assessed using the randomeffects model, and the I² statistic was calculated to determine the degree of variability across studies. Cochran's Q test was performed to evaluate whether the observed variation in effect sizes exceeded what would be expected by chance. The I² values were categorized as mild (25%), moderate (50%), or high (75%) to interpret the heterogeneity levels.

Sensitivity Analysis and Subgroup Analysis

A sensitivity analysis was undertaken to discern the influence of studies characterized by both highrisk and low-risk biases. Furthermore, the potential effect of studies manifesting significant shortcomings in one or multiple pivotal domains was evaluated. To further explore sources of heterogeneity, subgroup analysis and sensitivity analyses were conducted, with particular attention paid to factors such as sample size and treatment protocols, which were potential sources

of variation.

Statistical Analysis

We conducted our meta-analysis with RevMan R5.4.1 software (Nordic Cochrane Centre for the Cochrane Collaboration) and Stata 12 (StataCorp, LLC). For the synthesis of the data, a random-effects model was employed due to the anticipated variability between study designs and populations. Data analysis was performed with continuous variables, which were summarized as either means ± SDs or medians with interquartile ranges (IQR), depending on the distribution of the data. The confidence interval (CI) for all effect estimates was set at 95%. The control-group data were also compared with those of the intervention group to assess the overall effect of the treatments across studies.

RESULTS

A total of 658 records were identified through database searches, comprising 277 from PubMed, 234 from EMBASE, 97 from the Cochrane Library, and 50 from MEDLINE. After the removal of 168 duplicates, 490 records remained for screening. Of those, 407 records were excluded based on their titles and abstracts, including 53 conference abstracts, 2 letters, 14 comments, 72 reviews/meta-analyses, 9 trial protocols, and 257 observational studies. Consequently, 83 full-text articles were assessed for eligibility. Ultimately, 75 full-text articles were excluded due to inappropriate patient populations (4 studies), unsuitable interventions (69 studies), and lack of relevant outcomes (2 studies). This process resulted in the inclusion of 8 studies in both the qualitative synthesis and the meta-analysis (Fig. 1).

The risk of bias (Fig. 2) was assessed with the Cochrane tool across all included studies. Most studies were deemed to have a low risk of bias in random sequence generation, allocation concealment, blinding of patients and personnel, and incomplete outcome data. However, high risk of bias was noted in blinding of patients and personnel in one study (16). Some studies had unclear risks in certain domains (e.g., Elawamy A et al [17] in allocation concealment). The overall risk of bias suggests that the included studies were generally of high methodological quality, although some risks were present. Sensitivity analyses that excluded high-risk studies were not performed, limiting the assessment of how those biases might have influenced the results of the meta-analysis.

The meta-analysis included a total of 688 patients,

with 123 men (31.62%) and 266 women (68.38%) in the experimental group. The mean age of the patients was 62.14 years (SD = 9.44), and the mean follow-up time was approximately 30.75 weeks (SD = 18.73). Additionally, all included studies employed UG-PRF that targeted intraarticular (IA), saphenous nerve (SN) and genicular nerve (GN) treatments exclusively. The cohort comprised patients with mild-moderate-severe KOA (Kellgren-Lawrence [KL] grades 1-4), of whom 82% (564/688) exhibited advanced-stage disease (KL grades 3-4). Baseline pain severity, assessed using the VAS, averaged 7.23 (SD = 1.15), and a subset of patients reported prior knee surgical history (16-22) (Suppl. Tables 2-3).

The primary outcomes demonstrated a significant reduction in VAS scores at one month (MD = -14.40; 95% CI, [-19.61, -9.19]; P < 0.01) with substantial heterogeneity ($I^2 = 99\%$; P < 0.01). Subsequent assessments revealed progressively attenuated but sustained effects at 3 months (MD = -7.83; 95% CI, [-10.38, -5.27]; P < 0.01; $I^2 = 98\%$), 6 months (MD = -5.64; 95% CI, [-7.62, -3.66]; P < 0.01; $I^2 = 99\%$), and 12 months (MD = -1.08; 95% CI, [-1.94, -0.23]; P < 0.01; $I^2 = 91\%$), with persistent high heterogeneity across all timepoints.

For secondary outcomes, WOMAC scores showed pronounced early improvements at one month (MD = -20.71; 95% CI, [-27.43, -13.99]; P < 0.01; $I^2 = 77\%$), and those improvements peaked at 3 months (MD = -22.09; 95% CI, [-31.33, -12.84]; P < 0.01; $I^2 = 89\%$). This therapeutic effect diminished gradually, demonstrating moderate improvement at 6 months (MD = -15.62; 95% CI, [-26.00, -5.23]; P < 0.01; $I^2 = 96\%$) and ultimately losing statistical significance at 12 months (MD = -6.95; 95% CI, [-17.26, 3.35]; P = 0.19; $I^2 = 96\%$).

Sensitivity analysis (Fig. S3) demonstrated the robustness of pooled outcomes, since sequential exclusion of individual studies did not change the effect estimates for pain (VAS) or function (WOMAC) substantially. Subgroup analyses stratified by nerve targets (genicular, saphenous, intraarticular) (Fig. S4) showed no significant between-group differences and a minimal reduction in heterogeneity, suggesting that the targeted anatomical treatment site did not account for the outcome variability.

Publication bias (Fig. S5) was assessed with the fail-safe N analysis and trim-and-fill methods. For the twelfth-month VAS scores, 86 additional studies would be needed to change the estimate to no difference, indicating robust evidence against publication bias. The trim-and-fill method adjusted the pooled effect size by

incorporating 2 additional studies, resulting in an effect size of MD -1.86 (95% CI [-2.84, -0.88], P < 0.01), which did not alter the overall findings significantly. Similar robustness was observed for other outcomes, with high fail-safe N values and minimal adjustments required by the trim-and-fill method.

The quality of evidence was evaluated using the GRADE criteria (Fig. S6). For the primary outcomes, the evidence was rated as moderate quality for the first-month and sixthmonth VAS outcomes due to the inclusion of randomized trials that had no serious risk of bias or indirectness, though some imprecision was noted in confidence intervals. The third-month VAS outcome was downgraded to low quality because of serious imprecision (wide confidence intervals spanning both clinically significant and insignificant effects) and potential inconsistency. Notably, none of the VAS outcomes achieved a high-quality rating. The twelfth-month VAS outcome maintained

moderate quality but exhibited serious inconsistency among studies, as reflected in divergent effect estimates across trials. The twelfth-month WOMAC outcome was rated as low quality due to extreme inconsistency (with control-group baselines ranging from 53.30 to 65.79 points and intervention effects spanning both improvement and worsening) and possible imprecision rather than publication bias. These assessments underscore the critical importance of harmonizing measurement scales, ensuring adequate sample sizes, and standardizing study designs to enhance evidence certainty.

DISCUSSION

This meta-analysis synthesized data from 8 published studies to evaluate the impact of UG-PRF on pain caused by KOA. Our findings demonstrate statistically and clinically significant short-term pain reduction (measured on the VAS) and functional improvement (measured on the WOMAC), encompassing pain, stiffness, and physical function (e.g., daily activities like walking, stair-climbing, and rising from sitting), at one-6 months after the intervention, with diminishing efficacy by 12 months. Notably, heterogeneity remained high across all time points (I² = 77–99%), likely attributable to variability in treatment protocols, anatomical targets (genicular vs. intraarticular vs. saphenous nerve), and patient characteristics (Suppl. Tables 2-3).

The first key finding of this study is that UG-PRF

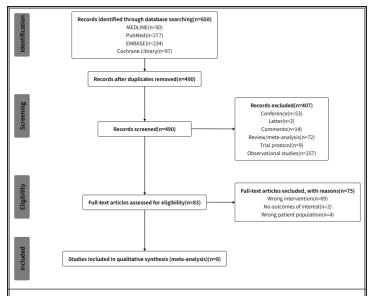
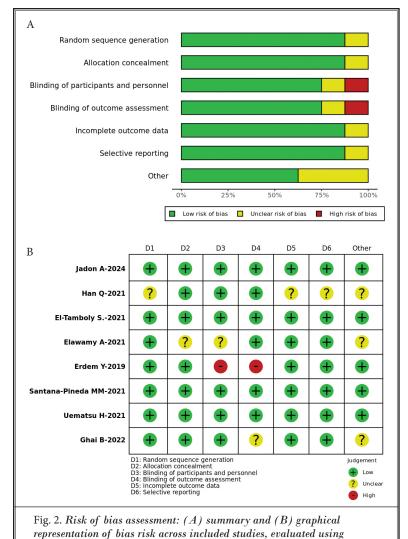


Fig. 1. PRISMA flowchart of the study selection: PRISMA flow diagram describing the selection of studies included in the systematic review and meta-analysis of the efficacy of UG-PRF in the management of knee osteoarthritis pain.

significantly reduces pain in patients with KOA at one, 3, and 6 months after treatment, as evidenced by the lower postoperative VAS scores. This outcome aligns with previous research demonstrating the safety and efficacy of RFA in pain alleviation without serious adverse events (8). Bhaskaran (23) has highlighted the longstanding clinical applications of RFA for various conditions since its introduction in 1891, supporting the foundational effectiveness of the technique. Additionally, Gofeld (24) reported that patients in the PRF group showed significant improvements in Numeric Rating Scale (NRS) scores compared to patients who received sham procedures, further corroborating the short-term benefits observed in this meta-analysis. Similarly, Soetjahjo (25) found that both CRFA and PRFA significantly reduced KOA pain at 6 months, with PRFA also improving function up to 3 months. Collectively, these findings collectively confirm that UG-PRF is an effective and safe modality for short-term pain relief and functional improvement in KOA patients, a pattern consistent with existing literature.

The second key finding reveals that the pain reduction achieved through UG-PRF is not significant after 12 months, potentially because of nerve regeneration mechanisms. Mintarjo (26) has explained that UG-PRF modulates nerve conduction without causing permanent damage, allowing for axon regeneration and the retransmission of pain signals approximately one year



Cochrane Collaboration criteria (random sequence generation, allocation

after treatment. This regenerative process may lead to the recurrence of pain, as supported by Karaman (27), who observed a decrease in the effectiveness of pain relief over time. Moreover, Halim (11) and West and Wu (28) note an incomplete understanding of PRF mechanisms and their neuromodulatory effects, respectively, which may contribute to the variability in the long-term outcomes of the procedure. Sluijter (12) has suggested that PRF yields dual effects in joint applications, providing immediate relief and gradually influencing immune cells, which might explain the transient nature of pain alleviation. Additionally, Han (29) and Sari (30) discuss the relationship between pain relief and physical function recovery, noting that

concealment, blinding, attrition, reporting).

long-term functional improvements are insignificant because muscles waste from pain avoidance behaviors. These insights are consistent with the current study's observation of diminished pain relief after one year, highlighting the need for ongoing research into the durability of PRF benefits.

The third key finding indicates that PRF, when compared to traditional hightemperature RF, mitigates nerve damage risk through lower-temperature application, aligning with PRF's characterization as a less neurodestructive modality. Unlike CRFA, which amplifies thermal ablation through internal cooling to expand lesion size, PRF avoids coagulative necrosis by delivering pulsed energy at sub-ablative temperatures. This mechanistic divergence explains PRF's reduced neurodestructive profile, as evidenced by comparative studies (12). Recent evidence further supports this distinction: a retrospective study of CRFA demonstrated a mean pain relief duration of 7.2 months, aligning with the 6-month efficacy window for PRF observed in our metaanalysis. However, unlike CRFA's reliance on neuroablative lesions, PRF prioritizes neuromodulation and procedural safety, enabling repeat interventions without cumulative neurodestructive risks (24). Unlike fluoroscopy-guided PRF, which relies on ionizing radiation and indirect bony landmarks for nerve localization, ultrasound guidance allows real-time

visualization of soft tissue structures, neurovascular bundles, and intra-articular anatomy (32). This direct visualization facilitates precise needle placement adjacent to target nerves (e.g., genicular or saphenous) while minimizing risks of vascular injury or off-target thermal effects (33). Furthermore, ultrasound imaging avoids radiation exposure, making the technique preferable for repeated procedures and younger patients (32). Recent comparative studies suggest comparable efficacy between ultrasound and fluoroscopy in genicular nerve ablation, with ultrasound demonstrating superior patient comfort and less procedural time due to dynamic needle tracking (34). Gupta (4) has emphasized that the reduced neurodestructive effects

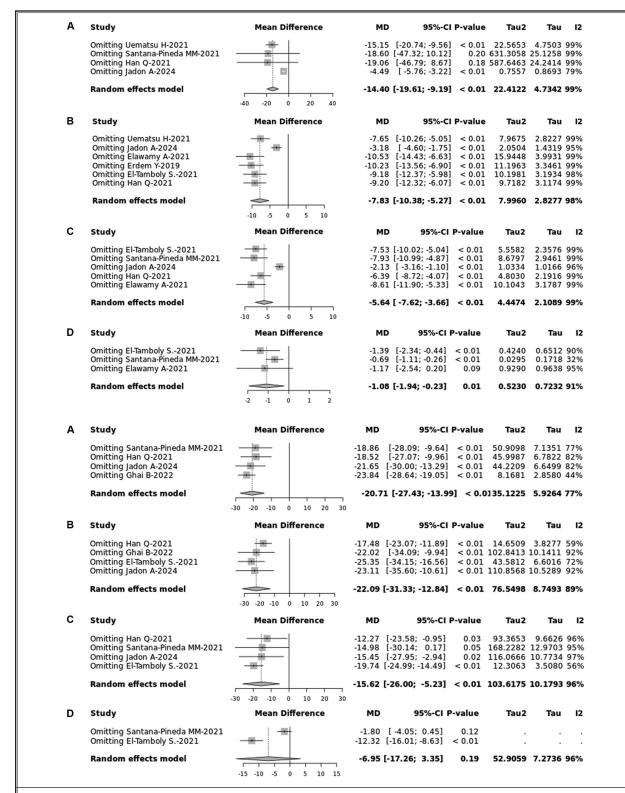
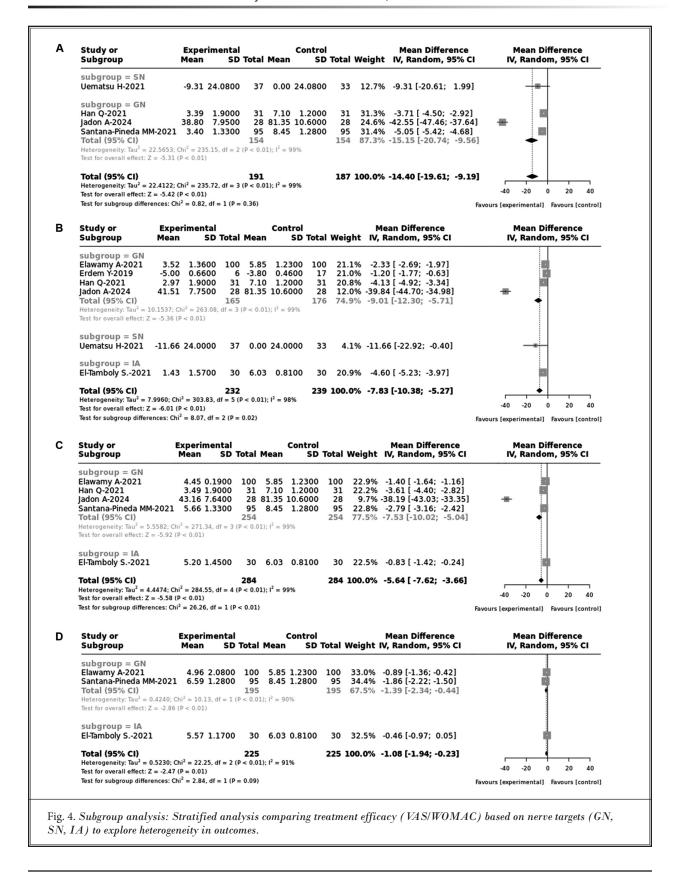
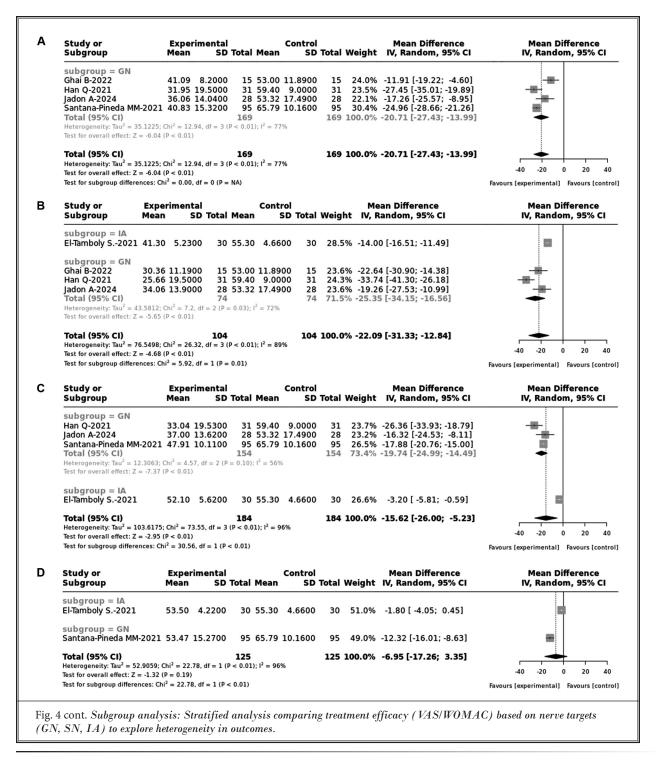


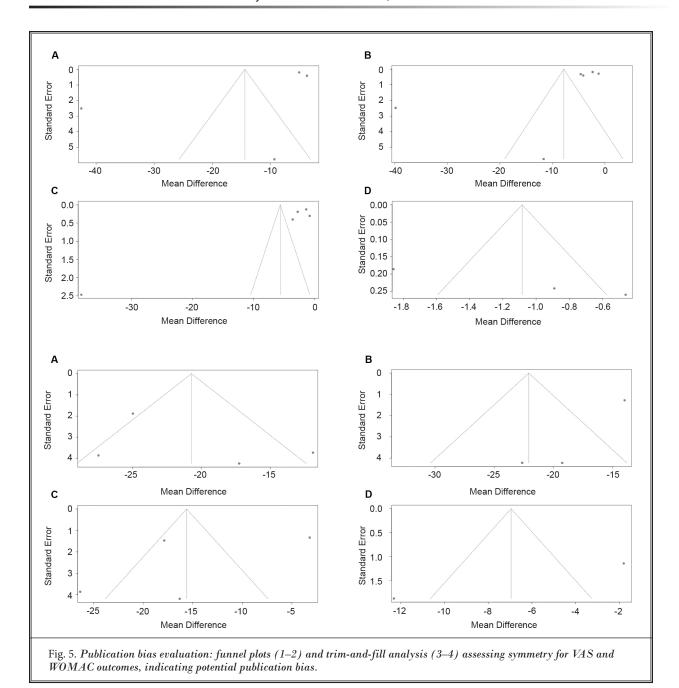
Fig. 3. Sensitivity analysis: forest plots for pain (VAS) and function (WOMAC) outcomes at one, 3, 6, and 12 months after the intervention, demonstrating effect size consistency after sequential exclusion of individual studies.

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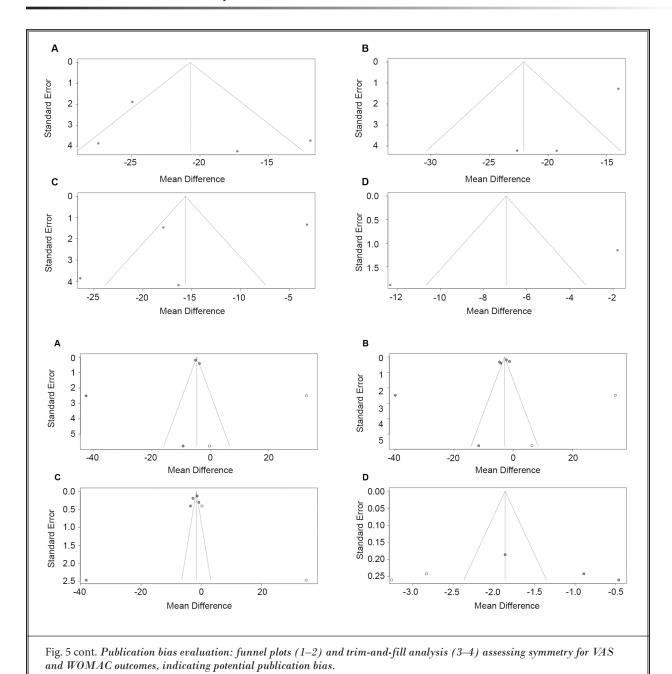


and minimized tissue damage and patient discomfort associated with PRF distinguish the procedure from conventional RFA. This safety advantage is further supported by studies demonstrating fewer adverse events with CRFA and PRFA techniques (14,35,36). Chou (37) found no significant differences in efficacy among various RFA techniques up to 6 months after treatment, reinforcing the comparatively short-term effectiveness



of PRFA. The diminishing of the analgesic effects at 12 months after treatment may reflect PRF's non-neurodestructive nature, as highlighted by Sam et al (6), who have identified that the technique leads to neuromodulatory effects on ion channels (e.g., Na,K-ATPase), inflammatory cytokines (IL-6, TNF α), and synaptic regulators (KCC2) without causing permanent neural disruption (6). Additionally, Wu (38) has recommended optimal temperature ranges for PRF to achieve analge-

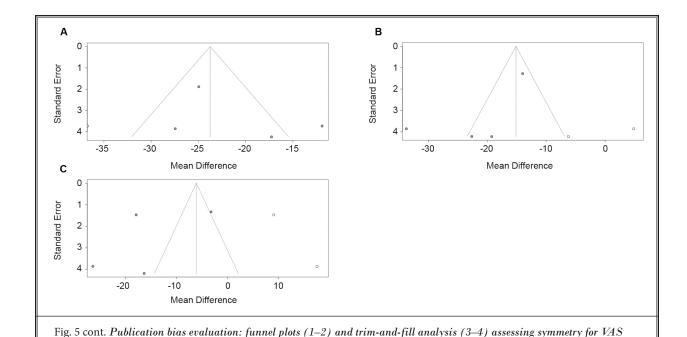
sia without enhancing duration, suggesting a balance between efficacy and safety. Although our study has focused on PRF's neuromodulatory effects, recent advances in thermal RFA techniques—such as V-shaped active tip needles designed to address anatomical variability among patients—highlight the importance of optimizing procedural precision (39). Future research could explore whether combining ultrasound guidance with similar anatomical innovations (e.g., multi-target



nerve mapping) might enhance the durability of PRF without compromising its nondestructive advantages. These findings are consistent with the current study, which observed significant short-term pain relief in association with PRF while acknowledging the trade-off of reduced long-term efficacy.

The findings of this meta-analysis hold significant clinical value by establishing PRFA as an effective shortterm treatment KOA pain. The demonstrated ability of PRFA to provide rapid pain relief and improve functional outcomes means that a viable alternative procedure can be offered to patients seeking minimally invasive interventions. This possibility is particularly relevant for individuals who have not achieved satisfactory results with conservative treatments such as pharmacotherapy or physical therapy, or for those who are not candidates for more invasive surgical options like knee replacement. The safety profile of PRFA, characterized

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and WOMAC outcomes, indicating potential publication bias.

Fig. 6. GRADE evidence profile: Summary of evidence certainty (high, moderate, low, very low) for pain and functional outcomes at different follow-up periods based on risk of bias, inconsistency, and imprecision.

by minimal adverse effects and reduced tissue damage, further enhances its practical applicability in clinical settings. By incorporating PRFA into treatment protocols, clinicians can offer a tailored pain management strategy that improves patients' quality of life and functional capacity in the short term. Additionally, the study's insights into the temporal efficacy of PRFA can inform clinical decision-making patient counseling, emphasizing the need for potential repeat treatments or complementary therapies to sustain pain relief and functional benefits.

Limitations

This meta-analysis is subject to several limitations that warrant consideration. Firstly, the incomplete reporting of WOMAC scores constrains the robustness of the study's conclusions, particularly as they pertain to long-term efficacy. Additionally,

the current study's limited data on nerve regeneration mechanisms after the administering of PRFA restricts a comprehensive understanding of the factors that contribute to pain recurrence at the 12-month mark. Future research should focus on elucidating the underlying biological processes of nerve regeneration and their impact on long-term outcomes.

Conclusion

In summary, this meta-analysis demonstrates that using UG-PRF to target the superior medial, superior lateral, and inferior medial genicular nerve branches—the primary sensory innervation of the anterior knee capsule—is an effective and safe intervention for reducing KOA pain and improving short-term function, supported by the absence of serious adverse events and standardized UG protocols that minimize procedural risks. The findings are consistent with existing

literature, highlighting significant pain relief and functional enhancement up to 6 months after treatment. However, the lack of sustained efficacy at 12 months underscores the need for further research into longterm outcomes and underlying mechanisms of nerve regeneration. The study's strengths lie in its systematic evaluation of high-quality RCTs and the emphasis on the minimally invasive nature of PRF, offering a valuable pain management option for patients. Addressing the identified limitations through future studies will be essential to fully establish the role of PRF in the comprehensive treatment of KOA. Future research should refine patient selection criteria based on pain generator topography (e.g., saphenous nerve targeting for medial knee pain) and optimize multi-session regimens to prolong therapeutic benefits. Fulfilling these priorities will solidify UG-PRF's role in minimally invasive KOA management.

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Suppl. Table 1. Search strategies.

	PUBMED		MEDLINE-ovid
#1	Osteoarthritis, knee[Title/Abstract]	#1	exp Osteoarthritis, Knee/
#2	Knee Osteoarthritis[Title/Abstract]	#2	(Knee osteoarthritis or Osteoarthritis of knee or Osteoarthritis of knee or KOA).ab.
#3	Osteoarthritis of knee[Title/Abstract]	#3	OR/1-2
#4	Osteoarthritis of the knee[Title/Abstract]	#4	Radiofrequency ablation.sh,ix,ab,ti.
#5	knee pain [Title/Abstract]	#5	
#6	OR/1-5	#6	(radiofrequency ablation OR Ablation, Radiofrequency OR Radio Frequency Ablation OR Ablation, Radio Frequency OR Radio-Frequency Ablation OR Ablation, Radio-Frequency OR RFA).ti,ab,kw.
#7	Radiofrequency Ablation[MeSH Terms]	#7	OR/4-5
#8	(radiofrequency [Title/Abstract]) OR (radiofrequency ablation [Title/Abstract]) OR (Ablation, Radiofrequency[Title/Abstract]) OR (Radio Frequency Ablation[Title/Abstract]) OR (Ablation, Radio Frequency[Title/Abstract]) OR (Radio-Frequency Ablation[Title/Abstract]) OR (Ablation, Radio-Frequency[Title/Abstract]) OR (RFA[Title/Abstract])	#8	3 AND 6
#9	OR/7-8		
#10	6 AND 9		
	EMBASE		Cochrane
#1	knee osteoarthritis'/exp	#1	MeSH descriptor: [Osteoarthritis, Knee] explode all trees
#2	(osteoarthritis or osteoarthrosis):ti,ab	#2	(Knee osteoarthritis or Osteoarthritis of knee or Osteoarthritis of knee or KOA):ab
#3	(knee):ti,ab	#3	OR/1-2
#4	2 AND 3	#4	(radiofrequency ablation):ab,ti,kw OR (Ablation, Radiofrequency):ab,ti,kw OR (Radio Frequency Ablation):ab,ti,kw OR (Ablation, Radio Frequency):ab,ti,kw OR (Radio-Frequency Ablation):ab,ti,kw OR (Ablation, Radio- Frequency):ab,ti,kw OR (RFA):ab,ti,kw
	OR ()	#5	MeSH descriptor: [radiofrequency ablation] explode all
#5	OR/1,4	π <i>3</i>	trees
#5 #6	OR/1,4 radiofrequency ablation'/exp	#6	OR/4-5
	,		
#6	radiofrequency ablation'/exp radiofrequency ablation ':ab,ti OR 'Ablation, Radiofrequency':ab,ti OR 'Radio Frequency Ablation':ab,ti OR 'Ablation, Radio Frequency':ab,ti OR 'Radio- Frequency Ablation':ab,ti OR 'Ablation, Radio-	#6	OR/4-5

 ${\bf Suppl.\ Table\ 2.}\ {\it Patient\ characteristics.}$

Study	No. of patients (rf/ control)	Country	Treatment gender (m/f)	Mean age	Follow-up
Erdem Y-2019 (33)	23/0	Turkey	7/16	69.8/78.0	3 mos
El-Tamboly S2021 (34)	30/30	Egypt	10/20	55.6/53.3	3,6,12mos
Elawamy A-2021 (35)	100/100	Egypt	50/50	47.78/48.45	3, 6, 12 mos
Han Q-2021 (22)	31/31	China	13/18	53.6/55.6	1, 3, 6 mos
Santana-Pineda MM-2021 (36)	93/95	Spain, Belgium	12/81	73.1/74.1	1,6,12 mos
Uematsu H-2021 (38)	37/33	Japan	14/56	73.10/74.30	12 week
Ghai B-2022 (39)	15/15	India	6/9	60.8/57.4	2 week,1,2,3mos
Jadon A-2024	27/28	India	11/16	63.3/59.6	1, 2, 3, 6 mos

Suppl. Table 3. Intervention characteristic.

Study	Intervention	RFA method	Intervention	Treatment target	Treatment pain score baseline	Ultrasound Guidance Universality	OA Severity Grading	Prior Knee Surgical History	Nerve Targeting Details	Number of Nerves Targeted per Treatment	Number of Treatments per Patient
Erdem Y-2019 (33)	PRF	paslud	42 °C, 120 s	ND	8.2(0.7)	Yes	KL Grade 3–4	6/23	SM, SL, IM GN	3	1
El-Tamboly S2021 (34)	PRF	palsed	42 °C, 120 s	IA	5.9(0.71)	Yes	KL Grade 1-2	09/0	SM, IM GN and IA	2	1
Elawamy A-2021 (35)	PRF	palsed	42 °C, 120 s	GN	5.85(1.23)	Yes	KL Grades 3-4	0/200	SMGN, IMGN, SLGN	3	1
Han Q-2021 (22)	PRF-PS	palsed	42°C 8min	GN	7.1 (1.2)	Yes	KL Grade 2-4	0/62	SMGN, IMGN, SLGN	3	3
Santana- Pineda MM- 2021 (36)	CNARF PNMRF	palsed	80 °C, 90 s	GN	8.36 (0.26) 8.45 (0.26)	Yes	KL Grade 3-4	20/188	SMGN, IMGN, SLGN	3	1
Uematsu H-2021 (37)	PRF	palsed	42 °C, 120 s	SN	7.2(1.4)	Yes	KL Grade 2–4	0/20	SN	1	1
Ghai B-2022 (38)	PRF	palsed	42 °C, 120 s	GN	8.0 (0.5)	Yes	KL Grade 2-3	0/30	SMGN, IMGN, SLGN	3	1
Jadon A-2024 (39)	PRF	paslud	42 °C, 120 s	GN	8.135(1.06)	Yes	KL Grade 2-4	0/55	SN, NVM, MFCN	3	1