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Genicular Artery Embolization and Genicular Nerve Radiofrequency Ablation for Knee Osteoarthritis: A Systematic Review of Sham-Controlled Randomized Trials

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ABSTRACT

Symptomatic knee osteoarthritis (KOA) may persist despite conservative care, and arthroplasty is not suitable for every patient. Genicular artery embolization (GAE) and genicular nerve radiofrequency ablation (RFA) target different proposed sources of knee pain. Because invasive procedures can produce substantial contextual responses, this review examined only sham-controlled randomized controlled trials (RCTs). PubMed, ScienceDirect, Europe PMC, and OpenAlex were searched for English-language reports published from January 2016 to June 2026. Eligible trials enrolled adults with symptomatic KOA and compared GAE or genicular nerve RFA with a sham procedure. Outcomes included pain, function, global improvement, analgesic use, imaging findings, and adverse events. Risk of bias was assessed with Cochrane Risk of Bias 2, and the evidence was synthesized narratively. Four RCTs randomized 221 participants. In the two embolization trials, pain improved in both active and sham groups, without significantly greater pain relief after GAE at 12 months; one exploratory analysis favored complete embolization for selected secondary outcomes. The two RFA trials differed: bipolar ablation of three genicular nerves was no better than sham RFA with local anesthetic and steroid at 12 months, whereas cooled RFA produced higher pain-responder rates than sham at 1, 3, and 6 months. No serious procedure-related complications were reported. The available sham-controlled evidence does not show a durable pain benefit of GAE beyond the sham response, whereas cooled RFA has the clearest evidence of short-term analgesic efficacy, although results vary by technique. Direct comparative trials with standardized procedures and longer follow-up are required.

Keywords: knee osteoarthritis; genicular artery embolization; genicular nerve radiofrequency ablation

INTRODUCTION

Knee osteoarthritis (KOA) commonly causes persistent pain and loss of mobility, limiting both everyday activity and employment[1]. Its prevalence continues to rise with population aging and obesity, adding to the demand for clinical care[2,3]. Total knee arthroplasty is effective for advanced disease, but it is not suitable or acceptable for every patient[4]. Comorbidity, less advanced radiographic disease, or a preference to postpone surgery may preclude this option. Patients who remain symptomatic after exercise, weight management, analgesia, non-steroidal anti-inflammatory drugs, or intra-articular injections consequently have few choices between conservative care and joint replacement.

Non-operative treatment remains central to KOA care. Guidelines recommend choosing among education, exercise, weight management, topical or oral medication, and selected intra-articular therapies according to the patient's needs[5,6]. Relief is not always sustained, and repeated medication or injection may be limited by adverse effects, contraindications, or patient preference. This unmet need has led to investigation of image-guided procedures directed at specific contributors to knee pain.

Genicular artery embolization is intended to reduce pain by occluding abnormal periarticular neovessels associated with synovial inflammation[7]. Synovitis and angiogenesis may be accompanied by sensory nerve growth and increased nociceptive signaling in painful KOA[8]. Selective embolization could therefore lessen local inflammatory activity while maintaining the major arterial supply. Prospective cohorts have reported improvement after GAE[9,10], but an uncontrolled change from baseline cannot separate a procedural effect from symptom fluctuation, regression to the mean, or the patient's expectation of benefit. Sham-controlled randomized evidence is needed before the procedure can be considered established care[11].

Genicular nerve RFA uses a different strategy by interrupting nociceptive input from sensory branches around the knee, usually the superomedial, superolateral, and inferomedial genicular nerves[12,13]. Conventional, pulsed, bipolar, and cooled techniques differ in lesion size, target coverage, imaging guidance, and patient selection. The 2019 American College of Rheumatology/ Arthritis Foundation guideline conditionally recommended RFA for knee OA, while noting uncertainty about technique, comparator choice, and longer-term safety[6]. These procedural differences matter because efficacy may depend on the ablation method, lesion geometry, use of a prognostic block, and the treatment delivered to the control group.

Placebo and contextual responses are particularly relevant when invasive treatments are assessed for pain[14]. KOA trials rely heavily on patient-reported pain, function, global change, and quality of life. These outcomes can be influenced by treatment expectations, the success of blinding, contact with the procedural team, and the apparent intensity of the intervention[15]. Sham procedures themselves may produce appreciable improvement[16,17]. Studies without a credible sham control may consequently attribute too much of the observed change to embolization or nerve ablation[18].

The place of GAE and genicular nerve RFA within KOA management is still uncertain. Published studies vary in disease severity, technical protocol, outcome definition, comparator, and follow-up duration. Their results also cannot support a reliable indirect comparison if the response in each sham group is ignored. Large improvement within an active-treatment cohort does not prove a specific procedural effect, and a short-term difference from sham does not establish durable improvement in function or a lower need for retreatment.

We therefore reviewed sham-controlled RCTs of GAE and genicular nerve RFA in adults with symptomatic KOA. The review examined whether either procedure produced benefit beyond its sham comparator and summarized pain, function, global improvement, analgesic use, imaging findings, durability, and adverse events. The two interventions were appraised within their own trial settings rather than treated as if they had been compared directly.

MATERIALS AND METHODS

Study design and reporting

This systematic review assessed the efficacy and safety of GAE and genicular nerve RFA for symptomatic KOA. Eligibility was restricted to randomized trials with a sham comparator, and reporting followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement[19]. Meta-analysis was inappropriate because few trials met the criteria and their procedures, sham designs, outcomes, and follow-up intervals differed.

Eligibility criteria

Eligibility was defined in advance according to population, intervention, comparator, outcomes, and study design. Participants had to be adults aged 18 years or older with clinically or radiographically diagnosed symptomatic KOA[20]. A mixed musculoskeletal pain study was eligible only when results for KOA could be separated. Studies of inflammatory arthritis, non-osteoarthritic knee pain, post-traumatic pain without KOA, or pain after total knee arthroplasty were excluded.

Eligible interventions were GAE or genicular nerve RFA. GAE included selective or superselective transcatheter embolization of genicular arterial branches or abnormal periarticular neovessels to treat KOA pain. Reports using the term transcatheter arterial embolization were accepted when the indication and vascular target matched this definition. Genicular nerve RFA included image-guided thermal ablation using conventional, cooled, or bipolar methods.

The control group had to undergo a sham procedure that reproduced the active intervention without delivering the intended embolic or ablative treatment. Trials were excluded when they compared GAE or RFA only with usual care, physical therapy, pharmacological treatment, intra-articular injection, a waiting list, or another active procedure.

Eligible trials reported at least one outcome involving pain, knee function, patient global assessment, quality of life, analgesic use, imaging, durability, retreatment, subsequent surgery, or adverse events. Non-randomized studies, observational cohorts, case reports or series, reviews, editorials, letters, animal or cadaveric research, technical reports, and conference abstracts without adequate clinical data were excluded.

Literature search and study selection

PubMed, ScienceDirect, Europe PMC, and OpenAlex were searched for English-language reports published from January 2016 through June 2026 (Figure 1). The final search was conducted in June 2026. The date range covered contemporary image-guided GAE and genicular nerve RFA techniques.

Controlled vocabulary and free-text terms covered KOA, GAE, genicular nerve RFA, randomization, and sham procedures. The PubMed search was '("knee osteoarthritis"[tiab] OR "osteoarthritis of the knee"[tiab] OR "knee OA"[tiab] OR gonarthrosis[tiab]) AND ("genicular artery embolization"[tiab] OR "genicular artery embolisation"[tiab] OR GAE [tiab] OR "genicular nerve radiofrequency"[tiab] OR "genicular nerve ablation"[tiab] OR "genicular radiofrequency ablation"[tiab] OR "cooled radiofrequency ablation"[tiab] OR "radiofrequency neurotomy"[tiab] OR "genicular denervation"[tiab])'. Syntax was adapted to the indexing and search functions of the other databases. Reference lists of eligible studies and relevant reviews were checked for additional trials.

Search records were transferred to a reference manager and deduplicated. Titles and abstracts were screened against the eligibility criteria, followed by full-text review of potentially relevant reports. Full-text articles were excluded if they lacked an eligible KOA population, did not study GAE or genicular nerve RFA, had no sham group, were not randomized, provided inadequate clinical outcomes, or were unavailable as an English-language full text.

The PRISMA flow diagram records each stage of selection and the reasons for full-text exclusion (Figure 1).

Data extraction

A standardized form was used to extract study setting and design, sample size, participant characteristics, diagnostic criteria, radiographic severity, eligibility criteria, intervention and sham protocols, co-interventions, follow-up, outcome measures, safety events, and the authors' conclusions. Procedural fields covered the embolic agent or RFA modality, arterial or nerve targets, and imaging guidance.

For embolization trials, extraction also covered the treated arteries, angiographic neovascularity, embolization endpoint, unilateral or bilateral treatment, technical success, and completeness of embolization when reported. For RFA trials, we recorded the type of ablation, temperature, duration, number and location of lesions, imaging method, use of prognostic blocks, and administration of local anesthetic or corticosteroid.

Outcomes

The primary outcome was improvement in pain with GAE or genicular nerve RFA relative to sham. Eligible measures included a visual analogue scale, numeric rating scale, the pain subscales of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)[21] or Knee injury and Osteoarthritis Outcome Score (KOOS)[22], and trial-defined responder outcomes.

Secondary outcomes were knee function, patient-reported global improvement, quality of life, use of analgesic or rescue medication, imaging change, durability, retreatment, subsequent knee surgery, and adverse events. Function could be measured with WOMAC, KOOS, the Oxford Knee Score, or another validated knee-specific instrument. Safety extraction included serious adverse events and reported vascular, cutaneous, infectious, neurologic, or pain-related complications.

Risk of bias assessment

Two reviewers assessed each trial with Cochrane Risk of Bias 2 (RoB 2)[23]. The tool addresses randomization, deviations from the assigned intervention, missing outcome data, outcome measurement, and selective reporting. Overall judgments were classified as low risk, some concerns, or high risk in accordance with RoB 2 guidance[24].

Because these were procedural trials with patient-reported outcomes, the appraisal examined the credibility of the sham procedure and maintenance of blinding in detail. Allocation concealment, co-intervention imbalance, missing data, and the possibility that participants knew their assignment were also considered.

Data synthesis

Narrative synthesis was used because the studies differed in intervention, technical protocol, sham procedure, outcome measure, response definition, and follow-up schedule[25]. GAE and RFA trials were summarized separately before their patterns of efficacy, durability, and safety were considered together.

Interpretation prioritized the contrast between active and sham groups. Change from baseline was also recorded, but it was not taken as proof of efficacy because symptom fluctuation, regression to the mean, co-interventions, and contextual effects could produce improvement in either group. Primary endpoints received the greatest weight; secondary and exploratory analyses were treated as supportive rather than confirmatory.

RESULTS

Study selection

Four sham-controlled RCTs, with 221 randomized participants, met the eligibility criteria. Two examined GAE or transcatheter arterial embolization against a sham angiographic procedure, and two compared genicular nerve RFA with sham RFA. None directly compared embolization with nerve ablation, so the studies were synthesized by intervention. Figure 1 presents the screening process.

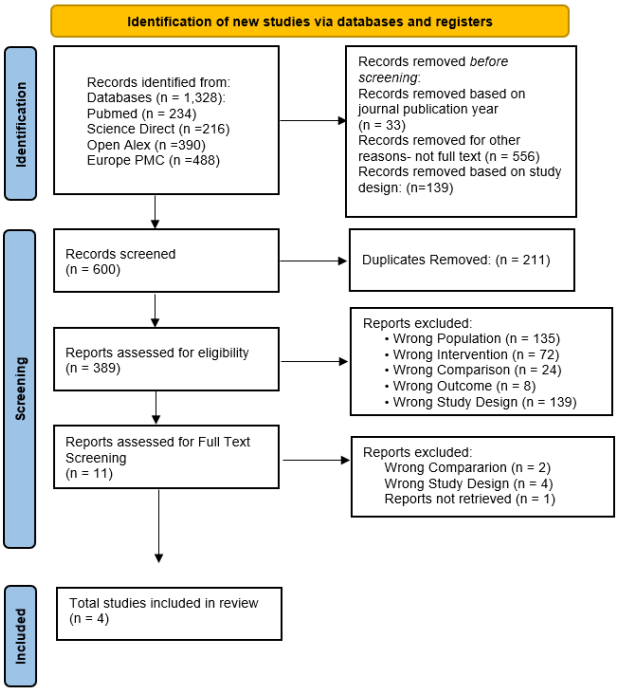


FIGURE 1: PRISMA flow diagram.

Characteristics of included studies

Two investigators (MFR and FA) independently extracted data. The embolization studies randomized 117 participants. Landers et al.[26] enrolled 59 patients with symptomatic Kellgren-Lawrence grade 2 KOA in a triple-blind, single-centre trial of transcatheter arterial embolization versus sham. KOOS pain at 12 months was the primary outcome; secondary measures included other KOOS domains, quality of life, global change, physical performance, and adverse events. Van Zadelhoff et al.[27] randomized 58 patients with mild-to-moderate KOA that had not responded to conservative care. GAE was compared with sham embolization, with clinical follow-up to 12 months and contrast-enhanced magnetic resonance imaging of synovitis.

The RFA studies randomized 104 participants. Malaithong et al.[28] enrolled 64 patients who had obtained more than 50% pain relief after prognostic blocks of the superomedial, superolateral, and inferomedial genicular nerves. Participants received bipolar RFA plus local anesthetic and steroid or the same medication with sham RFA. The primary endpoint was visual analogue scale pain at 12 months. Kwon et al.[29] compared cooled RFA with sham in 40 participants in a double-blind trial; the proportion of pain responders at 3 months was the primary endpoint. Table 1 summarizes the included studies.

TABLE 1: Characteristics of included sham-controlled randomized trials.

Study	Design	Participants	Intervention	Sham comparator	Primary outcome	Follow-up
Landers et al.[26]	Triple-blind, single-centre, sham-controlled RCT	59	Transcatheter arterial embolization / GAE	Sham angiographic procedure	KOOS pain	12 months
van Zadelhoff et al.[27]	Randomized sham-controlled trial	58	GAE	Sham embolization	Pain, KOOS, MRI synovitis	4 and 12 months
Malaithong et al. [28]	Double-blind, placebo-controlled RCT	64	Bipolar genicular nerve RFA	Sham RFA with local anesthetic and steroid	VAS pain	12 months
Kwon et al.[29]	Double-blind, sham-controlled RCT	40	Cooled genicular nerve RFA	Sham procedure	Pain responder rate	1, 3, and 6 months

Genicular artery embolization outcomes

In the trial by Landers et al.,[26] KOOS pain improved by 41.3% after embolization and by 29.4% after sham at 12 months. The between-group difference in the primary pain outcome was not statistically significant, and most secondary outcomes also did not differ. In an exploratory subgroup, complete embolization of all genicular arteries was associated with better KOOS Sports and Recreation, KOOS Quality of Life, and Global Change scores than sham. Because this analysis was exploratory, it cannot establish that technical completeness modifies treatment efficacy.

Van Zadelhoff et al.[27] also observed improvement in both groups. Mean KOOS pain increased from 44.44 to 65.61 after GAE and from 42.34 to 58.15 after sham over 12 months, with no significant difference between groups. Magnetic resonance imaging showed no significant change in synovitis within or between groups. Thus, this trial did not identify an embolization-specific effect on pain or the proposed imaging target.

Both embolization trials recorded improvement from baseline, but neither showed consistent superiority of the active procedure over sham.

Genicular nerve radiofrequency ablation outcomes

The RFA trials did not yield a uniform result. In the study by Malaithong et al.,[28] pain decreased in both groups during 12 months of follow-up. Mean visual analogue scale scores changed from 5.7 +/- 1.9 to 3.2 +/- 2.6 after bipolar RFA and from 5.0 +/- 1.4 to 2.6 +/- 2.4 after sham RFA with local anesthetic and steroid. The difference between groups was not significant, and neither WOMAC nor Patient Global Impression of Improvement favored active RFA at the primary endpoint.

Kwon et al.[29] reported a different pattern for cooled RFA. At 3 months, 76.5% of participants assigned to cooled RFA met the pain-responder criterion, compared with 33.3% assigned to sham. The active group also had higher responder rates at 1 and 6 months, and its pain reduction persisted through month 6. Functional status, medication change, and satisfaction, however, did not differ significantly between groups.

Safety outcomes

No trial reported a serious procedure-related complication. The embolization studies described no major vascular complication, and the RFA studies

reported no serious treatment-related adverse event. These findings provide limited short-term reassurance, but four small trials with differing techniques cannot reliably detect uncommon or delayed harms. Table 2 summarizes the efficacy and safety of included studies.

TABLE 2: Summary of efficacy and safety outcomes.

Study	Intervention	Pain outcome	Function and global outcomes	Safety	Overall interpretation
Landers et al[26]	TAE / GAE	KOOS pain improved in both groups; active treatment was not significantly better than sham at 12 months	Most secondary outcomes were similar; complete embolization favored selected outcomes in an exploratory analysis	No adverse events reported	No confirmed benefit beyond sham; the complete-embolization result was exploratory
van Zadelhoff et al. [27]	GAE	Pain improved in both groups, with no significant difference at 12 months	Function and MRI-assessed synovitis did not differ between groups	No serious procedure-related complications reported	No convincing efficacy beyond sham
Malaithong et al. [28]	Bipolar genicular RFA	Pain improved in both groups; bipolar RFA was not significantly better than sham plus local anesthetic and steroid at 12 months	WOMAC and PGI-I did not differ significantly	No serious treatment-related adverse events reported	No added benefit from bipolar RFA under the tested protocol
Kwon et al. [29]	Cooled genicular RFA	Pain-responder rates favored cooled RFA at 1, 3, and 6 months	Function, medication change, and satisfaction did not consistently differ	No serious treatment-related adverse events reported	Clearest short-term analgesic signal among the included trials

Risk of bias assessment

For the main pain outcome, one trial was judged at low risk of bias, and three raised some concerns under RoB 2. None was rated at high risk. Table 3 provides domain-level judgments.

The Landers trial had the strongest methodological profile, with triple blinding, a prespecified primary outcome, and little missing outcome data[26]. The trials by Van Zadelhoff, Malaithong, and Kwon raised concerns related to the description or handling of missing data, allocation concealment, or prespecified analyses[27-29].

Sham procedures reduced bias from treatment expectation in all four trials, an important design feature for participant-reported pain and function. Even so, small samples, procedural variation, and follow-up of no more than 12 months limit confidence in the evidence as a whole.

TABLE 3: Risk of bias assessment using Cochrane RoB 2.

Study	D1: Randomization	D2: Deviations	D3: Missing data	D4: Measurement	D5: Reporting	Overall
Landers et al.[26]	Low	Low	Low	Low	Low	Low
van Zadelhoff et al. [27]	Low	Low	Concerns	Low	Low	Concerns
Malaithong et al.[28]	Concerns	Low	Concerns	Low	Low	Concerns
Kwon et al.[29]	Concerns	Low	Concerns	Low	Concerns	Concerns

Legend: Low = low risk; Concerns = some concerns; High = high risk.

Overall synthesis

The trials do not show that GAE is superior to genicular nerve RFA. Such a claim would, in any event, be indirect because no head-to-head trial was found. In both embolization studies, active and sham groups improved without a consistent advantage for GAE at longer follow-up. Bipolar three-nerve RFA was also no better than its sham comparator at 12 months, while cooled RFA improved short-term pain-responder rates through 6 months. Among the included procedures, cooled RFA therefore had the clearest sham-controlled analgesic signal, but evidence for durable functional benefit remains sparse.

DISCUSSION

Four sham-controlled RCTs randomized 221 participants with symptomatic KOA[26-29]. Neither embolization trial showed a significant advantage over sham for its principal pain outcome at 12 months. Results from the RFA trials diverged. Bipolar ablation of three genicular nerves added no benefit to local anesthetic and steroid with sham RFA at 12 months, whereas cooled RFA increased pain-responder rates through 6 months. Because the interventions were not compared in the same trial, these data cannot establish that one procedure is superior.

The marked improvement in several sham groups is central to interpreting these studies. Pain, function, and global change can vary with expectation, regression to the mean, the natural course of symptoms, and interaction with clinicians. Meta-analytic work in osteoarthritis has also found substantial placebo responses, particularly for pain and self-reported function, with larger responses sometimes seen after more invasive interventions[14,16,17]. The parallel improvement after active and sham embolization illustrates why a favorable change from baseline is insufficient to show a specific effect of the procedure.

GAE has a plausible biological target. Painful KOA may involve synovial inflammation, neovascularity, and sensory nerve ingrowth, all of which could be affected by selective embolization. The randomized data, however, are less favorable than earlier uncontrolled reports[7,9,10]. In the Landers trial, the active and sham groups had similar KOOS pain results at 12 months, and most secondary outcomes were also comparable[26]. Better scores after complete embolization appeared only in an exploratory subgroup. This observation may inform procedural research, but limited power and post-randomization subgrouping prevent a confirmatory interpretation.

The trial by Van Zadelhoff provides a similar caution. Pain reduction at 4 months was comparable after GAE and sham, and assignment to GAE did not explain the degree of improvement. At 12 months, both groups retained some pain relief, yet pain, function, and magnetic resonance imaging measures of synovitis still did not differ[27]. The lack of an imaging effect leaves open whether embolization adequately altered the intended biological target in the studied population.

The RFA findings appear to depend on the technique and comparator. Malaithong et al. found no incremental pain or functional benefit from bipolar RFA of the superomedial, superolateral, and inferomedial genicular nerves[28]. This result applies to the tested protocol and should not be generalized to every form of genicular denervation. Local anesthetic and steroid were given in both groups, so an active analgesic effect in the comparator may also have narrowed the difference attributable to ablation.

Cooled RFA produced a more favorable pain result in the trial by Kwon et al.[29] Higher responder rates at 1, 3, and 6 months support a short-term analgesic effect beyond sham in selected patients. This is directionally consistent with a meta-analysis of placebo-controlled RFA trials that reported lower pain scores than placebo at 4, 12, and 24 weeks[13], and with an active-controlled trial in which cooled RFA outperformed intra-articular corticosteroid at 6 months[30]. A larger lesion or more reliable target coverage could explain the difference from bipolar RFA, but the trials were not designed to test that explanation. Moreover, the cooled RFA study was small, follow-up ended at 6 months, and measures of function, medication use, and satisfaction did not consistently favor treatment.

Any comparison between GAE and RFA must therefore remain descriptive. Participants, sham protocols, technical methods, endpoints, and follow-up differed across trials. The evidence is more favorable for short-term pain relief with cooled RFA than for GAE, but this pattern cannot be converted into a ranking of treatments. A direct, adequately powered randomized trial would be needed to determine comparative efficacy.

No serious procedure-related complication was reported, but 221 randomized participants provide little power to identify uncommon harms. Potential complications of GAE include non-target embolization, skin discoloration, a pain flare, vascular access injury, and tissue ischemia. RFA can cause neuritis, dysesthesia, vascular injury, burns, or persistent sensory symptoms. The available trials therefore offer preliminary safety information rather than evidence of long-term safety.

The main strength of this review was its restriction to sham-controlled RCTs. This design allowed each procedure to be judged against a credible procedural control rather than only against baseline[18]. Applying the same criterion to vascular and neural interventions also showed how the sham response can alter interpretation. Trial methods were appraised systematically with RoB 2[23].

Only four trials were eligible, and differences in KOA severity, participant selection, procedure, sham design, endpoint, and follow-up made meta-analysis inappropriate. Embolization protocols used different technical endpoints and imaging assessments. The RFA studies used different ablation methods and co-interventions. Most outcomes were patient-reported, and a sham procedure cannot eliminate every contextual influence. Data beyond 12 months are absent, so sustained benefit, retreatment, later arthroplasty, and cost-effectiveness remain unresolved.

Future research should first establish standardized protocols for each intervention, then compare them directly where appropriate. Embolization trials need explicit angiographic targets, embolic materials, endpoints, and imaging measures of synovitis or neovascularity.

RFA studies should prespecify nerve targets, lesion parameters, imaging guidance, prognostic block criteria, and any local anesthetic or corticosteroid given to either group. Longer follow-up should include validated responder thresholds, function, analgesic use, adverse events, retreatment, and progression to arthroplasty. Until those data are available, routine GAE for KOA remains investigational. Genicular nerve RFA, especbenefitsooled RFA, may be considered selectively, with patients informed that durability and functional benefit are still uncertain.

CONCLUSION

Four sham-controlled RCTs involving 221 participants do not establish that GAE is superior to genicular nerve RFA for symptomatic KOA. In both embolization trials, pain improved after the active and sham procedures, without a consistent advantage for embolization at 12 months. RFA results varied by technique: bipolar three-nerve RFA did not add benefit to sham RFA with local anesthetic and steroid, while cooled RFA increased pain-responder rates during 6 months of follow-up.

The sizable improvements seen in some sham groups caution against attributing every change from baseline to the procedure. Cooled RFA currently has the clearest evidence of a short-term analgesic effect, but durable functional improvement, reduced analgesic use, and long-term safety have not been established. The current evidence cannot support a direct ranking of treatments.

No serious procedure-related complication was reported, although the sample and follow-up were too limited to exclude uncommon or delayed harm. Larger multicentre trials should use standardized procedures, clinically meaningful responder definitions, and longer follow-up. Direct comparisons should assess pain, function, imaging biomarkers, medication use, retreatment, cost-effectiveness, adverse events, and progression to total knee arthroplasty.

DECLARATIONS

Ethics approval and consent to participate: Not applicable. This review used data from published studies and did not recruit participants.

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Conflict of interest: The authors declare that they have no conflicts of interest.

Data availability: All data analyzed in this review were obtained from the published studies.

Author contributions: Conceptualization, MFR; methodology, MFR and AAR; data extraction, MFR; risk of bias assessment, MFR and FA; writing, original draft, MFR and AAR; writing, review and editing, MFR, FA, and AAR; supervision, FA.

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