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Radiofrequency Ablation for Chronic Knee, Hip, and Shoulder Pain

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Rapid Review

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Abbreviations

ACR	American College of Rheumatology
AE	adverse event
ASPN	American Society for Pain and Neuroscience
IA-HA	intra-articular hyaluronic acid
IAS	intra-articular steroid
NICE	National Institute for Health and Care Excellence
OA	osteoarthritis
RCT	randomized controlled trial
RFA	radiofrequency ablation
SR	systematic review
VAS	visual analogue scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

Key Messages

- For patients with knee osteoarthritis (OA), radiofrequency ablation may reduce pain and improve function compared to other nonsurgical interventions without increasing adverse events.
- There is insufficient evidence to suggest that radiofrequency ablation reduces pain or improves function among patients with chronic hip pain.
- We did not find any studies or guidelines on the clinical effectiveness of radiofrequency ablation for treating chronic shoulder pain that met the inclusion criteria for this review.
- Three guidelines conditionally recommend the use of radiofrequency ablation for patients with knee OA, and 1 guideline conditionally recommends the use of radiofrequency ablation for hip joint pain following diagnostic blocks.

Context and Policy Issues

Why Is Chronic Pain of the Knee, Hip and Shoulder a Concern, and How Is it Currently Treated?

Chronic pain is characterized as pain lasting longer than 3 months.[1] An estimated 20% of Canadians are living with chronic pain, with 2 thirds experiencing moderate to severe pain and half experiencing long-term pain of over 10 years.[2] Chronic pain is recognized as a health condition in the 11th revision of the International Classification of Diseases.[3] It can be classified as chronic primary pain (pain associated with significant emotional distress and not otherwise accounted for by another diagnosis), or chronic secondary pain (pain as a symptom of another underlying health condition such as osteoarthritis).[2] Current treatments for chronic pain are typically multipronged and may include pharmaceutical, psychological, physical and rehabilitation, medical devices, practitioner administered or manual therapy, and/or interventional pain procedures.[2]

What Is Radiofrequency Ablation and How Is it Used?

Radiofrequency ablation (RFA) was introduced in the 1970s to treat back pain (via lumbar medial branch nerves of the facet joints),[4] and then its use was expanded to treat a range of conditions, including sacroiliac joint pain in the 1990s,[4] and chronic knee pain in 2008.[5] RFA is a procedure that disrupts the transmission of pain signals through the delivery of targeted thermal damage to nearby neural tissue.[6] Ideally, the chronic pain experienced by the patient will be attenuated while the damaged nerve structure is repaired by the body.[6] The duration of pain relief varies but is considered temporary and may last anywhere from 3 to 6 months,[7] or up to 12 months, or more.[8] A radiofrequency probe is inserted typically via fluoroscopic guidance, but sometimes via ultrasound guidance, adjacent to target nerve(s) and generates radiofrequency energy, which manifests as ionic heating (heating of the surrounding tissue, not the probe itself), causing destruction of the nerve(s).[6]Target temperatures typically range from 80°C to 90°C, for 90 to 120 seconds, but there is variation in procedure parametres.[9]

In addition to conventional (or thermal monopolar) RFA, there are other modalities available, each with the same overall objective of reducing pain through temporary damage of target nerves. Cooled RFA involves probes that allow the circulation of saline around the probe tip to help carry heat away from the tissue interface and thus reduce heat-related tissue damage. This also results in a larger heating area and lesion, because more energy can be delivered through the probe.[6] Therefore, more denervation is possible. Bipolar RFA involves 2 symmetrically placed electrodes that act as a conduit, also for the purpose of creating larger lesions than conventional RFA.[10] Pulsed RFA was more recently introduced (late 1990s) as an alternative to conventional RFA. This procedure involves the production of pulses of 45V lasting 20 milliseconds at a maximum tissue temperature of 42°C. Evidence suggests that pulsed RFA is less painful and causes less tissue damage compared to conventional RFA, but the duration of pain relief is generally less than RFA.[9] While pulsed RFA has similar effects on neural conduction, the treatment mechanism is different than that of nonpulsed RFA.

Why Is it Important to Do This Review?

Often, a combination of conservative treatment interventions (e.g., activity modification, intra-articular steroid injections, nonsteroidal anti-inflammatory drugs, etc.) effectively reduce chronic noncancer pain in the short-term (3 to 6 months).[11] Surgical interventions are an option for longer term pain relief or curative treatment, but some patients may not be eligible and those who are eligible may be faced with long surgical wait times.[12] This often results in the reliance on pharmaceuticals like opioids for pain relief. Therefore, the availability of alternative nonpharmaceutical (e.g., non-opioid) treatment options are required. Indeed, there is evidence that treatment with RFA among patients with chronic axial spine pain is associated with a decrease in the proportion of patients with opioid prescriptions compared to the proportion preprocedure.[13] However, whether RFA may be similarly effective for pain relief for patients with chronic knee, hip, or shoulder pain is unclear.

Objective

This report aims to summarize the evidence regarding the clinical effectiveness of, and guidelines with recommendations for, RFA for the treatment of chronic non-cancer knee, hip and shoulder pain.

Research Questions

1. What is the clinical effectiveness of radiofreqency ablation for adults with chronic knee pain?
2. What is the clinical effectiveness of radiofrequency ablation for adults with chronic hip pain?
3. What is the clinical effectiveness of radiofrequency ablation for adults with chronic shoulder pain?
4. What are the evidence-based guidelines regarding the use of radiofrequency ablation for adults with chronic knee, hip, or shoulder pain?

Methods

Literature Search Methods

An information specialist conducted a literature search on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were radiofrequency ablation and chronic knee, hip, and shoulder pain. CADTH-developed search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or indirect treatment comparisons, any types of clinical trials or observational studies, and guidelines. The search was completed on August 22, 2023 and limited to English-language documents published since January 1, 2018.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first screening level, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Criteria	Description
Population	Q1,4. Adults with chronic non-cancer knee pain Q2,4. Adults with chronic non-cancer hip pain Q3,4. Adults with chronic non-cancer shoulder pain
Intervention	Radiofrequency ablation[a]
Comparator	Q1-Q3: Alternative nonsurgical interventions (e.g., routine medical management, corticosteroid joint injection), placebo, or no treatment Q4. Not applicable
Outcomes	Q1-Q3: Clinical benefits (e.g., pain relief, health-related quality of life, functional improvement [e.g., activities of daily living]) and harms (e.g., fall risk) Q4. Recommendations regarding best practices for radiofrequency ablation (e.g., indications, number of lesions needed for effective treatment, who provides the procedure, setting for procedure)
Study designs	Health technology assessments, systematic reviews, randomized controlled trials, nonrandomized studies, evidence-based guidelines

[a]Excluding pulsed radiofrequency ablation unless volume of included evidence is low.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published before 2018. Systematic reviews in which all relevant studies were captured in other more recent or more comprehensive systematic reviews were excluded. Systematic reviews in which

there was partial overlap of relevant studies with 1 or more recent or comprehensive systematic reviews were excluded and the primary study(ies) missing from the more recent systematic review were retained and included in this review, even if published before 2018. Primary studies retrieved by the search were excluded if they were captured in 1 or more included systematic reviews. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included publications were critically appraised by 1 reviewer using the following tools as a guide: A MeaSurement Tool to Assess systematic Reviews 2 (AMSTAR 2)[14] for systematic reviews, the Downs and Black checklist[15] for randomized and nonrandomized studies, and the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument[16] for guidelines. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 449 citations were identified in the literature search. Following screening of titles and abstracts, 402 citations were excluded and 47 potentially relevant reports from the electronic search were retrieved for full-text review. 18 potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 57 publications were excluded for various reasons. After the assessment of overlap across the SRs meeting the inclusion criteria, 1 unique RCT[17] from an SR excluded for partial overlap[18] was retrieved. Nine publications met the inclusion criteria and were included in this report. These comprised 4 systematic reviews, 2 primary studies, and 3 evidence-based guidelines. Appendix 1 presents the PRISMA[19] flow chart of the study selection.

Two SRs[7,20] and 2 primary studies[10,17] were included for chronic knee pain, and 2 SRs[21,22] were included for chronic hip pain. No evidence was found for chronic shoulder pain. Three guidelines[23-25] were included.

Additional references of potential interest are provided in Appendix 7.

Summary of Study Characteristics

Three publications had broader inclusion criteria than the present review.

Fogarty et al. (2022)[7] examined the clinical effectiveness of fluoroscopically guided genicular RFA compared to non-surgical interventions including some not relevant to the present review (e.g., other forms of RFA). The 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip and Knee[24] makes recommendations for pharmacologic and nonpharmacologic management of OA, including for the use of RFA plus usual care for knee OA. Kao et al. (2018)[22] conducted an SR on the clinical effectiveness of RFA for hip pain. Two of the included studies (2/10) involved patients with postoperative hip pain and patients with cancer and 2/10 studies used pulsed RFA.

Only characteristics, results, and recommendations of the subset of relevant publications will be described in this report.

In addition, 1 SR did not identify any relevant studies. Chou et al. (2020)[21] evaluated the clinical effectiveness of 10 intervention procedures for 10 pain conditions, including cooled RFA versus usual care, sham, placebo, or no treatment for degenerative hip pain. However, no evidence was found for these comparisons. Due to the limited amount of evidence identified on the use of RFA for hip pain (1 SR with evidence[22]), 2 included studies in the SR that used pulsed RFA are included and summarized separately throughout this report.

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Study Design

Knee Pain

This review identified 2 SRs for RFA treatment of knee pain, 1 published in 2022,[7] and 1 in 2021.[20] The databases were searched from inception to October 10, 2020[7] and November 13, 2019.[20] Fogarty et al. (2022)[7] contained 5 RCTs across 8 publications, and 1 case series, of which 3 RCTs (3 publications) were relevant to the present review. The results were synthesized narratively. Chen at al. (2021)[20] included 7 RCTs and summarized the results via meta-analysis. A table describing the overlap of relevant studies within these 2 SRs is provided in Appendix. 5.

This review also identified 2 primary studies on RFA treatment of chronic knee pain, a triple-blinded RCT published in 2022[10] and an open-label, nonrandomized controlled trial published in 2011.[17]

Hip Pain

This review identified 2 SRs for RFA treatment of hip pain, 1 published in 2021[21] and 1 published in 2018.[22] The databases were searched from 1990 to April 2021[21] and from inception to January 20, 2017.[22] Chou et al. (2021) found no evidence relevant to this review and Kao et al. (2018)[22] included 6 case series or case reports on RFA and 1 nonblinded, uncontrolled, clinical trial and 1 case series using pulsed RFA.

Guidelines

This review identified 3 guidelines: 1 focuses on patients with knee osteoarthritis (OA)[23] and 2 are broader but included recommendations for the use of RFA for hip and knee pain.[24,25]

The National Institute for Health and Care Excellence (NICE) published their guidance in 2023.[23] A rapid review was conducted to gather evidence on the efficacy and safety of RFA for the treatment of patients with knee OA. All clinical study types were eligible for inclusion. Ratings of the quality of evidence and strength of the recommendations, and the methods used by the guideline development group to produce the recommendations, are not reported.

The American Society of Pain and Neuroscience (ASPN)[25] published their guidelines in 2021. A literature search of 3 databases was conducted to gather evidence on the use of RFA for 7 anatomic targets including the knee and hip joints. Systematic reviews, literature reviews, RCTs, prospective and retrospective observational studies were eligible for inclusion. The US Preventive Services Task Force criteria for quality of evidence and strength of recommendations is used. The quality of evidence is rated on a 5-level scale (I,

II-1, II-2, II-3 and III) where I is highest and III is lowest quality evidence. The strength of recommendations is rated from A (highest) to D (lowest), or I (insufficient evidence to make a recommendation).

The American College of Rheumatology (ACR) and the Arthritis Foundation published their guidelines in 2020.[24] A systematic search of the literature was conducted to identify evidence on the benefits and harms of available interventions for OA of the hand, hip and knee, including RFA. RCTs and observational studies were eligible for inclusion. The quality of evidence and strength of recommendations was graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology: the certainty of the evidence is assessed from very low to high, and the strength of a recommendation for or against an intervention can be weak or strong.

Country of Origin

Knee Pain

The first authors of the SRs were from the US.[7,20] The primary studies were conducted in Thailand[10] and Japan.[17]

Hip Pain

The first author of the SR on hip pain[22] was from the US.

Guidelines

The NICE guidelines[23] apply to the UK and the ASPN[26] and ACR guidelines[24] apply to the US.

Patient Population

Knee Pain

The SRs included adult patients diagnosed with knee OA. Studies were excluded if patients underwent knee arthroscopy. A total of 392 patients were included in the Fogarty et al. (2022)[7] review, while the total number of patients was not reported in Chen et al. (2021).[20] No other demographic or clinical information was reported in either SR. The primary studies enrolled 64[10] and 35[17] patients with knee OA. The mean age of patients in the primary studies was 66.7[10] and 77[17] years, and the majority was female.

Hip Pain

A total of 43 adult patients was included in the SR on hip pain: 26 patients received RFA (excluding pulsed RFA) and 17 patients received pulsed RFA.[22]

RFA (excluding pulsed RFA). Specific age was reported for 3 case reports (mean: 56 years).[22] Three publications involved patients with hip pain due to OA.[22] One case series involved patients with general chronic hip pain excluding metastasis to hip, a second case series involved chronic hip pain due to avascular necrosis of femoral head, and 1 case report focused on a patient with destructive coxopathy due to repeated radiation.[22]

Pulsed RFA: Age was not reported. Both studies involved patients with hip OA.[22]

Guidelines

The target population of the guidelines are patients with osteoarthritic knee pain,[23] patients with pain in the knee and hip joints,[25] and patients with OA of the knee or hip.[24] The intended users are health care providers, but the NICE[23] and ACR[24] guidelines also refer to patients and caregivers as a potential audience.

Interventions and Comparators

Knee Pain

The interventions included in the SRs were fluoroscopically guided cooled RFA,[7,20] conventional monopolar RFA,[7,20] and bipolar RFA.[7] Both SRs included medical management, intra-articular hyaluronic acid (IA-HA) injection, and intra-articular steroid (IAS) injection as comparators. Chen et al. (2021)[20] included 1 study with sham-RFA as a comparator.

Among the primary studies, interventions varied in target, frequency and method. Both were fluoroscopy guided and performed sensory/motor stimulation for localization.[10,17] The RCT did a prognostic nerve block before randomization[10] Malaithong et al. (2022) and the nonrandomized controlled trial did a nerve block 1 day before the intervention.[17] Malaithong et al. (2022)[10] conducted bipolar RFA on 3 genicular nerves simultaneously and Ikeuchi et al. (2011)[17] performed 2 RFA treatments 2 weeks apart on the medial retinacular nerve and the infrapatellar branch of the saphenous nerve. The lesions were made at 90° for 180s,[10] and 70°C for 90s.[17] Comparators were genicular nerve block at 3 target sites, local anesthetic and steroid injection plus sham-RFA,[10] and local anesthetic.[17]

Hip Pain

The specific intervention details varied across the 8 included publications within the SR identified for this report.[22]

RFA (excluding pulsed; 6 studies): A pre-treatment diagnostic nerve block was performed in 3 studies. Fluoroscopy guidance was used in 4 studies, ultrasound guidance was not used, and 2 studies did not report method of guidance. Sensory/motor stimulation was used in 3 studies. Five studies used thermal RFA, at varying temperature and duration: 90°C for 180 seconds (s) per target or 90s per target, 80°C for 120 seconds per target, 75°C to 80°C for 90 seconds per target, and 75°C to 90°C for 90s per target. When reported, a 22-gauge needle was used with a 100 mm electrode and 4 mm, 5 mm, and 10 mm exposed tip.

Pulsed RFA: Two studies used pulsed RFA. Both used fluoroscopic guidance, 42°C and 20 ms generator output of 45 V (1at 120s and 1 at 180s).

Guidelines

The NICE guidelines[23] describe the RFA intervention in general terms, including that it can be conducted under fluoroscopic or ultrasound guidance and that several targets have been identified including the genicular nerves. The ACR[24] guidelines are similarly general, citing the intervention as “radiofrequency ablation”. The ASPN[25] guideline includes a literature review and summary of the procedure techniques for both knee and hip RFA, including the general guidance on options for technique, electrode settings, target sites, and use of preprocedure diagnostic blocks. However, the recommendation statements are general:

they specify the target nerves (the genicular nerve or obturator and femoral nerve branches for knee or hip pain, respectively) but do not further specify recommended treatment protocols.

Outcomes

Knee Pain

All included SRs and primary studies measured pain via the visual analogue scale (VAS), function via the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the frequency of adverse events (AEs).[7,10,17,20] Additional function measures included the Oxford Knee Scale,[7] and the patient global impression of improvement Likert scale.[10,17]

Hip Pain

The outcomes from the Kao et al. (2018)[22] SR included pain measured via VAS, function measured via the Lower Extremity Functional Scale and the frequency of AEs.

Guidelines

The outcomes considered by the NICE guideline panel[23] were pain (VAS, the numeric rating scale), function (WOMAC, global perceived effort scale, timed up and go test and EQ-D5) and safety (pain, infection, numbness, damage to adjacent structures). ASPN[25] considered improvement in pain (any scale), function, analgesic use, subsequent need for surgery, health care utilization and return to work. ACR[24] considered pain, function (self-reported) and function (performance based).

Summary of Critical Appraisal

Knee

Systematic Reviews

The SRs had clear research questions, comprehensive literature reviews and study selection in duplicate. This increases the likelihood that relevant studies were not missed. With respect to the analysis, Fogarty et al. (2022)[7] extracted data in duplicate, and described the included studies in some detail, but additional patient characteristics would have enhanced interpretation. An important weakness of Chen et al. (2021)[20] is the lack of demographic, clinical and other information about the included patients: it's neither in the publication nor the supplementary information. Therefore, it is difficult to interpret the results and assess the external validity of the findings.

Primary Studies

The primary studies[10,17] had clearly defined objectives, main outcomes, characteristics of the included patients, and interventions. The presented results were described in the methods, the statistical tests were appropriate, compliance with the intervention was reliable and the main outcome measures were valid and reliable. Malaithong et al. (2022)[10] was a blinded (both study subjects and those measuring the main outcomes), randomized trial. There was sufficient power to detect a clinically important effect in VAS at all time points except 10 and 12 months. By contrast, Ikeuchi et al. (2011)[17] was an unblinded, nonrandomized trial with insufficient information provided to determine whether the study had sufficient power to detect clinically important differences between the treatment groups (a total of 35 patients were enrolled). Neither

study provided sufficient information to assess external validity, or whether confounding was assessed adequately.

Hip

Both SRs[21,22] had clear research questions containing the components of PICO, had comprehensive literature reviews with searches of at least 4 databases, justified their selection of included study types, conducted study selection in duplicate and reported no conflicts of interest. Neither performed data extraction in duplicate nor provided a list of excluded studies. Kao et al. (2018[22] provided a satisfactory explanation for, and discussion of, the heterogeneity observed but there were concerns with the risk of bias [RoB]). The method to assess RoB was not reported, but the authors stated there was a large RoB within the included studies due to lack of blinding and small sample sizes which is inherent in the design of included studies (i.e., case series/reports).[22]

Guidelines

The ACR guideline[24] performed well across all AGREEII domains, except applicability, and has strengths that the other 2 guidelines do not. The scope and purpose of the ACR guideline[24] is clear, all relevant professional groups and the target population participated in the development group, and the target users are clearly defined. The guideline was developed using rigorous methods for evidence synthesis and recommendations development, and with editorial independence, with the only area of uncertainty being whether external review occurred. The guideline's weakness relates to its applicability: facilitators and barriers to application are not mentioned, and no advice or tools are provided to enable implementation. Conversely, both NICE[23] and ASPN[25] did have resources available for implementation (methods for putting evidence into practice,[23] best practice summary).[25] However, the rigour of development is unclear for both NICE[23] and ASPN.[25] Systematic methods were used to identify evidence, but the strengths and limitations of the body of evidence and the methods for formulating recommendations are not provided. While ASPN[25] did have an explicit link between the evidence and the recommendation, the assigned evidence level of II-1 (defined as evidence from a "well-designed, controlled, nonrandomized clinical trial (p. 2809)"[25]) did not align with the stated source evidence (uncontrolled studies). NICE[23] did not include an explicit link between the evidence and the recommendation. Additional concerns with the NICE guideline are uncertainty around editorial independence (there is no statement on conflict of interest, and it is unclear whether the views of the funding body have influenced the content of the guideline. This leads to difficulty in understanding the rationale for the recommendation statements. The clarity of presentation for all 3 guidelines is good: recommendations are specific and easy to find.

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Summary of Findings

Appendix 4 presents the main study findings.

Clinical Effectiveness of Radiofrequency Ablation for Chronic Knee Pain

Evidence from 2 SRs[7,20] and 2 additional primary studies[10,17] suggests that the use of RFA for chronic knee pain is clinically effective (Table 8; Table 9; Table 10; Table 11). There is general agreement across studies

in favour of RFA versus nonsurgical or sham interventions for nearly all measured outcomes, follow-up time points, and treatment comparisons, with infrequent AEs.

There was some overlap in the primary studies included in the SRs; therefore, to avoid duplication of results, outcome data from an individual primary study are only reported once. The extent of overlap is summarized in Appendix 5. Due to methodologic heterogeneity, neither SR pooled results by meta-analysis.

Pain

Pain was measured by VAS at baseline and at 4, 8 and 12 weeks, and at 6 and 12 months (Table 8).

For patients with knee OA, there were inconsistent findings at 4 weeks. Namely, there was no difference between bimodal RFA and sham-RFA groups in mean change from baseline, but a statistically significant between-group difference in mean VAS among those receiving RFA compared to local anesthetic (1 nonrandomized study with 35 patients; 1 RCT with 64 patients).

From 8 weeks to 6 months, VAS measures generally favoured the intervention groups compared to the control groups (2 SRs[7,20] and 2 primary studies;[10,17] 35 to 392 patients):

- RFA was favourably associated with pain compared to intra-articular injections (IA-HA and IAS), at 12 weeks and 6 months (2 SRs;[7,20] 24 to 158 patients per primary study).
  - There were statistically significant between-group differences in mean VAS at 12 weeks and 6 months (1 SR,[20] 24 to 96 patients).
  - There were statistically significant between-group differences in the relative risk of patients experiencing at least 50% pain relief (1 SR;[7] 151 to 158 patients).
- There was a statistically significant between-group difference in VAS 12 weeks and 6 months in favour of RFA compared to oral analgesics (2 SRs;[7,20] 60 patients).
- When compared to sham-RFA, the evidence of treatment effectiveness was inconsistent.
  - There was a statistically significant between-group difference in mean VAS at 12 weeks in favour of the intervention (1 SR;[20] 35 patients)
  - There were no between-group differences at 6 and 12 months (1 RCT;[10] 53 to 59 patients). Note that the RCT had insufficient power to detect a clinically significant difference at 12 months.

Function

Function (WOMAC score) was measured at baseline and at 4 weeks, 8 weeks, 12 weeks, and 6 months (Table 9).

- At 4 to 8 weeks, RFA had no impact on function, compared with sham-RFA or local anesthetic:
  - At 4 weeks, there was no between-group difference in mean WOMAC score change from baseline (1 RCT;[10] 64 patients).
  - At 4 and 8 weeks, there were no between-group difference in WOMAC scores (1 nonrandomized trial;[17] 35 patients).

- At 12 weeks, there was consistent, statistically significant, improvement in function among the RFA groups, compared to IA-HA, IAS and sham control groups, but not compared to local anesthetic.
  - There were significant between-group differences in mean WOMAC score versus IA-HA, IAS and sham-RFA at 12 weeks (1 SR;[20] 35 to 133 patients).
  - There was no difference in WOMAC score between the RFA and local anesthetic groups (1 nonrandomized trial;[17] 35 patients).
- At 6 months, there was consistent, statistically significant, improvement in function among the RFA groups compared to medical management, IA-HA and IAS, but not sham-RFA or local anesthetic.
  - There was a statistically significant difference between groups in mean WOMAC score change from baseline (1 SR;[7] 177 patients) and statistically significant between-group difference in WOMAC scores (1 SRs;[7,20] 96 to 125 patients).
  - There was no difference between groups (bimodal RFA vs. sham RFA) in mean change from baseline (1 RCT;[10] 64 patients) and no between-group difference in mean WOMAC score (RFA vs. local anesthetic) (1 nonrandomized trial;[17] 35 patients).

Other Outcomes

Additional measures were summarized in a subset of the included studies:

- There was no between-group difference in mean Patient Global Impression at any time point, for bimodal RFA versus sham-RFA or RFA versus local anesthetic (2 primary studies;[10,17] 35 to 64 patients) (Table 10).
- There was a statistically significant between-group difference in mean Oxford Knee Score at 6 months, but not 12 months (1 SR; 7 52 to 126 patients; cooled RFA versus IAS). There was a statistically significant within-group difference from baseline among the intervention arm at 24 months (1 SR;7) (Table 11).

Adverse Events

All studies reported the frequency of adverse events (AE).[7,10,17,20] (Table 12).

- One serious AE – significant swelling -- was reported in 1 patient receiving RFA (1 RCT,[10] 64 patients).
- The frequency of any AE was 3.9% (n = 3/76) among those receiving cooled RFA compared to 9% (n = 7/75) in those receiving IAS (1 SR,[7] 392 patients).
- Subcutaneous bleeding at the site of needle insertion occurred in 67% (n = 12/18) of RFA group patients, compared to 82% (n = 11/14) receiving local anesthetic (1 nonrandomized trial, 32 patients).[17]
- Prolonged hypoesthesia at the infrapatellar branch of the saphenous nerve occurred in 78% (n = 14/18) of RFA group patients, compared to 0% receiving local anesthetic (1 nonrandomized trial, 32 patients).[17]
- Four studies reported no AEs in either the intervention or control groups (2 SRs,[7,20] total number of patients not reported).

Clinical Effectiveness of Radiofrequency Ablation for Chronic Hip Pain

We identified 2 SRs[21,22] that sought evidence regarding the use of RFA, including pulsed RFA, for chronic non-cancer hip pain. Chou et al. (2021)[21] did not identify evidence meeting our inclusion criteria. Kao et al. (2018)[22] summarized clinical outcomes (pain, function, AE) from a small number of low-quality studies (1 nonrandomized trial, 1 prospective before-and-after study, and 6 uncontrolled case series/reports) involving 43 patients.

The quality and quantity of this identified evidence is therefore insufficient to determine the comparative effectiveness of RFA, including pulsed RFA, for patients with chronic hip pain.

Pain

For patients receiving RFA (n = 25):

- There was significant within-group improvement in VAS from baseline to 6 months (1 prospective before-and-after study from 1 SR,[22] Table 13).
- Four case series and reports in 1 SR[22] found some improvement in VAS for 8 patients at 4 weeks, 8 weeks, 12 weeks and/or 6 and 24 months of follow-up (Table 13).

For patients receiving pulsed RFA (n = 17):

- There was some improvement in VAS at 1, 4, 12, and 16 weeks (1 nonrandomized trial and 1 case series in 1 SR)[22] (Table 13).

Function

One patient with chronic hip pain experienced functional improvement at 6 months after the RFA procedure (1 case report reported in 1 SR,[22] Table 14).

Adverse Events

AEs were reported in 4 of 25 patients who received RFA and 1 of 15 patients who received pulsed RFA (2 nonrandomized controlled trials, 2 case series in 1 SR,[22] Table 15).

Clinical Effectiveness of Radiofrequency Ablation for Chronic Shoulder Pain

No relevant evidence regarding the use of RFA for chronic shoulder pain was identified; therefore, no summary can be provided.

Guidelines Regarding the Use of Radiofrequency Ablation for Chronic Knee, Hip and Shoulder Pain

Knee and Hip Pain

This review identified 3 guidelines for the use of RFA for the treatment of adults with chronic knee pain (Table 16).

- The NICE guideline[23] states that RFA may be used "…if standard arrangements are in place for clinical governance, consent and audit (p.2)."[23] The guideline also specifies that the procedure should be done by clinicians with appropriate training. The quality of the evidence supporting this guideline was not summarized and there is no strength given to this statement.

- The ACR guideline[24] conditionally recommends the use of RFA for patients with knee OA, based on moderate quality evidence. The recommendation is conditional due to the methodologic heterogeneity in the supporting evidence (i.e., various intervention techniques and control procedures) and lack of long-term safety data.
- The ASPN guideline[25] states that RFA may be used to treat knee joint pain due to post OA and postsurgical pain (moderate to high certainty that the net benefit is moderate/substantial, based on well-designed, controlled trial).

This review identified 1 guideline for the use of RFA for the treatment of chronic hip pain (Table 16).

- The ASPN guideline[25] states that RFA may be used for the treatment of hip joint pain following diagnostic blocks. The guideline specifies that the obturator and femoral nerve branches should be targeted (recommendation with moderate to high certainty that the net benefit is moderate/substantial, based on well-designed, controlled trials).

Shoulder Pain

No relevant guidelines were found regarding the use of RFA for chronic shoulder pain.

Limitations

There was considerable methodological heterogeneity in the body of evidence gathered for this report. The 2 SRs on knee pain[7,20] included studies with 2 to 3 different RFA approaches (cooled, conventional monopolar and bipolar) and between 4 and 5 different comparator treatments. Meta-analysis was therefore not justified, and results were summarized narratively. Similarly, there was inconsistency across the RCTs: 1 RCT compared bipolar RFA to IAS plus sham-RFA, whereas the other RCT compared a two-treatment RFA regimen to local anesthetic. This makes concise interpretation across the body of included evidence challenging.

The generalizability of these results is limited to patients with OA-related knee pain. The patient population from the hip pain-related evidence was more diverse (e.g., 50% of patients experience chronic hip not related to OA), but not sufficiently to be generalizable due to small numbers (n = 26 patients). Further, no demographic, clinical or other confounding variables were summarized in the SRs. Without basic information like the age and sex distribution of the patients, it is difficult to assess the generalizability of the findings to the Canadian context.

The quantity and quality of available evidence on the use of RFA for the treatment of chronic hip pain is low. Two SRs[21,22] and 1 guideline[25] were identified for hip pain. One well conducted SR did not find any relevant evidence.[21] Several reasons for this may exist. First, the authors limited the interventions for this SR to cooled and pulsed RFA; therefore, evidence may have been missed regarding the broader clinical effectiveness of other/all RFA modalities on chronic hip pain. Second, the use of RFA for large joints is relatively new compared to its use for spinal and cranial nerves, so the volume of comparative trials may be low. This is reflected in the SR by Kao et al. (2018),[22] which included 6 low-quality observational studies with a total of 26 patients across them.[22] Further, the methodological heterogeneity among these studies was substantial

so the results could not be pooled to increase the sample size and power to detect differences across the intervention groups.

There is discordance between this review and the ASPN guideline[25] regarding the evidence assessment for the use of RFA on hip pain. The ASPN recommendation[25] that RFA may be used for the treatment of hip joint pain is informed by 4 nonrandomized studies: 2 retrospective uncontrolled studies, 1 prospective uncontrolled study, and 1 case series. Two of these studies were also captured in the Kao et al. (2018)[22] SR (although 1 was not summarized in this review because it included patients with cancer-related pain); 2 were excluded due to study design (i.e., uncontrolled studies). ASPN[25] assigned an evidence level of II-1 to this body of evidence which is defined as "well-designed, controlled, nonrandomized clinical trial (p. 2809)"[25] despite there not being a controlled trial in the included body of evidence. Due to the discordance between the included evidence and the assigned evidence level, and its unclear interpretation and application to the "best practice summary," the resulting recommendation should be interpreted and applied with caution.

This report is also limited by the lack of relevant evidence identified on the use of RFA for the treatment of chronic shoulder pain.

Conclusions and Implications for Decision- or Policy-Making

Summary

This review identified 2 SRs[7,20] and 2 primary studies[10,17] on the clinical effectiveness of RFA for chronic knee pain; 2 SRs[21,22] on the clinical effectiveness of RFA for chronic hip pain; and no evidence on the clinical effectiveness of chronic shoulder pain. Three guidelines were identified: 2 for the use of RFA for knee OA[23,24] and 1 for the use of RFA for knee or hip OA.[25]

Despite the considerable methodological heterogeneity across the included studies due to variation in RFA procedures and choice of comparators, there is consistency in the direction of the effect for pain (VAS) and function (WOMAC) across several time points for the use of RFA on knee OA. This increases the certainty that the use of RFA is clinically effective in reducing pain and improving function among adult patients with chronic OA knee pain. Conversely, there is a lack of certainty around the evidence of effectiveness for the use of RFA on chronic hip pain, despite consistency in the direction of the effect for pain (VAS), due to the small number of low-quality, heterogeneous studies.

Three guidelines[23-25] were identified that conditionally recommend the use of RFA for patients with knee OA. These recommendations align with the consistent clinical findings summarized in this review. One guideline[25] conditionally recommends using RFA for hip pain following diagnostic blocks. This recommendation is inconsistent with the findings summarized in this review, primarily due to discordance in the interpretation of the quality of evidence, where this review concludes that the small quantity and low-quality evidence available is insufficient to suggest that RFA reduces pain and improves function among patients with chronic non-cancer hip pain.

Considerations for Future Research

A research gap exists for good-quality RCTs that evaluate the effectiveness of RFA on chronic hip and shoulder pain. While this review identified an SR focused on the use of RFA for hip pain, that SR identified 1 uncontrolled trial and 5 case series or reports relevant to this review. No RCTs of RFA versus alternative nonsurgical interventions (e.g., routine medical management, corticosteroid joint injection), placebo, or no treatment were identified – either directly through this report's search or indirectly via included SRs. Further, no evidence was identified on the effectiveness of RFA for chronic shoulder pain going back to January 1, 2018. Decision-makers should consider that this represents a substantial gap in evidence for the use of a nonpharmacological intervention for 2 joint sites affected by OA.[1]

In addition, the available guidelines lacked recommendations with specificity for best practices for the RFA technique. An opportunity exists to create an evidence-informed resource to support clinicians' ability to optimally perform this procedure. Selection of key procedural parametres such as electrode size, lesioning time, and selection of the target sensory nerves have an impact on the lesion size and the likelihood of denaturing the target nerves.[7]

Ultrasound-guided RFA is increasingly being explored as an alternative to, or in conjunction with,[25] fluoroscopy-guided RFA. As complementary to fluoroscopic guidance, the addition of ultrasound may help with needle placement, improve safety, and decrease the risk of vascular and/or nerve injury, particularly for the challenging anatomy of the hip joint.[25] Suggested advantages as an alternative to fluoroscopic guidance include decreased cost, increased availability, and lack of ionizing radiation.[7] This review did not identify any studies using ultrasound guidance. Well-designed and adequately powered comparative studies on the effectiveness of ultrasound guidance versus fluoroscopy may expand the opportunities for the application of this technology for knee OA.

Implications for Clinical Practice

The findings of this report suggest that RFA may be an effective treatment option for chronic knee pain due to OA as an alternative to other nonsurgical interventions such as intra-articular injections or oral analgesics in patients with postsurgical pain, those not eligible for surgery or those who are awaiting surgery. In addition, this treatment may provide an alternative nonpharmacologic (e.g., opioid) option for patients with chronic knee OA who are no longer experiencing (or have never experienced) pain relief with existing treatments.

While identified guidelines supported the use of RFA in patients with knee OA, only one[25] specified parametres for electrode settings, target nerves, and use of pre-ablative diagnostic blocks and motor testing. The guideline also noted the required knowledge for application of this procedure, so there may be an opportunity for clinician training and knowledge of the anatomic innervation of the knee, the principles surrounding RFA, and experience with fluoroscopy, ultrasound, and the variety of RFA modalities.

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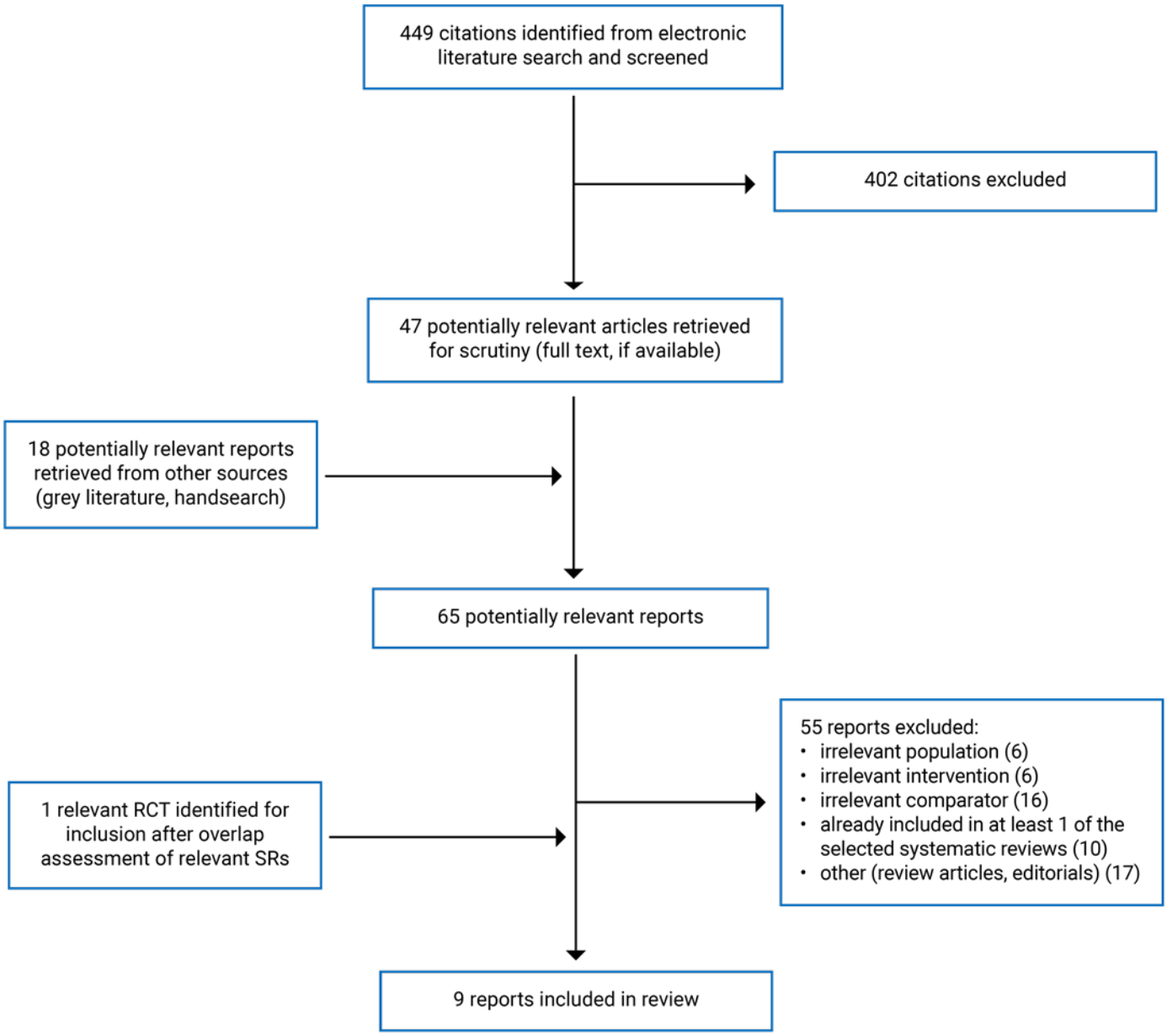
Appendix 1: Selection of Included Studies

Note that this appendix has not been copy-edited.

Figure 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Note that this appendix has not been copy-edited.

Table 2: Characteristics of Included Systematic Reviews

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Knee pain				

Fogarty et al. (2022)[7]
US
Funding source: NR
	A total of 5 RCTs (across 8 publications) and 1 case series) were included; 3 RCTs relevant to this present review.[a]
	Results were synthesized mnarratively.
		Patients > = 18 years with chronic knee pain due to OA.
		392 patients were included in the relevant studies.
		Studies were excluded if patients underwent total knee arthroplasty.
			Intervention: fluoroscopically guided genicular nerve RFA:
			• cooled
			• conventional monopolar
			• bipolar
			Comparator:
			Relevant to present review:
			• Medical management
			• intra-articular injection of:
			  ○ steroid;
			  ○ HA
			Not relevant:
			• Conventional RFA
				Outcome (measure): ≥ 50% pain reduction (VAS), function (WOMAC, OKS), and adverse events (n).
				Follow-up: 6, 12, 18 and 24 months.

Chen et al. (2021)[20] US **Funding source:** Hangzhou medical and Health Technology Planning Program	A total of 7 RCTs were included (5 high quality and 2 moderate quality).	Patients with symptomatic knee OA. No other demographic and clinical details were NR.	**Intervention:** Cooled RFA (1 trial) and RFA (6 trials). **Comparator:** • Sham (1 trial) • IA-HA (2 trials) • Oral analgesic (1 trial) • Control; details not specified (1 trial) • IAS (2 trials)	**Outcome (measure):** Pain (VAS), function (WOMAC) and adverse events (n). **Follow-up:** 12 and 24 weeks.
Hip pain				
Chou et al. (2021)[21] US **Funding source:** AHRQ	RCTs and cohort studies (if RCTs not available). 37 RCTs were included. No evidence on the efficacy or safety of RFA for hip pain was found.	**Population:** Adults with pain, of any duration, due to: vertebral compression fracture; degenerative back or hip pain; presumed discogenic back pain; radicular low back pain; trigeminal neuralgia; headache; piriformis syndrome; or ulnar, median or radial neuropathy.	**Intervention:** vertebral augmentation procedures; intradiscal and facet joint platelet-rich plasma; intradiscal stem cells; intradiscal methylene blue; intradiscal ozone; sphenopalatine block; occipital stimulation; piriformis injection; peripheral nerve stimulation. **Relevant intervention:**	**Outcomes:** primary outcomes were pain and function. Secondary outcomes were quality of life, emotional function, global improvement, and harms. **Follow-up:** 1 to 2 weeks, 2 to 4 weeks, 1 to 6 months, 6 to 12 months and ≥ 12 months.

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
		Relevant population: Adults ≥ 18 years of age undergoing RFA for hip pain of any duration	cooled or pulsed RFA for degenerative hip pain. **Comparators**: usual care, sham, placebo, no treatment or conventional RFA.	

Kao et al. (2018)[22]
US
Funding source: Veteran's Affairs Rehabilitation Research and Development Service
	Clinical trials, case series' and case reports were included.
	Number of studies: 2 unblinded, noncontrolled clinical trials and 8 case series/reports were included and synthesized qualitatively.
	Number of relevant studies: 1 clinical trial and 7 case series/ reports, including 2 studies using pulsed RFA which were not excluded, but reported separately, due to limited amount of evidence for the hip joint identified through the present review.
		Population: Adults ≥ 18 years of age with chronic (≥ 3 months) with nonmalignant hip-related pain. Despite the exclusion of malignancy, one trial included patients with cancer so was excluded from the present review.
		Relevant population: patients with nonmalignant and nonsurgical hip pain.
		A total of 43 patients was included in the review:
		• RFA (n = 26 patients)
		  ○ Age was reported in 3/6 studies (range: 53 to 39 years).
		  ○ 3/6 studies focused on OA pain.
		• Pulsed (n = 17 patients)
		  ○ Age not reported.
		  ○ 2/2 studies focused on OA pain.
			Intervention: thermal, cooled and pulsed RFA. Four studies reported pre-treatment diagnostic block. One case report involved 2 treatments (conventional single needle, then bipolar).
			Relevant intervention: thermal and cooled RFA
			Comparator: nonblinded control (standard therapy).
				Outcome (measure): pain (VAS), function, (Lower Extremity Functional Scale) and adverse events (n).
				Follow-up: 4 weeks to 2 years.

AHRQ = The Agency for Health care Research and Quality; CRF = cooled radiofrequency ablation; CRMRF = capacitive resistive monopolar radiofrequency; GPE = global perceived effort; HA = hyaluronic acid; NaHA = sodium hyaluronate; IA-HA = intra-articular hyaluronic acid; IAS = intra-articular steroid; NR = not reported; OA = osteoarthritis; RF = radiofrequency; RFA = radiofrequency ablation; VAS = visual analogue scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

[a]2 RCTs included in this SR were outside the scope of the present review. Jadon (2018)[27] compared 2 RFA modalities (monopolar vs. bipolar conventional RFA); and McCormick (2018)[28] examined the effectiveness of RFA on knee pain, with and without prognostic block..

Table 3: Characteristics of Included Primary Clinical Studies

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Malaithong et al. (2022)[10] Thailand **Funding source:** internal funding	RCT Patients, outcome assessors and statisticians were blind to treatment allocation	A total of 64 patients with severe OA chronic knee pain, (32 in each group) were enrolled in the trial: • Mean age: 66.7 ± 9.8 years • 81% female • Moderate baseline pain (VAS): 6.5 ± 1.7 • Average pain duration at baseline: 5.1 ± 3.6 years	**Intervention:** genicular nerve bipolar RFA with fluoroscopic guidance, plus local anesthetic and steroid injection. 10cm, 18 gauge cannula with 10mm active tip. Sensory stimulation for localization. Lesioning occurred simultaneously at each of the 3 target nerves. **Comparator**: genicular block at 3 target sites, local anesthetic and steroid injection (same dose as intervention group) plus sham-RFA. All patients underwent a prognostic block before randomization to exclude patients with a negative response to the block (< 50% pain relief).	**Outcome (measure):** pain (VAS), function (WOMAC, PGI-I), adverse events (n) **Follow-up**: 12 months. Outcomes measured at 1, 2, 4, 6, 8, 10 and 12 months.
Ikeuchi et al. (2011)[17] Japan **Funding source:** NR	Prospective, nonrandomized open-label and controlled study. Recruitment through convenience sample at a clinic (clinic details not provided). Eligible patients presenting to the clinic between August and December 2005 were assigned as candidates for the intervention group. Eligible patients presenting between January and May 2006 were candidates for the control group.	A total of 35 patients with moderate or severe refractory anteromedial knee pain associated with knee OA were enrolled (n = 18 in the intervention group and n = 17 in the control group): • mean age: 77 years • 89% female • disease duration: 9.5 years • baseline pain (VAS): 57 to 58mm	**Intervention:** 2 RFA treatments 2 weeks apart. 50mm cannula with 5mm active tip. Sensory stimulation for localization. **Control:** local anesthetic Both intervention and control treatments were applied to the medial retinacular nerve and the infrapatellar branch of the saphenous nerve. 3 weeks before the first intervention, other treatments were stopped: physical therapy, acupuncture,	**Outcome (measure):** pain (VAS); function (WOMAC), patient's global assessment, adverse events (n). **Follow-up:** outcomes assessed at baseline, 4, 8, 12 weeks and 6 months after the first procedure.

Study citation, country, funding source	Study design	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
			regular use of Aspirin or NSAID, IAS or IA-HA. These were allowed to resume after 12 weeks after the first procedure. Home exercises were allowed to continue throughout. Loxoprofen sodium was allowed up to 3 tablets per day, as a rescue analgesic	

IA-HA = intra-articular hyaluronic acid; IAS = intra-articular steroid NR = not reported; NSAID = nonsteroidal anti-inflammatory drug; PGI-I = patient global impression of improvement Likert scale; VAS = visual analogue scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Table 4: Characteristics of Included Guidelines

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
NICE 2023[23]						
Intended users: not explicitly reported, but accompanying tools available for both public (e.g., "questions to ask") and health professionals (e.g., auditing and monitoring tracking spreadsheet) **Target population**: patients with osteoarthritic knee pain	RFA (conventional, cooled and pulsed)	**Efficacy** • VAS • NRS • WOMAC • Global Perceived Effect scale • Timed Up and Go test • EQ-5D **Safety** • Pain • Infection • Numbness • Damage to adjacent structures	Rapid review on the efficacy and safety of RFA. Databases were searched from inception to 10 February 2023. A grey literature search was conducted as well (date NR). **Study types:** clinical studies. Abstracts were included if they reported outcomes No information on method for evidence assessment or selection Study characteristics of key included studies (n = 9) summarized in table format. N = 51 studies met the inclusion criteria, but only 9 were included in the evidence summary.	NR	Methods used by the guideline development group to produce recommendations was NR Strength of recommendation NR	No information on internal/external consultation for this guideline, but NICE's general procedure is available on its website.[29] **External review:** by the public, national patient organizations if applicable, medical device companies, professional organizations and other stakeholders. **Internal review:** NR

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
ASPN 2021[25]						
Intended Users: clinicians **Target Population**: people with chronic pain in the cervical, thoracic, lumbar spine; posterior sacroiliac joint; hip and knee joints; and occipital neuralgia.	RFA	**Primary:** • Improvement in pain (any scale) **Secondary:** • Function • Analgesic use • Subsequent need for surgery • Health care utilization • Return to work	Formal literature search of 3 databases (date of search NR). **Study types:** Systematic reviews, literature reviews, RCTs, prospective and retrospective observational studies. A meta-analysis was not conducted. Evidence is summarized in table format by anatomic target (e.g., knee joints, hip joints).	The USPSTF criteria for quality of evidence was used (I, II-1, II-2, II-3 and III).	Recommendations were produced via consensus. Each recommendation statement was assigned a strength of recommendation as per the USPSTF criteria (A, B, C, D or I). The recommendation for use of RFA for knee pain is based on evidence from 4 studies. The recommendation for use of RFA for hip pain is based on evidence from 5 studies.	Methods for internal and external review were NR.
ACR 2021[24]						
Intended Users: health care providers, caregivers and patients. **Target Population**: patients with osteoarthritis of hand, hip and/or knee and no specific contraindicators to the recommended therapies.	Pharmacologic and nonpharmacologic management of OA of the hand, hip and knee, including RFA plus usual care (maximally tolerable therapeutic doses of acetaminophen or nonsteroidal anti-inflammatory drugs).	**Critical outcomes** • Pain • Function (self-reported) • Function (performance based)	A systematic search of the literature was conducted. Databases were searched from inception to October 15, 2017 which update search on August 1, 2018. **Study types:** RCTs, observational studies	The quality of the evidence was assigned as per the GRADE methodology which characterizes the certainty of evidence on a four-level scale: • very low; • low;	Voting panel members voted on the direction and strength of reach recommendation. A threshold of 70% agreement among members was required to accept a recommendation. If not reached, additional discussions were held before re-voting. The strength of	Methods for internal and external review were NR.

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
				• moderate; or • high.	recommendations was assigned as per the GRADE methodology: • Strong against • Weak against • Weak for • Strong for	

ACR = American College of Rheumatology; EQ-5D = standardized measure of health-related quality of life; GRADE = Grading of Recommendations Assessment, Development and Evaluation; NA = not applicable; NICE = National Institute for Health and Care Excellence; NR = not reported.; NRS = Numeric Rating Scale; RCT = randomized controlled trial; RFA = radiofrequency ablation; VAS = visual analogue scale; USPSTF = United States Preventive Services Task Force; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Appendix 3: Critical Appraisal of Included Publications

Note that this appendix has not been copy-edited.

Table 5: Strengths and Limitations of Systematic Reviews Using AMSTAR 2[14]

Strengths	Limitations
Knee pain	
Fogarty (2022)[7]	
• The research questions and inclusion criteria included components of PICO. • A comprehensive literature search strategy was used. • Study selection was conducted in duplicate. • Data extraction was performed in duplicate. • The included studies were described in adequate detail. • The authors used Cochrane's RoB tool for the individual studies included in the review. • The authors reported on the sources of funding for the studies included in the review. • The authors accounted for RoB when interpreting and discussing the results. • The authors reported no conflicts of interest.	• There was no statement to confirm that the review methods were established before conducting the search. • No justification for selection of study design for inclusion in the review. • The list of excluded studies was not provided. • The authors did not explain the impacts of heterogeneity on the results.
Chen (2021)[20]	
• The research questions and inclusion criteria included components of PICO. • A comprehensive literature search strategy was used. • Study selection was conducted in duplicate. • The list of excluded studies with justification for exclusion was provided. • The authors used a satisfactory technique to assess RoB. • Appropriate methods for the combination of results were used. • The authors accounted for RoB when interpreting and discussing the results.	• There was no statement to confirm that the review methods were established before conducting the search. • No justification for selection of study design for inclusion in the review. • Unable to determine if data extraction was performed in duplicate. • The includes were not described in adequate detail. • The authors did not report the sources of funding for the included studies. • The authors did not explain the impacts of heterogeneity on the results. • There was no investigation of publication bias. • Conflict of interest was not reported.
Hip pain	
Chou (2021)[21]	
• The research questions and inclusion criteria included components of PICO. • The review methods were established before conducting the search. • Justification of preference for RCTs vs. observational studies was provided.	• It is unclear whether data extraction was performed in duplicate. • The list of excluded studies was not provided. • The remaining AMSTAR 2 questions are NA since no evidence was found.

Strengths	Limitations
• A comprehensive literature search strategy was used. • Study selection was conducted in duplicate. • The authors reported no conflicts of interest. • The remaining AMSTAR 2 questions are NA since no evidence was found.	
Kao (2018)[22]	
• The research questions and inclusion criteria included components of PICO. • The authors explained their selection of the study designs included in the review. • The included studies were described in adequate detail. • A satisfactory explanation for, and discussion of, the heterogeneity observed in the results of the review. • The authors reported no conflicts of interest.	• There was no statement to confirm that the review methods were established before conducting the search. • It is unclear whether data extraction was performed in duplicate. • The list of excluded studies was not provided. • The authors did not report on the sources of funding for the included studies. • The method to assess RoB was not reported. The authors stated that there was a large risk of bias within the included studies due to lack blinding and small sample sizes. There was also a large risk of bias across the studies due to positive reporting biases and small sizes within the studies.

AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2; NA = not applicable; PICO = population, intervention, comparator, outcome, study type; RoB = risk of bias.

Table 6: Strengths and Limitations of Clinical Studies Using the Downs and Black Checklist[15]

Strengths	Limitations
Malaithong (2022)[10]	
• The objective, main outcomes, characteristics of the included patients, and interventions were clearly defined. • The main study findings are clearly described. • Actual P values were reported. • The study subjects and those measuring the main outcomes were blinded to treatment received (intervention or control). • All reported results were described in the methods. • The main outcomes were reported by time of follow-up. • The statistical tests used were appropriate. • Compliance with the intervention was reliable. • The main outcome measures were accurate (valid and reliable). • The study subjects were randomized to the intervention groups. • Losses to follow-up were considered. • The study had sufficient power to detect a clinically important effect at all time points except months 10 and 12.	• Potential confounders were not described, and no adjustment for confounding was made in the analysis. • The authors did not identify potential adverse events a priori; instead, all adverse events that occurred during follow-up were reported. • No information was provided on the population from which the subjects were recruited. • No information was provided about the facility where the patients were treated. • Unable to determine whether the patients in different intervention groups were recruited from the same population. • No information was provided on the recruitment timeline. • Unable to determine whether the randomization assignment was concealed from both the patients and health care staff until recruitment was complete and irrevocable.

Strengths	Limitations
Ikeuchi (2011)[17]	
• The objective, main outcomes, characteristics of the included patients, and interventions were clearly defined. • Estimates of random probability are provided via error bars (standard error of the mean) in figures. • Subjects who were prepared to participate were likely representative of the population from which they were recruited. • All results were described in the methods. • All subjects included in the analyses had the same length of follow-up. • The statistical tests used were appropriate. • Compliance with the intervention was reliable. • The main outcome measures were accurate (valid and reliable). • The patients in the intervention groups were recruited from the same population. • There was adequate adjustment for confounding.	• Potential confounders were not described in the methods; however, the characteristics of patients table included some potential confounders and there was no significant difference in their distribution across the 2 groups. • The main findings are presented in graphical format with no accompanying data table or in-text quantitative summary. Therefore, it is not possible to obtain precises measures of effect. • The authors did not identify potential adverse events a priori; instead, all adverse events that occurred during follow-up were reported. • The reason for loss-to-follow-up was provided but no additional characteristics of these 3 patients was included. • Actual P values were not reported. • Unable to determine whether the subjects asked to participate were representative of the entire population from which they were recruited. • Unable to determine whether staff, places and facilities were representative of the treatment that the majority of patients receive. • No attempt to blind study subjects or assessors. • Study subjects were not recruited from the same time period. • The study subjects were not randomized to intervention groups. • The intervention assignment was not concealed. • Patients lost to follow-up were excluded from the analysis. They left the trial because they did not experience pain relief so opted for surgery. • Unable to determine whether the study had sufficient power to detect clinically important differences between groups.

Table 7: Strengths and Limitations of Guidelines Using AGREE II[16]

Item	NICE (2023)[23]	ASPN (2021)[25]	ACR 2021[24]
Domain 1: Scope and purpose			
1. The overall objective(s) of the guideline is (are) specifically described.	Yes	No Can be implied but not specifically described	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	No	No Can be implied but not specifically described	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	No	No Can be implied but not specifically described	Yes

Item	NICE (2023)[23]	ASPN (2021)[25]	ACR 2021[24]
Domain 2: Stakeholder involvement			
4. The guideline development group includes individuals from all relevant professional groups.	Unsure	No Development group limited to pain experts	Yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	Unsure	Unsure	Yes Two patients were part of the guideline development group
6. The target users of the guideline are clearly defined.	No	Yes	Yes
Domain 3: Rigour of development			
7. Systematic methods were used to search for evidence.	Yes	Yes	Yes
8. The criteria for selecting the evidence are clearly described.	No	Yes	Yes
9. The strengths and limitations of the body of evidence are clearly described.	No	No	Yes
10. The methods for formulating the recommendations are clearly described.	No	No	Yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	Yes	No	Yes
12. There is an explicit link between the recommendations and the supporting evidence.	No	Yes	Yes
13. The guideline has been externally reviewed by experts before its publication.	Unsure	Unsure	Unsure
14. A procedure for updating the guideline is provided.	Yes	No	No
Domain 4: Clarity of presentation			
15. The recommendations are specific and unambiguous.	Yes	Yes	Yes
16. The different options for management of the condition or health issue are clearly presented.	No	Yes	No
17. Key recommendations are easily identifiable.	Yes	Yes	Yes
Domain 5: Applicability			
18. The guideline describes facilitators and barriers to its application.	Yes There is a patient-focused section of the NICE website for this guideline that describes key questions to consider	Yes Best practice summaries were provided for each anatomic target which include some clinical barriers	No

Item	NICE (2023)[23]	ASPN (2021)[25]	ACR 2021[24]
	and how to have the discussion about the procedure with their health care professional[30]	and facilitators to treatment, if applicable.	
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	Yes NICE has a document describing general principles for putting evidence-based guidance into practice (i.e., not specifically for this guideline)[31]	Yes The best practice summaries contain some clinical advice on implementation	No
20. The potential resource implications of applying the recommendations have been considered.	No	No	No
21. The guideline presents monitoring and/or auditing criteria.	Yes NICE has a generic tool (spreadsheet) to facilitate the audit of interventional procedures[32]	No	No
Domain 6: Editorial independence			
22. The views of the funding body have not influenced the content of the guideline.	Unsure	Yes	Yes
23. Competing interests of guideline development group members have been recorded and addressed.	No	Unsure	Yes

ACR = American College of Rheumatology; AGREE II = Appraisal of Guidelines for Research and Evaluation II; ASPN = American Society of Pain and Neuroscience; 0NICE = National Institute for Health and Care Excellent; NR = not reported.

Appendix 4: Main Study Findings

Table 8: Summary of Findings by Outcome for Knee Pain — Pain (VAS)

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
VAS at 4 weeks									
Malaithong et al. (2022)[10] RCT	1	NA	Mean difference from baseline (SD)	64	Fluoroscopy guided bimodal RFA	Sham-RFA	Intervention: 2.7 (2.3) Control: 1.9 (2.2)	0.15	No difference between groups
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Mean VAS (narrative summary)	35	RFA	Local anesthetic	The authors concluded that mean VAS was lower among the intervention group, compared to the control group.	0.007	Favours intervention
VAS at 8 weeks									
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Mean VAS (narrative summary)	35	RFA	Local anesthetic	The authors concluded that mean VAS was lower among the intervention group, compared to the control group.	0.028	Favours intervention
VAS at 12 weeks									
Chen et al. (2021)[20] Systematic Review	6	Choi et al. (2011)	Mean difference between	35	RFA	Sham-RFA	−3.55 (−4.84, −2.26)	NR	Favours intervention

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
			groups (95% CI)						
		Shen et al. (2011)		54	RFA	Control	−2.09 (−2.38, −1.80)	NR	Favours intervention
		El-Hakeim et al. (2018)		60	Conventional RFA	Oral analgesic	−2.10 (−3.16, −1.04)	0.004	Favours intervention
		Ray et al. (2018)		24	RFA	IA-HA	−4.50 (−5.84, −3.16)	NR	Favours intervention
		Xiao et al. (2017)		96	RFA	IA-HA	−3.28 (−3.72, −2.84)	NR	Favours intervention
		Davis et al. (2018)		133	Cooled RFA	IAS	−2.40 (−3.12, −1.68)	NR	Favours intervention
VAS at 6 months									
Fogarty et al. (2022)[7] Systematic review	3	Chen et al. (2020)	≥ 50% pain relief (RR [95% CI])	158	Cooled monopolar RFA	IA-HA	1.88 (1.38 to 2.57)	NR	Favours intervention
		El-Hakeim et al. (2018)	Mean (SD)	60	Conventional RFA	Oral analgesic	Intervention: 3.13 (0.3) Control: 5.73 (0.26)	< 0.001	Favours intervention
		Davis et al. (2018)	≥ 50% pain relief (RR [95% CI])	151	Cooled RFA	IAS	4.58 (2.61 to 8.04)	NR	Favours intervention
Chen et al. (2021)[20] Systematic review	1	Xiao et al. (2017)	Mean difference (95% CI)	96	RFA	IA-HA	−2.72 (−3.36, −1.82)	NR	Favours intervention

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
Malaithong et al. (2022)[10] RCT	1	NA	Mean difference from baseline (SD)	59	Fluoroscopy guided bimodal RFA	Sham-RFA	Intervention: 2.4 (2.7) Control: 1.7 (2.7)	0.29	No difference between groups
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Narrative summary	35	RFA	Local anesthetic	The authors concluded mean VAS was lower among the intervention group, compared to the control group.	0.006	Favours intervention
VAS at 12 months									
Malaithong et al. (2022)[10] RCT	1	NA	Mean difference from baseline (SD)	53	Fluoroscopy guided bimodal RFA	Sham-RFA	Intervention: 2.3 (2.8) Control: 2.2 (2.4)	0.73	No difference between groups

CI = confidence interval; HA = hyaluronic acid; IA-HA = intra-articular hyaluronic acid; IAS = intra-articular steroid injection; NA = not applicable; NR = not reported; RCT = randomized controlled trial; RFA = radiofrequency ablation; RR = relative risk; SD = standard deviation; VAS = visual analogue scale.

Note that this table has not been copy-edited.

Table 9: Summary of Findings by Outcome for Knee Pain — Function (WOMAC)

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
WOMAC at 4 weeks									
Malaithong et al. (2022)[10] RCT	1	NA	Mean difference from baseline, within-group (SD)	64	Fluoroscopy guided bimodal RFA	Sham-RFA	Intervention: 26.6 (37.7) Control: 27.2 (37.7)	0.78	No difference between groups
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Narrative summary	35	RFA	Local anesthetic	The authors concluded there was no difference in WOMAC scores between the intervention and control groups.	NR	No difference
WOMAC at 8 weeks									
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Narrative summary	35	RFA	Local anesthetic	The authors concluded there was no difference in WOMAC scores between the intervention and control groups.	NR	No difference
WOMAC at 12 weeks									
Chen et al. (2021)[20] Systematic review	4	Choi et al. (2011)	Mean difference between groups (95% CI)	35	RFA	Sham-RFA	−11.50 (−16.65, −6.15)	NR	Favours intervention
		Shen et al. (2011)		54	RFA	Control	−9.55 (−15.02, −4.08)	NR	Favours intervention

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
		Xiao et al. (2017)		96	RFA	IA-HA	−12.50 (−14.48, −10.52)	NR	Favours intervention
		Davis et al. (2018)		133	Cooled	IAS	−10.00 (−12.71, −7.29)	NR	Favours intervention
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Narrative summary	35	RFA	Local anesthetic	The authors concluded there was no difference in WOMAC scores between the intervention and control groups.	NR	No difference
WOMAC at 6 months									
Fogarty et al. (2022)[7] Systematic review	2	El-Hakeim et al. (2018)	Mean (SD)	60	Monoplar RFA	Medical management	Intervention: 33.13 (4.1) Control: 43.5 (2.0)	< 0.0001	Favours intervention
		Chen et al. (2020)	Proportion improvement from baseline	177	Cooled RFA	IA-HA	Intervention: 48.2% Control: 22.6%	< 0.0001	Favours intervention
Chen et al. (2021)[20] Systematic review	2	Xiao et al. (2017)	Mean difference between groups (95% CI)	96	RFA	IA-HA	−14.20 (−16.76, −11.64)	NR	Favours intervention
		Davis et al. (2018)		125	RFA	IAS	−13.30 (−10.26)	NR	Favours intervention
Malaithong et al. (2022)[10] RCT	1	NA	Mean difference from baseline, within-group (SD)	59	Fluoroscopy guided bimodal RFA	Sham-RFA	Intervention: 27.1 (42.7) Control: 34.7 (54.4)	0.81	No difference between groups

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Narrative summary	35	RFA	local anesthetic	The authors concluded there was no difference in WOMAC scores between the intervention and control groups.	0.0066	No difference between groups
WOMAC at 12 months									
Malaithong et al. (2022)[10] RCT	1	NA	Mean difference from baseline, within-group (SD)	53	Fluoroscopy guided bimodal RFA	Sham-RFA	Intervention: 17.7 (49.2) Control: 24.6 (38.5)	0.7	No difference between groups

HA = hyaluronic acid; IA-HA = intra-articular hyaluronic acid; IAS = intra-articular steroid injection; NA = not applicable; NR = not reported; RCT = randomized controlled trial; RFA = radiofrequency ablation; RR = relative risk; SD = standard deviation; VAS = visual analogue scale.

Note that this table has not been copy-edited.

Table 10: Summary of Findings by Outcome for Knee Pain — Function (PGI-I)

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
Malaithong et al. (2022)[10] RCT	1	NA	Mean (SD)	64	Fluoroscopy guided bimodal RFA	Sham-RFA	**4 weeks:** Intervention: 2.3 (0.8) Control: 2.5 (0.8) **6 months:** Intervention: 2.6 (1.0) Control: 2.4 (0.9) **12 months:** Intervention: 2.8 (1.3) Control: 2.6 (1.3)	0.65 0.46 0.56	No difference between groups
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Mean (SD)	35	RFA	Local anesthetic	**6 months:** Intervention: 1.5 (0.8) Control: 1.1 (0.6)	0.126	No difference between groups

PGI-I = patient global impression of improvement Likert scale; RFA = radiofrequency ablation; PGI-I = SD = standard deviation.

Note that this table has not been copy-edited.

Table 11: Summary of Findings by Outcome for Knee Pain — Function (OKS)

Study citation, design	N studies	Substudy (if applicable)	Measure (summary statistic)	N patients	Intervention	Comparator	Treatment group difference	P value	Direction of effect
OKS at 6 months									
Fogarty et al. (2022)[7] Systematic review	1	Davis et al. (2018)	Mean (SD)	126	Cooled RFA	IAS	Intervention: 35.7 (8.5) Control: 22.4 (8.5)	< 0.001	Favours intervention
OKS at 12 months									
Fogarty et al. (2022)[7] Systematic review	1	Davis et al. (2019)	Mean (SD)	52	Cooled RFA	IAS	Intervention: 34.3 (11.1) Control: 22.0 (16.0)	0.11	No difference between groups
OKS at 24 months									
Fogarty et al. (2022)[7] Systematic review	1	Hunter et al. (2020)	Mean difference from baseline (SD)	NR	Cooled RFA	NA	Baseline: 20.2 (7.3) 24 months: 46.8 (10.3)	< 0.001	Significant improvement from baseline

IAS = intra-articular steroid; OKS = Oxford Knee Score; RFA = radiofrequency ablation; NA = not applicable; SD = standard deviation.
Note that this table has not been copy-edited.

Table 12: Summary of Findings by Outcome for Knee Pain — Adverse events

Study citation, design	N studies	Substudy (if applicable)	Adverse event	Intervention group	Comparator group
Fogarty et al. (2022)[7] Systematic review	2	Davis et al. (2018)	Any	Cooled RFA: 3/76 = 3.9%	IAS: 7/75 = 9.3%
		El-Hakeim et al. (2018)	Serious AE	Conventional RFA: No serious AE	Medical management: No serious AE
Chen et al. (2021)[20] Systematic review	3	Choi et al. (2011)	Any	RFA: No AE	Sham-RFA: No AE
		Sari et al. (2018)	Any	RFA: No AE	IAS: No AE
		Ray et al. (2018)	Any	RFA: No AE	IA-HA: No AE
Malaithong et al. (2020)[10] RCT	1	NA	Serious AE (significant swelling)	Bimodal RFA: 1/32 = 3.1%	Sham-RFA: 0/32 = 0%
Ikeuchi et al. (2011)[17] Nonrandomized trial	1	NA	Serious AE	RFA: No serious AE	Local anesthetic: No serious AE
			Subcutaneous bleeding at the site of needle insertion	RFA: 12/18 = 66.7%	Local anesthetic: 11/14 = 82.4%
			Prolonged hypoesthesia at the IPBSN region	RFA: 14/18 = 77.8%	Local anesthetic: No AE

AE = adverse event; IA-HA = intra-articular hyaluronic acid; IAS = intra-articular steroid; IPBSN = infrapatellar branch of the saphenous nerve; RFA = radiofrequency ablation; RCT = randomized controlled trial.

Note that this table has not been copy-edited.

Table 13: Summary of Findings by Outcome for Hip Pain — Pain (VAS)

Primary Study Within Kao (2018),[22] Systematic Review	Preprocedure VAS score, mean	Postprocedure VAS score, mean	Duration of follow-up
RFA[a]			
Fukui (2001) Case report	9.5 (range: 9 to 10)	1.5 (range: 1 to 2)	2 years
Malik (2003) Case series (n = 3)	8.2 (range: 7 to 9.5)	3 (range: 2 to 4) 3 (range: 2 to 4) 4 (range: NR)	4 weeks 8 weeks 12 weeks
Rivera (2012) Prospective uncontrolled study (n = 17)	9.5 (range: 7 to 10) SD: 0.79	6.35 (range: 6 to 10) SD: 2.17, P < 0.05	6 months

Primary Study Within Kao (2018),[22] Systematic Review	Preprocedure VAS score, mean	Postprocedure VAS score, mean	Duration of follow-up
Cortinas-Saenz (2014) Case series (n = 3)	NR	Average 68.3% improvement	4 weeks
Gupta (2014) Case report	NR	90% relief after first RFA procedure. 20% to 50% relief after second RFA procedure.	6 months NR
Pulsed RFA			
Chye (2015) Nonrandomized controlled trial (n = 15)	6.7 (SD: 0.6)	2.2 (SD: 1.5) 2.4 (SD: 1.4) 3.0 (SD: 1.8)	1 week 4 weeks 12 weeks
Wu (2007) Case series (n = 2)	9 (range: 8 to 10)	0 (range: NR) 3.5 (range: NR)	Immediately postprocedure 3 and 4 months

NR = not reported; SD = standard deviation; VAS = visual analogue scale.

[a]RFA excluded pulsed RFA.

Note that this table has not been copy-edited.

Table 14: Summary of Findings by Outcome for Hip Pain — Function (Lower Extremity Function Scale)

Primary Study Within Kao (2018),[22] Systematic Review	Preprocedure score	Postprocedure score	Duration of follow-up	Direction of effect
Austria (2016) Case report	18/80	49/80	6 months	Favours intervention

Note that this table has not been copy-edited.

Table 15: Summary of Findings by Outcome for Hip Pain — Adverse events

Primary study within Kao (2018),[22] systematic review	Description of adverse event(s)
RFA[a]	
Malik (2003) Case series (n = 3)	Persistent lateral surface hip numbness for unknown duration (n = 1)
Rivera (2012) Prospective uncontrolled trial (n = 17)	Transient hematoma from vessel puncture (n = 3)
Cortinas-Saenz (2014) Case series (n = 3)	Persistent lateral surface hip numbness for unknown duration (n = 1)
Pulsed	
Chye (2015) Nonrandomized controlled trial (n = 15)	Subcutaneous hematoma (n = 1)

[a]RFA excluding pulsed RFA.

Note that this table has not been copy-edited.

Table 16: Summary of Recommendations in Included Guidelines

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
NICE 2023[23]	
"Radiofrequency denervation for osteoarthritic knee pain may be used if standard arrangements are in place for clinical governance, consent and audit (p. 2)."[23] **Efficacy outcomes** **Pain relief (measured by VAS):** Evidence from an NMA of 16 RCTs (at 3 months follow-up) and 10 RCTs (at 6 months follow-up), 2 meta-analyses, 1 RCT, and 2 cohort studies showed that radiofrequency ablation was associated with a statistically significant decrease in pain compared to control at all time points (varied by study, but includes 1 week, and 1, 3, 6, 12, 18 and 24 months). **Composite knee function and pain measures (WOMAC):** Evidence from 1 NMA, 1 meta-analysis, 1 RCT and 1 cohort study showed that radiofrequency ablation was associated with a statistically significant decrease in WOMAC compared to control at all time points (varied by study, but includes 1, 3, 6, 18 and 24 months). **Functional outcomes** • Evidence from 1 RCT found no significant difference in **walking ability** among patients who received capacitive resistive monopolar radiofrequency compared to sham. • Evidence from 1 RCT found a significant difference **in knee range of motion** between groups pre-treatment, post-treatment, 1 month and 3 months after treatment. **Quality of life (measured by EQ-5D-5L):** Evidence from 1 cohort study showed that total EQ-5D-5L among patients who received cooled radiofrequency ablation significantly increased from baseline at 18 and 24 months. **Efficacy by treatment modality:** Evidence from 1 NMA "found that whilst all modalities of RF denervation were typically more effective than placebo or exercise, patients responded better to the cooled modality than the conventional and pulsed modalities, and bipolar is more effective than monopolar for pain function in conventional and pulsed modalities…However, the authors caution that the number of studies, including for cooled modality, is insufficient (p. 28)."[33] **Safety outcomes** **Complications and major complications:** Evidence from 1 NMA found evidence of adverse events reported in 6 studies: 8.4% of those in the treatment group with any adverse events, and 3.9% with major adverse events. Evidence from 1 meta-analysis found no significant difference in risk of adverse events between treatment and control groups. **Other:** • Evidence from 1 NMA found 5 people experienced **falls**, 1 person had **stiffness**, and 2 people had **swelling.** There were considered major adverse events possibly related to the treatment. • Evidence from 1 narrative review summarized a report of 1 person with **septic arthritis**, 1 person with a pes answerine tendon injury, and 1 person with a **skin burn** after treatment. • An instance of **foot drop** after treatment was summarized in 1 case report. And a second case report summarized the evidence of 1 person with **vascular injury** after treatment.	NR

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
• A list of anecdotal and theoretical adverse events was generated through expert consultation: numbness, osteomyelitis, injuries to motor nerves, post ablation neuritis and Charcot neuropathy.	
"The procedure should only be done by clinicians with specific training and experience in this procedure (p. 2)."[23] Supporting evidence NR	NR
"For auditing the outcomes of this procedure, the main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes and audit took (for use at local discretion) (p. 2)."[23] Supporting evidence NA	NA
ASPN (2021)[25]	
"Genicular nerve radiofrequency neurotomy may be used for the treatment of osteoarthritis related and post-surgical knee joint paint. GRADE II-I B (p. 2821)."[25] **Evidence overview** This recommendation was informed by 4 studies: a meta-analysis of 12 RCTs, a systematic review of 13 publications, 1 RCT (which was included in the systematic review) and 1 literature review. **Efficacy outcomes** **Pain relief:** The body of evidence included in this guideline (n = 4 studies) showed reduction in pain scores among those who received RFA compared to the control group at various time points (1, 3 and 12 months). **Function:** Evidence from the systematic review and RCT (which was included in the systematic review) showed improved function about the treatment groups compared to the controls. **Safety outcomes** **Adverse events:** The systematic review did not report any adverse events associated with RFA treatment.	**Quality of evidence:** Well-designed, controlled, nonrandomized clinical trial. **Strength of recommendation:** "…high certainty that the net benefit is moderate or there is a moderate certainty that the net benefit is moderate to substantial (p. 2810)."[25]
Best practices summary: • "Radiofrequency ablative technologies for the nociceptive sensory innervation of the knee have been shown to be an effective therapy for chronic knee pain due to conditions, such as osteoarthritis and postsurgical pain (p. 2821)."[25] • "Utilization of RFN on the knee obviates a comprehensive knowledge and understanding of the anatomical innervation of the knee, experience with fluoroscopy or ultrasound, and knowledge regarding the principles surrounding RFN (p. 2821).[25] • "Evidence-based parametres for electrode settings are the use of 70–80°C for 90–180 seconds p. 2821)."[25] • "In terms of technique, targeted genicular nerves for conventional and cooled RFN include the SM, SL, and IM nerves. Due to the variable anatomy of these branches, larger lesion sizes increase the likelihood of success p. 2821)."[25] • "Pre-ablative diagnostic blocks with a low volume anesthetic may enable more accurate prognostication of the analgesic response to RFN (p. 2821)."[25] • "Avoiding unnecessary injury or inadvertent neurotomy of motor nerves, nontargeted sensory nerves, blood vessels, and other nontargeted anatomic structures is essential. Motor testing prior to ablation should be considered (p.	NR

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
2821)."[25] **Evidence overview** The link between the evidence and the best practice summary is not clearly defined: there is no evidence quality or strength assessment assigned to each summary point. No additional publications are cited to inform this practice summary.	
"Hip joint radiofrequency neurotomy targeting the obturator and femoral nerve branches may be used for the treatment of hip joint pain following diagnostic blocks. GRADE II-I-B (p. 2824)."[25] **Evidence overview** The efficacy of RFA for hip pain was informed by evidence from 4 studies: 2 retrospective uncontrolled studies, 1 prospective uncontrolled study, and 1 case series. **Efficacy outcomes** **Pain relief:** Evidence from the 4 studies showed improvement in pain scores from baseline.	**Quality of evidence:** Well-designed, controlled, nonrandomized clinical trial. **Strength of recommendation:** "…high certainty that the net benefit is moderate or there is a moderate certainty that the net benefit is moderate to substantial (p. 2810)."[25]
Best practices summary: • "At a minimum, fluoroscopy is necessary to ensure proper identification of hip bony landmarks and to navigate challenging anatomy. More investigation is required to determine the optimal use of ultrasound in hip denervation. Ultrasound is often used in conjunction with fluoroscopy for optimal needle placement (p. 2823)."[25] • "Patient body habitus and mobility are also important considerations. In the morbidly obese (BMI >40), it can be extremely difficult to place needles comfortably and easily. Patients must be able to lie supine with the hip in neutral extension (p.2823)."[25] • "Diagnostic blocks should be performed prior to neurotomy but data implying their prognostic value is limited (p.2823)."[25] • "Neurotomy of both the femoral and articular branches has become standard practice using lateral to medial approaches with the patient in the supine position (p.2823)."[25] • "Evidence best supports the use of conventional RF at 80 degrees for 90 seconds, although efficacy for cooled-RF has been shown in recent cohort and case series (p.2823)."[25] **Evidence overview** The link between the evidence and the best practice summary is not clearly defined: there is no evidence quality or strength assessment assigned to each summary point. In addition to the 4 studies on the hip joint referenced above, one additional anatomic study may have been used to inform this practice summary (it is summarized in a table with the other 4 studies). The authors assessed the contribution of the femoral, obturator and accessory obturator nerves and found that the femoral and obturator nerves contributed to the capsular innervation in all specimens (n = 3).	NR

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
ACR 2021[24]	
"Radiofrequency ablation is conditionally recommended for patients with knee OA. "A number of studies have demonstrated potential analgesic benefits with various ablation techniques but, because of the heterogeneity of techniques and controls used and lack of long-term safety data, this recommendation is conditional (p. 156)."[24] **Efficacy outcomes** **Pain relief:** Evidence from 1 moderate quality and 2 high-quality RCTs found RFA was associated with decreased pain compared to sham ablation for OA knee. Evidence from 4 low-quality RCTs found that RFA was associated with decreased pain compared to intra-articular injections for OA knee. **Function:** Evidence from 1 low-quality RCT found that RFA was associated with improved SF-36 physical function score compared to intra-articular injections for OA knee. Evidence from 1 low-quality RCT found that RFA was associated with a higher rate of walking at 3 months compared to intra-articular injections for OA knee. Evidence from 1 low-quality RCT found that RFA was associated with improved stair climbing at 3 months compared to intra-articular injections for OA knee. **Safety outcomes** NR for knee or hip.	**Quality of evidence:** "Quality of evidence across all critical outcomes: moderate (for direct comparison data) (p. 322)."[24] **Strength of recommendation:** Conditional

ACR = American College of Rheumatology; ASPN = American Society of Pain and Neuroscience; NA = not applicable; NICE = National Institute for Health and Care Excellence; NMA = network meta-analysis; NR = not reported; OA = osteoarthritis; RCT = randomized controlled trial; RFA = radiofrequency ablation; VAS = visual analogue scale; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Note that this table has not been copy-edited.

Appendix 5: Overlap Between Included Systematic Reviews

Note that this appendix has not been copy-edited.

Table 17: Overlap in Relevant Primary Studies Between Included Systematic Reviews

Primary study citation	Fogarty (2022)[7]	Chen (2021)[20]
Chen AF, et al. J Bone Joint Surg Am. 2020;102:1501 to 10.	Yes	—
Chen AF, et al. BMC Musculoskelet Disord. 2020;21:363.	Yes	—
Hunter C, et al. Pain Pract. 2020;20:238 to 46.	Yes	—
Davis T, et al. Reg Anesth Pain Med. 2019;44:499 to 506.	Yes	—
Davis T, et al. Reg Anesth Pain Med. 2018;43:84 to 91.	Yes	Yes
El-Hakeim EH, et al. Pain Physician. 2018;21:169 to 77.	Yes	Yes
Reddy RD, et al. Anesth Pain Med. 2016;6:e39696.	—	Yes
Xiao L, et al. Exp Ther Med. 2018;5:3973 to 77.	—	Yes
Sari S, et al. Int J Rheum Dis. 2018;21:1772 to 78.	—	Yes
Ray D, et al. Indian J Pain. 2018;1:36 to 39	—	Yes
Shen WS, et al. Am J Ther. 2017;6:e693-e700.	Yes	—
Choi WJ, et al. Pain. 2011;3:481 to 87.	—	Yes

Appendix 6: References of Potential Interest

Note that this appendix has not been copy-edited.

Systematic Reviews

Network Meta-Analysis With Methodological or Administrative Issues

Wu L, Li Y, Si H, et al. Radiofrequency ablation in cooled monopolar or conventional bipolar modality yields more beneficial short-term clinical outcomes versus other treatments for knee osteoarthritis: a systematic review and network meta-analysis of randomized controlled trials. *Arthroscopy*. 2022 07;38(7):2287-2302. PubMed

Note: This SR with network meta-analysis was identified in the search and reviewed at full text. It was also a key piece of evidence used to inform the NICE guideline.[23] It was excluded from the present review due to issues with critical citations: there were numerous instances where the references for the included studies were inaccurate in-text (i.e., they cross-referenced to a different citation in the reference list). Due to the presence of multiple publications from the same author, and one reference missing completely from the study's reference list (i.e., Ahmed et al. was the first included study in-text, but not listed in the reference list). It was difficult to assess overlap between other SRs included in this review, and to interpret findings. Therefore, it was excluded from this review but shared here as it has relevant findings from direct and indirect comparisons of RFA effectiveness on knee pain.

Systematic Reviews That Met Inclusion Criteria but Were Excluded Due to Complete Overlap With Included SRs

Ajrawat P, Radomski L, Bhatia A, Peng P, Nath N, Gandhi R. Radiofrequency procedures for the treatment of symptomatic knee osteoarthritis: a systematic review. *Pain Med*. 2020 02 01;21(2):333-348. PubMed

Li G, Zhang Y, Tian L, Pan J. Radiofrequency ablation reduces pain for knee osteoarthritis: a meta-analysis of randomized controlled trials. *Int J Surg*. 2021 Jul;91:105951. PubMed

Zhang H, Wang B, He J, Du Z. Efficacy and safety of radiofrequency ablation for treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. *J Int Med Res*. 2021 Apr;49(4):3000605211006647. PubMed

Additional References

Case Report or Series Identified Through the Literature Search

Belba A, Vanneste T, Jerjir A, et al. Complex regional pain syndrome of the knee after conventional radiofrequency ablation of the genicular nerves treated successfully with dorsal root ganglion stimulation: a case report. *Pain Pract*. 2022;22(5):541-546. PubMed

Koshi E, Cheney CW, Sperry BP, Conger A, McCormick ZL. Genicular nerve radiofrequency ablation for chronic knee pain using a three-tined electrode: a technical description and case series. *Pain Med*. 2020;21(12):3344-3349. PubMed

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Questions or requests for information about this report can be directed to Requests@CADTH.ca.