07.01.73 Ablative Procedures of the Peripheral Nerves to Treat Pain*

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Related Policies:

- 07.01.41 Pulsed Radiofrequency Ablation
- 07.01.58 Radiofrequency Ablation and Alternative Ablative Methods for Chronic Facet Joint Mediated Neck, Back, and Sacroiliac Joint Pain*
- 07.01.66 Treatment for Occipital Neuralgia, Chronic Headaches and Persistent Idiopathic Facial Pain*

Summary

Description

Ablative procedures such as radiofrequency ablation (RFA) (standard, pulsed, cooled), cryoneurolysis (cryoablation) and chemical neurolysis (phenol, alcohol, glycerol) of the nerves have been proposed as a

treatment for several different types of pain. These ablative procedures have been used to treat a number of clinical pain syndromes such as trigeminal neuralgia, cervical and lumbar facet joint pain and headache syndromes, s*ee Related Polices above.* This evidence review evaluates the application of RFA (standard, pulsed, cooled), cryoneurolysis (cryoablation, cryoanalgesia) and chemical neurolysis (phenol, alcohol, glycerol) in peripheral sites distant from the spine.

Summary of Evidence

Osteoarthritis of Knee

For individuals who have knee osteoarthritis (OA) who receive radiofrequency ablation (RFA) (conventional RFA, pulsed RFA, or cooled RFA) of the peripheral nerves, the evidence includes systematic reviews of randomized controlled trials (RCTs), RCTs with 24 to 200 individuals, and non-randomized comparative studies with up to 12 months of follow-up. Relevant outcomes include symptoms, functional outcomes, and quality of life (QOL). Knee OA is a common disorder in older adults. RFA of the genicular nerves has the potential to alleviate pain and improve function in this population and might also delay or eliminate the need for TKA. At this time, there is high heterogeneity in methods and comparators. The systematic reviews generally found that RFA had a benefit on pain, function and composite scores compared to the control treatments at 3 and 6-month follow-up; however, most estimates were determined to have moderate to high heterogeneity. The network meta-analysis compared multiple RFA modalities and found that cooled RFA had significantly improved efficacy for pain and function through 6 months follow-up compared with traditional pulsed RFA. The 2 multicenter trials conducted in the U.S. used anesthetic nerve block under fluoroscopic guidance and compared efficacy of cooled RFA to either steroid injection or hyaluronic acid injection. Both studies reported a responder rate of approximately 70% at 6 months, which was significantly greater than the control conditions. A small, double-blind RCT of bipolar RFA with genicular nerve block compared to genicular nerve block and sham found no differences between groups for visual analog score (VAS) pain or the Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores through 12 months follow-up. Given that OA of the knee is a common condition; adequately powered studies, preferably blinded with active and sham controls and follow-up at least 12 months, is needed to determine the benefits and potential harms of this treatment. The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have knee OA or total knee arthroplasty (TKA) who receive cryoneurolysis (cryoablation) of peripheral nerves, the evidence includes 2 RCTs with a total of 304 participants, a comparative, retrospective cohort study of 57 participants, and a registry study of 140 individuals. Relevant outcomes include symptoms, functional outcomes, and QOL. In one RCT, cryoneurolysis (cryoablation) in individuals with knee OA resulted in a greater decrease in WOMAC pain score, WOMAC total score, and VAS score at 30 days compared with sham-treated controls. However, subsequent measurements showed no significant benefit of cryoneurolysis on WOMAC score at 60 days or VAS scores at 60 or 90 days. Another RCT investigated cryoneurolysis (cryoablation) compared to standard of care for patients with knee OA who were planning to undergo TKA. Cryoneurolysis (cryoablation) resulted in a lower rate of opioid consumption, a reduction in numeric rating scale (NRS) pain scores and Knee Injury and Osteoarthritis Score for Joint Replacement (KOOS JR) functional performance at 12 weeks post discharge. The retrospective cohort study reported superiority of cryoneurolysis (cryoablation) on the KOOS JR and Short-Form-12 item (SF-12) mental score at 1 year follow-up; no significant differences were observed on the SF-12 physical score at 1 year follow-up or any outcome at earlier 3-month assessment. A registry study found improved pain and lowered opioid use with cryoneurolysis prior to TKA; however, functional outcomes through 6 months were similar. Several technical issues including the optimal number of applications to each nerve, the duration of treatment, and the duration of thawing before moving the cannula have not been resolved. The most effective method for determining probe

insertion location (e.g., ultrasound-guided or based on anatomic landmarks) also needs to be established. The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have knee osteoarthritis (OA) who receive chemical neurolysis (phenol, alcohol, glycerol) the evidence includes a systematic review that includes case series, case report, observational prospective cohort study and RCTs. Relevant outcomes include symptoms, functional outcomes, and QOL. In the systematic review by Tan et. al. (2022) included case series, case report, observational prospective cohort study and randomized controlled trials for individuals with chronic knee OA. Relevant outcomes include symptoms, functional outcomes, and (QOL). In this systematic review the only study that utilized phenol as the therapeutic treatment (1.5 mL of 7% glycerinated phenol solution) was a noncomparative observational prospective cohort study (n=43) by Risso et. al. (2021). Patients experienced pain reduction early within one day > 50 reduction and maintained for up to 6 months (NRS-11 improvement from 7.2 at baseline to 4.2) in 43 patients and improvement in WOMAC from 48.7 at baseline to 20.7 at 6 months. Adverse events included local pain, hypoesthesia, swelling and bruising at 2 weeks which resolved within 2 months. While this observational prospective cohort study showed promise in improving pain this was limited to 6-month follow-up, and it was noncomparative. RCTs are needed with larger sample sizes and longer follow-up to determine the efficacy of chemical neurolysis (phenol, alcohol, glycerol) in the treatment of chronic knee OA. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Osteoarthritis of Hip

For individuals who have hip OA who receive RFA (standard, pulsed and cooled), the evidence includes nonrandomized controlled trial, observational study and case series. Relevant outcomes include symptoms, functional outcomes, and QOL. While these studies may have shown promising results in reducing pain and increasing function through the use of VAS and WOMAC scores the time on follow-up was of short duration 12 weeks to 6 months, and when comparing groups from baseline pain and function scores there were no statistical differences noted between the groups. These studies did not include any comparisons between RFA and non-RFA groups. Comparative RCTs are needed to investigate the efficacy of RFA to include longer observation periods in the treatment of chronic hip pain. The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have hip OA who receive chemical neurolysis (phenol, alcohol, glycerol), the current evidence is limited, but does includes a RCT. Relevant outcomes include symptoms, functional outcomes, and QOL. The current evidence includes two double blinded RCTs. Crema et al (2022) single RCT included individuals with severe hip OA to compare hip pain and functional performance after obturator nerve with phenol (PG) or 1% lidocaine that failed conservative treatment. Treatment responses were evaluated utilizing VAS scores and WOMAC scores. The pain intensity reported by VAS during the study included the following: baseline pain intensity was similar in both groups (phenol: 87.0 ± 15.0 vs lidocaine 90.0 ± 11.0; p>0.05). After one month of a single nerve block, pain intensity reduced in both groups, although slightly more in those subjects injected with phenol, without statistical difference (phenol: 58.0 vs 29.0 vs lidocaine: 70.0 ± 27.0; p>0.05); and both groups finished the follow-up period with very similar pain intensities (phenol: 59.0 ± 29.0 vs lidocaine: 60.0 ± 32.0; p>0.05). Similar results concerning functioning using WOMAC were observed in both groups which had similar baseline scores and improved QOL after one month and four months. Although the scores were better than baseline there was no statistical difference between the groups. Reysner et al (2025) evaluated the efficacy and safety of chemical ablation of the pericapsular nerve utilizing ultrasound guided ethanol (95%) neurolysis compared with sham neurolysis procedure in individuals with chronic osteoarthritis of the hip who failed conservative management. The primary outcome was pain intensity (numeric rating scale [NRS]) assessed at 7 days, 30 days, 3 months, and 6 months. Secondary outcomes included opioid consumption

(oral morphine equivalents), quality of life (EQ-5D-5L), and neurological deficits. Ethanol neurolysis significantly reduced NRS scores at all follow-ups (P <0.0001). The mean NRS scores decreased from baseline 6.0 ($_{SD}$ 0.9) to 3.1 (0.8) at 7 days, 2.9 (0.7) at 30 days, 2.8 (0.7) at 3 months, and 3.0 (0.7) at 6 months. Opioid consumption was lower in the neurolysis group at 7 days (median [IQR]: 1.5 [0.5-3.5] mg vs 11.5 [9.1-13.7] mg, P=0.002) and remained reduced through 6 months. Quality of life improved significantly (P<0.0001), and no neurological deficits were observed. While studies may show promise, additional RCTs are warranted to further investigate the efficacy of chemical neurolysis in the treatment of chronic hip pain. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Chronic Shoulder Pain

For individuals who have chronic shoulder pain who receive RFA (standard, cooled and pulsed) the evidence includes systematic review and cohort study. Relevant outcomes include symptoms, functional outcomes, and QOL. In a systematic review by Orhurhu et. al. (2019) on the use of RFA and pulsed radiofrequency ablation (PRF) for the management of shoulder pain which included 6 RCTs, 1 prospective study, 1 retrospective study, and 10 case series or case reports. While studies may have shown an improvement in pain and functional outcomes, there were numerous limitations that reduced the strength of this evidence. First, heterogeneity in concomitant therapies used in combination with PRF and RFA (steroids and physical therapy) made it difficult to evaluate the efficacy of PRF. Additionally, different techniques of ablation as well as varying study lengths and follow-up periods were utilized which confounds the actual duration of pain relief provided by PRF. The prospective and retrospective studies evaluating RFA suggested a potential benefit of RFA, however, the results were limited by varying treatment protocols and small sample sizes. Further RCTs determining standardized protocols, larger sample sizes with longer follow-up are needed to assess safety and efficacy of radiofrequency ablation for the treatment chronic shoulder pain. The evidence is insufficient to determine the effects of the technology on net health outcomes.

For individuals who have chronic shoulder pain who receive chemical neurolysis (alcohol, phenol, glycerol) no published literature was identified in-regards to individuals receiving this ablative treatment for this condition. Relevant outcomes include symptoms, functional outcomes, and QOL. RCTs are needed to determine the efficacy of this ablative method in the treatment of chronic shoulder pain. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Intercostal Neuralgia

For individuals who have intercostal neuralgia who receive RFA (standard, cooled and pulsed) the evidence includes case series. Relevant outcomes include symptoms, functional outcomes, and QOL. In the two-case series one utilized cooled radiofrequency and the other utilized standard RFA in the treatment of intercostal neuralgia, while both studies showed that RFA may reduce pain one study was not standardized and long-term assessment could not be concluded. RCTs are needed with larger patient populations to determine ideal candidates and standardize protocols to further elucidate the effectiveness of this intervention, safety profile and its scope of use in the treatment of intercostal neuralgia, The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have intercostal neuralgia who receive chemical neurolysis (alcohol, phenol, glycerol) no published literature was identified in-regards to individuals receiving this ablative treatment for this condition. Relevant outcomes include symptoms, functional outcomes, and QOL. RCTs are needed to

determine the efficacy of this ablative method in the treatment of intercostal neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Chronic Inguinal Neuralgia

For individuals who have chronic inguinal neuralgia who receive RFA (standard, cooled and pulsed) the evidence includes two RCTs, retrospective studies, and case series. Relevant outcomes include symptoms, functional outcomes, and QOL. In Makharita (2015) longer duration of pain relief was noticed in Group 1 (p=0.005) after the first PRF block, while durations of pain relief of the second PRF block were comparable (4 months in each group; p=0.59). All patients in Group 2 received 3 blocks (the first was a sham PRF) during the one-year follow-up period. In Kastler (2012) mean VAS scores were 7.72 in the RFA group and 7.46 in the infiltration group. Maximum early pain relief did not statistically differ (77% in the RFA group and 81.5% in the injection group) from baseline. Study limitations for both studies were small sample size and that they did not address key health outcomes. Results need to be confirmed by additional RCTs with larger sample sizes and longer follow-up to determine the efficacy of RFA in the treatment of chronic inguinal neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have chronic inguinal neuralgia who receive chemical neurolysis (alcohol, phenol, glycerol) no published literature was identified in-regards to individuals receiving this ablative treatment for this condition. Relevant outcomes include symptoms, functional outcomes, and QOL. RCTs are needed to determine the efficacy of this ablative method in the treatment of chronic inguinal neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Plantar Fasciitis

For individuals who have plantar fasciitis who receive RFA or cryoneurolysis (cryoablation), the evidence includes 2 RCTs and a meta-analysis. Relevant outcomes include symptoms, functional outcomes, and QOL. One of the randomized trials only evaluated 17 individuals, and assessment of randomized outcomes was limited to 4 weeks post-treatment. A second RCT evaluated 36 individuals out to 12 weeks. Both trials found RFA associated with pain reduction, but to be more confident in the efficacy of this treatment, controlled trials with larger samples and longer follow-up would be necessary. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have plantar fasciitis who receive chemical neurolysis (alcohol, phenol, glycerol) no published literature was identified in-regards to individuals receiving this ablative treatment for this condition. Relevant outcomes include symptoms, functional outcomes, and QOL. RCTs are needed to determine the efficacy of this ablative method in the treatment of plantar fasciitis. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Peripheral Neuromas

For individuals who have peripheral neuromas who RFA or cryoneurolysis (cryoablation), the evidence includes case series. Relevant outcomes include symptoms, functional outcomes, and QOL. In the case series studies utilizing radiofrequency and cryosurgery for lower extremity peripheral neuromas, while both studies may have shown a relief of pain symptoms a portion of the patients experienced minimal relief to no relief based on these treatment modalities. RCTs with larger patient populations and longer follow-up are needed to assess the safety and efficacy of RFA in the treatment of peripheral neuromas. The evidence is insufficient to determine the effects of the technology on net health outcomes.

For individuals who have chronic inguinal neuralgia who receive chemical neurolysis (alcohol, phenol, glycerol) no published literature was identified in-regards to individuals receiving this ablative treatment for this condition. Relevant outcomes include symptoms, functional outcomes, and QOL. RCTs are needed to determine the efficacy of this ablative method in the treatment of chronic inguinal neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Chronic Orchialgia

For individuals who have chronic orchialgia who receive RFA (standard, cooled and pulsed) the evidence includes one RCT. Relevant outcomes include symptoms, functional outcomes, and QOL. In the RCT by Hetta et. al. 2018 which evaluated the analgesic effect of PRF applied to the ilioinguinal nerve and the genital branch of the genitofemoral nerve for individuals suffering from chronic post-surgical orchialgia there was a significant reduction of the mean post-procedural VAS pain score at 2-, 4-, 6-, 8-, and 12-weeks ($p = 0.001$) in the PRF group in comparison to the sham group. Likewise, there was a significant improvement of the GPE in the PRF group in comparison to the sham group ($p = 0.00$), however, this study was limited by the follow-up period, which was only 3 months. While the RCT showed promising results it was limited by short follow-up period and did not evaluate key health outcomes such as QOL or achievement of pre-specified clinically significant improvement thresholds. Additional RCTs are needed to determine the efficacy of this ablative method in the treatment of chronic orchialgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have chronic inguinal neuralgia who receive chemical neurolysis (alcohol, phenol, glycerol) no published literature was identified in-regards to individuals receiving this ablative treatment for this condition. Relevant outcomes include symptoms, functional outcomes, and QOL. RCTs are needed to determine the efficacy of this ablative method in the treatment of chronic inguinal neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Postherpetic Neuralgia

For individuals who have postherpetic neuralgia who receive RFA (standard, cooled and pulsed) the evidence includes systematic review, observational study and case report. Relevant outcomes include symptoms, functional outcomes, and QOL. Hayes Inc. (May 2024) completed an a health technology assessment regarding pulsed radiofrequency for the treatment of chronic postherpetic neuralgia of various sites. The evidence was considered low-quality. While the limited evidence may show promise in reducing pain there remains an uncertainty in PRF treatment protocols, heterogeneity in comparators and treatment sites/targeted nerves, the clinical benefit of this treatment and lack of long-term follow-up. In the systematic review Lin (2019), which included 4 RCTs evaluating the efficacy of pulsed radiofrequency ablation for the treatment of post herpetic neuralgia all study outcomes, including VAS, average rescue medication dosage, most SF-36 index scores (e.g., general health perceptions, social function, emotional role, mental health index, bodily pain index, physical function, and physical role), and the Pittsburgh Sleep Quality Index scale, favored pulsed radiofrequency. The observed effects began on Day 2 or 3 after treatment and persisted for 2-6 months (i.e., study endpoint). No side effects such as pneumothorax, infection, nerve injury, postoperative paresthesia, pain exacerbation, or any other serious adverse effects were observed in all studies. While this systematic review shows promise these RCTs are limited by short follow-up of 6 months. Additional RCTs are needed to verify these results to include adequate sample size and longer follow-up to determine the efficacy of radiofrequency ablation for the treatment of post herpetic neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have postherpetic neuralgia who receive chemical neurolysis (alcohol, phenol, glycerol) no published literature was identified in-regards to individuals receiving this ablative treatment for this condition. Relevant outcomes include symptoms, functional outcomes, and QOL. RCTs are needed to determine the efficacy of this ablative method in the treatment of postherpetic neuralgia. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Cryoablation for Individuals undergoing Nuss Procedure for Pectus Excavatum

For individuals who are undergoing Nuss procedure for pectus excavatum who receive intercostal nerve cryoablation (ICN) the evidence includes systematic review and meta-analysis, 1 RCT, and several observational studies. Relevant outcomes include symptoms, functional outcomes, and QOL. A study of 20 adolescent to young adults, upon which the FDA 510k clearance for using cryoablation nerve block therapy device in adolescents (12–21 years of age) was based, demonstrated analgesia equivalence to thoracic epidurals and shorter hospital length of stays. However, as noted in a commentary by Chidambraran et al (2022), "this is not enough evidence to demonstrate safety of this technique in children and that larger studies are needed, and we should therefore be cautious in its application. In a systematic review and meta-analysis in 2020 by Daemen et. al. reviewing the outcomes of intercostal nerve cryoablation (INC) in comparison to thoracic epidural (TE) after the Nuss procedure found the meta-analyses demonstrated a significantly shortened length of hospital stay [mean difference -2.91 days; 95% confidence interval (CI) -3.68 to -2.15; P < 0.001]. However, the meta-analyses demonstrated significant level heterogeneity (both I^2 = 91%; P < 0.001). Post hoc subgroup analysis was performed to assess the effect of the use of concomitant analgesic methods on the length of hospital stay and heterogeneity. Subgroup analysis revealed a statistically significant difference among studies that did (n = 3) and did not (n = 2) use additional modalities of analgesia (PCA, intercostal nerve block or local infusion catheters) (I 2 = 91.1%; P < 0.001). The subgroup using additional analgesic techniques demonstrated a lower decrease in hospitalization for the cryoablation group (MD -2.19, 95% CI -2.50 to -1.89; P < 0.001), compared to the subgroup without additional analgesic methods (MD -3.76, 95% CI -4.63 to -2.90; P < 0.001). In addition, no heterogeneity was detected among studies in the subgroup that used concomitant analgesic methods (I 2 = 0.0%; P = 0.38). Despite shorter hospitalization time in favor of cryoablation, postoperative pain scores based on the numeric rating scale (NRS) didn't significantly differ between groups. Despite diverging definitions, 3 studies demonstrated a statistically significant difference in opioid usage that favored cryoablation. Dekonenko et al., total opioid usage during inpatient stay was 420.0 MME for the thoracic epidural and 60.0 MME for the cryoablation group (p < 0.001), Graves et al. found statistically significant reduced mean opioid usage in the cryoablation group [268.0 MME (SD 165.2) vs 684.0 MME (SD 191.8) for the epidural group; p < 0.001]. Keller et al. only reported the mean total intravenous opioid usage and revealed similar results [49.0 (SD 32.7) vs 119.8 MME (SD 95.1) for the cryoablation and epidural group; p = 0.001]. Harbaugh et al. was the only one to find no statistically significant mean difference in postoperative opioid usage. In regard to adverse effects eleven (11.0%) complications occurred in the cryoablation group, in comparison to 3 (3.1%) complications in the thoracic epidural group. Limitations associated with this review included a low number of included studies and participants; only one randomized trial included, the overall methodological quality that ranged from some concerns to serious risk of bias, the use of data conversion methods and the heterogeneity among included studies. The authors concluded "Cryoablation of the intercostal nerves during the Nuss procedure may be an attractive alternative to thoracic epidural analgesia with reduced length of hospital stay of 2.91 days. However, given the overall low methodological quality and heterogeneity of studies, well-designed randomized controlled trials are necessary to corroborate the current evidence." Additional comparative RCTs are needed with larger sample sizes, longer follow-up, and outcome measures (functional outcomes and QOL) related to the use of ICN for individuals undergoing Nuss procedure for pectus excavatum to determine safety and efficacy. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Additional Information

Not applicable

OBJECTIVE

The objective of this evidence review is to determine whether the use of radiofrequency ablation (RFA) (standard, cooled and pulsed), cryoneurolysis (cryoablation, cryotherapy, cryoanalgesia), and chemical neurolysis (alcohol, phenol, glycerol) of peripheral nerves improves the net health outcome in individuals with chronic pain due to osteoarthritis of the knee and hip, chronic orchialgia (may also be referred to as one of the following: testicular pain syndrome; chronic testicular pain; testialgia; chronic scrotal content pain (CSCP); post-vasectomy orchialgia; post-vasectomy pain syndrome (PVPS); congestive epididymitis), chronic shoulder pain, inguinal neuralgia, intercostal neuralgia, peripheral neuromas, plantar fasciitis, postherpetic neuralgia and pain management regarding pectus excavatum related to the Nuss procedure.

PRIOR APPROVAL

Prior approval is required.

Note: *Refer to Wellmark Authorization Table to determine applicable prior approval requirements for the procedure code(s) to be performed and the medical necessity clinical coverage criteria using InterQual® criteria.*

POLICY

Radiofrequency ablation (standard, cooled, pulsed), cryoneurolysis (cryoablation, cryotherapy, cryoanalgesia) or chemical neurolysis (alcohol, phenol, glycerol) of the peripheral nerves to treat pain including but not limited to the following is considered **investigational** because the evidence is insufficient to determine the effects of this technology on net health outcomes:

- Chronic knee pain/Osteoarthritis of the knee
    - As a treatment prior to partial or total knee replacement
    - As a treatment following partial or total knee replacement
    - As a treatment for individuals who are not candidates for partial or total knee replacement surgery
- Chronic hip pain/Osteoarthritis of the hip
    - As a treatment prior to partial or total hip replacement
    - As a treatment following partial or total hip replacement

    - As a treatment for individual who are not candidates for partial or total hip replacement surgery
- Chronic orchialgia (may also be referred to as one of the following: testicular pain syndrome; chronic testicular pain; testalgia; chronic scrotal content pain (CSCP); post-vasectomy orchialgia; post-vasectomy pain syndrome (PVPS); congestive epididymitis)
- Chronic shoulder pain
- Inguinal neuralgia
- Intercostal neuralgia
- Peripheral neuromas
- Plantar Fasciitis
- Postherpetic neuralgia
- Pre-operative, intraoperative and post-operative for pain management related to pectus surgery including Nuss procedure

POLICY GUIDELINES

Coding

See the Codes table for details.

BACKGROUND

Nerve Radiofrequency Ablation

Nerve RFA is a minimally invasive method that involves the use of heat and coagulation necrosis to destroy tissue. A needle electrode is inserted through the skin and into the tissue to be ablated. A high-frequency electrical current is applied to the target tissue and a small sphere of tissue is coagulated around the needle by the heat generated. It is theorized that the thermal lesioning of the nerve destroys peripheral sensory nerve endings, resulting in the alleviation of pain. Cooled RFA is a variation of nerve RFA using a water-cooled probe that applies more energy at the desired location without excessive heat diffusing beyond the area, causing less tissue damage away from the nerve (see Table 1). The goal of ablating the nerve is the same.

RFA is also distinguished from pulsed radiofrequency (PRF) treatment, which has been investigated for different types of pain. The mechanism of action of PRF treatment is uncertain, but it is thought not to destroy the nerve. It does produce some degree of nerve destruction but is thought to cause less damage than standard RFA. Some studies refer to PRF treatment as ablation.

For the indications assessed in this evidence review, nerve RFA should be distinguished from RF energy applied to areas other than the nerve to cause tissue damage. Some individuals have been treated for plantar fasciitis with a fasciotomy procedure using an RF device. This procedure does not ablate a specific nerve.

Table 1. Types of Radiofrequency Ablation

Type	Procedure	Tissue Temperature	Key Differences
Standard RFA	Electrode tip provides thermal energy for 90 – 130 seconds	70 – 90° C	Longer term pain relief but with more adjacent thermal tissue injury and limitation in size and shape of lesion.
Pulsed RFA	Non-ablative - provides 20 ms pulses every 30 seconds	42° C	Limits tissue damage but results in shorter duration of pain relief.
Cooled RFA	Water circulates through RF electrode to cool the tip	60° C	Larger lesion with limited thermal injury to tissue. Longer term pain relief.

RF: radiofrequency; RFA: radiofrequency ablation
Adapted from Oladeji et al (2019)

Cryoneurolysis

Cryoneurolysis (cryoablation cryotherapy, cryoanalgesia) is being investigated to alleviate pain. Temperatures of -20° to -100°C applied to a nerve cause Wallerian (anterograde axonal) degeneration, with disruption of nerve structure and conduction but maintenance of the perineural and epineural elements of the nerve bundle. Wallerian degeneration allows complete regeneration and recovery of nerve function in about 3 to 5 months. The iovera° cryoablation system is a portable handheld device that applies percutaneous and targeted delivery of cold to superficial peripheral nerves.

Chemical Neurolysis

Chemical neurolysis (phenol, alcohol, glycerol) may be utilized as an option to provide pain relief and maintain mobility. Chemical neurolysis causes nerve destruction and has a local anesthetic effect on smaller nerve fibers.

Regulatory Status

In January of 2021, the U.S. Food and Drug Administration (FDA) cleared additional labeling for cryo nerve block (cryoNB) therapy to include the treatment of adolescent patients 12-21 years of age. The cryoICE® and cryoSPHERE™ cryoablation probes are designed to temporarily block pain by ablating intercostal nerves under direct visualization in adolescent patients of at least 12 years of age. AtriCure's cryoICE technology uses a unique freezing method to block nerves from transmitting pain signals for several months.

A number of radiofrequency (RF) generators and probes for the peripheral nervous system have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process, some examples are listed in the Table 2.

In 2017 the U.S. Food and Drug Administration (FDA) cleared for marketing COOLIEF cooled radiofrequency (Cooled RF) probe (Avanos, previously known as Halyard Health) to be used in conjunction with a radiofrequency generator to create lesions in nervous tissue (K163461). One of the indications is specifically for "creating radiofrequency lesions of the genicular nerves for the management of moderate to severe knee pain of more than 6 months with conservative therapy, including medication,

in patients with radiologically confirmed osteoarthritis (grade 2-4) and a positive response (> 50% reduction in pain) to a diagnostic genicular nerve block."

Table 2. Radiofrequency and Cryoneurolysis Devices

Device	Manufacturer	Date
SInergy®/Baylis Pain Management Probe	Kimberly-Clark/Baylis	2005
NeuroTherm® NT 2000	NeuroTherm	2011
iovera	Myoscience4	2014
COOLIEF® Cooled Radiofrequency Kit	Avanos, previously known as Halyard Health	2016
COOLIEF® Cooled RF Probe	Avanos, previously known as Halyard Health	2017
Rulo(TM) Radiofrequency Lesion Probe	Epimed International	2019
Intracept Intraosseous Nerve Ablation System	Relievant Medsystems, Inc.	2022
Apex 6 Radiofrequency Lesion Generator	RF Innovations, Inc.	2023
CyroICE™, cryoFORM™ cryoablation probe	AtriCure Inc.	2016
cryoICE™ cryoablation probe (Cryo2), cryosphere cyroablation probe (CryoS, Cryo S-L)	AtriCure Inc.	2020
the cryoICE™ cryosphere + cryoablation Probe (CRYOSP, cryoICE cryosphere+Cryoablation Probe (CRYOSP-L), cryoICE cryosphere MAX cryoablation probe (CRYOSMAX), and cryosphere MAX Cryoablation Probe (CRYOSMAX-L)	AtriCure Inc.	2023

RATIONALE

This evidence review was created in January 2017 and has been updated regularly with PubMed database. The most recent literature update was performed through November 2025.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life (QOL), and

ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to individuals and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Radiofrequency Ablation for Knee Osteoarthritis

Clinical Context and Therapy Purpose

The purpose of RFA in individuals with knee OA who have severe refractory pain is to provide a treatment option that is an alternative to intra-articular injections or total joint replacement. Pain in OA can be transmitted via the genicular sensory nerves, which are branches of the femoral, tibial, peroneal, saphenous and obturator nerves around the knee. The genicular nerve branches can be divided into a four-quadrant system: superomedial, superolateral, inferomedial, and inferolateral. Nerves in the superomedial, superolateral, and inferomedial quadrants are located near the periosteum, but the inferolateral branch is close to the peroneal nerve and is usually avoided. The exact neuroanatomy around the knee is variable and can also be affected by chronic OA. Although the location of the target nerves is aided by palpating the bony landmarks and fluoroscopy, variability may prevent the exact localization. Diagnostic nerve blocks have been evaluated to confirm the location of the genicular nerves and predict efficacy. In addition to the genicular nerves, studies have reported RFA of the saphenous nerve, the sciatic nerve, the femoral, tibial, saphenous nerves, and peripatellar plexus in combination, and the intra-articular joint space.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with knee OA.

Knee OA is common, and often the cause of substantial disability. Prevalence increases with age, from about 24% among those 60 to 64 years of age to as high as 40% in those 70 to 74 years of age. Knee osteoarthritis is characterized by pain upon initiation of movement or walking. As osteoarthritis progresses, the pain becomes continuous and joint functionality is severely impaired.

Interventions

The therapy being considered is RFA of the superomedial, inferomedial, and superolateral genicular nerves. Due to the variable location of the genicular nerves, it is thought that the increased area of denervation associated with cooled-RFA may be more effective than standard or PFA.

Comparators

The following therapy is currently being used to treat OA: conservative management which may include analgesics, physical therapy (PT) or intra-articular injections.

Treatment of OA of the knee aims to alleviate pain and improve function. However, most treatments do not modify the natural history or progression of OA and are not considered curative. Nonsurgical modalities used include exercise; weight loss; various supportive devices; acetaminophen or nonsteroidal anti-inflammatory drugs (e.g., ibuprofen); nutritional supplements (glucosamine, chondroitin); and intra-articular viscosupplements. Corticosteroid injection may be considered when relief from nonsteroidal anti-inflammatory drugs is insufficient, or the patient is at risk of gastrointestinal adverse events. If symptom relief is inadequate with conservative measures, invasive treatments may be considered. Total knee arthroplasty is an operative treatment for symptomatic OA of the knee.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most commonly measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The Oxford Knee Score is scaled between 12 and 60, with 12 representing the best outcome. Quantifiable pre- and posttreatment measures of functional status are also used, such as the12-Item and 36-Item Short-Form Health Survey.

The Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) is also frequently used to evaluate pain and function due to OA. The WOMAC includes three subscales: pain, stiffness, and physical functioning. Scores range from 0 to 96, with higher scores indicating greater disability.

The Lysolm Knee Score (LKS) has 8 domains to assess limitations in function, including limp, use of supports, locking, instability, pain, swelling, stair-climbing, and squatting. Scores range from 0 to 100, with lower scores indicating greater disability.

Because of the variable natural history of OA and the subjective nature of the outcome measures, RCTs are needed to determine whether outcomes are improved with interventions for pain. Trials should include a homogenous population of patients with a defined clinical condition, use standardized outcome measures when possible, and define a priori the clinically significant magnitude of response.

The effect of RFA is likely to be transient, so the period for follow-up is within a month to determine procedural success and at least one year to evaluate durability. Longer follow-up is needed to evaluate whether denervation of sensory nerves of the knee could have adverse long-term effects on knee anatomy in patients with OA.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months of outcomes, and systematic reviews of RCTs. It is preferred to have double-blinded sham interventions to control for placebo effects.
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.

- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Systematic Reviews

Characteristics of systematic reviews are described in Tables 3 and 4.

Chen et al (2021) conducted a systematic review of RFA for the treatment of knee OA. The authors (including several affiliated with the American Academy of Orthopaedic Surgeons) identified 7 randomized controlled trials (RCTs) published through 2019 that met inclusion criteria. Quality of the studies was assessed based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology for risk of bias of randomization, allocation concealment, blinding, incomplete data, selective reporting, and other bias. Five of the trials were rated as high quality despite lack of blinding in most and moderate risk of bias for allocation concealment and other biases. Two were rated as moderate quality. A majority of the studies were conducted outside of the U.S., with a number of participants ranging from 24 to 151. Techniques included radiofrequency ablation (RFA) and cooled RFA (C-RFA). RFA was compared to non-treated controls or sham procedures, intra-articular corticosteroids, or hyaluronic acid. There was high heterogeneity due to the variability in comparators and outcome measures that limited meta-analysis, but analysis of the mean differences for the individual studies showed general agreement that RFA had a benefit on pain, function, and composite scores compared to the control treatments at 3- and 6-month follow-up.

Liu et al (2022) performed a systematic review of RFA, pulsed RF, C-RFA, and RF thermocoagulation to either the genicular nerve or intra-articular nerves in patients with knee OA. The authors identified 15 RCTs which met their inclusion criteria. This assessment concluded that all studies had a low risk of bias for random sequence generation, 12 (80%) had a low risk of bias for allocation concealment, 6 (40%) had a low risk of bias for blinding of participants, and personnel as well as blinding of outcome assessment. A low risk of selective reporting was identified in 12 (80%) studies, and all studies were reported as having a low risk of other biases. No overall assessment of study quality was provided. The authors reported a mean pain score difference in favor of the radiofrequency group over the control group at 1 to 2 weeks (-1.72; 95% confidence interval [CI], -2.14 to -1.30), 4 weeks (-1.49; 95% CI, -1.76 to -1.21), 12 weeks (-1.83; 95% CI, -2.39 to -1.26), and 24 weeks (-1.96; 95% CI, -2.89 to -1.04); however, all these estimates had significant heterogeneity ranging from 66% to 97% ($p<.00001$). A subgroup analysis limiting the site of radiotherapy to the genicular nerve included 5 trials and found a weighted mean difference between RF and control of -1.64 (95% CI, -2.19 to -1.09; $p<.001$) with a high level of heterogeneity (I^2, 84%; $p<.001$) at 1 to 2 weeks post-treatment. The mean difference in Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores also favored the radiofrequency group over control groups at 4 weeks (-10.64; 95% CI, -13.11 to -8.17), 12 weeks (-6.12; 95% CI, -7.67 to -4.57), and 24 weeks (-10.89; 95% CI, -12.28 to -9.51). No significant heterogeneity was observed in the 4- and 12-week WOMAC score pooled estimates, but the evidence was limited to being pooled from 4 trials. The rate of adverse events appeared equivalent between groups when observed when pooling data from 13 RCTs (risk difference, 0.03; 95% CI, -0.01 to 0.06; $p=.14$) with no significant heterogeneity.

Wu et al (2022) conducted a systematic review and network meta-analysis of multiple RFA modalities versus other treatments for osteoarthritis (OA) with a focus on short-term clinical outcomes through 6 months post-treatment. Twenty-one RCTs were identified that were eligible for inclusion. The evidence base consisted of 1818 individuals with a range of 24 to 260 participants across the included RCTs. Outcomes of interest included VAS Pain and WOMAC function scores as well as adverse events. The authors found that C-RFA has better efficacy for pain and function than conventional or pulsed modalities

and that conventional RFA outperforms pulsed RFA. Visual analog scale (VAS) pain scores were reported in 16 studies at 3 months follow-up (n=1401). All interventions, with the exception of exercise, had significant improvement compared with placebo. In a ranked surface under the cumulative ranking curve (SUCRA) analysis, monopolar C-RFA of the genicular nerve ranked first in analgesia performance, followed by conventional monopolar RFA of the genicular nerve, intraarticular platelet-rich plasma injection (IAPRP), pulsed monopolar RFA of the genicular nerve, intraarticular anesthesia injection (IAA), intraarticular dextrose injection (IAD), intraarticular sodium hyaluronate injection (IAHA), pulsed monopolar RFA of the saphenous nerve, intraarticular corticosteroid injection, nonsteroidal anti-inflammatory drugs (NSAIDs). At 6 months, 10 trials reported on 1,021 individuals for VAS pain outcomes. All treatments, save NSAIDs, had a significantly decreased VAS score compared with exercise at 6 months follow-up. A SUCRA analysis showed that the best-performing intervention was conventional bipolar RFA of the genicular nerves (MD, -5.5; 95% CI, -4.3 to -6.7) followed by conventional monopolar RFA of the genicular nerves, pulsed monopolar intraarticular RFA, pulsed monopolar RFA of the genicular nerve, IACS, IAHA, IAPRP, and NSAIDs. WOMAC scores were reported in 14 studies (n=1091) at 3 months and by 9 studies (n=821) at 6 months follow-up. At 3 months, except for exercise, NSAIDs, and pulsed monopolar IPRFA, all treatments had a significant reduction in WOMAC scores compared to placebo. SUCRA analysis suggested the first rank intervention for improved knee performance at 3 months follow-up was cooled monopolar RFA of the genicular nerve followed by conventional bipolar RFA of the genicular nerve, pulsed monopolar intraarticular RFA, conventional monopolar RFA of the genicular nerve, pulsed monopolar intraarticular RFA plus IAPRP, IAA, pulsed monopolar RFA of the genicular nerves, pulsed monopolar IPRFA, IAS, and IAHHA. All interventions had a significant improvement in WOMAC scores at 6 months compared to exercise. SUCRA analysis showed the best performance for cooled monopolar RFA of the genicular nerve followed by conventional bipolar RFA of the genicular nerve, conventional monopolar RFA of the genicular nerve, pulsed monopolar RFA of the genicular nerve, IACS, IAHA, NSAIDs and exercise. The authors also reported that adverse events were recorded in 6 RCTs (n=836) and found 43 (8.3%) in the RFA groups, which were likely attributable to RFA; major adverse events included: pain (n=5), post-procedural pain (n=7), fall (n=5), stiffness (n=1) and swelling (n=2).

The trials by Davis et al (2018), El-Hakeim et al (2018), Xiao et al (2018), and Chen et al (2020), along with later RCTs that are not included in the systematic reviews, are described in greater detail below.

Table 3. Systematic Review Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Chen et al (2021)	1966 - 2019	7	Individuals with OA of the knee who were treated with RFA or C-RFA	NR (24 to 151)	RCT	up to 12 months
Liu et al (2022)[,]	Database inception - 2021	15	Individuals with OA of the knee who were treated with RFA, C-RFA, pulsed radiofrequency, or RF thermocoagulation	1009 (16 to 177)	RCT	up to 24 months
Wu et al (2022)[,]	Database inception - 2021	21	Individuals with OA of the knee who were treated with RFA, C-RFA, pulsed radiofrequency, bi-polar RFA, IAA, IAD, IAPRP, IAHA, intra-articular erythropoietin, IACS, NSAIDs, or exercise	1818 (24 to 260)	RCT	6 months

C-RFA: cooled radiofrequency ablation; IAA: intra-articular anesthesia; IACS: intra-articular corticosteroid; IAD: intra-articular dextrose; IAHA: intra-articular sodium hyaluronate; IAPRP: intra-articular platelet rich plasma; NR: not reported; NSAIDs: non-steroidal anti-inflammatory drugs; OA: osteoarthritis; RCT: randomized controlled trial; RF: radiofrequency; RFA: radiofrequency ablation.

Table 4. Comparison of Trials/Studies Included in Systematic Review and Meta-Analysis

Study	Trial Size	Nerve Target	Prognostic Block	RF Method	Comparator	Follow-up	Chen et al (2021)	Liu et al (2022)	Wu et al (2022)
Choi et al (2011)	38	GN	Yes	RFA	Sham	3 months	●	●	●
Yi et al (2012)	36	GN	No	RFA	IA Hyaluronic Acid	3 months		●	
Rahimzadeh et al (2014)	50	IA	No	PRF	IA Sham	3 months		●	●
Hashemi et al (2016)	72	IA+GN	NR	PRF	IA Steroid	3 months			●
Yang et al (2015)	62	GN	No	RFA	IA Hyaluronic Acid	3 months		●	
Hu et al (2016)	92	IA	No	PRF	NSAIDs	6 months		●	
Sari et al (2016)	50	GN	NR	RFA	Ultrasound	3 months			●
Yuan (2016)	24	IA	Yes	PRF	IA Steroid	6 months		●	●
Gulec et al (2017)	100	IA	NR	PRF	Monopolar RFA	3 months			●
Shen et al (2017)	54	IA	No	RFA	Standard Treatments	3 months	●	●	
Sari et al (2018)	73	GN	No	RFA	IA Steroid	3 months	●	●	●
Davis et al (2018)	151	GN	Yes	C-RFA	IA Steroid	6 months	●	●	
El-Hakeim et al (2018)	60	GN	No	RFA	Acetaminophen and NSAIDs	6 months	●	●	●
Jadon et al (2018)	30	GN	NR	RFA	Monopolar RFA	6 months			●
Ray et al (2018)	24	GN	Yes	RFA	IA Hyaluronic Acid	3 months	●		●
Xiao et al (2018)	96	GN	No	RFA	IA Hyaluronic Acid	6 months	●	●	●
Davis et al (2019)	151	GN	NR	C-RFA	IACS	12 months			●
Monerris et al (2019)	28	GN	NR	PRF	Placebo	6 months			●
Kumaran et al (2019)	30	IA	No	RFA	Sham	3 months		●	
Chen et al (2020)	177	GN	Yes	C-RFA	IA Hyaluronic Acid	6 months		●	●

Study	Trial Size	Nerve Target	Prognostic Block	RF Method	Comparator	Follow-up	Chen et al (2021)	Liu et al (2022)	Wu et al (2022)
Han et al (2020)	62	GN	NR	C-RFA	Exercise	6 months			●
Hong et al (2020)	53	GN	No	RF thermocoagulation	IA Steroid	6 months		●	
Santana et al (2022)	216	GN	NR	PRF	IA Hyaluronic Acid	12 months			●
Carpenedo (2021)	16	IA	Yes	PRF	Sham PRF	6 months		●	
Abdelraheem et al (2021)	200	GN	NR	PRF	IA-PRP	12 months			●
Sameh et al (2021)	60	GN	NR	PRF	IARFA+IAPRP	12 months			●
Roberta et al (2021)	20	SN	NR	PRF	Placebo	6 months			●
Ahmed et al (2021)	58	GN	NR	RFA	IACS	6 months			●

C-RFA: cooled radiofrequency ablation; IA: intra-articular; NSAIDS: nonsteroidal anti-inflammatory drug; PRF: pulsed radiofrequency; RCT: randomized controlled trial; RFA: radiofrequency ablation; SN: saphenous nerve.

Randomized Controlled Trails

Characteristics and results of relevant RCTs that are not included in the above systematic reviews are described in Tables 5 and 6. Study limitations are described in Tables 8 and 9.

Twelve to 24-month follow-up of a subset of individuals treated with RFA in the RCT by Davis et al (2018) was reported by Hunter et al (2020) and is shown in Table 7. There were 42 individuals randomized to RFA and 41 randomized to the control group who crossed over to RFA at 6 months and qualified for follow-up at participating sites. Of the 83 potential participants, 15 had additional procedures (e.g. steroid injection, total knee arthroplasty, hyaluronic injection, repeat RFA) and were not included in the analysis, 35 (42.2%) could not be reached or declined to participate, and 33 (40%) consented for the study. Although 44% of individuals who participated in follow-up maintained their improvement in pain scores, this was a small percentage of the individuals who received treatment. Interpretation of this study is limited due to the small number of individuals and the potential for bias in this non-blinded study.

Lyman et al (2022) published an extension study of the manufacturer-sponsored trial on cooled RFA for knee osteoarthritis that was reported by Chen et al (2020) to assess long-term outcomes through 24 months for participants in this trial who received RFA. Of the initial 66 RFA patients who had 12 months follow-up, 36 signed the informed consent to participate in the extension study. Thirty-two of these participants completed 18-month follow-up and 27 completed 24-month follow-up; the primary reason for loss to follow-up was receiving another knee procedure (Table 7). At baseline, the participants had a mean NRS of 6.8±0.8 which was reduced to 2.4 ± 2.5 (64% reduction) at 18 months and 3.4 ± 3.2 (51% reduction) at 24 months; a ≥ 50% improvement in NRS pain scores was experienced by 22 (69%) of patients at 18 and 17 (63%) at 24 months. Mean WOMAC scores at baseline for these participants were 64.4 ± 14.7, which were reduced by a mean of 34.7±27.5 (54%; $p<0.0001$ versus BL) and 24.8±32.8

(35%; p<0.0007) at 18 and 24 months respectively. No serious or non-serious adverse events related to cooled RFA were reported by the authors at 18- or 24-months post-treatment.

An independent study by Elawamy et al (2021) compared pulsed radiofrequency to a single injection of platelet-rich plasma in 200 individuals with OA (NCT03886142). VAS scores showed an improvement of 50% (from a score of 6 to 3) in both groups at 3 months, with values returning to a score of 5 by the sixth month. Scores on the Index of Severity for OA of the Knee were reduced from 7 at baseline to 4 at the third month, increasing to 5 at the sixth month. Twelve-month scores were not reported. Platelet-rich plasma is not considered a standard of care treatment for OA and there were a number of additional limitations in conduct and reporting of this study. Limitations of these studies, which include potential for bias due to lack of blinding of study participants and insufficient number of individuals in follow-up, are described in Tables 8 and 9.

A single-center, double-blind RCT by Malaithong et al (2021) compared bipolar radiofrequency to a sham RFA procedure using low-level sensory stimulation in 64 individuals with OA (Thailand Clinical Trial Registration 20170130003). Both treatment groups received genicular nerve blocks prior to RFA or sham procedure. The bipolar RFA and sham RFA treatment arms experienced significant improvements in pain at 12 months from baseline, but no differences between groups were observed (Table 6). Similar findings were observed for WOMAC scores through 12 months follow-up as well as the Patient Global Improvement Index.

A single-center, double-blind RCT by Ma et al (2024) compared RFA to usual care in patients over 50 years of age with moderate to severe knee OA. A total of 112 patients were randomized. Mean NRS scores were lower among patients in the RFA group at the 6-month follow-up (2.25 vs. 4.53; p<.01) as were worst NRS scores (3.27 vs. 5.42; p<0.01). WOMAC scores for pain and physical function were lower in patients receiving RFA; however, stiffness scores were similar between groups.

A single-center, open-label RCT by Anwar et al (2025) compared intraarticular platelet-rich plasma injection to genicular nerve RFA in 200 patients with Grade II-III knee OA. Patients received either a single platelet-rich plasma injection or genicular nerve RFA targeting the superomedial, superolateral, and inferomedial genicular nerves after diagnostic nerve blocks. Both groups showed significant pain and disability improvements at early time points, but the PRP group exhibited significantly lower Visual Analog Scale (VAS) and Oswestry Disability Index (ODI) scores at 12 and 24 months. No adverse effects were reported in either group.

Table 5. Summary of Key RCT Characteristics

Study	Countries	Sites	Participants	Interventions	
				Active	***Comparator***
Xiao et al (2018)	China	1	96 individuals with OA with VAS >6 and LKS <60 who had abandoned other therapeutic measures	RFA of the genicular nerves guided by a plexus nerve stimulator (n=49)	Single intra-articular hyaluronic acid injection (n=47)
Elawamy et al (20210)	Egypt	2	200 individuals with knee OA grade III or IV refractory to conservative management	Pulsed RFA with identification of the genicular nerves based on proximity to the arteries by ultrasound and sensory stimulation (n=100)	Single intra-articular platelet rich plasma (n=100)

Study	Countries	Sites	Participants	Interventions	
				Active	***Comparator***
Malaithong et al (2022)	Thailand	1	64 individuals with chronic OA grade III or IV refractory to conservative management with a positive diagnostic genicular nerve block[b]	Bipolar RFA of the genicular nerves under fluoroscopic guidance (n=32)	Sham RFA with a genicular nerve block (n=32)
Ma et al (2024)	China	1	112 individuals older than 50 years of age with chronic knee joint pain (grade III or IV and NRS ≥4) for more than 6 months	RFA of the genicular nerves with ultrasound guidance plus nerve block(n=56)	Nerve block (n=56)
Anwar et al 2025	Pakistan	1	200 individuals diagnosed with Grade II-III knee OA	RFA of the genicular nerves (n=100)	Single intra-articular platelet rich plasma (n=100)

LKS: Lysolm Knee Score; OA: osteoarthritis; RCT: randomized controlled trial; RFA: radiofrequency ablation; VAS: visual analog score.
[a]Conservative treatment included physical therapy, oral analgesics: ≤60 mg morphine equivalence, stable for 2 months; intra-articular injections with steroids and/
or viscosupplementation, body mass index (BMI) <40, and reporting ≥50% response to blocks as
[b]At least 50% reduction in numeric rating scale for pain with anesthetic injection to the superomedial and inferomedial branches of the saphenous nerve and the superolateral branch of the femoral nerve.

Table 6. Summary of Key RCT Results

Study	Mean Pain Scores (SD)				Function	
	1 Month	***3 Months***	***6 Months***	***Responders at 6 Months, %[a]***	***Mean Oxford Knee Score at 6 Months (SD)***	***Global Perceived Effect at 6 Months, %***
Xiao et al (2018)	**VAS**			**Lysolm Knee Score**		
	3 Days	***6 Months***	***12 Months***	***3 Days***	***6 Months***	***12 Months***
n	96	96	96	96	96	96
RFA	3.38 (1.02	2.41 (1.06)	3.12 (1.03)	78.1 (7.5)	68.3 (6.6)	84.6 (4.3)
Hyaluronic Acid	5.11 (1.13)	5.13 (1.12)	7.01 (1.01)	61.1 (5.3)	54.1 (6.2)	43.2 (6.1)
p-value	<.05	<.05	<.05	<.05	<.05	<.05
Elawamy et al (2021)	**VAS**			**ISK**		
	1 Week	***6 Months***	***12 Months***	***1 Week***	***6 Months***	***12 Months***
n	200	NR	NR	200	NR	NR
RFA	3	5	5	5	4	NR

Study	Mean Pain Scores (SD)				Function	
	1 Month	***3 Months***	***6 Months***	***Responders at 6 Months, %[a]***	***Mean Oxford Knee Score at 6 Months (SD)***	***Global Perceived Effect at 6 Months, %***
Platelet-rich Plasma	3	5	6	6	6	NR
p-value	NR	NR	NR	NR	NR	
Malaithong et al (2022)	**VAS**			**WOMAC**		
	1 Month	***6 Months***	***12 Months***	***1 Month***	***6 Months***	***12 Months***
n	64	59	53	64	59	53
RFA	3.0 (2.3)	3.3 (2.7)	3.2 (2.6)	63.6 (51.8)	74.6 (50.3)	67.1 (51.9)
Sham RF	3.1 (1.9)	3.1 (2.3)	2.6 (2.4)	66.8 (42.4)	66.2 (43.5)	24.6 (38.5)
p-value	.15	.29	.73	.78	.81	.70
Ma et al (2024)	**NRS**			**WOMAC**		
	1 Month	***3 Months***	***6 Months***	***1 Month***	***3 Months***	***6 Months***
n	110	107	104	110	107	104
RFA + block	2.67 (1.22)	3.18 (1.09)	3.27 (1.06)	34.69 (3.54)	36.09 (3.36)	37.25 (4.35)
Block alone	4.38 (1.16)	4.81 (0.94)	5.42 (1.23)	43.15 (3.84)	43.72 (3.97)	47.86 (4.47)
p-value	<.01	<.01	<.01	<.01	<.01	<.01
Anwar et al (2025)	**VAS**			**ODI**		
	6 Months	***12 Months***	***24 Months***	***6 Months***	***12 Months***	***24 Months***
n	200	200	200	200	200	200
RFA	1.89 (0.94)	4.73 (2.63)	6.06 (2.01)	17.72 (4.00)	32.89 (6.53)	40.18 (9.91)
Platelet-rich Plasma	1.82 (0.93)	2.99 (1.78)	4.05 (1.82)	22.37 (4.74)	18.40 (4.13)	17.45 (3.97)
p-value	.599	<.05	<.05	<.05	<.05	<.05

CI: confidence interval; ISK: Index of Severity for Osteoarthritis of the Knee; NR: not reported; NRS: numeric rating scale; RCT: randomized controlled trial; RFA: radiofrequency ablation; SD: standard deviation; VAS: visual analog score; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

[a] Greater than 50% reduction in the NRS.

Table 7. Extended Follow-up of Individuals Treated with RFA

Study	Mean Pain Scores (SD)				Function	
	At 12 Months	***At 18 Months***	***At 24 Months***	***Responders at 18 Months, %[a]***	***Oxford Knee Score at 18 Months (SD)***	***Oxford Knee Score at 24 Months (SD)***
Davis et al (2018), Hunter et al (2020)	NRS					
N (randomized and crossover)	30	25	18	25	25	18
RFA	3.0 (2.5)	3.1 (2.7)	3.6 (2.8)	44.0	47.2 (8.1)	46.8 (10.3)
	At 12 Months	***At 18 Months***	***At 24 Months***	***Responders at 24 Months, %[a]***	***WOMAC Score at 18 Months (SD)***	***WOMAC Score at 24 Months (SD)***
Chen et al (2020), Lyman et al (2022)	NRS					
N (randomized and crossover)	32	32	27	27	32	27
RFA	1.9 (1.9)	2.4 (2.5)	3.4 (3.2)	63.0	34.7 (27.5)	24.8 (32.8)

NRS: numeric rating scale; RFA: radiofrequency ablation; SD: standard deviation;
[a] Greater than 50% reduction in the NRS.

Table 8. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Xiao et al (2018)	4. Study population was not selected by a positive response to a nerve block		2. Efficacy of a single injection of hyaluronic acid as an active comparator is not supported by evidence		
Elawamy et al (2021)	4. Study population was not selected by a positive response to a nerve block	1. Both groups received analgesics and physical therapy, but these were not recorded	2. Efficacy of a single injection of platelet-rich plasma as an active comparator is not supported by evidence		
Malaithong et al (2022)		1. Both groups received analgesic therapy, but these were not recorded			
Ma et al (2024)	4. Study population was not selected by a positive response to a nerve block				1. Follow-up >6 mo is needed to evaluate durability of the procedure
Anwar et al (2025)		1. Both groups received analgesic therapy, but these were not recorded	2. Efficacy of a single injection of platelet-rich plasma as an active comparator is not supported by evidence		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 9. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Xiao et al (2018)	2. Allocation concealment not described	1. Study population was not blinded to treatment assignment, which might have affected subjective scores			1. Power calculations were not reported	2. The study did not use a repeated-measures test for the different time points.
Elawamy et al (2021)		1. Study population was not blinded to treatment assignment, which might have affected subjective scores		6. It is unclear how many individuals completed the 12 month follow-up		2, 4. The study did not use a repeated-measures test and there was no comparison between groups.
Malaithong et al (2022)	2. Allocation concealment not described				4. Power calculations may have underestimated the number of patients needed to recruit; effect size based on older study	
Ma et al (2024)						3. Confidence intervals not reported
Anwar et al 2025		1. Study population was not blinded to treatment assignment, which might have affected subjective scores			1. Power calculations were not reported	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
RFA: radiofrequency ablation.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Nonrandomized Studies

Kapural et al (2022) reported a retrospective assessment of pain relief in 340 consecutive patients with chronic knee pain at a single center who were treated with either C-RFA (n=170) or conventional RFA (n=170) (Table 10). The mean age at treatment was 63 years in the C-RFA group and 61 years in the conventional RFA group; both treatment groups had similar levels of baseline VAS pain reported prior to nerve block (8.4 in the C-RFA group and 8.3 in the traditional RFA group). Included patients had at least one year of follow-up after treatment and were evaluated on short-term and long-term pain outcomes on the VAS and opioid use (Table 11). The authors reported that at the first follow-up, approximately 4 to 6 weeks post-treatment, individuals in the C-RFA group had superior pain reduction on the VAS when compared to traditional RFA as well as significantly longer durability of pain relief. This reduction in pain, however, did not translate into a reduction in the usage of opioids from baseline which showed no significant differences in either treatment arm.

Wu and colleagues (2022) published a retrospective cohort study of C-RFA versus traditional RFA of the genicular nerves in patients who had chronic knee pain despite attempts at conservative management. The mean age of treatment was 72 years of age in the C-RFA group and 69.6 after matching; both groups reported similar levels of baseline NRS pain prior to treatment and similar Kellgren-Lawrence grade for classification of OA. Patients were followed for one year after administration of RFA and were evaluated for treatment success (defined as a reduction of 2 or more on the NRS), duration of pain relief, and the probability of having total knee arthroplasty (TKA) within 1-year post-RFA. In this cohort, patients treated with traditional RFA were significantly more likely to report treatment success at 1-, 3- and 6-months follow-up (p<.01); the mean duration of relief was 175 days in the c-RFA group and 156 days in the traditional RFA group and did not vary significantly (p=.69). The traditional RFA group had a significantly greater reduction in NRS pain scores at 1-month post-RFA (-3.59 versus 4.71; p=.02), but this was not sustained at 3-, 6-, 9- and 12-months follow-up. A higher probability of having TKA was observed in the C-RFA group (14%) compared to traditional RFA (7.7%), but this difference did not reach statistical significance (p=.18).

Table 10. Summary of Key Nonrandomized Trials or Observational Comparative Study Characteristics

Study	Study Type	Country	Dates	Participants	C-RFA	Traditional RFA	Follow-Up
Kapural et al (2022)	Retrospective	U.S.	2013-2019	340 consecutive individuals with chronic knee pain who had either C-RFA or conventional RFA at a single center. Median	C-RFA of the genicular nerves under fluoroscopic guidance following	Conventional RFA of the genicular nerves under fluoroscopic guidance	1 year

Study	Study Type	Country	Dates	Participants	C-RFA	Traditional RFA	Follow-Up
				VAS pain prior to treatment was 8 prior to nerve block.	geniculate block (n=170)	following geniculate block (n=170)	
Wu et al (2022)	Retrospective	U.S.	NR	208 patients with chronic knee pain who were unresponsive to conservative treatments and had either C-RFA or conventional RFA at a single center. Mean BL NRS pain scores were 7 prior to treatment and the mean Kellgren-Lawrence grade was 3.6.	C-RFA of the genicular nerves (n=104)	Conventional RFA of the genicular nerves (n=104)	1 year

BL: baseline; C-RFA: cooled radiofrequency ablation; NR: not reported; NRS: numeric rating scale; RFA: radiofrequency ablation; VAS: visual analogue scale

Table 11. Summary of Key Nonrandomized Trias or Observational Comparative Study Results

Study	VAS Pain Score Baseline ± SD	VAS Pain Score at 4-6 Wks f/u ± SD	Mean Duration of Pain Relief (≥50% VAS pain decrease)	≥50% VAS Pain Decrease at 6 Mos, n (%)	≥50% VAS Pain Decrease at 12 mos, n (%)	Opioid Usage
Kapural et al (2022)	340	340	340	340	340	340
C-RFA (n=170)	8.4 ± 1.5	4.26 ± 3.2; p=.001	11.1 mos	107 (63%)	78 (46%)	Mean 53 mg at BL; 53.2 ± 32 mg OME at 12 mos f/u; p=.954
RFA (n=170)	8.3 ± 1.4	5.07 ± 2.8; p=.001	2.6 mos	35 (20.6%)	15 (8.8%)	Mean 48.6mg at BL; 41.5 ± 20 mg OME at 12 mos f/u; p=.054
Diff; p-value	NA	p=.010	8.5 mos; p=0.001	42.6%; NR	37.2%; NR	No between-group comparison
	Treatment Success, % (95% CI) at 1 mo	**Treatment Success, % (95% CI) at 3 mo**	**Treatment Success, % (95% CI) at 6 mo**	**Mean Change in NRS Pain Score (95% CI) at 3 mo**	**Mean Change in NRS Pain Score (95% CI) at 6 mo**	**Mean Change in NRS Pain Score (95% CI) at 12 mo**
Wu et al (2022)	104	104	104	104	104	104
C-RFA (n=104)	43 (34 to 53)	55 (45 to 64)	59 (49 to 68)	-1.14 (-2.2 to -0.1)	-0.83 (-2.1 to 0.4)	1 (-2 to 4)

Study	VAS Pain Score Baseline ± SD	VAS Pain Score at 4-6 Wks f/u ± SD	Mean Duration of Pain Relief (≥50% VAS pain decrease)	≥50% VAS Pain Decrease at 6 Mos, n (%)	≥50% VAS Pain Decrease at 12 mos, n (%)	Opioid Usage
RFA (n=104)	62 (51 to 71)	59 (49 to 68)	79 (70 to 86)	-2.05 (-2.9 to -1.2)	-1.18 (-2.4 to 0.03)	-0.83 (-2.4 to 0.7)
Diff; p-value	.01	<.001	<0.01	.18	.68	.22

BL: baseline; C-RFA: cooled radiofrequency ablation; CI: confidence interval; Diff: difference; f/u: follow-up; mos: months; NR: not reported; NRS: numeric rating scale; OME: oral morphine equivalent; RFA: radiofrequency ablation; SD: standard deviation; VAS: visual analagoue scale; wks: weeks.

Safety

In 2021, the Spine Intervention Society's Patient Safety Committee published an article on the safety of genicular nerve RFA. The committee reviewed case reports of septic arthritis, pes anserine tendon injury, third-degree skin burn, and clinically significant hematoma and/or hemarthrosis with RFA of the genicular nerves, concluding that larger cohort studies are needed to determine the incidence of these complications for this emerging technology.

Section Summary: Radiofrequency Ablation for Knee Osteoarthritis

Knee OA is a common disorder in older adults. RFA of the genicular nerves has the potential to alleviate pain and improve function in this population and might also delay or eliminate the need for TKA. To date, the evidence on RFA for knee pain includes systematic reviews and meta-analyses of RCTs, RCTs with 24 to 200 individuals, and prospective observational studies with up to 24 months of follow-up. The systematic reviews generally found that RFA had a benefit on pain, function, and composite scores compared to the control treatments at 3 and 6-month follow-up; however, most estimates were determined to have moderate to high heterogeneity. The network meta-analysis compared multiple RFA modalities and found that cooled RFA had greater efficacy for pain and function through 6 months follow-up than traditional or pulsed RFA. Trials have compared RFA to sham procedures, intra-articular steroid injection, intra-articular hyaluronic acid injection, and platelet-rich plasma injection. Few of the studies were blinded, which may have biased the subjective outcome measures. Additional limitations in design and conduct include suboptimal statistical analyses and reporting of loss to follow-up. Given that OA of the knee is a common condition, adequately powered studies, preferably blinded with active and sham controls and follow-up of at least 12 months, are needed to determine the benefits and potential harms of this treatment.

Cryoneurolysis for Knee Osteoarthritis or Total Knee Arthroplasty

Clinical Context and Therapy Purpose

The purpose of cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) in individuals who have OA or total knee arthroplasty (TKA) is to provide a treatment option that is an alternative to standard therapies. Pain control in individuals with knee OA can delay TKA, while pain control following TKA is essential for patients to participate in physical therapy and promote recovery.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with OA or who have undergone TKA.

Interventions

The therapy being considered is percutaneous cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) of the anterior femoral cutaneous nerve and/or the infrapatellar branch of the saphenous nerve.

Comparators

The following therapies are currently being used to treat OA or pain with TKA: conservative management which may include corticosteroid injections or oral medications for OA; and opioid or peripheral nerve blocks with anesthetics for TKA.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is most commonly with a VAS or NRS. The Oxford Knee Score is scaled between 12 and 60, with 12 representing the best outcome. Quantifiable pre - and post-treatment measures of functional status are also used, such as the 12-Item and 36-Item Short-Form Health Survey. The WOMAC score is also frequently used to evaluate function due to OA. The time for follow-up is within days to determine procedural success and at least 6 months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Systematic Reviews

Hayes (March 2025) completed the annual review of their evolving evidence review regarding the iovera (Pacira Biosciences Inc.) system for pain associated with total knee arthroplasty (TKA), to include the presurgical period to assist in the treatment of chronic pain and long-term opioid use/misuse. This updated evidence review found 2 retrospective chart reviews and 1 analysis of registry data. Based on the prior evidence review (2024) included RCTs and systematic reviews. Findings from 3 very- poor or poor-quality studies did not show a clear benefit in pain management or improvement in function with the use of iovera over standard of care, however, it was associated with lower opioid use. Current follow-up is up to 1-year. Cryoanalgesia using the iovera system is usually performed 3 to 9 days prior to TKA surgery as part of pain management program, but there is no consensus regarding timing prior to (or during)

surgery on when this should be delivered, Also, there is currently no consensus on the nerves to treat, the freeze duration (minimum critical length has not been established), or number of freezing cycles needed for pain relief efficacy.

Hayes (December 2024) completed the annual review of their evolving evidence review regarding the iovera (Pacira Biosciences Inc.) system for knee osteoarthritis (OA) there was no new evidence regarding efficacy or safety since their evolving evidence review in 2022. Based on the prior evidence review (2023) which included RCTs and systematic reviews regarding the iovera system for the treatment of knee OA, one sham-controlled RCT suggested that treatment with the iovera system may have shown an improvement in OA knee pain with post-treatment improvements in pain and function compare with sham up to 90 days follow-up depending on the scale utilized. At 6-months follow-up from baseline the patient's pain was improved, however, the sham-treated individuals showed an improvement in these measures at 180-days follow-up which may suggest a placebo effect. The use of cyroneurolysis in the treatment of knee OA is expected to lose effectiveness over time, however, no studies have been completed evaluating the clinical benefit of repeat treatment for knee pain due to OA using the iovera system. Also, no studies were identified that compared iovera with standard of care or other treatment alternatives for OA knee pain, additional studies are needed to inform treatment selection.

Randomized Controlled Trials

In addition to the RCTs included in the Hayes review summarized above, Mahalko et. al. (2021) reported a non-blinded single-center RCT of cryoneurolysis for individuals with OA planning to undergo TKA. Patients were randomized 1:1 to either cryoneurolysis targeting the superficial genicular nerves or standard of care treatment prior to receiving TKA (Table 12). A significant reduction in the primary outcome of opioid consumption was not reported in the intention to treat (ITT) analysis, but PP analysis found that patients in the cryoneurolysis group had significantly lower opioid consumption 72 hours, 6 weeks, and 12 weeks post-discharge ($p<.05$) (Table 13). A significant reduction in pain from baseline was reported at 12 weeks post-discharge but not for earlier evaluated time points when analyzing the PP population. Improvements in the Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS JR) were noted from 72 hours to 12 weeks follow-up in the PP analysis ($p<.0001$). The authors noted an adverse event rate of 17% in the cryoneurolysis group and 35% in the standard of care comparator.

Nygaard et al (2025) conducted a double-blinded, single-center RCT investigating the efficacy of cryoneurolysis for patients with chronic OA not undergoing imminent surgery. Eighty-seven patients were randomized 1:1 to receive either cryoneurolysis targeting the anterior femoral cutaneous and infrapatellar branch of the saphenous nerves or a sham intervention, followed by a standardized 8-week exercise program (Table 12). In the ITT analysis, the primary outcome of average 24-hour pain intensity 14 days postintervention did not differ significantly between the groups ($p =.198$) (Table 13). However, secondary outcomes in the PP analysis showed significantly lower pain scores in the cryoneurolysis group at 14 days and 6 months ($p =.022$ and.024, respectively). No significant differences were reported for functional measures (sit-to-stand, maximum voluntary contraction) or quality-of-life indexes. Adverse events were mostly mild and transient, with numbness and swelling reported more frequently in the cryoneurolysis group.

Table 12. Summary of Key Randomized Controlled Trial Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	***Comparator***
Radnovich et al (2017)	U.S.	17	2013-2016	180 individuals with mild-to-moderate (grade II-III) knee OA with knee pain ≥40 mm/100-mm VAS and ≥50% reduction in pain on diagnostic block	n=121 percutaneous cryoneurolysis targeting the IBSN with anatomic landmarks (visual and palpation)	n=59 sham cryoneurolysis with a sham tip and local anesthetic
Mihalko et al (2021)	U.S.	1	2017-2019	124 individuals with severe knee OA who were scheduled to under TKA	n=62 cryoneurolysis targeting the superficial genicular nerves (ISN and AFCN) 3 to 7 days prior to TKA	n=62 standard of care prior to TKA
Nygaard et al (2025)	Denmark	1	2019-2023	87 individuals with knee OA (grade II-IV) who had experienced knee pain for >6 months with a pain intensity of at least 4 on the NRS	n=44 cryoneurolysis targeting anterior femoral cutaneous and infrapatellar branch of the saphe nous nerves	n=43 sham cryoneurolysis

AFCN: anteroior femoral cutaneous nerve; IIBSN: infrapatellar branch of the saphenous nerve; NRS, numeric rating scale; OA: osteoarthritis; RCT: randomized controlled trial; TKA, total knee arthroplasty; VAS: visual analog score.

Table 13. Summary of Key RCT Results

Study	Change in WOMAC Score (SEM)				VAS Score (SEM)		
	Pain at 30 Days	***Total at 30 Days***	***At 60 Days***	***At 90 Days***	***At 30 Days***	***At 60 Days***	***At 90 Days***
Radnovich et al (2017)							
N	180	180	180	180	180	180	180
Cryoneurolysis	-16.65 (1.26)	-78.78 (5.81)	-75.75 (5.87)	-80.31 (5.89)	-40.09 (2.87)	-38.53 (2.91)	-37.90 (3.01)
Sham	-9.54 (1.63)	-48.26 (7.51)	-56.28 (7.58)	-56.51 (7.60)	-27.83 (3.68)	-32.44 (3.73)	-31.58 (3.86)
Diff (95% CI)	-7.12 (-11.01 to -3.22)	-30.52(-48.52 to -12.53)	-19.47(-37.64 to -1.30)	-23.80(-42.02 to -5.57)	-12.25(-21.16 to -3.35)	-6.09(-15.11 to 2.94)	-6.32(-15.66 to 3.01)
p	.004	.001	.036[a]	.011			.183
Mihalko et al (2021)	**Opioid consumption in TDME (SEM) at 6 weeks post discharge, PP**	**Opioid consumption in TDME (SEM) at 12 weeks post discharge, PP**	**Individuals not opioid free, n (%) from discharge to 6 weeks, PP**	**Mean change in NRS (SD) from BL to 6 Weeks, PP**	**Mean changein NRS (SD) from BL to 12 Weeks, PP**	**Mean change in AUC for KOOS JR from BL to 6**	**Mean change in AUC for KOOS JR from BL to 12 weeks, PP**

Study	Change in WOMAC Score (SEM)				VAS Score (SEM)		
						weeks, PP	
N	48	48	48	48	48	48	48
Cryoneurolysis	4.2 (0.5)	2.4 (0.3)	7 (15%)	2.2 (2.2)	3.2 (2.3)	9.7	16
Standard of care	5.9 (0.6)	3.4 (0.4)	19 (40%)	1.6 (2.0)	2.3 (2)	7.7	14.1
Diff (95% CI)	1.6 (0.1 to 3.2)	1 (0 to 2)	25%	0.6 (-0.2 to 1.5)	0.9 (0 to 1.7)	2	1.9
p	.0186	.0234	.006	.068	.0256	<.0001	<.0001
Nygaard et al (2025)	**Average pain during the last 24 h at 14 days on an 11-point NRS, ITT**	**Average pain during the last 24 h after completion of GLA:D on an 11-point NRS, ITT**	**Average pain during the last 24 h at 6 months days on an 11-point NRS, ITT**	**Average pain during the last 24 h at 12 months on an 11-point NRS, ITT**			
N	84	58	68	63			
Cryoneurolysis, predicted difference over time [95% CI]	−1.9 [−2.4 to −1.3]	−2.3 [−2.9 to −1.7]	−2.5 [−3.0 to −1.9]	−1.9 [−2.4 to −1.3]			
Sham, predicted difference over time [95% CI]	−1.4 [−1.9 to −0.8]	−1.5 [−2.1 to −0.9]	−1.4 [−2.0 to −0.8]	−1.2 [−1.8 to −0.6			
Difference between groups across time [95% CI]	0.49 [−0.3 to 1.2]	0.8 [−0.1 to 1.6	1.1 [0.3 to 1.9]	0.7 [−0.2 to 1.5			
p	.198	.064	.009	.111			

AUC: are under the curve; BL: baseline; CI: confidence interval; Diff: difference; GLA:D, Good Life with osteoArthritis in Denmark program; KOOS JR: Knee Injury and Osteoarthritis Outcome Score for Joint Replacement; NRS: numeric rating scale; PP: per protocol; RCT: randomized controlled trial; SEM: standard error of mean; TDME: total daily mean morphone equiavelnts; VAS: visual analog score; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

[a] Statistical significance was set at a 1-sided level of 0.025.

Tables 14 and 15 display notable limitations identified in the studies evaluated.

Table 14. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Radnovich et al (2017)	4. A more relevant population would be individuals with moderate-to-severe knee osteoarthritis				

Mihalko et al (2021)	3.Baseline level of pain for individuals prior to TKA unclear				
Nygaard et al (2025)				2. GLA:D program was managed by external physiotherapists at specialized GLA:D clinics	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 15. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Radnovich et al (2017)						2. Unclear whether data were modeled for each time point independently or longitudinally
Mihalko et al (2021)				1,2: Almost 25% missing data 6. Per protocol analysis for many outcomes	4. Per protocol analysis below the required number of participants per group in the power calculation	
Nygaard et al (2025)				1. Study was performed during a period with COVID-19, and some uncertainty and data loss occured		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Nonrandomized Studies

Lung et al (2022) reported a retrospective study of pain relief in 57 individuals with OA and chronic knee pain planning to undergo TKA at a single center who were treated with either cryoneurolysis of the anterior femoral cutaneous nerve (AFCN) or infrapatellar branch of the saphenous nerve (ISN) or conventional TKA without cryoneurolysis. Included patients had at least 1 year of follow-up after treatment and were assessed for the primary outcome of total opioid morphine milligram equivalents (MME) at 6 weeks post-treatment as well as VAS pain, knee injury and osteoarthritis scores (KOOS JR), and short form survey (SF12) outcome measures (Tables 16 and 17). No significant between group differences were found for the outcome of mean total MME during the inpatient stay or follow-up visits at 4- and 6-weeks post-treatment (p>.05). KOOS scores at 12 months follow-up (p=.007) favored the cryoneurolysis group over standard TKA controls, as did SF-12 mental scores (p=.01). However, between-group comparisons on these outcomes at other time points as well as SF12 physician scores and VAS pain at all time points reported, failed to reach significance. Complications were rare and appeared equivalent between groups.

Mont et al (2024) evaluated the Innovations in Genicular Outcomes Registry (iGOR) for outcomes associated with preoperative cryoneurolysis prior to TKA. A total of 80 individuals who had received preoperative cryoneurolysis and 60 who had not been identified from 2021 to 2024. The study is summarized in Tables 16 and 17.

Table 16. Summary of Key Nonrandomized Trials or Observational Comparative Study Characteristics

Study	Study Type	Country	Dates	Participants	Cryoneurolysis	Control	Follow-Up
Lung et al (2022)[1]	Retrospective	U.S.	2013-2019	57 individuals with OA planning to undergo TKA who had pre-TKA cryoneurolysis of ISN or AFCN nerves compared matched individuals with OA from the same center who received TKA.	Cryoneurolysis delivered by Iovera handheld device of the ISN or AFCN nerves (n=29)	Conventional TKA without cryoneurolysis (n=28)	1 year
Mont et al (2024)	Prospective	U.S.	2021-2024	140 individuals undergoing TKA from the iGOR	Cryoneurolysis delivered by iovera handheld device to the genicular nerves (n=80)	Conventional TKA without cryoneurolysis (n=60)	

AFCN: anteroior femoral cutaneous nerve; iGOR: Innovations in Genicular Outcomes Registry; ISN: infrapatellar branch of the saphenous nerve; OA: osteoarthritis; TKA: total knee arthroplasty

Table 17. Summary of Key Nonrandomized Trials or Observational Comparative Study Results

Study	KOOS Score MD BL to 3 mos (SD)	KOOS Score MD BL to 12 mos (SD)	SF12 Physical Score MD BL to 3 mos (SD)	SF12 Physical Score MD BL to 12 mos (SD)	SF12 Mental Score MD BL to 3 mos (SD)	SF12 Mental Score MD BL to 12 mos (SD)
Lung et al (2022)	57	57	57	57	57	57
Cryoneurolysis (n=29)	27.5 (10)	38.8 (11.2)	8.8 (4.3)	12.9 (11.4)	-0.6 (7.8)	3.6 (9.7)

Study	KOOS Score MD BL to 3 mos (SD)	KOOS Score MD BL to 12 mos (SD)	SF12 Physical Score MD BL to 3 mos (SD)	SF12 Physical Score MD BL to 12 mos (SD)	SF12 Mental Score MD BL to 3 mos (SD)	SF12 Mental Score MD BL to 12 mos (SD)
Standard TKA (n=28)	25.7 (22.1)	11.1 (9.6)	2.5 (18.2)	4 (7.8)	3.5 (6.8)	-3.8 (6.2)
Diff; p-value	.4	.007	.1	.2	.2	.2
Mont et al (2024	**Pain Response through 6 mos[a], (%)**	**Overall Opioid Use through 6 mos (%)**	**Function Response through 6 mos[b], (%)**			
Cryoneurolysis	71.7	31.4	86.6			
Standard TKA	62.2	62.8	87.3			
Diff; p-value	OR: 1.55; 95% CI, 1.15 to 2.07; p=.004	OR: 0.27; 95% CI, 0.19 to 0.38; p<.001	OR: 0.94; 95% CI, 0.62 to 1.41; p=.761			

BL: baseline; Diff: difference; KOOS: Knee Injury and Osteoarthritis Outcome Score; LSM: least squares means; MD: mean difference; mos: months; NR: not reported; OR: odds ratio; SD: standard deviation; SF: short form; TKA: total knee arthroplasty

[a] Proportion of patients achieving a pre-determined minimal clinically important difference decrease from baseline in pain score.

[b] Proportion of patients achieving a pre-determined minimal clinically important difference in function outcome.

Observational Studies

Shi et al (2024) published a retrospective study in 73 individuals following genicular nerve RFA and found that at 6-month follow-up the overall success rate was similar for the osteoarthritic group and the post-total knee arthroplasty group. However, conclusions about the comparative effectiveness of genicular nerve RFA cannot be drawn from this study due to the lack of an active treatment control group.

Technical Issues

As noted in a review by Gabriel and Ilfeld (2018), several technical issues have yet to be resolved, including the optimal number of applications for each nerve, the duration of treatment, and the duration of thawing before moving the cannula. The most effective method for determining the location of the probe (e.g., ultrasound or using anatomic landmarks) also needs to be established.

Section Summary: Cryoneurolysis for Knee Osteoarthritis or Total Knee Arthroplasty

Two RCTs and 2 nonrandomized studies were identified. One RCT with 180 individuals compared cryoneurolysis with sham treatment in individuals who had knee OA. Cryoneurolysis resulted in a greater decrease in WOMAC pain, WOMAC total, and VAS score at 30 days compared with sham-treated controls. Subsequent measurements showed no significant benefit of cryoneurolysis on WOMAC score at 60 days or in VAS scores at 60 or 90 days. Another RCT with 124 individuals compared cryoneurolysis to standard of care treatment for patients with knee OA who were planning to undergo TKA. Cryoneurolysis had a significantly lower rate of opioid consumption, reduction in NRS pain, and KOOS JR performance at 12 weeks from discharge compared to standard of care. A retrospective cohort study reported superiority of cryoneurolysis on the KOOS JR and SF-12 mental score at 1 year follow-up; no significant differences were observed on the SF-12 physical score at 1 year follow-up or on any outcome for 3-month

follow-up. A registry study found improved pain and lowered opioid use with cryoneurolysis prior to TKA; however, functional outcomes through 6 months were similar. Several technical issues including the optimal number of applications for each nerve, the duration of treatment, and the duration of thawing before moving the cannula, have yet to be resolved.

Chemical Neurolysis for Treatment of Osteoarthritis of the Knee

Clinical Context and Therapy Purpose

The purpose of chemical neurolysis (phenol, alcohol, glycerol) in individuals with knee OA who have chronic pain is to provide a treatment option that is an alternative to existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with knee osteoarthritis (OA).

Knee OA is common, and often the cause of substantial disability. Prevalence increases with age, from about 24% among those 60 to 64 years of age to as high as 40% in those 70 to 74 years of age. Knee osteoarthritis is characterized by pain upon initiation of movement or walking. As osteoarthritis progresses, the pain becomes continuous and joint functionality is severely impaired.

Interventions

The therapy being considered is chemical neurolysis (phenol, alcohol, glycerol). Chemical neurolysis causes nerve destruction and has a local anesthetic effect on smaller nerve fibers.

Comparators

The following therapy is currently being used to treat OA: conservative management which may include analgesics, physical therapy (PT) or intra-articular injections.

Treatment of OA of the knee aims to alleviate pain and improve function. However, most treatments do not modify the natural history or progression of OA and are not considered curative. Nonsurgical modalities used include exercise; weight loss; various supportive devices; acetaminophen or nonsteroidal anti-inflammatory drugs (e.g., ibuprofen); nutritional supplements (glucosamine, chondroitin); and intra-articular viscosupplements. Corticosteroid injection may be considered when relief from nonsteroidal anti-inflammatory drugs is insufficient, or the patient is at risk of gastrointestinal adverse events. If symptom relief is inadequate with conservative measures, invasive treatments may be considered. Total knee arthroplasty is an operative treatment for symptomatic OA of the knee.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require

quantifiable pre- and posttreatment measures. Pain is most commonly measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The Oxford Knee Score is scaled between 12 and 60, with 12 representing the best outcome. Quantifiable pre- and posttreatment measures of functional status are also used, such as the12-Item and 36-Item Short-Form Health Survey.

The Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) is also frequently used to evaluate pain and function due to OA. The WOMAC includes three subscales: pain, stiffness, and physical functioning. Scores range from 0 to 96, with higher scores indicating greater disability.

The Lysolm Knee Score (LKS) has 8 domains to assess limitations in function, including limp, use of supports, locking, instability, pain, swelling, stair-climbing, and squatting. Scores range from 0 to 100, with lower scores indicating greater disability.

Because of the variable natural history of OA and the subjective nature of the outcome measures, RCTs are needed to determine whether outcomes are improved with interventions for pain. Trials should include a homogenous population of patients with a defined clinical condition, use standardized outcome measures when possible, and define a priori the clinically significant magnitude of response.

The effect of RFA is likely to be transient, so the period for follow-up is within a month to determine procedural success and at least one year to evaluate durability. Longer follow-up is needed to evaluate whether denervation of sensory nerves of the knee could have adverse long-term effects on knee anatomy in patients with OA.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months of outcomes, and systematic reviews of RCTs. It is preferred to have double-blinded sham interventions to control for placebo effects.
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

The below systematic review is a comprehensive review of the current evidence which includes one case report, 2 case series, one observational cohort study and 5 randomized controlled trials (RCTs).

Systematic Review

In 2022, Tan et. al. completed a systematic review to determine the clinical characteristics of patients with chronic knee osteoarthritis (OA) selected for ultrasound-guided (ULSD-g) genicular nerve blocks (GNB) and described the various ULSD-g techniques and pharmacological agents used to target the genicular nerves and evaluate the primary outcomes of pain and function. A total of 280 patients were included with a confirmed diagnosis of symptomatic knee OA with a mean duration of at least 3 months and a severity ranging from grade 2 to grad 4 on the Kellgren and Lawrence classification system and received ULSD guidance for GNB using either local anesthetic agents and/or corticosteroids or alcohol. All 9 studies described the targeting of 3 nerves - the superior medial genicular nerve (SMGN), the superior lateral

genicular nerve (SLGN), and the inferior medial genicular nerve (IMGN). Only one study included the inferior lateral genicular nerve (ILGN), the middle genicular nerve, and the recurrent peroneal nerve. For diagnostic GNB used either lidocaine or bupivacaine with one to 2 successful blocks achieved before progression to therapeutic GNB. For therapeutic GNB, this was performed with either betamethasone and lidocaine, 50% alcohol and bupivacaine, 99% alcohol and lidocaine or glycerinated phenol 7%. All studies described pain outcomes in the form of Visual Analog Scale (VAS) or Numeric Rating Scale (NRS-11). For other outcomes the Knee Osteoarthritis and Outcome score, Oxford Knee Scale (OKS) and total WOMAC for stiffness, function and disability as well as the Global Perceived Effect Scale, and the 36-item Short-Form Survey for quality of life (QOL).

In the observational studies (case report [Demir 2017]**,** case series [Ahmed 2019, Dass 2019], cohort study [Risso 2021]) patients experienced a reduction in pain following GNB. The only study that utilized phenol as the therapeutic treatment (1.5 mL of 7% glycerinated phenol solution) was in the observational prospective cohort study (n=43) Risso et. al. (2021). Patients experienced pain reduction early within one day > 50 reduction and maintained for up to 6 months (NRS-11 improvement from 7.2 at baseline to 4.2) in 43 patients and improvement in WOMAC from 48.7 at baseline to 20.7 at 6 months. Adverse events included local pain, hypoesthesia, swelling and bruising at 2 weeks which resolved within 2 months. While this observational prospective cohort study showed promise in improving pain this was limited to 6-month follow-up.

The majority of studies reported no adverse effects. Study limitations included heterogeneity in study design (number of studies that met inclusion criteria were low); use of different pharmacological agents with varying doses, diverse descriptions of ULSD technique and different time intervals for documentation of outcomes rendered meta-analysis impossible; and a general lack of technical descriptors such as experience level of interventionist, needling approach and accuracy of needle placement. While this systematic review may suggest that ULSD-g GNB using local anesthetic agents with corticosteroids or alcohol for the treatment of Knee OA provides effective pain relief and functional knee improvement by targeting the SMGN, SLGN, and IMGN, for a duration of up to 6 months the authors concluded “there was heterogeneity in the interventional approaches and were unable to make specific recommendations for the optimal approach.”

Section Summary: Chemical Neurolysis for Treatment of Osteoarthritis of the Knee

In the systematic review by Tan et. al. (2022) included case series, case report, observational prospective cohort study and RCTs for individuals with chronic knee OA. Relevant outcomes include symptoms, functional outcomes, and QOL. In this systematic review the only study that utilized phenol as the therapeutic treatment (1.5 mL of 7% glycerinated phenol solution) was in the observational prospective cohort study (n=43) Risso et. al. (2021). Individuals experienced pain reduction early within one day > 50 reduction and maintained for up to 6-months (NRS-11 improvement from 7.2 at baseline to 4.2) in 43 individuals and improvement in WOMAC from 48.7 at baseline to 20.7 at 6-months. Adverse events included local pain, hypoesthesia, swelling and bruising at 2-weeks which resolved within 2-months. While this observational prospective cohort study showed promise in improving pain this was limited to 6-month follow-up. RCTs are needed with larger sample sizes and longer follow-up to determine the efficacy of chemical neurolysis (phenol, alcohol, glycerol) in the treatment of chronic knee OA.

Ablative Procedures for Osteoarthritis of the Hip

Clinical Context and Therapy Purpose

The purpose of ablative procedures including RFA, cryoneurolysis, and chemical neurolysis in individuals with OA of the hip who have chronic pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with hip OA.

Interventions

The therapy being considered is RFA (standard, cooled and pulsed), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (phenol, alcohol, glycerol).

Comparators

The following therapy is currently being used to treat OA: lifestyle modifications: minimizing activities that aggravate the condition, such as climbing stairs, switching from high impact activities to lower impact activities, losing weight can reduce stress on the hip joint, resulting in less pain and increased function; physical therapy; assistive devices (cane, crutches, walker); medications (acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids either orally or injected into the painful joint.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most commonly measured with a visual analog scale (VAS) or numeric rating scale (NRS). Quantifiable pre- and posttreatment measures of functional status are also used, such as the12-Item and 36-Item Short-Form Health Survey. The Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) is also frequently used to evaluate pain and function due to OA. The WOMAC includes three subscales: pain, stiffness, and physical functioning. Scores range from 0 to 96, with higher scores indicating greater disability.

Because of the variable natural history of OA and the subjective nature of the outcome measures RCTs are needed to determine whether outcomes are improved with interventions for pain.

The effect of RFA is likely to be transient, so the period for follow-up is within a month to determine procedural success and at least one year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months of outcomes, and systematic reviews of RCTs. It is preferred to have double-blinded sham interventions to control for placebo effects.
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Radiofrequency Ablation

Nonrandomized Controlled Trial

Chye et. al. (2015) completed a prospective comparative study of 29 patients with chronic hip pain > 3 months that were divided into two groups, pulsed radiofrequency (PFR) and conservative treatment. Fifteen patients received PRF of the articular branches of the femoral or obturator nerves, and 14 patients received conservative treatment. Visual Analog Scale (VAS) score, Oxford Hip Scores (OHS) and pain medications were used for outcome measurement before treatment and at 1 week, 4 weeks, and 12 weeks after treatment. After 1 week, changes in VAS scores ($p<0.001$) and revised OHS values ($p<0.001$) were significantly greater in the PRF group than in the conservative group. These changes remained significantly greater at 4 weeks and 12 weeks. The VAS scores in the PRF group were significantly lower than those in the conservative group at 1 week ($p<0.001$), 4 weeks ($p<0.001$), and 12 weeks ($p=0.017$). The OHS values were also lower in the PRF group at 1 week ($p<0.001$), 4 weeks ($p<0.001$), and 12 weeks ($p=0.04$). Friedman analysis indicated that for both groups, there were significant differences ($p<0.001$) in the VAS scores after treatment. However, the differences in OHS were only significant in the PRF group ($P<0.001$). No significant differences in OHS values were found after treatment in the conservative group. The pain medication scores were significantly lower in the PRF group at 1 week ($p=0.01$), 4 weeks ($p=0.007$), and 12 weeks ($p=0.01$). Eight participants in the control group switched to PRF treatment group after 12 weeks, six (75%) of them had improvement of > 50% with their pain, whereas two patients had no improvement (25%). Limitations included nonrandomized study with patients either consenting or refusing PRF, self-selection bias and 12 weeks observation is not enough time to evaluate long-term pain relief. How exactly PRF acts to produce a resolution of pain remains unclear. The authors concluded “although this study produced promising results, caution is advised in drawing conclusions from this single study. Controlled, randomized investigations with longer observation periods are necessary to further clarify the role of PRF in the treatment of chronic hip pain.”

Observational Study

Kapural et. al. (2018) conducted a retrospective chart review in an interventional pain management urban private practice. Chronic hip joint pain is a common condition with an estimated prevalence of 7% in men and 10% in women, in a population sample aged over 45. Conservative treatment can include physical therapy, weight loss, a variety of pharmacologic agents ranging from nonsteroidal anti-inflammatory drugs (NSAIDS) to opioids, and intraarticular injections with various substances. Definitive treatment of hip pain, however, has primarily centered on hip arthroplasty. Data on 52 radiofrequency (RF) ablations of the hip in 23 patients were retrospectively collected. RF ablation was conducted with patient supine and under guidance of fluoroscopy and ultrasound (US). While fluoroscopy was used to place RF probes to appropriate landmarks, sole purpose of using US was to avoid femoral neurovascular bundle. Data were collected on needle placement, stimulation parameters, and short- and long-term complications. A total of 62 patients underwent 2 diagnostic blocks. Fifty-two of them had greater than 50% relief and agreed to

RF ablation. Until now, the ablation was conducted in 23 patients. There were no adverse events, except one case of neuritis. Expectedly, the needle approach to the lateral articular branches of the femoral nerve was easily achieved with more than a 1 cm passage distance from the femoral nerve in all 52 RF cases (median 2.5 range 1-3.5 cm). Placement of the second trocar to the incisura acetabuli was more challenging; in 21 RF cases the passing distance was less than 1 cm (range 0.5 to 1.9 cm, median 0.8). Motor stimulation (2 Hz) at less than 1 V was positive for the obturator nerve in 26 cases, which resulted in electrode repositioning more laterally (2-5 mm). Change in the pain scores was from the baseline 7.61 ± 1.2 to 2.25 ± 1.4 after the RF ablation (P < 0.01). The time interval of pain relief was much longer for RF ablation. Limitations of this retrospective, observational study include lack of blinding and absence of a comparator group.

Case Series

In 2022, Tran et. al. performed a prospective pilot study to establish the effectiveness of cooled radiofrequency ablation in the management of chronic hip pain from osteoarthritis (OA) who failed conservative treatments and not surgical candidates. Eleven patients were included and initially underwent anesthetic blocks of the obturator and femoral nerve branches to determine cooled radiofrequency ablation candidacy. After adequate response to the anesthetic blocks (> 50% immediate pain relief), patients were subjected to the procedures 2-3 weeks later. Treatment response was evaluated utilizing clinically validated questionnaires and visual analog score in order to assess impact on pain severity, stiffness, and functional activities of daily living. Follow-up outcome scores were collected up to 6 months after cooled radiofrequency ablation procedure. The mean total HOOS score improved significantly from baseline at 17.0 ± 6.0 to 52.9 ± 5.4 at a mean of 6.2 months after treatment (p < 0.0001), with significant improvement in mean pain score from 16.1 ± 6.6 to 53.4 ± 7.4 (p < 0.0001) and mean stiffness score from 15.0 ± 8.1 to 53.6 ± 11.0 (p < 0.0001). No major complications were encountered.

Rivera et. al. (2012) completed a prospective study of 18 patients with chronic hip pain with several contraindications for total hip arthroplasty (THA). Predenervation diagnosis was osteoarthritis in 16 patients and prolonged post-operative hip pain in 2 (1 THA, 1 Girdlestone). The hip pain was treated by percutaneous radiofrequency lesioning of the sensory branches of the obturator and femoral nerves. Six-month follow-up data revealed a statistically significant decrease in Visual Analog Scale (VAS) scores and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scores, and a statistically significant increase of Harris Hip Score. Before radiofrequency and at 6-month follow-up, mean VAS scores were 9.52 (range 7-10; standard deviation 0.79) and 6.35 (range 3-10; standard deviation 2.17), respectively; mean Harris Hip Scores were 28.64 (range 19-41; standard deviation 6.98) and 43.88 (range 23.71; standard deviation 16.38), respectively; and mean WOMAC scores were 75.70 (range 92-59; standard deviation 9.70) and 63.70 (range 78-44; standard deviation 11.37), respectively. All values were statistically significant (P<.05) for Student’s t test and Wilcoxon signed-rank test. Eight patients reported > 50% pain relief at 6-month follow-up. No side effects were reported. The authors concluded “the use of this technique for hip pain control is controversial. In our experience, percutaneous radiofrequency lesioning of the sensory branches of the nerves innervating the hip joint can be an option for patients with intractable hip pain.”

Chemical Neurolysis

Randomized Controlled Trial

Reysner et al (2025) conducted a prospective double-blinded, single-center, randomized controlled trial that evaluated the efficacy and safety of chemical ablation of the pericapsular nerve utilizing ultrasound

guided ethanol neurolysis compared with sham neurolysis procedure in individuals with chronic osteoarthritis of the hip. This study included 100 patients (median age 82 years [IQR 74-89]; 49% male) and chronic hip pain who were unresponsive to conservative management. Participants were randomly assigned in a 1:1 ratio to ultrasound-guided 95% ethanol neurolysis (n=50) or sham neurolysis (n=50) prior to the diagnostic PENG block to ensure the patients were assigned to either the control or neurolysis group before undergoing any procedural intervention. The primary outcome was pain intensity (numeric rating scale [NRS]) assessed at 7 days, 30 days, 3 months, and 6 months. Secondary outcomes included opioid consumption (oral morphine equivalents), quality of life (EQ-5D-5L), and neurological deficits. Ethanol neurolysis significantly reduced NRS scores at all follow-ups (P <0.0001). The mean NRS scores decreased from baseline 6.0 ($_{SD}$ 0.9) to 3.1 (0.8) at 7 days, 2.9 (0.7) at 30 days, 2.8 (0.7) at 3 months, and 3.0 (0.7) at 6 months. Opioid consumption was lower in the neurolysis group at 7 days (median [IQR]: 1.5 [0.5-3.5] mg vs 11.5 [9.1-13.7] mg, P=0.002) and remained reduced through 6 months. Quality of life improved significantly (P<0.0001), and no neurological deficits were observed. Limitations included the study performed at single center and the short-term follow-up of only 6-months. While the study may show promise the authors concluded “future research should focus on multicenter trials with extended follow-up periods to validate long-term benefits of ethanol neurolysis. Additional comparative studies examining ethanol neurolysis against alternative techniques such as RFA and cryoablation could further clarify its role in comprehensive pain management strategies.”

In 2022, Crema et. al. completed a randomized, double-blind clinical trial for patients with severe hip osteoarthritis to compare hip pain and functional performance after obturator nerve with phenol (PG) or 1% lidocaine that failed conservative treatment. Forty-four patients scheduled for total arthroplasty due to severe osteoarthritis were randomized to the anterior branch of the obturator nerve with phenol (PG) or 1% lidocaine (LG), guided by electrical stimulation. Treatment response was evaluated utilizing Visual Analog Scale (VAS) scores and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scores. The pain intensity reported by VAS during the study included the following: baseline pain intensity was similar in both groups (phenol: 87.0 ± 15.0 x lidocaine90.0 ± 11.0; p>0.05); after one month of a single nerve block, pain intensity reduced in both groups, although slightly more in those subjects injected with phenol, without statistical difference (phenol: 58.0 ± 29.0 x lidocaine: 70.0 ± 27.0; p>0.05); and both groups finished the follow-up period with very similar pain intensities (phenol: 59.0 ± 29.0 x lidocaine: 60.0 ± 32.0; p>0.05). Similar results concerning functioning using WOMAC were observed in both groups which had similar baseline scores and decreased the compromise in quality of life after one month and four months, without statistical difference. Limitations included the evaluation of function through questionnaire by the patient that had multiple comorbidities and not through physical testing. While these results for both groups improved pain control and functioning in the first month with reduced effect after 4 months, although the scores were still better then baseline there was no statistical difference noticed between groups.

Section Summary: Ablative Procedures for Osteoarthritis of the Hip

For RFA (standard, cooled and pulsed) for the treatment of chronic hip pain related to OA the evidence includes nonrandomized controlled trial, observational study and case series. While these studies may have shown promising results in reducing pain and increasing function through the use of Visual Analog Scale (VAS) scores and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scores the time on follow-up was of short duration 12-weeks to 6-months and when comparing groups from baseline there were no statistical differences noted between the groups. RTCs are needed to investigate the efficacy of RFA to include longer observation periods in the treatment of chronic hip pain.

For chemical neurolysis (phenol, alcohol, glycerol) for the treatment of chronic hip pain related to OA of the hip. The evidence is limited currently there are two double blinded RCTs. In a review of the current

evidence Crema et al (2022) for patients with severe hip OA compared hip pain and functional performance after obturator nerve with phenol (PG) or 1% lidocaine that failed conservative treatment. Treatment responses were evaluated utilizing Visual Analog Scale (VAS) scores and Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) scores. The pain intensity reported by VAS during the study included the following: baseline pain intensity was similar in both groups (phenol: 87.0 ± 15.0 x lidocaine 90.0 ± 11.0; p>0.05); after one month of a single nerve block, pain intensity reduced in both groups, although slightly more in those subjects injected with phenol, without statistical difference (phenol: 58.0 ± 29.0 x lidocaine: 70.0 ± 27.0; p>0.05); and both groups finished the follow-up period with very similar pain intensities (phenol: 59.0 ± 29.0 x lidocaine: 60.0 ± 32.0; p>0.05). Similar results concerning functioning using WOMAC were observed in both groups which had similar baseline scores and decreased the compromise in quality of life after one month and four months. Although the scores were better than baseline there was no statistical difference between the groups. Reysner et al (2025) evaluated the efficacy and safety of chemical ablation of the pericapsular nerve utilizing ultrasound guided ethanol (95%) neurolysis compared with sham neurolysis procedure in individuals with chronic osteoarthritis of the hip who failed conservative management. The primary outcome was pain intensity (numeric rating scale [NRS]) assessed at 7 days, 30 days, 3 months, and 6 months. Secondary outcomes included opioid consumption (oral morphine equivalents), quality of life (EQ-5D-5L), and neurological deficits. Ethanol neurolysis significantly reduced NRS scores at all follow-ups (P <0.0001). The mean NRS scores decreased from baseline 6.0 (SD 0.9) to 3.1 (0.8) at 7 days, 2.9 (0.7) at 30 days, 2.8 (0.7) at 3 months, and 3.0 (0.7) at 6 months. Opioid consumption was lower in the neurolysis group at 7 days (median [IQR]: 1.5 [0.5-3.5] mg vs 11.5 [9.1-13.7] mg, P=0.002) and remained reduced through 6 months. Quality of life improved significantly (P<0.0001), and no neurological deficits were observed. While studies may show promise additional RCTs are warranted to further investigate the efficacy of chemical neurolysis in the treatment of chronic hip pain.

Ablative Procedures for Chronic Shoulder Pain

Clinical Context and Therapy Purpose

The purpose of ablative procedures RFA, cryoneurolysis, and chemical neurolysis in individuals with chronic shoulder pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with chronic shoulder pain.

Interventions

The therapy being considered is RFA (standard, cooled and pulsed), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (phenol, alcohol, glycerol).

Comparators

The following therapy is currently being used to make decisions about treating chronic shoulder pain: conservative management is aimed at relieving pain and preserving range of motion, options include anti-inflammatory medications, corticosteroid injections, and physical therapy.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most commonly measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The time for follow-up is within days to determine procedure success and at least six months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months of outcomes, and systematic reviews of RCTs. It is preferred to have double-blinded sham interventions to control for placebo effects.
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Radiofrequency Ablation

The below systematic review is a comprehensive review of the current evidence.

Systematic Review

In 2019 Orhurhu et. al. completed a systematic review on the use of radiofrequency ablation (RFA) and pulsed radiofrequency ablation (PRF) for the management of shoulder pain. The treatment options for the management of shoulder pain are broad but evolving process. Modalities for controlling shoulder pain have commonly focused on pharmacotherapy, physical therapy, rehabilitation, and invasive procedures (surgical procedures, surgical, intra-articular steroid injections, many times, being sub-optimal). The use of radiofrequency ablation (RFA) for managing shoulder pain is on the rise. This review investigated the evidence for the use of RFA in the management of shoulder pain. A review of the literature was completed, and eighteen studies were included which included 6 randomized controlled trials (RCTs), 1 prospective study, 1 retrospective study, and 10 case series or case reports. The studies were published from 2003 to 2017, with a follow-up period of up to 2 years. Sixteen of the studies performed pulsed radiofrequency ablation (PRF). Pain outcomes were reported by Visual Analog Scale (VAS) or Numerical Rating Scale (NRS) and functional outcome data by shoulder pain, Oxford shoulder score and disability

index or range of motion (SPADI – Shoulder Pain and Disability Index). Functional outcomes were limitedly reported. In the RCTs the dropout rates were significant in the placebo arms and in all but one study highlighting an intra-articular application of PRF the pain scores improved using PRF or continuous ablative techniques. Limitations related to this systematic review include, the study structures and designs of the intervention arm included combination of PRF with other treatment modalities (steroids and physical therapy) which made it difficult to evaluate the efficacy of PRF. Additionally, different techniques of ablation as well as varying study lengths and follow-up periods were utilized which confounds the actual duration of pain relief provided by PRF. The prospective and retrospective studies evaluating RFA suggested a potential benefit of RFA, however, the results were limited by varying methodologies and small sample sizes. The authors concluded “further research with standardized protocol, large sample size and with longer follow-up are needed to better assess the efficacy and safety of RFA for patients with shoulder pain.”

Observational Study

Abd-Elsayed et al (2025) completed a retrospective analysis of data from patient records who received radiofrequency ablation (RFA) and pulsed radiofrequency ablation of the suprascapular nerves for managing chronic shoulder pain from June 2017 through May 2024. All patients in this study were previously diagnosed with chronic shoulder pain refractory to conservatory management. Thirty-one (n=31) suprascapular RFA were reviewed for inclusion in this study, however, six procedures were excluded due to lack of incomplete documentation (absence of pre or postoperative VAS pain scores or data on improvement). The final analysis included 25 procedures with 14 unique patients (7 males and 7 females) with a mean age 63.86 ± 19.57 years and a mean BMI of 31.28 ± 7.34 who underwent more than one procedure during the study, either due to bilateral shoulder involvement or recurrent symptoms that required a repeat RFA. The data included was patient demographics (age, sex and BMI), diagnoses, pre RFA pain score utilizing Visual Analog Scale (VAS), post-RFA pain score, percentage of pain improvement and adverse events. The mean pre-RFA pain score was 6.08 ± 2.15, and the mean post-RFA pain score was 2.95 ± 2.27 (n = 25). A two-tailed paired t-test revealed a statistically significant difference in pre- and postoperative pain scores with a $p < 0.001$. Five procedures did not result in any improvement in the patients reported pain scores. The mean percentage improvement in the procedures that yielded pain relief (n = 20) was 63.3 ± 18.4%. Limitations include retrospective analysis, small sample size and lack of patient follow-up. Authors noted that “further research should aim to conduct prospective randomized controlled trials with standardized protocols, stratified patient cohorts and more cases to compare the therapeutic effects for pulsed and conventional radiofrequency ablation of the suprascapular nerve for patients with chronic shoulder pain.”

Chemical Neurolysis

Per review of the current peer reviewed medical literature regarding chemical neurolysis (alcohol, phenol, glycerol) for the treatment of chronic shoulder pain no studies were found. RCTs are needed to evaluate the safety and efficacy of this ablative method for the treatment of this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Section Summary: Ablative Therapies for Chronic Shoulder Pain

In a systematic review by Orhurhu et. al. (2019) on the use of RFA and PRF for the management of shoulder pain which included 6 RCTs, 1 prospective study, 1 retrospective study, and 10 case series or case reports while studies may have shown an improvement in pain and functional outcomes, the limitations related to this systematic review included: the study structures and designs of the intervention

arm included combination of PRF with other treatment modalities (steroids and physical therapy) which made it difficult to evaluate the efficacy of PRF. Additionally, different techniques of ablation as well as varying study lengths and follow-up periods were utilized which confounds the actual duration of pain relief provided by PRF. The prospective and retrospective studies evaluating RFA suggested a potential benefit of RFA, however, the results were limited by varying methodologies and small sample sizes. Further RCTs determining standardized protocols, larger sample sizes with longer follow-up are needed to assess safety and efficacy of radiofrequency ablation for the treatment chronic shoulder pain.

Ablative Procedures for Chronic Intercostal Neuralgia

Clinical Context and Therapy Purpose

The purpose of ablative procedures RFA, cryoneurolysis, and chemical neurolysis in individuals with intercostal neuralgia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with chronic intercostal neuralgia.

Interventions

The therapy being considered is RFA (standard, cooled and pulsed), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (phenol, alcohol, glycerol).

Comparators

The following therapy is currently being used to make decisions about treating intercostal neuralgia: systemic medications, topical or invasive nerve blocks.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most commonly measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The time for follow-up is within days to determine procedure success and at least six-months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Radiofrequency Ablation

Per review of the current peer reviewed medical literature no systematic reviews for RCTs were identified.

Case Reports

In 2023, Fiala et. al. in a case series assessed the efficacy of cooled radiofrequency ablation (CRFA) for the treatment of intercostal neuralgia in 6 patients (3 females and 3 males) who failed conventional treatment including intercostal nerve blocks, nonsteroidal anti-inflammatory drugs, transcutaneous electrical nerve stimulation, topical medications, opioids, tricyclic antidepressants, and anticonvulsants. Because of the retrospective nature of this case series, no standardized methodology for reporting pain relief following the CRFA procedure was established. All 6 patients reported pain reduction after CRFA with an overall average pain reduction of 81.3%. Since this case series was not standardized, a long-term assessment of these 6 cases could not be concluded. The authors concluded “further studies should be concluded to assess the duration of effect for CRFA for the treatment of intercostal neuralgia and to determine the side effects, ideal candidates and safety.”

Abd-Elsayed et. al. (2018) completed a case series presenting 2 cases on the safety and efficacy of radiofrequency ablation (RFA) for the treatment of intercostal neuralgia who failed conservative management. Patient 1 was a 62-year-old female that developed chronic chest pain following lumpectomy for breast cancer and Patient 2 was a 67-year-old female with a history of esophageal carcinoma (treated with chemotherapy-radiation) and non-small cell lung cancer (treated with right upper lobe resection) that developed chronic chest pain following treatment. Both patients underwent RFA. Both patients reported their pain 0/10 at 2-month follow-up. Patient 1 continued to report good pain relief at 1 year and Patient 2 did not return to the pain clinic. While RFA for the treatment of intercostal neuralgia appears to be promising the authors concluded “additional research is needed to further elucidate the effectiveness of this intervention, safety profile and its scope of use.”

Chemical Neurolysis

Per review of the current peer reviewed medical literature regarding chemical neurolysis (alcohol, phenol, glycerol) for the treatment of intercostal neuralgia no studies were found. RCTs are needed to evaluate the safety and efficacy of this ablative method for the treatment for this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Section Summary: Ablative Procedures for Intercostal Neuralgia

In the two case series studies one utilized cooled radiofrequency and the other utilized standard RFA in the treatment of intercostal neuralgia, while both studies showed that RFA may reduce pain one study was not standardized and long-term assessment could not be concluded. RCTs are needed with larger

patient populations to determine ideal candidates and standardize protocols to further elucidate the effectiveness of this intervention, safety profile and its scope of use in the treatment of intercostal neuralgia.

Ablative Procedures for Inguinal Neuralgia

Clinical Context and Therapy Purpose

The purpose of ablative procedures RFA, cryoneurolysis, and chemical neurolysis in individuals with inguinal neuralgia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with chronic inguinal neuralgia involving the ilioinguinal and iliohypogastric nerves.

Interventions

The therapy being considered is RFA (standard, cooled and pulsed), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (phenol, alcohol, glycerol).

Comparators

The following therapies are currently being used to make decisions about treatment chronic inguinal neuralgia: nonsteroidal anti-inflammatory medications (NSAIDs), nerve block, surgery, and nerve stimulation.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The time for follow-up is within days to determine procedure success and at least six months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs

- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Radiofrequency Ablation

Randomized Controlled Trials

In 2015, Makharita et. al. completed a randomized, double-blind controlled trial to evaluate the efficacy of pulsed radiofrequency in management of chronic inguinal neuralgia. Chronic inguinal neuralgia has been reported after inguinal herniorrhaphy, caesarean section, appendectomy, and trauma to the lower quadrant of the abdomen or inguinal region. Twenty-one adult patients aged between 20 and 60 years were allocated into 2 groups. Group 1 received 2 cycles of pulsed radiofrequency (PRF) for each nerve root. In Group 2, after stimulation, the same time was spent to mimic PRF. Both groups received bupivacaine 25% plus 4mg dexamethasone in 2mL for each nerve root. Visual Analogue Scale (VAS) was assessed. Duration of the first block effective pain relief was reported. Repeated PRF blockade was allowed for any patient who reported a VAS > 30 mm in both groups during the one-year follow-up period. The number and duration of blocks were reported, and adverse effects were reported. Significantly longer duration of pain relief was noticed in Group 1 (P=0.005) after the first block, while the durations of pain relief of the second block were comparable (P=0.59). In Group 1 the second PRF produced pain relief from the twenty-fourth week until the tenth month while in Group 2, pain relief was reported from the sixteenth week until the eighth month after the use of PRF. All patients in Group 2 received 3 blocks (the first was a sham PRF) during the one-year follow-up period. Meanwhile, 2 PRF blocks were sufficient to achieve pain relief for patients in Group 1 except 4 patients who needed a third PRF block. No adverse events were reported. Limitations include small sample size, and the study was not powered.

In 2012, Kastler et. al. evaluated the efficacy of computed tomography (CT)-guided radiofrequency ablation in the treatment of chronic inguinal neuralgia which compared ilioinguinal and iliohypogastric radiofrequency neurolysis and local injection. Forty-two patients suffering from chronic inguinal pain refractory to specific medication were included. A total of 18 radiofrequency neurolysis (RFN) procedures (14 patients) and 28 injections (28 patients) were performed. Pain was assessed in both groups using Visual Analog Scale (VAS) scores measured immediately before and after the procedure at 1-, 3-, 6-, 9- and 12- months after the procedure. Mean duration of pain prior to the procedure and mean duration of pain relief post procedure were noted. Moreover, mean maximum early pain relief was assessed. All procedures were ambulatory under computed tomography (CT) guidance. Injections contained 1.5 mL of cortivazol and 3 mL of lidocaine-ropivacaine (30%-70%). Radiofrequency neurolysis was performed using a Neurotherm RF Generator. Mean VAS scores were 7.72 in the RF group and 7.46 in the infiltration group. Maximum early pain relief did not statistically differ (77% in the RFN group and 81.5% in the injection group). Mean duration of pain relief was statistically significant (P=.005) in the RF group (12.5 months) compared to the infiltration group (1.6 months). Mean VAS scores during the year following the procedure were all significantly in favor of radiofrequency neurolysis management. Limitations of this study include small study samples and retrospective study.

Chemical Neurolysis

Per review of the current peer reviewed medical literature regarding chemical neurolysis (alcohol, phenol, glycerol) for the treatment of inguinal neuralgia no studies were found. RCTs are needed to evaluate the

safety and efficacy of this ablative method for the treatment for this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Section Summary: Ablative Procedures for Inguinal Neuralgia

Review of the current peered reviewed medical literature found two RCTs Kastler (2012) and Makharita (2015) using RFA (standard and pulsed) with pain measured based on a visual analog scale (VAS). In Makharitia (2015) longer duration of pain relief was noticed in Group 1 (P=0.005) after the first PRF block, while the durations of pain relief of the second PRF block were comparable (P=0.59). In Group 1 the second PRF produced pain relief from the twenty-fourth week until the tenth month while in Group 2, pain relief was reported from the sixteenth week until the eighth month after the use of PRF. All patients in Group 2 received 3 blocks (the first was a sham PRF) during the one-year follow-up period. In Kastler (2012) mean VAS scores were 7.72 in the RF group and 7.46 in the infiltration group. Maximum early pain relief did not statistically differ (77% in the RFN group and 81.5% in the injection group). Study limitations for both studies were small sample size. Results need to be confirmed by additional RCTs with larger sample sizes.

Radiofrequency Ablation for Plantar Fasciitis

Clinical Context and Therapy Purpose

The purpose of RFA (standard, pulsed and cooled) in individual who have plantar fasciitis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with plantar fasciitis.

Plantar fasciitis is a common cause of foot pain in adults, characterized by deep pain in the plantar aspect of the heel, particularly on arising from bed. While the pain may subside with activity, in some individuals the pain persists and can impede activities of daily living. On physical examination, firm pressure will elicit a tender spot over the medial tubercle of the calcaneus. The exact etiology of plantar fasciitis is unclear, although a repetitive injury is suspected. Heel spurs are a common associated finding, although it has never been proven that heel spurs cause the pain. Asymptomatic heel spurs can be found in up to 10% of the population.

Interventions

The therapy being considered is RFA (standard, pulsed, and cooled), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (phenol, alcohol, glycerol).

Comparators

The following therapy is currently being used to make decisions about treating plantar fasciitis: conservative management which may include corticosteroid injection.

Most cases of plantar fasciitis are treated with conservative therapy, including rest or minimization of running and jumping, heel cups, and nonsteroidal anti-inflammatory drugs. Local steroid injection may also be used. Improvement may take up to 1 year in some cases.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most commonly measured using a VAS. Quantifiable pre- and posttreatment measures of functional status are also used, such as the American Orthopedic Foot and Ankle Society (AOFAS) ankle-hindfoot score. The AOFAS ankle-hindfoot scores range from 0 to 100, with up to 40 points for pain, 50 points for functional aspects, and 10 points for alignment. A high score indicates a better outcome. The time for follow-up is within days to determine procedure success and at least 6 -months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Because of the variable natural history of plantar fasciitis and the subjective nature of the outcome measures, RCTs are needed to determine whether outcomes are improved with interventions for pain. Trials should include a homogenous population of individuals with a defined clinical condition, use standardized outcome measures when possible, and define a priori the clinically significant magnitude of response.

Review of Evidence

Systematic Reviews

A meta-analysis published by Guimaraes et al (2022) reviewed multiple therapeutic interventions to relieve pain from plantar fasciitis. A total of 8 studies of RFA were identified, but only 2 RCTs were included in the pooled analysis of RFA compared to a control group (n=117). The authors performed a dual assessment of the risk of bias of the included studies using the Cochrane Risk of Bias tool and found

a low quality of evidence for RFA to relieve pain from plantar fasciitis. The pooled mean difference between groups for pain outcomes was -1.19 (95% CI, -3.54 to 1.15; p=.32), favoring the RFA group, but this estimate did not achieve statistical significance and had a high level of heterogeneity (I^2, 84%).

Randomized Controlled Trials

Two double-blind sham-controlled randomized trials have assessed RFA for the treatment of chronic heel pain (Table 18). Wu et al (2017) randomized 36 individuals to ultrasound-guided pulsed radiofrequency of the posterior tibial nerve. First step pain, average pain, and the AOFAS ankle-hindfoot score were assessed at baseline and at 1, 4, 8, and 12 weeks. Scores at 12 weeks are shown in Table 19. Changes in VAS score in the sham group were modest (<1 on a 10-point VAS) and of short duration (statistically significant at weeks 1 and 4 but not weeks 8 and 12). The AOFAS ankle-hindfoot score was 60.55 at baseline and 60.05 at 12 weeks in the sham group. In the RFA group, VAS scores at weeks 1, 4, 8, and 12 were all significantly lower than baseline (p<.001), and the AOFAS ankle-hindfoot score increased from 55.5 to 87.6 (p<.001). The improvements in pain and function were greater in the RFA group than in the control group (p<.001 for all measures).

Landsman et al (2013) reported on a double-blind randomized crossover trial (N=17) of RFA applied along the medial aspect of the heel. Crossover to the alternate treatment was allowed at 4 weeks. Outcomes assessed weekly were a pain VAS score reported at the first step in the morning, average pain level, and peak pain level (Table 19). In a graphic presentation of results, patient pain levels for all 3 outcomes decreased after RFA but showed minimal change after sham. Following crossover from sham to RFA, there was a steep drop in all pain outcomes. The maximum follow-up assessment was at 16 weeks and appeared to show similar pain levels throughout the follow-up period.

Table 18. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	***Comparator***
Wu et al (2017)	Taiwan	1	2014-2016	36 individuals (40 feet) with recalcitrant plantar fasciitis	Ultrasound-guided pulsed RF stimulation of the posterior tibial nerve	Sham with ultrasound-guided lidocaine injection
Landsman et al (2013)	U.S.	Multicenter	NR	17 individuals failed at least 3 prior types of treatments, pain for >3 mo, and VAS score ≥5	RFA procedure, including stimulation of sensory nerves in an awake patient	Sham with all aspects of the RFA procedure, except delivery of RF energy at the final step

NR: not reported; RCT: randomized controlled trial; RF: radiofrequency; RFA: radiofrequency ablation; VAS: visual analog scale.

Table 19. Summary of Key RCT Results

Study	First Step Pain on VAS Score	Average VAS Pain Score		AOFAS Ankle-Hindfoot Score
	At 12 Weeks	***At 12 Weeks***		
Wu et al (2017)				
N	36	36		36

Study	First Step Pain on VAS Score	Average VAS Pain Score		AOFAS Ankle-Hindfoot Score
	At 12 Weeks	***At 12 Weeks***		
RFA (SD)	1.79 (1.62)	1.54 (1.26)		87.60 (9.12)
Sham (SD)	6.13 (1.75)	6.09 (1.70)		60.05 (11.38)
	Change At 4 Weeks	Change Score	Change in Peak Pain	
Landsman et al (2013)				
N	17	17	17	
RFA	5.0	4.06	5.33	
Sham	1.33	0.8	1.80	
p	.30	.047	.048	

AOFAS: American Orthopedic Foot and Ankle Society; RCT: randomized controlled trial; RFA: radiofrequency ablation; SD: standard deviation; VAS: 10-cm visual analog score.

Tables 20 and 21 display notable limitations identified in each study.

Table 20. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-Up[e]
Wu et al (2017),	3. Study did not report a minimum VAS for inclusion criteria				
Landsman et al (2013)		1. Targeted nerve not clearly defined			1. Crossover allowed at 4 wk

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
VAS: visual analog score.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 21. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Wu et al (2017),						
Landsman et al (2013)				3. Crossovers at 4 wk prevented longer-term assessments	1. Power calculations not reported	3. Confidence intervals not reported

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Case Series

Kurtoglu et al (2022) reported the largest case series of standard RFA for plantar fasciitis. The retrospective study, conducted in Turkey, included 261 individuals with plantar heel pain for at least 6 months and at least 2 failed conservative treatments. Mean VAS (scale 0-10) was 8 (range 8-9) at baseline and 0 (range 0-7) at the final mean follow-up of 15 months (p<.001). At follow-up, 16 (6.1%) individuals felt the RFA procedure was unsuccessful.

Cozzarelli et al (2010) reported the case series with the longest follow-up. This study reported on a 12-year follow-up of 82 individuals who had undergone RFA for heel pain. Study participants had undergone RFA between 1994 and 1995 and had been interviewed at 5-, 10-, and 12-years post procedure. Baseline pain levels before the procedure were recalled retrospectively at the follow-up interviews. Of 99 individuals potentially eligible to be interviewed, the study evaluated 82 individuals. The results were presented without statistical testing. It appears that 73 of 82 individuals reported being pain-free at 12 years. On a 0-to-10 pain VAS, the pain-free study participants rated their preprocedural pain at a mean of 7.1 and at 0 post procedure.

Section Summary: Radiofrequency Ablation Plantar Fasciitis

A meta-analysis found that a pooled assessment of 2 RCTs investigating RFA for pain alleviation in plantar fasciitis did not demonstrate a significant improvement compared to the control group. The analysis revealed significant heterogeneity, and the overall quality of evidence was graded as low. Two randomized, double-blind trials (total N for both trials=53) and 2 case series found consistent reductions in pain after RFA for individuals with heel pain due to plantar fasciitis. In one trial, improvements in pain and function were greater in the RFA group than in the control group at 12 weeks. In the second trial, the randomized comparison only evaluated outcomes to 4 weeks. No conclusions about RFA effectiveness can be drawn from the 2 retrospective case series with methodological limitations. To be more confident in the efficacy of this treatment, studies with larger samples and longer follow-up would be necessary. The safety of the procedure cannot be fully evaluated in the small samples studied so far.

Chemical Neurolysis for Plantar Fasciitis

For individuals with plantar fasciitis no published literature were identified in-regards to individuals receiving chemical neurolysis (alcohol, phenol, glycerol) for the treatment of this condition. RCTs are needed to evaluate the safety and efficacy of this ablative method for the treatment for this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Ablative Procedures for Peripheral Neuromas

Clinical Context and Therapy Purpose

The purpose of ablative procedures RFA, cryoneurolysis, and chemical neurolysis in individuals with peripheral neuromas is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with peripheral neuromas.

Interventions

The therapy being considered is RFA (standard, cooled and pulsed), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (alcohol, phenol, glycerol).

Comparators

The following therapy is currently being used to make decisions about treating peripheral neuromas: pharmacotherapy and steroid injections.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The time for follow-up is within days to determine procedure success and at least six months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Radiofrequency Ablation

Case Series

In 2012, a review related to the effectiveness of radiofrequency thermoneurolysis in alleviating symptoms was completed in patients with symptomatic neuroma. This review looked at 32 feet in 29 patients treated between January 2007 and January 2010. Overall relief of symptoms was rated as complete by 24 (83%) patients, with 5 patients experiencing minimal to no relief. Two patients were lost to follow-up after 1 month, 2 patients opted for no further intervention, and 1 patient went to open resection of the neuroma. Average follow-up was 13 months.

In 2002, Caporusso et. al. in a prospective study assessed the efficacy of cryosurgery on lower extremity neuromas, thirty- one neuromas in 20 patients who failed prior conservative treatment were percutaneously denervated. Patient evaluation consisted of a 10-point visual analog scale (VAS) that was administered pre- and postoperatively. Periodic evaluation with the VAS and patient satisfaction was conducted for a 1-year period following the procedure. Immediately after the procedure, all patients reported complete relief of pain and were permitted to return to full activity. Two weeks after the index procedure, patients were categorized into one of three groups: those who remained completely pain free (38.7%), those who had reduced pain (45.2%), and those who had reverted to preprocedure pain levels (16.1%). The pain score of those patients who had reduced pain decreased from a mean of 8.5+/-0.4 preprocedure to 3.5+/-0.4 ($p < .002$). Fewer than 40% of the patients had completed pain relief.

Chemical Neurolysis

Per review of the current peer reviewed medical literature regarding chemical neurolysis (alcohol, phenol, glycerol) for the treatment of peripheral neuromas no studies were found. RCTs are needed to evaluate the safety and efficacy of this ablative method for the treatment for this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Section Summary: Ablative Procedures for Peripheral Neuromas

Two case series were found related to radiofrequency and cryosurgery for lower extremity peripheral neuromas. While both studies may have shown a relief of pain symptoms a portion of the patients experienced minimal relief to no relief based on these treatment modalities. RCTs with larger patient populations and longer follow-up are needed to assess the safety and efficacy of radiofrequency ablation (standard, cooled or pulsed) in the treatment of peripheral neuromas.

Ablative Procedures for Chronic Orchialgia

Clinical Context and Therapy Purpose

The purpose of ablative procedures RFA, cryoneurolysis, and chemical neurolysis in individuals with chronic orchialgia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with chronic orchialgia, may also be referred as one of the following: testicular pain syndrome; testalgia; chronic testicular pain; chronic scrotal content pain (CSCP); post-vasectomy orchialgia; post-vasectomy pain syndrome (PVPS); and congestive epididymitis.

Interventions

The therapy being considered is RFA (standard, cooled and pulsed), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (alcohol, phenol, glycerol).

Comparators

The following therapy is currently being used to make decisions about treating chronic orchialgia: nonsteroidal anti-inflammatory drugs (NSAIDs) and antibiotics, particularly when there is evidence of infection; antidepressants such as amitriptyline or nortriptyline may be used to reduce neuropathic pain; and nerve blocks as a single injection or in a series with or without steroids.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The time for follow-up is within days to determine procedure success and at least six months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Radiofrequency Ablation

Randomized Controlled Trial

Hetta et. al. (2018) evaluated the analgesic effect of pulsed radiofrequency (PRF) applied to the ilioinguinal nerve and the genital branch of the genitofemoral nerve for patients suffering from chronic post-surgical orchialgia in a prospective, double-blind, sham-controlled, randomized trial. The inclusion criteria were patients with chronic scrotal pain (orchialgia) that fulfilled the following criteria: pain intensity > 5 on the visual analog scale (VAS); pain that lasted more than 3 months after groin surgeries; failed conservative treatment with non-steroidal anti-inflammatory drugs (NSAIDs); and showed more than 50% reduction of their orchialgia on the VAS for at least 6 hours following spermatic cord block with 6 mL of lidocaine 2%. Seventy patients complaining of chronic post-surgical orchialgia were randomized into 2 groups: PRF group (n = 35), received pulsed radiofrequency on the ilioinguinal nerve and genital branch of the genitofemoral nerve, or sham group (n = 35). The percentage of patients that showed > 50 % reduction of their visual analog scale (VAS) pain score as well as the percentage of patients that did not require additional analgesic drugs was assessed. The VAS pain score and the global perceived effect (GPE) were reported during the 3-month follow-up period. The percentage of patients that showed > 50% reduction of their VAS pain score was 80% (24/30) in the PRF group versus 23.33% (7/30) in the sham group. The percentage of patients that did not require analgesic drugs was 50% (15/30) in the PRF group versus 3.3% (1/30) in the sham group. There was a significant reduction of the mean post-procedural VAS pain score at 2-, 4-, 6-, 8-, and 12- weeks (p = 0.001) in the PRF group in comparison to the sham group. Likewise, there was a significant improvement of the GPE in the PRF group in comparison to the sham group (p = 0.00). This study was limited by the follow-up period, which was only 3 months.

Chemical Neurolysis

Per review of the current peer reviewed medical literature regarding chemical neurolysis (alcohol, phenol, glycerol) for the treatment of chronic orchialgia no studies were found. RCTs are needed to evaluate the safety and efficacy of this ablative method for the treatment for this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Section Summary: Ablative Procedures for Chronic Orchialgia

In the randomized controlled trial by Hetta et. al. 2018 which evaluated the analgesic effect of pulsed radiofrequency (PRF) applied to the ilioinguinal nerve and the genital branch of the genitofemoral nerve for patients suffering from chronic post-surgical orchialgia there was a significant reduction of the mean post-procedural VAS pain score at 2-, 4-, 6-, 8-, and 12- weeks (p = 0.001) in the PRF group in comparison to the sham group. Likewise, there was a significant improvement of the GPE in the PRF group in comparison to the sham group (p = 0.00), however, this study was limited by the follow-up period, which was only 3 months.

Ablative Procedures for Postherpetic Neuralgia

Clinical Context and Therapy Purpose

The purpose of ablative procedures RFA, cryoneurolysis, and chemical neurolysis in individuals with postherpetic neuralgia (PHN) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with PHN.

Interventions

The therapy being considered is RFA (standard, cooled, and pulsed), cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation) and chemical neurolysis (alcohol, phenol, glycerol).

Comparators

Multiple medications have shown benefit in reducing PHN symptoms. However, PHN can be difficult to treat, and some individuals require multimodal therapy to manage symptoms. The choice among treatments for PHN should be individualized according to the severity and location of pain, comorbid conditions, medication side effect profile, treatment cost and availability, and patient values and preferences. Because the pain of PHN may be chronic, long-term therapy is often required.

Outcomes

The most clinically relevant outcome measures for pain treatments are measures of pain severity and functional limitations. Pain is a subjective, patient-reported measure. Therefore, pain outcomes require quantifiable pre- and posttreatment measures. Pain is most measured with a visual analog scale (VAS) or numeric rating scale (NRS).

The time for follow-up is within days to determine procedure success and at least six months to a year to evaluate durability.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Radiofrequency Ablation

Systematic Review

Hayes (June 2025) completed annual review of the health technology assessment regarding percutaneous pulsed radiofrequency (PRF) for chronic postherpetic neuralgia of various sites. There was no change in this assessment. This assessment found the evidence overall was considered to be low-quality. A single study comparing PRF with stellate ganglion (SG) blockade and cervical nerve root block (CNRB) suggested PRF provided greater pain relief than these comparators. When PRF was compared to short-term spinal cord stimulation (SCS), results were conflicting with one study finding that PRF was less effective than SCS and the other finding no difference between the two treatments. While the limited evidence may show promise in reducing pain there remains an uncertainty regarding variability of PRF treatment protocols, heterogeneity in comparators and treatment sites/targeted nerves, the clinical benefit of treatment and a lack of long-term follow-up. Additional comparative studies are needed to determine which patients would benefit from PRF treatment and evaluate comparative effectiveness.

In 2019 Lin et. al. completed a systematic review that focused on interventional therapies that have been subjected to randomized controlled trials for the treatment of postherpetic neuralgia (PHN), including transcutaneous electrical nerve stimulation; local botulinum toxin A, cobalamin, and triamcinolone injection; intrathecal methylprednisolone and midazolam injection; stellate ganglion block; dorsal root ganglion destruction; and pulsed radiofrequency therapy. Thirty-three studies were included in this review, 20 were randomized controlled trials and the remaining 13 were nonrandomized studies case series. Of the 20 RCTs evaluated pulsed radiofrequency (n=4). Two of these RCTs regarding pulsed radiofrequency (PRF) targeted areas near the dorsal root ganglion via the angulus costae and paravertebral puncture, whereas the other 2 trials targeted the intercostal nerves and provided no further descriptions. All study outcomes, including VAS, average rescue medication dosage, most SF-36 index scores (e.g., general health perceptions, social function, emotional role, mental health index, bodily pain index, physical function, and physical role), and the Pittsburgh Sleep Quality Index scale, favored pulsed radiofrequency. The observed effects began on Day 2 or 3 after treatment and persisted for 2-6 months (i.e., study endpoint). No side effects such as pneumothorax, infection, nerve injury, postoperative paresthesia, pain exacerbation, or any other serious adverse effects were observed in all studies. In a 2016 meta-analysis (Shi et. al.) similarly demonstrated the effectiveness of pulsed radiofrequency, including significant pain improvement after 1 day, 1 week, and 1 and 3 months, with only minor adverse events (e.g., local symptoms and transient bradycardia). The authors concluded “the current evidence is insufficient for determining the single best interventional treatment. Despite the lack of conclusive evidence these interventional therapies remain valuable, especially for patients with postherpetic neuralgia refractory to standard conservative treatments.” Limitations include short follow-up of 6 months.

Observational study

Lin et. al. (2021) in a retrospective study investigated the use of computed tomography (CT)-guided radiofrequency ablation (RFA) of the cervical dorsal root ganglia (DRG) for treatment of cervical and occipital postherpetic neuralgia (PHN) in 27 patients at a single center. Patients were followed 2 days later and at 1-, 3-, 6-, and 12- months after RFA. Observation at each follow-up visit included rating of pain on a visual analog scale (VAS) and assessment of complications and adverse events. VAS scores significantly decreased in patients with PHN after RFA compared with their scores before RFA ($p < 0.05$). Study limitations include small sample size, conducted in a single center and there was no control group. The authors concluded “this study showed that CT-guided percutaneous RFA of cervical DRGs was safe and effective for reducing cervical and occipital postherpetic neuralgia in the short term. In the future we plan to conduct a multicenter study with a more comprehensive design and a larger sample size.”

Case Report

In 2019, Weber et. al. reported on a case of 71-year-old gentleman with refractory postherpetic neuralgia (PHN) in the intercostobrachial nerve distribution treated with cryoneurolysis/cryoanalgesia therapy. Multiple cycles of cryotherapy were administered in which the patient tolerated well without any complications reported. At one-month post-procedure the patient reported greater than 50% pain relief (NRS <4 on the NRS scale) and self-reported improvement in quality of life and activity. No further interventions were needed. This report concluded that given the severity of pain PHN with limited treatment options, cryoablation offers an alternative that is minimally invasive, however, authors acknowledged additional studies are necessary.

Chemical Neurolysis

Per review of the current peer reviewed medical literature regarding chemical neurolysis (alcohol, phenol, glycerol) for the treatment of post herpetic neuralgia no studies were found. RCTs are needed to evaluate the safety and efficacy of this ablative method for the treatment for this indication. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Section Summary: Ablative Procedures for Post Herpetic Neuralgia

The current evidence includes systematic review, observational study and case report regarding RFA for the treatment of refractory PHN. In the systematic review Lin et. al. 2019, which included 4 RCTs evaluating the efficacy of pulsed radiofrequency ablation for the treatment of post herpetic neuralgia all study outcomes, including VAS, average rescue medication dosage, most SF-36 index scores (e.g., general health perceptions, social function, emotional role, mental health index, bodily pain index, physical function, and physical role), and the Pittsburgh Sleep Quality Index scale, favored pulsed radiofrequency. The observed effects began on Day 2 or 3 after treatment and persisted for 2-6 months (i.e., study endpoint). No side effects such as pneumothorax, infection, nerve injury, postoperative paresthesia, pain exacerbation, or any other serious adverse effects were observed in all studies. While this systematic review shows promise these RCTs are limited by short follow-up of 6 months. Additional RCTs are needed to verify these results to include adequate sample size and longer follow-up to determine the efficacy of radiofrequency ablation for the treatment of post herpetic neuralgia.

Cryoablation in Individuals Undergoing Nuss Procedure for Pectus Excavatum

Clinical Context and Therapy Purpose

The purpose of cryoneurolysis (cryoablation) in individuals with pectus excavatum undergoing pectus surgery using minimally invasive Nuss procedure is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest are individuals undergoing pectus surgery using minimally invasive Nuss procedure to correct chest wall deformity for pectus excavatum.

Interventions

The therapy being considered is cryoneurolysis (cryoanalgesia, cryotherapy, cryoablation).

Comparators

Thoracic epidural analgesia.

Outcomes

The most clinically relevant outcome measures are reduction in length of stay (LOS) and opioid requirements.

The Nuss procedure is associated with significant postoperative pain, prolonged hospital stays and high opiate requirements.

Study Selection Criteria

We selected methodologically credible studies, using these principles:

- To assess efficacy outcomes, we sought comparative controlled prospective trials, with a preference for RCTs with a minimum of 6 months outcomes, and systematic reviews of RCTs
- To assess long-term outcomes and adverse effects, we sought single-arm studies with longer periods of follow-up and/or larger populations.
- Within each category of study design, we included studies with larger sample sizes and longer duration.

Review of Evidence

Systematic Review and Meta-Analysis

Daemen et. al. (2020) completed a systematic and meta-analysis reviewing the outcomes of intercostal nerve cryoablation (INC) in comparison to thoracic epidural (TE) after the Nuss procedure. The primary outcome was postoperative length of stay. Four observational and 1 randomized study were included, enrolling a total of 196 patients of which 100 (51%) in the TE group and 96 (49%) in the INC group. Meta-analyses demonstrated a significantly shortened length of hospital stay [mean difference -2.91 days; 95% confidence interval (CI) -3.68 to -2.15; P < 0.001]. However, the meta-analyses demonstrated significant level heterogeneity (both I^2 = 91%; P < 0.001). Post hoc subgroup analysis was performed to assess the effect of the use of concomitant analgesic methods on the length of hospital stay and heterogeneity. Subgroup analysis revealed a statistically significant difference among studies that did (n = 3) and did not (n = 2) use additional modalities of analgesia (PCA, intercostal nerve block or local infusion catheters) (I 2 = 91.1%; P < 0.001). The subgroup using additional analgesic techniques demonstrated a lower decrease in hospitalization for the cryoablation group (MD -2.19, 95% CI -2.50 to -1.89; P < 0.001), compared to the subgroup without additional analgesic methods (MD -3.76, 95% CI -4.63 to -2.90; P < 0.001). In addition, no heterogeneity was detected among studies in the subgroup that used concomitant analgesic methods (I 2 = 0.0%; P = 0.38). The mean operative time ranged from 62.7 to 109.0 min for the epidural group and 101.0 to 145.3 min for the cryoablation group. The difference in operative time reached statistical significance in 3 [19, 20, 23] out of 4 [19–21, 23] studies, favoring thoracic epidural analgesia. Pooled analysis demonstrated a statistically significant increased operative time among participants who received cryoablation during surgery (MD 40.91, 95% CI 14.42 to 67.40; P = 0.002). However, again meta-analysis detected a significant level of heterogeneity (I 2 = 91%; P < 0.001). Despite shorter hospitalization time in favor of cryoablation, postoperative pain scores based on the numeric rating scale (NRS) didn't significantly differ between groups. Keller et. al. only reported pain scores for the cryoablation group.

Additional PCA pumps with hydromorphone were given to all participants of both groups by Graves et al., whereas Harbaugh et al. used PCA in 4 (30.8%) patients in the epidural, and 13 (68.4%) patients in the cryoablation group due to inadequate pain control. Moreover, an additional intercostal nerve block was given to 2 patients in the cryoablation group. In the study by Keller et. al. 7 (26.9%) participants received local subcutaneous infusion catheters in the epidural group, in contrast to 24 (92.3%) participants in the cryoablation group. Two studies reported the time to oral pain medications alone to be 2- to 3- fold lower for cryoablation ($p < 0.01$ and $p < 0.001$). Total postoperative opioid usage was reported by 4 out of 5 studies. Despite diverging definitions, 3 studies demonstrated a statistically significant difference in opioid usage that favored cryoablation. For the study of Dekonenko et al., total opioid usage during inpatient stay was 420.0 MME for the thoracic epidural and 60.0 MME for the cryoablation group. This difference was statistically significant ($p < 0.001$). The most recent study of Graves et al. found statistically significant reduced mean opioid usage in the cryoablation group [268.0 MME (SD 165.2) vs 684.0 MME (SD 191.8) for the epidural group; $P < 0.001$]. Keller et al. only reported the mean total intravenous opioid usage and revealed similar results [49.0 (SD 32.7) vs 119.8 MME (SD 95.1) for the cryoablation and epidural group; $p = 0.001$]. Harbaugh et al. was the only one to find no statistically significant mean difference in postoperative opioid usage. In regard to adverse effects eleven (11.0%) complications occurred in the cryoablation group, in comparison to 3 (3.1%) complications in the thoracic epidural group. None of these complications could be directly related to the technical performance of the analgesic therapies. The majority of complications in the cryoablation group were bar displacements (n = 6; 6.0%). Limitations associated with this review included a low number of included studies and participants; only one randomized trial included, the overall methodological quality that ranged from some concerns to serious risk of bias, the use of data conversion methods and the heterogeneity among included studies. The authors concluded “Cryoablation of the intercostal nerves during the Nuss procedure may be an attractive alternative to thoracic epidural analgesia with reduced length of hospital stay of 2.91 days. However, given the overall low methodological quality and heterogeneity of studies, well-designed randomized controlled trials are necessary to corroborate the current evidence.”

Randomized Controlled Trial

Rim et al (2024) in a randomized, single-blind clinical trial evaluated the use of cryoanalgesia for pain management following pectus excavates repair in 101 patients who were randomly assigned to one of two groups: cryoanalgesia (group C, n = 24) or noncryoanalgesia (group N, n=24). Intrathoracic cryoablation was performed bilaterally on the fourth and seventh intercostal nerves using a cryoprobe at -80°C for 2 minutes. Comparing the results the pain levels were measured using the visual analog scale (VAS-R for resting and VAS-D for dynamic) and the total rescue analgesic consumption was determined. The two groups had similar baseline-patient characteristics; however, group C had a longer mean operative time (159 vs. 125 minutes, $p < 0.01$) and experienced significantly less pain throughout the postoperative course, with VAS at 6 hours (5.38 vs. 7.04, $p < 0.01$) and 48 hours (3.17 vs. 5.67, $p < 0.01$). While cryoanalgesia may have shown improvement in postoperative pain control at rest and during movement following the repair, this outcome was less favorable than expected due to VAS greater than 4 (moderate pain), even though after a day or two it decreased to lower levels VAS <4 in the cryoanalgesia group. The authors concluded that the routine use of cryoanalgesia for pectus surgery is yet to be determined.

Graves et. al. (2019) in a prospective randomized clinical trial (RCT) of patients undergoing the Nuss procedure for pectus excavatum between May 2016 and March 2018 hypothesized that intercostal nerve cryoablation during the Nuss procedure would reduce hospital length of stay (LOS) compared to thoracic epidural analgesia and to validate results of previous retrospective studies. Twenty patients were recruited and were randomized evenly via closed-envelope method to receive either cryoanalgesia or

thoracic epidural analgesia. Patients and physicians were blinded to study arm until immediately preoperatively cryoablation (n = 10) or thoracic epidural (n = 10). Primary outcome was postoperative LOS. Secondary outcomes included total operative time, total/daily opioid requirement, inpatient/outpatient pain score, and complications. Primary outcome data were analyzed by the Mann–Whitney U-test for nonparametric continuous variables. Other continuous variables were analyzed by two-tailed t-test, while categorical data were compared via Chi-squared test, with alpha = 0.05 for significance. Postoperative care and analgesic protocol were identical for all patients with the exception of continuous epidural infusion (no bolus or patient-controlled epidural analgesia). Local field block was performed intraoperatively at all incision sites. All patients received a hydromorphone PCA, standing intravenous acetaminophen, and 48 h of standing ketorolac immediately postoperatively. Once patients were tolerating a diet, they were converted to oral oxycodone, acetaminophen, and ibuprofen. Per institutional protocol, all epidurals were weaned at the discretion of the pediatric pain management team in consultation with the primary surgical team. Narcotic usage was recorded and tracked through the hospital's electronic medical record. In addition to standard postoperative nursing assessments and service rounds, patients' pain (including neuropathic-specific pain described as “burning”, “electrical” or “tingling” sensations) was assessed by study questionnaire via numerical pain scale (1 to 10, with 10 representing a maximum score) twice per day in sitting and lying position. Discharge was determined by the pediatric surgery attending based on adequate pain control with oral medications, ability to walk independently, and diet tolerance. All patients receiving thoracic epidural were followed for one year. Patients undergoing cryoanalgesia received postoperative follow-up to one year with the exception of one patient who had not yet reached the one-year mark, and one patient who was lost to follow-up after seven months (Median follow-up 12 months in both groups; Cryoablation follow-up range: 7–12 months). Both patients who did not reach one year of follow-up reported return of normal chest wall sensation and pain scores of 3 or lower at the 3-month follow-up exams. Median LOS decreased by 2 days in patients undergoing cryoablation, relative to those receiving an epidural. Specifically, patients receiving cryoablation were discharged on median postoperative day (POD) 3 (range: POD 2–4), while those receiving an epidural were discharged on median POD 5 (range: POD 4–6; Mann–Whitney U p = 0.0001). All 10 patients undergoing cryoablation were discharged home by POD 4. In the epidural analgesia group, 4 of 10 patients were discharged on POD 4, while the remaining six patients were discharged on POD 5 or POD 6. In regard to analgesic requirements patients who underwent cryoablation required significantly less opioid analgesia than those undergoing epidural. For the entire postoperative stay, patients in the intercostal nerve cryoablation group required a mean 268 mg (range 150–386 mg; Std Dev 165.2 mg) total oral morphine equivalents, compared to a mean 684 mg (range 547–821 mg; Std Dev 191.8 mg) in patients receiving thoracic epidural (mean difference: 416 mg; p = 0.0001). The decreased opioid requirement was not attributable to the shorter length of postoperative stay based on comparison of daily opiate requirements. Patients who underwent cryoanalgesia received 52% less opioid on POD 1, 76% less on POD 2, and 82% less on POD 3 (p-value b0.01 for all three time points). Additionally, patients who received cryoablation required less total ketorolac (mean decrease 89.3 mg, p = 0.02) and less acetaminophen (mean decrease 848.1 mg, p = 0.01). There was no difference in mean pain scores between the two randomization groups at any in-hospital or outpatient time points, up to one- year. The biggest limitation was small sample size and even though the study demonstrated differences in LOS and opioid requirements between the two groups, the groups were not exactly matched as evidenced by statistically significant differences in age between the groups. Also blinding to the intervention was not feasible for the surgeon or the patient who awoke with or without epidural catheter. Additionally, to ensure patient safety and to optimize individualized analgesia regimens it was critical for the healthcare team to be aware of the which treatment the patient received.

Observational Studies

Braak et. al. (2024) conducted a retrospective chart review that compared the efficacy of intercostal nerve cryoablation combined with patient controlled systemic opioid analgesia (PCA) compared with continuous epidural analgesia (CEA) with PCA in children undergoing Nuss procedure. This study was conducted between January 2019 through July 2022. The primary outcome was length of stay (LOS), and secondary outcomes were operation time, postoperative pain, opioid consumption, and gabapentin use. Numeric Rating Scale (NRS) was utilized to evaluate pain scores. Minimum follow-up period was 12 months. Based on the number of patients undergoing the Nuss procedure during the study period 66 patients (n=66) were included. Thirty-three patients were included in each cohort (n=33). Of all patients, 84.8% were male (n=56/66) and the median age was 16 years. Most patients received one Nuss bar (84.8%, n=56/66). No patients were lost to follow-up and no readmissions were reported. Mean operation room time was 15.6 (95% confidence interval [CI]: -2.2 to -29.0) minutes shorter for the CEA group, $p < 0.010$) compared with the cryoablation group. There was no significant difference in operation room time between the Nuss procedure with one or two bars (127.0 vs. 132.0, $p = 0.365$). NRS pain scores at day 1 and 2 were lower in the cryoablation group (respectively -1.3 (95% CI: -2.2 to -0.4), $p = 0.002$ and -2.0 (IQR: -.5 to -3.0), $p = 0.001$). Use of gabapentin (78.8%, n = 26/33 vs. 18.2%, n = 6/33) was higher in the CEA group ($p < 0.001$). Fewer patients used opioids at discharge (n = 10/33, 30.3% vs. n = 32/33, 97.0%; $p < 0.001$)) and 1 week after surgery (n = 2/33, 6.1% vs. n = 15/33, 45.4%; $p < 0.001$)) in the cryoablation group. After 6 weeks two patients still used opioids, one in each group. The use of PCA after surgery was shorter in the cryoablation group (1.6 vs. 4.1 days, $p < 0.001$). Median LOS was 3 days shorter in the cryoablation group. In the cryoablation group, seven patients stayed for 5 days or longer (18 in the CEA group). In two cases, the prolonged stay was related to the cryoablation procedure (large bilateral pneumonia [n = 1], pain due to unilateral cryoablation [n = 1]). Other reasons for prolonged hospital stay were social problems (n = 2), opioid related gastrointestinal problems (n = 2), and persistent pain (n = 1). Limitations included small sample size and lack of long-term follow-up.

Holguin et. al. (2023) completed a retrospective chart review for all patients who underwent Nuss procedure for pectus excavatum from 2002 to 2020. Patients were stratified by pain management strategy, intercostal nerve cryoablation (INC) vs. thoracic epidural (TE). Chi-square and Fisher's exact were used to compare categorical variables. Wilcoxon tests were used to evaluate continuous variables and costs. A total of 158 patients were identified. Of these, 80.4% (N = 127) were treated with epidural, while 19.6% (N = 31) were treated with intercostal nerve cryoablation. The INC group had lower rates of PCA use (35.5% vs. 93.7%, $p < 0.001$), lower total morphine milligram equivalent requirement (27.0 vs. 290.8, $p < 0.001$), and shorter length of stay (3.2 days vs. 5.3 days, $p < 0.001$) compared to the TE group. INC was also associated with longer operative times (153.0 min vs. 89.0 min, $p < 0.001$) and higher hospital costs.

Lai et. al. (2022) completed a retrospective single-center chart review on patients undergoing Nuss procedure for pectus excavatum with intercostal cryoablation which evaluated the relationship between cryoablation and clinical outcomes. Demographics, hospital course, and postoperative complications were abstracted. To evaluate the evolution of outcomes over time, the earliest quarter (Q1) of cryoablation patients were compared to the last quarter (Q4). Over 45 months, 350 Nuss procedures with cryoablation were performed. The mean age at operation was 15.7 ± 2.3 years with an average Haller Index of 5.4 ± 4.2. The mean operative time was 136 ± 40.5 minutes. On average, patients used 2.8 ± 2.5 OME/kg of opioid in hospital with a LOS of 2.7 ± 1.1 days. The Q4 patients were discharged 1.3 days earlier ($p<0.05$) than Q1 patients, with 80% of Q4 discharged by postoperative day #2 vs. 23% in Q1 ($p<0.05$). Q4 patients received 74% ($p<0.05$) less opioid in hospital and 21% ($p<0.05$) less on discharge. Within 90 days postoperatively, complication rates (chest tube placement, wound infection, readmission, neuropathic pain) were similar. Only two patients (0.6%) required reoperation for bar migration/slippage.

Clark et. al. (2022) completed a single-center retrospective chart review for patients less than 18 years old who underwent minimally invasive repair of pectus excavatum (MIRPE) which involved placement of a transthoracic, retrosternal support bar under thoracoscopic guidance. This study evaluated the effects of intraoperative intercostal nerve cryoablation (CA) on postoperative pain control, opioid requirement and perioperative outcomes. Data collection included demographics, preoperative characteristics, intraoperative findings, and postoperative outcomes. It was hypothesized that CA would be associated with improved pain scores, lower doses of total inpatient opioid requirement, and shorter length of stay (LOS). One hundred sixty-one patients met inclusion criteria: 75 underwent intraoperative CA and 86 underwent MIRPE without CA (NCA group). CA significantly decreased median LOS from 4 days in NCA to 2 days; the use of CA was the only significant predictor of LOS on linear regression. CA was also associated with decreased total PCA, intravenous opioid, and oral opioid dosages. There was no difference in inpatient pain scores and a slight increase in mean procedure time.

Aiken et. al. (2021) conducted a retrospective study for patients undergoing Nuss procedure from 2016-2019. Patients who received cryoablation were compared to those that received traditional pain control (patient-controlled analgesia or epidural). Outcome variables included postoperative opioid usage (milligram morphine equivalents, MME) and length of stay (LOS). Thirty-five of 73 patients studied (48%) received intercostal nerve cryoablation. LOS (1.0 vs 4.0 days, $p<0.01$) was decreased in the cryoablation cohort and cryoablation was also associated with decreased opioid usage (15.0 versus 14.6 MME, $p<0.01$) during the 24 hours following surgery and this persisted over the entire postoperative period, including discharge opioid prescription (112.5 vs 300.0 MME, $p<0.01$). Limitations related to this study include retrospective single institution study that limits generalizability and introduces the potential for selection bias and cohort imbalance in both measured and unmeasured confounders. However, all consecutive patients received cryoablation once it was introduced, reducing the chance for selection bias. It is possible that other aspects of the cryoablation protocol, such as pre-operative pregabalin and intercostal nerve blocks with bupivacaine, contributed to the overall decreased opioid use. However, the persistent opioid reduction beyond the first 24 hours suggests that these factors were not solely responsible for the overall opioid reduction. Finally, it is also possible that the introduction of cryoablation led to differences in opioid prescribing unrelated to the efficacy of the intervention (novelty bias).

Section Summary: Cryoablation in Individuals undergoing Nuss Procedure for Pectus Excavatum

A study of 20 adolescent to young adults, upon which the FDA 510k clearance for using cryoablation nerve block therapy device in adolescents (12–21 years of age) was based, demonstrated analgesia equivalence to thoracic epidurals and shorter hospital length of stays. However, as noted in a commentary by Chidambraran et al (2022), “this is not enough evidence to demonstrate safety of this technique in children and that larger studies are needed, and we should therefore be cautious in its application. In a systematic review and meta-analysis in 2020 by Daemen et. al. reviewing the outcomes of intercostal nerve cryoablation (INC) in comparison to thoracic epidural (TE) after the Nuss procedure found the meta-analyses demonstrated a significantly shortened length of hospital stay [mean difference -2.91 days; 95% confidence interval (CI) -3.68 to -2.15; $P < 0.001$]. However, the meta-analyses demonstrated significant level heterogeneity (both $I^2 = 91\%$; $P < 0.001$). Post hoc subgroup analysis was performed to assess the effect of the use of concomitant analgesic methods on the length of hospital stay and heterogeneity. Subgroup analysis revealed a statistically significant difference among studies that did ($n = 3$) and did not ($n = 2$) use additional modalities of analgesia (PCA, intercostal nerve block or local infusion catheters) ($I 2 = 91.1\%$; $P < 0.001$). The subgroup using additional analgesic techniques demonstrated a lower decrease in hospitalization for the cryoablation group (MD -2.19, 95% CI -2.50 to -1.89; $P < 0.001$), compared to the subgroup without additional analgesic methods (MD -3.76, 95% CI -

4.63 to -2.90; P < 0.001). In addition, no heterogeneity was detected among studies in the subgroup that used concomitant analgesic methods (I 2 = 0.0%; P = 0.38). Despite shorter hospitalization time in favor of cryoablation, postoperative pain scores based on the numeric rating scale (NRS) didn't significantly differ between groups. Despite diverging definitions, 3 studies demonstrated a statistically significant difference in opioid usage that favored cryoablation. Dekonenko et al., total opioid usage during inpatient stay was 420.0 MME for the thoracic epidural and 60.0 MME for the cryoablation group (p < 0.001), Graves et al. found statistically significant reduced mean opioid usage in the cryoablation group [268.0 MME (SD 165.2) vs 684.0 MME (SD 191.8) for the epidural group; p < 0.001]. Keller et al. only reported the mean total intravenous opioid usage and revealed similar results [49.0 (SD 32.7) vs 119.8 MME (SD 95.1) for the cryoablation and epidural group; p = 0.001]. Harbaugh et al. was the only one to find no statistically significant mean difference in postoperative opioid usage. In regard to adverse effects eleven (11.0%) complications occurred in the cryoablation group, in comparison to 3 (3.1%) complications in the thoracic epidural group. Limitations associated with this review included a low number of included studies and participants; only one randomized trial included, the overall methodological quality that ranged from some concerns to serious risk of bias, the use of data conversion methods and the heterogeneity among included studies. The authors concluded "Cryoablation of the intercostal nerves during the Nuss procedure may be an attractive alternative to thoracic epidural analgesia with reduced length of hospital stay of 2.91 days. However, given the overall low methodological quality and heterogeneity of studies, well-designed randomized controlled trials are necessary to corroborate the current evidence."

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Orthopaedic Surgeons et al

In 2021, the American Academy of Orthopaedic Surgeons published a clinical practice guideline, endorsed by the American Association of Hip and Knee Surgeons and the American Physical Therapy Association, on management of osteoarthritis (OA) of the knee. The guideline did not specifically address RFA or cryoneurolysis, but did include a guideline statement on denervation therapy that included various ablation techniques (e.g., RFA, cryoneurolysis, thermal ablation and chemical ablation). The guideline stated, "denervation therapy may reduce pain and improve function in patients with symptomatic osteoarthritis of the knee" (strength of recommendation: limited).

American College of Foot and Ankle Surgeons

In 2018, the American College of Foot and Ankle Surgeons issued a clinical consensus statement on the diagnosis and treatment of adult acquired infracalcaneal heel pain. The safety and efficacy of bipolar radiofrequency were listed as “uncertain – neither appropriate nor inappropriate.”:

American College of Rheumatology and Arthritis Foundation

In 2019, the American College of Rheumatology and Arthritis Foundation gave a conditional recommendation for radiofrequency ablation for the treatment of knee OA. The recommendation was based on evidence of a potential analgesic benefit, but the studies used heterogeneous techniques and there was a lack of long-term safety data.

American Society of Pain and Neuroscience

The American Society of Pain and Neuroscience (2021) issued consensus guidelines using U.S. Preventive Services Task Force (USPSTF) grading criteria on the use of RFA to treat various pain conditions. The guidelines stated that genicular RFA may be used for the treatment of osteoarthritis-related and post-surgical knee joint pain (Grade B), and may be selectively offered for the treatment of occipital neuralgia pain when greater or lesser nerves have been identified as the etiology of pain via diagnostic blocks (Grade C).

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review can be located at clinicaltrials.gov.

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CODES

To report provider services, use appropriate CPT codes, HCPCS codes, Revenue codes, and/or ICD diagnosis codes.

Codes	Number	Description
CPT		
	64620	Destruction by neurolytic agent, intercostal nerve (destruction by a neurolytic agent may include chemical (e.g., alcohol, glycerol, phenol), cold, or radiofrequency techniques)

	64624	Destruction by neurolytic agent, genicular nerve branches including imaging guidance, when performed
	64640	Destruction of neurolytic agent; other peripheral nerve or branch (destruction by a neurolytic agent may include chemical (e.g., alcohol, glycerol, phenol), cold, or radiofrequency techniques)
	64999	Unlisted procedure code, nervous system (may be used RF neurolytic peripheral nerve)
	0440T	Ablation percutaneous cryoablation includes imaging guidance upper extremity distal/peripheral nerve
	0441T	Ablation percutaneous cryoablation includes imaging guidance lower extremity distal/peripheral nerve
	0442T	Ablation, percutaneous, cryoablation, includes imaging guidance; nerve plexus or other truncal nerve (e.g., brachial plexus, pudendal nerve)
HCPCs		
	C2618	Probe/needle cryoablation
	C9808	Nerve cryoablation probe (e.g., cryoice, cryosphere, cryosphere max, cryoice cryosphere, cryoice cryo2), including probe and all disposable system components, non-opioid medical device
	C9809	Cryoablation needle (e.g., iovera system), including needle/tip and all disposable system components, non-opioid medical device
	G0571	Intraoperative nerve(s) cryoablation for post-surgical pain relief (list separately in addition to code for primary service)
Type of Service	Surgery	
Place of Service	Outpatient/Inpatient	

POLICY HISTORY

Date	Action	Action
November 2025	Annual Review	Policy Revision
November 2024	Annual Review	Policy Revised

Date	Action	Action
November 2023	Annual Review	Policy Revised
January 2023	Annual Review	Policy Revised
March 2022	Interim Review	Policy Revised
January 2022	Annual Review	Policy Revised
January 2021	Annual Review	Policy Renewed
January 2020	Annual Review	Policy Revised
January 2019	Annual Review	Policy Revised
January 2018	Annual Review	Policy Revised
January 2017		New Medical Policy

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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