Review Article

Radiofrequency Ablation in Chronic Pain Syndromes: An Evidence- and Consensus-Based Indian Society for the Study of Pain Guidelines, 2022

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Abstract

Chronic pain is a frequent, intricate, and adverse condition that has a considerable influence on individuals and society at large. In India, its prevalence is around 20%. Although a spectrum of conservative treatment modalities is available, a significant proportion of patients with chronic pain syndromes remain refractory and require surgical intervention. In these groups of patients, radiofrequency ablation (RFA) techniques are safe minimally invasive treatments and provide significant and durable pain relief. Thus, we aimed to formulate the Indian Society for the Study of Pain (ISSP) guidelines for the management of chronic pain syndromes with various RFA techniques. An in-depth literature review by experts in Pain Medicine practising in India, was used to produce 16 statements across 4 common chronic pain syndromes, including knee pain, headache and facial pain, lumbar facet joint pain, and sacroiliac joint pain. The quality of evidence was assessed with the Third US Preventive Service Task Force guidance document and the strength of the recommendation was determined by the Delphi consensus process. The level of evidence for most of the statements was I. Moreover, for most statements, the level of agreement between the experts was good (≥80% of the experts). The ISSP guidelines for the management of chronic pain syndromes are developed by experts in pain medicine. For most of the statements, the highest level of evidence was available and inter-expert agreement was good. However, further high-quality research is required to formulate more inclusive guidelines in this evolving pain medicine speciality.

Keywords: Chronic pain, conventional radiofrequency, cooled radiofrequency, Delphi process, guidelines, pain medicine, pulsed radiofrequency, radiofrequency ablation, thermal radiofrequency

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Introduction

Pain is an unpleasant sensory and emotional experience associated with, or resembling that associated, actual or potential tissue damage.[1] Moreover, chronic pain is pain which has remained beyond the normal duration of tissue healing, which, in the absence of other factors, is generally taken to be 3 months.[2] As a frequent, intricate, and adverse condition, chronic pain has a considerable influence on individuals and society at large.[3] It is usually attributed to a disease or an injury. Nevertheless, it is a standalone condition in its own right, not just an associated symptom of an underlying disease. Thus, it has its medical definition as well as taxonomy.[4-6]

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The term "chronic primary musculoskeletal (MSK) pain" suggests chronic pain in the muscles, tendons, joints, or bones that is characterized by substantial functional disability or emotional distress.[7] Globally, the disease burden due to chronic pain is rising exponentially, with 1.9 billion individuals being affected by recurring tension-type headaches, one of the most

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common symptomatic chronic disorders. Moreover, estimation of years lived with disability, low back pain (LBP) and neck pain have persistently been the predominant factors responsible for disability, with other chronic painful conditions featuring notably in the 10 most frequent factors leading to disability.[8]

As per a study, the prevalence of chronic pain in the US population ranges from 11% to 40%, with a point prevalence of 20.4%.[9] A pooled analysis suggested the prevalence of chronic pain in those residing in the UK is 43.5%, with the rate of moderate-to-severe disabling pain between 10.4% and 14.3%.[10] Similarly, in India, the estimated prevalence of chronic pain is 19.3%.[11] The order of chronic pain reported is back pain (24.84%) followed by body pain (22.98%), knee (16.77%), chest (13.97%), and upper limb (10.87%).[11]

However, chronic pain does not affect all individuals equally. It frequently affects females, those belonging to lower socioeconomic status, military veterans, and individuals living in rural areas.[9] Moreover, as a leading cause of disability, it affects an individual's ability to work and has a significant economic cost. As per an estimate, one in three Americans is affected by chronic pain, costing between 560 and 635 billion USD yearly in medical costs and lost productivity.[12] According to another estimate, the mean nonfinancial yearly cost for one of the 15.4% of Australian individuals suffering from chronic pain ranges from 22,588 to 42,979 AUD.[13] Thus, considering the enormous disease burden and disabilities arising from it, chronic pain requires active management.

Various modalities, including physiological therapies, pharmacotherapy, complementary medicine, various minimally invasive pain and spine interventions (MIPSI) by pain physicians, psychotherapeutic interventions, and rehabilitative interventions are available for chronic pain.[14] Despite these multiple options, this cohort of patients usually has refractory pain and requires other modalities besides surgery. Introduced initially in the 1970s, radiofrequency ablation (RFA) was initially used to treat trigeminal neuralgia (TN). However, subsequently, its indications were diversified to treat vertebral radiculopathy pain and are currently used to manage conditions ranging from sympathetic-derived nerve pain to chronic knee pain.[15,16]

The conventional RFA, a minimally invasive novel technique, uses a high-temperature probe (60°C–90°C for 60–90 s) that targets particular nerves eliciting the pain, resulting in thermo-coagulation and destruction of the neural tissue. Subsequently, introduced in 1998, pulse RFA (P-RFA) is performed in short pulses (20 msec pulses every 0.5 s) to decrease the target temperature (does not exceed 42°C) by allowing for cooling of tissues, making it a nonneuroablative technique.[17] Finally, the cooled RFA (C-RFA) provides the ability to produce a larger local neuronal lesion to increase the chances of effective denervation. In C-RFA, water circulates inside the probe to remove heat, modulating the thermal heat in the tissue to around 60°C, and alters the overall size, shape, and projections of lesions compared to conventional RFA.[18] Various studies have reported excellent short- and long-term pain relief of RFA in a variety of chronic pain painful conditions. Moreover, RFA interventions are associated with a favorable safety profile in comparison to major surgical options available for chronic pain syndromes. Thus, Indian Society for the Study of Pain (ISSP) aimed to develop pragmatic guidelines, based on both evidence and consensus among Pain Physicians with extensive experience in RFA that can be used to guide clinical care and simultaneously improve the research quality.

Methods

Guideline development committee

The ISSP convened a Special Interest Group (SIG) for Guidelines Development consisting of 10 members with expertise in pain medicine and the use of various RFA modalities. The SIG reviewed the evidence and formulated the recommendations on efficacy and safety of various RFA techniques, including conventional/thermal RFA, P-RFA, and C-RFA in a spectrum of chronic pain syndromes. Two co-chairs (G. D., and P. S.) were selected by the ISSP to lead the panel, which also included the past president of ISSP as guidelines committee chairman (G. D.). All participants were identified to have an area of needed expertise, which could include extensive experience in the practice of RFA procedures, basic science research, clinical studies, or expertise in evidence assessment or publication. Invitations were subsequently sent to potential panelists and accepted before formal engagement. Meetings were held regularly during the composition and drafting of the guideline, with meetings to rank evidence and develop consensus surrounding the use of RFA.

Guideline development process

The population, intervention, comparator, outcome, and healthcare setting principles were used as the basis of the statements. The SIG was proposed during the General Body Meeting of ISSP during the national conference held at Bengaluru, in February 2019, and the SIG met in person on May 18, 2019 and December 21, 2019. At the first meeting, the SIG developed the scope and key questions used to guide the systematic evidence review. At the second meeting, the group reviewed the results of the evidence review and drafted initial potential recommendation statements. Subsequently, additional draft recommendation statements were proposed.

The SIG was then involved in a multistage modified Delphi process, in which each draft recommendation was ranked according to clinical importance and usefulness, and revised. At each stage of the Delphi process, the lowest-ranked recommendations were eliminated. For a recommendation to be approved, a two-thirds majority was required. However, a unanimous or near-unanimous consensus was achieved for all recommendations. After the finalization of the recommendations, the guideline was written by various panel members, and drafts were distributed to the panel for feedback and revisions. Three external peer reviewers (K. S., D. B.,

SD and PB.), not part of the SIG, from different professional societies, were solicited for additional comments. After another round of revisions and panel approval, the guideline was finalized.

The panel formulated the recommendations to be generally applicable in adult populations with various chronic pain syndromes.

Evidence review

This guideline is informed by a systematic evidence review that addressed a variety of topics related to the efficacy and safety of RFA procedures commissioned by ISSP. Literature searches were conducted in multiple electronic databases (PubMed, Cochrane Library, and Google Scholar) from their start date through October 2019. An update search was performed in September 2020. In addition, reference sections of all manuscripts were examined to find any relevant study. There was no limitation on the types of articles used to develop the guidelines; however, the search was restricted to the English language. Based on the chronic pain conditions, search terms were: chronic knee pain ("analgesia," "chronic pain," "conventional radiofrequency," "cooled radiofrequency," "functional outcome," "genicular nerve (GN)," "hyaluronic acid," "intra-articular (IA)," "knee arthroplasty," "knee pain," "knee osteoarthritis (OA)," "nerve ablation," "pain relief," "pulsed radiofrequency," "quality of life (QoL)," "radiofrequency," "steroid," "thermal radiofrequency," and "water-cooled (WC) radiofrequency"); Headache disorders and Facial pain ("chronic headache disorders," "chronic neck pain," "cooled radiofrequency," "dorsal root ganglion," "Gasserian ganglion," "greater occipital nerve," "migraine," "occipital nerve," "occipital neuralgia," "pericranial neuralgias," "peripheral nerve stimulation," "pulsed radiofrequency," "radiofrequency thermoablation (RFTA)," "radiofrequency thermocoagulation," "steroid," "thermal radiofrequency," and "TN"); Lumbar facet joint pain ("conventional radiofrequency," "cooled radiofrequency," "IA," "LBP," "lumbar facet joint pain," "medial branch block (MBB)," "pulsed radiofrequency," and "radiofrequency neurotomy"); and sacro-iliac joint (SIJ) pain ("conventional radiofrequency," "cooled radiofrequency," "functional improvement," "LBP," "nerve ablation," "QoL," "radiofrequency," "RFA," "SIJ pain," and "WC radiofrequency"). Each author performed independent literature searches and the information was cross-referenced and compiled for evidence analysis and consensus review. These searches yielded 78 articles, which were found relevant to the RFA treatment of chronic pain syndromes. Investigators reviewed abstracts from electronic databases, reference lists, and suggestions from expert reviewers. Meta-analysis (MA), systematic reviews (SRs), original articles, case series, case reports, and experimental studies were included in the evidence report.

Wherever pertinent, proposed mechanisms of action are provided followed by a critical review. Literature published before the dates stated above is cited when relevant. After reviewing the literature, the ISSP panel convened to develop recommendations for RFA analgesia. Supporting literature is included following these recommendations and discussions of the panel.

Evidence ranking

The United States Preventative Services Task Force developed hierarchies of studies and degrees of recommendations according to the evidence rankings as outlined in Tables 1 and 2.[19] The 2022 ISSP guideline has adopted these classifications. In areas with strong evidence, recommendations were formulated based on peer-reviewed references. While, in areas with weak or no evidence, recommendations were formulated based on the consensus opinion.

Each author of the guideline completed a reference form for the statements assessed. These forms were then reviewed by the executive committee of the SIG and the mean was calculated, serving as a means for review and consensus development. The SIG developed recommendations based on evidence ranking, or consensus when evidence was lacking, followed by assigning consensus rankings. The consensus determination

Table 1: Hierarchy of studies by the type of design (U.S. Preventive Services Task Force)[19]

Evidence level	Study type
I	The systematic review, meta-analysis, or at least one properly designed controlled and RCT
II-1	Well-designed, controlled, non-RCTs
II-2	Cohort or case studies and well-designed controls, preferably multicenter
II-3	Multiple series compared over time, with or without intervention, and surprising results in noncontrolled experiences
III	Clinical experience-based opinions, descriptive studies, clinical observations or reports of expert committees

RCTs: Randomized clinical trials

Table 2: Meaning of recommendation degrees (U.S. Preventive Services Task Force)[19]

Degree of recommendation	Meaning
A	Extremely recommendable (good evidence that the measure is effective and benefits outweigh the harms)
B	Recommendable (at least, moderate evidence that the measure is effective and benefits exceed harms)
C	Neither recommendable nor inadvisable (at least moderate evidence that the measure is effective, but benefits are similar to harms and a general recommendation cannot be justified)
D	Inadvisable (at least moderate evidence that the measure is ineffective or that the harms exceed the benefits)
I	Insufficient, low quality or contradictory evidence; the balance between benefits and harms cannot be determined

Table 3: Strength of consensus

Strength of consensus	Definition*
Strong	≥80% consensus
Moderate	50%-79% consensus
Weak	<49% consensus

*Quorum is defined as 80% of participants available for vote

was performed during in-person meetings or via teleconference with a quorum of 80% of the contributing authors determining recommendation strength. Based on the agreement, consensus rankings were classified as strong, moderate, or weak, as defined in Table 3.

As with any guideline, this document serves only as a recommendation regarding the implementation and management of RFA therapy. The opinions and recommendations offered are not intended to promote the off-label use of RFA procedures. In addition, these recommendations should not be construed as a standard of care. While making clinical decisions, pain physicians should consult their national approval processes.

It is critical to highlight the conflicting nature of evidence and the requirement for consensus. Evidence and consensus are not mutually exclusive, which may be the perception at first glance. Evidence assessment, regardless of the strength, needs interpretation for clinical application whenever used. Thus, the good clinical judgment of pain physicians should guide individual patient care.

Quality of evidence

The quality of evidence suggests the level of certainty in the recommendation and the possibility that further research could alter the recommendations. As suggested, a recommendation based on low-quality evidence has a high chance of being affected by new evidence, and a recommendation based on high-quality evidence has a low probability. Strong recommendations based on low-quality evidence suggest that until better evidence becomes available, the panel determined that the benefits of following the recommended course of action outweigh the harm.

Target audience and scope

The guideline intends to provide, where possible, evidence-based recommendations for use of RFA in adults for the treatment of chronic pain syndromes in specialty settings. The target audience is all practicing pain physicians.

Dissemination of the guidelines and revision plans

The developed guidelines will be published in the "Clinical practice guidelines" in the Indian Journal of Pain, the official journal of ISSP, and also on the official website of ISSP. In addition, this guideline will be presented at medical symposia, conferences, and hospitals. The ISSP intends to update its clinical practice guidelines regularly. This guideline and the evidence report used to develop it will be reviewed and updated by 2025, or earlier if critical new evidence becomes available.

Editorial independence

Funding for the guideline was provided by the ISSP. The guideline was approved by ISSP, but the content of the guideline is the responsibility of the authors and panel members. All panelists were required to disclose conflicts of interest within the preceding 5 years at all face-to-face meetings and before submission of the guideline for publication, and to recuse themselves from votes, if a conflict was present. Conflicts of interest between the authors and panel members are listed in Appendix 1.

Recommendations of 2022 Indian Society for the Study of Pain Guideline

In this guideline, we explored the evidence-weighted and consensus recommendations of the ISSP regarding the following painful conditions:

1. Chronic knee pain
2. Headache disorders and facial pain
3. Lumbar facet joint (LFJ) pain
4. SIJ pain.

Chronic Knee Pain

Statement 1

In patients with chronic OA knee pain, GN-RFA results in a clinically significant degree of pain relief and mid-to long-term functional improvement.

Recommendation

In patients with chronic OA knee pain, ISSP recommends that GN-RFA may be used for mid-to-long-term pain control and functional improvement.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 80%; Mostly agree: 20%; Partially agree: 0%; Mostly disagree: 0%; Completely disagree: 0%; and Not sure: 0%.

Rationale

In an SR, Orhurhu *et al*. evaluated the findings of 19 studies, including 4 randomized controlled trials (RCTs). GN-RFA was used to mitigate chronic OA KNEE pain. They observed that patients with chronic OA KNEE pain had a significant reduction in pain scores and improvement in functional outcomes. The use of RFA resulted in immediate, short-term, and long-term pain relief, with pain relief lasting for as long as 12 months. Moreover, only two studies reported spontaneously resolving periosteum pain and difficulty to manage recurrent pain as adverse events (AEs) associated with RFA. While others reported no safety concerns. Thus, demonstrating the safety of RFA.[20]

In a randomized, double-blind, sham lesion-controlled study, Choi *et al*. evaluated if the GNRF neurotomy was effective in relieving chronic pain in 38 elderly patients with Osteoarthritis of Knee. Patients received either percutaneous GNRF neurotomy (RF group; $N = 19$) or the same procedure without effective neurotomy (control group; $N = 19$). In the RF group, compared with baseline, Visual Analog Scale (VAS) knee pain scores were lower at 1-, 4-, and 12 weeks ($P < 0.001$). Contrarily, in the control group, the VAS pain scores were only lower than baseline at 1 week. When comparing knee pain improvement from baseline, the RF group showed superior improvement compared with the control group at both 4 and 12 weeks (both $P < 0.001$). Moreover, 10 (59%) patients in the RF group achieved at least 50% pain relief at 12 weeks, while none of the patients in the control group achieved this pain relief. In the RF group, Oxford knee scores (OKS) improved at all assessment points compared with baseline ($P < 0.001$). The OKS, at 4 and 12 weeks, was significantly better in the RF than in the control group (both $P < 0.001$).[21]

In an RCT, Sari *et al*. compared the clinical effects and reliability of the GNRF neurotomy using fluoroscopy and ultrasound techniques in patients with OA KNEE pain. The decrease in VAS score and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total score in the 1 and 3 months was significant in both groups ($P < 0.001$). While the groups did not differ in terms of pain relief and functional status. Moreover, the application time was significantly shorter in the ultrasound group (20.2 ± 6.4 min) than in the fluoroscopy group (25 ± 4.8 min) ($P < 0.05$). Thus, GNRF neurotomy under ultrasound guidance was easily applicable, safe and dynamic, and required no radiation to achieve the same benefit as the fluoroscopy-guided interventions.[22]

In a single-blind RCT, El-Hakeim *et al*. evaluated the efficacy of fluoroscopic-guided GNRF neurotomy for the alleviation of chronic pain and improvement of function in patients with OA KNEE. The RF group ($N = 30$) received GNRF neurotomy, while the conventional group ($N = 30$) received conventional analgesics only. In both, groups, the VAS and WOMAC score decreased significantly at 2 weeks, 3 months, and 6 months from the baseline (all $P < 0.05$). The VAS score was significantly lower in the RF group at 2 weeks ($P = 0.004$), 3 months ($P < 0.001$), and 6 months ($P < 0.001$). However, the total WOMAC score was significantly less in the RF group only at 6 months ($P < 0.001$). Thus, improvement in pain and WOMAC score resulted in improved QoL.[23]

In a prospective, observational, longitudinal study, Santana Pineda *et al*. attempted to manage intractable knee pain, in 25 patients with grade 3-4 arthrosis, with RF neurotomy of superior medial, superior lateral, and inferior medial GNs. Compared to baseline, the VAS and WOMAC scores decreased significantly at 1, 6, and 12 months (all $P < 0.001$). Moreover, both the scores decreased significantly at 12 months from 1 and 6 months (both $P < 0.01$). Global evaluation of therapy consisted in assessing the proportion of patients with at least 50% improvement in VAS scores in comparison to the baseline value. These values are 88%, 64%, and 32% at 1, 6, and 12 months, respectively. The beneficial effect of treatment started to decline after 6 months, but even 1 year after the intervention, 32% of patients reported 50% improvement or greater in pretreatment VAS scores.[24]

In a prospective study, Kirdemir *et al*. investigated the short- and medium-term effectiveness of GN-RFA in 49 patients with chronic OA KNEE pain. The mean pretreatment VAS and WOMAC scores were 8.9 ± 0.8 and 64.26 ± 7.29, respectively. There was a statistically significant improvement in mean VAS scores at 1-(4.73 ± 3.23), 4-(3.89 ± 2.9), and 12 weeks (3.93 ± 2.95) posttreatment compared to the pretreatment values (all $P < 0.01$). Similarly, there was a statistically significant improvement in mean WOMAC scores at 1 (44.93 ± 13.18), 4 (42.81 ± 13.15), and 12 weeks (43.04 ± 13.36) posttreatment compared to the pre-treatment values (all $P < 0.01$). Thus, GN-RFA led to significant pain reduction and functional improvement.[25]

In a case series, Bellini and Barbieri discussed the findings of 9 patients with chronic OA KNEE pain treated with GNs C-RFA. Following the procedure, they observed an improvement in VAS pain scores 2 ± 0.5 at 1 month, 2.3 ± 0.7 at 3 months, 2.1 ± 0.5 at 6 months, and 2.2 ± 0.2 at 12 months, and WOMAC scores 20 ± 2, at 1 month, 22 ± 0.5 at 3 months, 21 ± 1.7 at 6 months, and 20 ± 1.0 at 12 months. Thus, the majority of patients experienced a clinically relevant degree of pain relief and improved function.[26]

Future direction

Currently available literature does not provide evidence of pain and functional improvement for 12 months and beyond following the index RFA procedure. Thus, future studies need to evaluate the effectiveness and safety of RFA for 12 months and beyond following the index procedure.

Statement 2

In patients with chronic OA knee, the use of C-RFA or WC RFA leads to significant pain relief, decreased disability, and improved QoL.

Recommendation

In the patient with chronic OA knee, ISSP recommends that C-RFA or WC-RFA should be used to receive significant pain relief, decrease disability, and improve the QoL.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 80%; mostly agree: 20%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In a prospective, randomized, comparative trial, McCormick *et al*. evaluated the utility of GN blocks to predict the outcome of GN C-RFA in patients with chronic OA KNEE pain. Patients were randomized to receive a GN block (N = 29, 36 knees) or no block (N = 25, 35 knees) before C-RFA. At 6 months, 17 (58.6%) patients in the prognostic block group and 16 (64.0%) in the no-block group had ≥50% pain relief (P = 0.34). During a similar period, a 15-point decrease in the WOMAC was present in 17 (55%) patients in the prognostic block group and 15 (60%) in the no prognostic block group (P = 0.36). The improved or very much improved Patients' Global Impression of Change (PGIC) was observed in 9 (31%) patients in the prognostic block group compared with 9 (36%) in the no prognostic block group (P = 0.65). The patients in each group had a significant decrease in the Numerical Rating Scale (NRS) pain scores and WOMAC functional assessments at the follow-up assessments compared with baseline, while there was no difference between the groups. The percentage of participants who met the criteria for a successful outcome was increased at prognostic block improvement levels of 80% and 90% compared with 50%; however, the increase in participants with a 50% reduction in NRS even at a prognostic block improvement of 90% was not different than at 50% relief (difference = 18%, 95% confidence interval [CI] of the difference = –12% to 49%, P = 0.19). Thus, at up to 6 months, the findings demonstrated a clinically meaningful improvement in pain and physical function in nearly 50% of patients. However, prognostic GN block with a local anaesthetic (1 mL) at each injection site and a threshold of 50% pain relief for subsequent C-RFA eligibility did not improve the rate of treatment success.[27]

In a cross-sectional survey, McCormick *et al*. determined the outcomes of C-RFA of the GNs for the treatment of 33 patients (52 knees) with chronic OA knee pain. At a minimum follow-up of 6 months, on the NRS scale, the median reduction in pain was 2 (interquartile range [IQR] = 0–6). Thirty-seven per cent (95% CI = 24%–50%) and 50% (95% CI = 36%–64%) of procedures resulted in ≥50% and a reduction of ≥2 points in NRS score, respectively. Complete pain relief was observed in 19% (95% CI = 10%–33%) procedures. The median reduction in Medication Quantification Scale III (MQSIII) score was 3 (IQR = 0–6), and the proportion of patients with a reduction of 3.4 or more was 40% (95% CI = 27%–54%). An improved or very much improved PGIC score was observed in 35% (95% CI = 22%–48%) procedures. Moreover, 35% (95%CI = 22%–48%) procedures fulfilled the stringent definition of treatment success based on the criteria of ≥50% reduction in NRS score improved or very much improved PGIC score, and no total knee arthroplasty (TKA). There were no reported serious AEs related to the C-RFA procedure.[28]

In a prospective, observational study, House *et al*. evaluated the factors associated with treatment success after 91 fluoroscopy-guided GN C-RFA procedures for chronic knee pain in 64 patients. There were 34 C-RFA procedures for unique knees, in which there was both ≥50% NRS reduction and no TKA (37%, 95% CI = 27%–47%). The mean NRS reduction was 3.3 ± 0.4 (P < 0.001). Univariate analysis showed that shorter duration of knee pain (OR = 0.98, 95% CI = 0.97–1.00, P < 0.005), higher baseline MQSIII (OR = 1.04, 95% CI = 1.03–1.05, P < 0.01), and Kellgren Lawrence (KL) grade <4 (OR = 4.03, 95% CI = 1.25–12.5, P < 0.02) were associated with successful treatment. In the multivariate model, success was associated with shorter pain duration and a KL grade <4 when controlling for bilateral procedures and knees with prior meniscal procedures. Patients with a KL grade of ≤3 were more likely to benefit from C-RFA versus those with a KL grade of 4 (30 of 67 [45%] vs. 4 of 24 [17%], respectively, P < 0.05). No significant difference was found in MQSIII values after C-RFA procedures (premedian = 6.8, IQR = 3.4-10.4, vs. postmedian = 6.8, IQR = 4.4–10.1, respectively, P = 0.89). This investigation demonstrated a reduction in pain scores following GN C-RFA, with one-third of participants receiving a clinical benefit. End-stage OA KNEE and longer symptom duration were associated with less pain relief after GN C-RFA for chronic OA knee pain.[29]

In a retrospective study, Kapural *et al*. evaluated the long-term effectiveness of C-RFA in 275 consecutive patients with general chronic knee pain. The average baseline VAS pain scores were 8.5 cm, which decreased to 2.2 cm after the block, and to 4.2 cm after C-RFA. A total of 65% of the patients claimed >50% pain relief, whereas 77% had ≥2 VAS points decrease, and 26 patients claimed no pain after C-RFA. The mean duration of >50% of pain relief after C-RFA was 12.5 months (0–35 months). There was no significant decrease in opioid use over that time, despite improved pain scores. Patients who received a repeated procedure (N = 43) achieved similar pain relief (P = 0.402). The study demonstrated the clinical effectiveness of C-RFA in the treatment of chronic OA KNEE pain, and even in those patients who maintained chronic knee pain after TKA.[30]

In a retrospective study, Eshraghi *et al*. evaluated the effectiveness of GN C-RFA in 205 patients with general chronic knee pain. At a minimum of 3 months, the mean Pain Disability Index (PDI) decreased significantly following C-RFA (P < 0.001). Similarly, the mean numerical pain rating scale score decreased significantly following C-RFA (P < 0.001). This study suggests that C-RFA provides significant pain relief and reduces the disability caused by chronic knee pain.[31]

Future direction

Although the current literature supports the significant improvement in pain, function, and QoL, recent MA failed to show significant improvement in function and QoL. Thus, well-designed RCTs with a larger sample size and longer study duration are required.

Statement 3

In patients with pain and dysfunction following TKA, the use of RFA results in significant pain relief and improved performance.

Recommendation

In patients with pain and dysfunction following TKA, ISSP recommends that RFA (Conventional and Cooled) may be used to provide significant pain relief and improved performance.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 80%; Mostly agree: 20%; partially agree: 0%; Mostly disagree: 0%; Completely disagree: 0%; and Not sure: 0%.

Rationale

In a double-blind, RCT, Qudsi-Sinclair *et al*. evaluated the effect of RFA (RAF group, $N = 15$) and compared it with an analgesic block with anesthetic and corticosteroids (AC group, $N = 15$) of the superolateral, superomedial, and inferomedial branches of the knee GNs in patients with persistent pain following TKA. In both RFA and AC groups, the mean NRS score decreased significantly from baseline to 6 months and 12 months (both $P < 0.001$). Similarly, significant functional improvement, estimated by OKS and Knee Society Score was observed in both groups, from baseline to 6 months and 12 months (both $P < 0.01$). No AEs were recorded during either the procedure or the follow-up period. However, there was no significant difference between the groups in any of the outcomes assessed.[32]

In a retrospective study, Erdem and Sir evaluated the effect of ultrasound-guided GN P-RFA on knee pain and function in patients who had severe OA knee (nonoperated, $N = 17$) or who had previous TKA (operated, $N = 6$). A total of 14 (82%) nonoperated patients and 4 (67%) operated patients had at least a 50% reduction in the VAS scores at 3 weeks. Similarly, at 3 months, 15 (88%) nonoperated patients and 4 (67%) operated patients had at least a 50% reduction in the VAS scores. In both the groups, mean WOMAC scores decreased significantly between the baseline and 3-week scores, baseline and 3-month scores, and 3-week and 3-month scores (all $P < 0.05$). However, in both the groups, mean VAS scores decreased significantly between the baseline and 3-week scores, and baseline and 3-month scores (both $P < 0.05$). Moreover, the mean VAS and WOMAC scores were significantly greater in operated patients at 3 weeks and 3 months (both $P < 0.05$). It was further observed that the groups were homogenous at baseline in terms of pain, but not in terms of function (VAS $P = 0.515$, and WOMAC $P = 0.038$).[33] In another retrospective study, Kapural *et al*. observed that improvements were comparable among patients who had previous TKA ($n = 21$) and the rest of the treated patients ($P = 0.542$).[30]

In a case series, Baber and O'Conniell reported the outcome of GN-RFA in 8 patients (3 non-TKA and 5 postunilateral TKA) with chronic knee pain. They reported clinically significant improvements in the majority of patients. At 3 months, 4 of the cases reported >50% pain relief and 1 case reported 40% pain relief. Another case reported 45% improvement at 3 weeks but 0% relief at 3 months. Moreover, 2 patients reported 0% pain relief at 3 weeks and thus were not re-evaluated. Interestingly, non-TKA patients experienced superior overall pain reductions in comparison to post-TKA patients, at least for the diagnostic block procedures.[34]

In a case report, Menzies and Hawkins described the case of a 68-year-old, nonsmoking, morbidly obese, Caucasian male who presented with unsatisfactory bilateral TKAs. He was referred for nerve ablation as he had persistent knee pain, immobility, and reduced function. Following C-RFA of the superior lateral, superior medial, and inferior medial GNs, the patient reported marked improvements in OKS for both knees. Indeed, pain and overall score ratings each increased after CRF indicating sustained pain relief and better knee function up to 9 and 6 months for the left and right knees, respectively. Moreover, the patient reported a significant improvement in QoL, as indicated by minimal knee pain, less reliance on analgesics, and the ability to walk more freely, including on stairs.[35]

In another case report, Protzman *et al*. reported the feasibility of treating chronic knee pain following TKR with RFA of right inferomedial, superomedial, and superolateral GN branches. Following RFA, at 2 weeks and 3 months, the VAS score was 0. However, following physical therapy, the VAS score was a 3 of 10. At the 3-month visit, the right knee demonstrated an active range of motion of 4°–108° and a passive range of motion of 0°–112°. There was a gain of strength and range of motion, with a marked improvement in ambulating upstairs and downstairs without the hand rail. The patient scored a 70.30% on the Knee Injury and Osteoarthritis Outcome Score, with a 71.43% on the symptom subscale, 69.44% on the pain subscale, 72.06% on the function and daily living subscale, and 62.50% on the QoL subscale.[36] Moreover, Sylvester and Goree reported a case of a 68-year-old woman with 6 months of chronic unilateral posterior thigh pain following TKA. Her pain was refractory to various modalities of treatments. Following diagnostic tests, RFA of GN block was performed, which resulted in significant pain relief at the 3-month follow-up.[37]

Future direction

Although the findings of currently available studies are promising, a recently published SR by Meiling *et al*.[38] concluded that there is low certainty to support the use of GN-RFA to ameliorate chronic knee pain following TKA, mostly due to inconsistency and risk of bias. Thus, well-designed, double-blind RCTs with a large sample size should be performed to evaluate the role of GN-RFA in ameliorating chronic knee pain following TKA.

Statement 4

In patients with chronic OA knee pain, C-RFA is a safe and effective alternative to IA injections for improving long-term pain, physical function, and QoL.

Recommendation

In patients with chronic OA knee pain, ISSP recommends that C-RFA should be preferred over IA injections for significant improvement in long-term pain, physical function, and QoL.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 80%; Mostly agree: 20%; Partially agree: 0%; Mostly disagree: 0%; Completely disagree: 0%; and Not sure: 0%.

Rationale

In a prospective, randomized, survey study, Sari *et al*. compared the efficacy of GNRF neurotomy ($N = 37$) and IA injection ($N = 36$; 2.5 mL of bupivacaine, 2.5 mg of morphine and 1 mL of betamethasone) in patients with chronic OA knee pain. In both the groups, compared to baseline, significant improvement was observed in VAS-pain and WOMAC scores at the 1-and 3-month ($P < 0.001$). Compared to the IA group, the GNRF group had a significant reduction in VAS score at 1 and 3 months (both $P < 0.001$). Moreover, in the GNRF group, a significant reduction was observed in the mean WOMAC score at 1 month ($P < 0.001$), but not at 3 months ($P = 0.263$). None of the patients developed any AE or complications in either treatment group. This was the first study to compare GNRF neurotomy to IA injections and demonstrated that GNRF neurotomy is a safe and efficient treatment modality and provides functional improvement along with analgesia.[39]

In a randomized, open-label, multicenter study, Davis *et al*. compared the long-term clinical safety and effectiveness of C-RFA ($N = 76$) with IA steroid (IAS, $N = 75$) injection in managing chronic OA KNEE pain. In both the groups, at 1-, 3-, and 6 months, the mean NRS score reduced significantly relative to baseline (all $P < 0.0001$). At each follow-up, the mean NRS score was significantly less in the C-RFA group than in the IAS group (1-month: $P = 0.025$; 3-months: $P < 0.0001$; 6 months: $P < 0.0001$). The mean reductions in the average NRS scores from baseline in the C-RFA group were greater than those in the IAS group at all follow-ups (1-month: $P = 0.02$; 3-months: $P < 0.0001$; 6-months: $P < 0.0001$). At 6 months, 74% of patients in the C-RFA group and 16% in the IAS group received ≥50% reduction in NRS score ($P < 0.0001$). During a similar period, none of the patients in the C-RFA group reported worse pain, while 15% of patients in the IAS group experienced an exacerbation of knee pain ($P < 0.002$). Moreover, for 6 months, 20% of patients in the C-RFA group and 4% in the IAS group reported: "no pain" ($P < 0.002$). In both the groups, at 1-, 3-, and 6 months, mean OKSs improved significantly relative to baseline scores (all $P < 0.0001$). The mean OKSs were greater in the C-RFA group than in the IAS group at 1-($P = 0.004$), 3-($P < 0.0001$), and 6 months ($P < 0.0001$). While index knee function improved in the C-RFA group, it declined in the IAS group from 1 to 6 months after treatment. Beginning at 1 month, more subjects in the C-RFA group than in the IAS group had satisfactory joint function ($P = 0.56$), and at 3 and 6 months, more subjects in the C-RFA had satisfactory joint function than in the IAS group (both $P < 0.0001$).[40]

In a prospective, multicenter, randomized study, Hunter *et al*. performed the extension of the study performed by Davis *et al*.[40] They evaluated the long-term outcomes, including pain, function, and perceived effect of treatment, of GNs C-RFA ($N = 42$) in patients with chronic OA KNEE and compared it with IAS ($N = 41$). After 6 months, patients in the IAS group were crossed-over to the C-RFA group (XO group). Finally, 33 patients (19 original C-RFA and 14 XO) participated in the study, of which 25 were evaluated at 18 months and 18 were evaluated at 24 months following C-RFA. The mean baseline NRS pain score for patients treated with C-RFA was significantly decreased at 18 and 24 months (both $P < 0.0001$). The results demonstrate that patients can have clinically significant pain relief through 24 months following a single C-RFA treatment; 48% (12/25) patients at 18 months and 61.1% (11/18) patients at 24 months continued to experience at least 50% reduction in pain from baseline values. The mean OKS scores continued to increase significantly from baseline to 18 months and remained stable at 24 months compared to the baseline ($P < 0.0001$). At baseline, 54.6% (13/33) of patients reported having symptoms consistent with severe arthritis, and this decreased to 0% at 18 and 24 months. The functional improvements noted in the first 12 months continued through the 24-month follow-up, with 66.7% of those returning at 24 months still indicating satisfactory joint function. Moreover, 80% (20/25) patients at 18 months and 66.7% (12/18) at 24 months reported a perceived improvement in chronic pain.[41]

In a prospective, multi-center, randomized, cross-over trial, Davis *et al*. investigated the analgesic effect of C-RFA ($N = 67$) in patients with chronic OA knee pain 12 months postintervention and its ability to provide pain relief in patients who experienced unsatisfactory effects of IAS ($N = 71$). At 6 months, 58 (87%) and 68 (96%) of treated patients in the C-RFA and IAS cohorts, respectively, completed the study. While 58 (82%) patients of the IAS group were crossed-over to receive C-RFA (XO group). At 12 months, 52 (78%) patients were in the original C-RFA group and while at 6 months post-C-RFA, 51 (88%) patients in the XO group completed the study. In the original C-RFA group, at 12 months, the mean decrease in NRS and increase in OKS from baseline was statistically significant (both $P < 0.0001$). At 1-, 3-, 6-, and 12 months, 70% (47/67), 72% (47/65), 74% (43/58), and 65% (34/52) patients experienced ≥50% pain relief relative to baseline. The percentage of patients reporting OKS "severe arthritis" was progressively reduced from baseline to 6 months and was nearly 7-fold less at 12 months compared with baseline. At 12 months, 75% (39/52) of patients perceived improved health, which was similar to values at

1-(79%, 53/67) and 3 months (80%, 52/65) and substantially different than the baseline value of 17% (12/72). However, the proportions for all of the above follow-ups were less than that observed at 6 months (91%, 53/58). In the XO group, at 1-, 3-, and 6 months, a statistically significant reduction in mean NRS was observed ($P < 0.0001$). At 6 months, 49% of patients experienced ≥50% pain relief. Moreover, at 6 months, the mean increase in the OKS from baseline was statistically significant ($P < 0.0001$). At baseline (6 months post-IAS), none of the patients reported OKS satisfactory joint function. However, at 1 month after C-RFA, nearly 20% of patients reported OKS satisfactory joint function and by 6 months, this condition progressively increased to 25%. Furthermore, at the baseline (6 months post-IAS), 7.1% (3/42) perceived improved health due to C-RFA, while this increased to 65% (26/40), 79% (30/38), and 57% (21/37) this outcome at 1-, 3-, and 6-months post-C-RFA, respectively.[42]

In a prospective, randomized, multi-center, cross-over study, Chen *et al*. compared pain relief, functional improvement, and the safety of C-RFA of GNs ($N = 89$) to a single IA hyaluronic acid injection (HA, $N = 88$) to treat OA knee pain in patients with a minimum of 50% pain relief on diagnostic block injections. After 6 months, patients were crossed-over to another treatment arm. In the C-RFA group, 76 and 66 patients completed a follow-up of 6 and 12 months, respectively. While, in the HA group, 82 completed the 6-month follow-up. Of these, 68 were crossed-over to receive C-RFA and 62 of them returned for their 6-month crossover follow-up. Of 14 patients in the original HA, groups were not crossed-over and 11 of them completed their 12-month follow-up. At 12 months, 43/66 (65.2%) patients of the original C-RFA group had pain reduction ≥50%. During the original 6-month posttreatment interval (i.e., 1-, 3-, and 6-month timepoints following HA injection), those within the cross-over group reported diminishing pain relief, with only 20/68 (29.4%) reporting ≥50% relief at 6 months. However, upon crossing-over, the cross-over group saw improvements in pain relief, with 40/62 (64.5%) patients reporting ≥50% relief at the 12-month follow-up or the 6-month cross-over timepoint compared to their baseline pain, measured at the 6-month timepoint post-HA injection but before crossing-over. Of those originally treated with C-RFA, NRS pain scores decreased significantly at all timepoints and maintained pain relief through the 12-month ($P < 0.0001$). Those within the cross-over group saw an initial decrease in NRS pain score at 1-month after HA treatment, but this score steadily increased at the 3-and 6-month. At the 6-month timepoint, the cross-over group had a significant decrease in the mean NRS score ($P < 0.0001$). Moreover, this group had a significant reduction in mean NRS from 6 to 12 months ($P < 0.0001$). At 12 months, patients in the original C-RFA group had a significant and durable improvement in the total WOMAC score ($P < 0.0001$). Within the cross-over group, after an initial decrease in mean total WOMAC score after HA treatment, there was a steady increase in WOMAC score from the 3-to 6-month. After crossing-over to receive C-RFA treatment, those within this group had a significant decrease in the mean total WOMAC score ($P < 0.0001$). Thus, findings suggest that subjects who received HA before C-RFA can still receive substantial benefits from C-RFA. At the 12-month timepoint, patients in both C-RFA and cross-over groups reported lowered NRS pain scores. These study results suggest that patients may benefit by receiving C-RFA initially rather than HA, but those that receive C-RFA after HA may still expect improvement in outcomes.[43]

In a multicenter, randomized study, Chen *et al*. compared the efficacy and safety of GNs C-RFA ($N = 88$) with those of a single IA HA injection ($N = 87$). In the C-RFA group, the mean NRS scores decreased significantly relative to the HA group at 1-($P = 0.0085$), 3-($P < 0.0001$), and 6 months ($P < 0.0001$). Moreover, at 6 months, a significantly greater proportion of patients in the C-RFA than the HA group had ≥50% decrease in pain (71% vs. 38%, $P < 0.0001$). Similar to the NRS scores, the mean WOMAC scores were improved significantly in the C-RFA group at 1-($P = 0.023$), 3-($P < 0.0001$), and 6 months ($P < 0.0001$). The QoL as assessed by Global Perceived Effect (GPE) score and EuroQol-5 Dimensions-5 Level (EQ-5D-5 L) questionnaire suggested that significantly greater proportions of patients in the C-RFA group reported their condition as "improved" on the GPE questionnaire at 1 ($P = 0.012$), 3 ($P = 0.0001$), and 6 ($P < 0.0001$). Moreover, the mean EQ-5D-5 L index scores at 1 ($P = 0.025$), 3 ($P = 0.0002$), and 6 ($P < 0.0001$) were significantly greater in patients of the C-RFA group.[44]

Future direction

The available evidence supports the superiority of C-RFA over IA injections. However, future studies should compare IA injections with other RFA modalities. Moreover, SRs and meta-analyses are required to demonstrate the superiority of a particular RFA modality over IA injections.

In knee pain, the use of RF depends on the grading of knee pathology, functional disability, and anatomical indication (e.g. meniscal or ACL tear injury) causing chronic pain.

A summary of recommendations for patients with chronic knee pain is depicted in Table 4.

Headache Disorders and Facial Pain

Statement 1

In patients with chronic headache disorders associated with pericranial neuralgias, RFA is safe and results in significantly improved analgesia and decreased disability.

Recommendation

In patients with chronic headache disorders associated with pericranial neuralgias, ISSP recommends that RFA is safe and should be used for significantly improved analgesia and decreased disability.

Table 4: Summary of recommendations in patients with chronic knee pain

Recommendations	Grade of recommendation	Level of evidence	Strength of consensus	References
In patients with chronic OA knee pain, ISSP recommends that GN-RFA should be used for mid-to-long-term pain control and functional improvement	A	I	Strong	[20-26]
In a patient with chronic OA knee, ISSP recommends that C-RFA or WC-RFA should be used to receive significant pain relief, decrease disability, and improve the QoL	A	I	Strong	[27-31]
In patients with pain and dysfunction following TKA, ISSP recommends that RFA (conventional and cooled) may be used to provide significant pain relief and improved performance	A	I	Strong	[30,32-37]
In patients with chronic OA knee pain, ISSP recommends that C-RFA should be preferred over IA injections for significant improvement in long-term pain, physical function, and QoL	A	I	Strong	[39-44]

OA: Osteoarthritis; ISSP: Indian Society for the Study of Pain; RFA: Radiofrequency ablation; GN-RFA, Genicular nerve RFA; C-RFA: Cooled RFA; WC-RFA: Water-cooled RFA; QoL: Quality of life; TKA: Total knee arthroplasty

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 80%; mostly agree: 20%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In a double-blind RCT, Yang *et al*. evaluated the efficacy and safety of P-RFA ($N = 20$) of cervical 2-3 posterior medial branches in the treatment of patients with chronic migraine and compared it with a sham procedure ($N = 20$). At 1 ($P < 0.001$), 2 ($P < 0.001$), and 6 months ($P < 0.01$), the decrease in mean VAS score was significantly greater in the P-RFA group than in the sham group. At 6 months, a significantly greater proportion of patients in the P-RFA group than in the sham group had a 30% reduction in VAS score ($P < 0.05$). None of the patients in either group achieved a 50% decrease in pain intensity. At 1, 2, and 6 months, the decrease in mean headache duration was significantly greater in the P-RFA group than in the sham group (all $P < 0.001$). At 6 months, the mean migraine disability assessment score in the treatment group was 21.57 points lower than that in the sham group. The migraine disability assessment scores were significantly decreased after P-RFA treatment compared to the baseline ($P < 0.001$) and between the two groups ($P < 0.001$). None of the patients experienced any major complications during the peri-operative period. In the P-RFA group, 1 patient reported mild pain at the injection site following the second round of treatments and the pain resolved spontaneously within 6 h. No complications were recorded during the follow-up period.[45]

In a retrospective study, Abd-Elsayed *et al*. evaluated the efficacy of RFA ($n = 353$) of pericranial nerves in the treatment of 211 patients with headache disorders. Pain scores decreased significantly (from 5.62 ± 2.18 to 2.93 ± 2.29; $P < 0.001$) with an average relief of $61.31 \pm 33.8\%$. Moreover, headache-related emergency department visits decreased significantly (from 1.62 ± 3.79 to 0.36 ± 1.52; $P < 0.001$). The mean duration of relief was 199 ± 168 days.[46]

In another retrospective study, Abd-Elsayed *et al*. evaluated the efficacy and safety of RFA ($n = 72$) of pericranial nerves in 57 patients with chronic headache conditions. Postprocedure, mean pain scores decreased significantly (from 6.6 ± 1.7 to 1.9 ± 1.9; $P < 0.001$). Of all patients, 90.3% (65/71) had an improvement, while 9.7% (7/71) had no improvement. The overall mean improvement was $71.7\% \pm 28.8\%$. Of 65 patients, 46 had ongoing improvement and reported $81.2\% \pm 18.7\%$ improvement. RFA with an endpoint at follow-up (improvement is not ongoing and pain is back) was associated with a mean improvement of $75.2\% \pm 14.1\%$ and a mean duration of 127 ± 79.2 days (8–270 days). There were no major complications. However, following bilateral supraorbital and supratrochlear RFA, two patients reported spontaneously resolving swelling of the eyelids.[47]

Future directions

Further well-designed, double-blind RCTs should be performed to evaluate the long-term effectiveness and safety of RFA procedures.

Statement 2

In patients with occipital neuralgia, refractory to conservative treatment, P-RFA of the occipital nerve may be an alternative treatment option.

Recommendation

In patients with occipital neuralgia, refractory to conservative treatment, ISSP recommends that P-RFA of the occipital nerve may be used as an alternative.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 90%; mostly agree: 10%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In a prospective study, Vanelderen *et al*. evaluated the P-RFA of greater and/or lesser occipital nerve in 19 patients with occipital neuralgia. Compared to baseline (7.5 ± 0.4), the mean VAS score decreased significantly at 1 (3.5 ± 0.8; $P < 0.001$), 2 (3.5 ± 0.7; $P < 0.001$), and 6 months (3.9 ± 0.8; $P = 0.002$). For pain evaluated on a 7-point Likert scale, 13 (68.4%), 11 (57.9%), and 10 (52.6%) patients mentioned a score of ≥6 on the 1, 2, and 6 months, respectively. No AEs were reported.[48]

In a retrospective study, Choi *et al*. reported the finding of P-RFA of the occipital nerve in 10 patients with occipital neuralgia, refractory to conservative management. Pain evaluated on VAS score and total pain index decreased significantly in 1 − 6 months ($P < 0.05$). Compared to the baseline (6.9), the mean VAS score decreased significantly post P-RFA (1.2) and last follow-up (0.8) (both $P < 0.001$). Similarly, compared to the baseline (232.7), the mean total pain index score decreased significantly post P-RFA (53.7) and last follow-up (40.6) (both $P < 0.001$). Following P-RFA, 8 (80%) patients completely stopped using analgesics. One patient (10%) reported a substantial reduction in analgesic requirements and pharmacotherapy was maintained in 1 patient who had a partial recurrence of headaches. There were no intra-or postprocedure complications that would lead to any type of significant morbidity or mortality. No AEs were observed.[49]

Describing the ALblation technique, Abd-Elsayed reported the outcome of RFA for bilateral supraorbital, supratrochlear, lesser occipital, and greater occipital nerves for treating severe bilateral migraine headache in 13 patients, refractory to conservative management. Compared to preprocedure levels, pain decreased significantly after the procedure (4.7 ± 0.3 vs. 2.2 ± 0.5; $P < 0.0001$). Patients reported 10%–100% improvement in their headache frequency and intensity with a mean improvement of 70.5% ± 27.6%. The mean duration of improvement was 331.2 ± 202.1 days (41–726 days).[50]

In a case report, Kwak and Cheng reported the outcomes of P-RFA of GON in two patients with refractory chronic migraine. In these patients, the headache intensity was 7–8 on NRS. In both patients, 2 weeks following the P-RFA, the pain score reduced to 3. The P-RFA effect lasted for at least 3 months, and no AEs were observed.[51]

In a case report, Hasoon and Berger described the experience with RFA of the third occipital nerve along with the medial branches of C3-4 in a male in his late 50s with chronic neck pain and occipital headache, refractory to conservative therapy. Following this procedure, the patient obtained >80% improvement in headache intensity and frequency. He was able to discontinue all analgesics. The pain improved for 9 months, following which the procedure was repeated with positive results.[52]

In a case report, Navani *et al*. described the outcome of P-RFA of GON in a 62-year-old man with chronic greater occipital neuralgia, refractory to conservative treatment and interventional therapy. Following P-RFA, the patient reported 60%–70% pain relief that lasted for 4 months. Subsequently, repeat P-RFA was performed that produced the same level of analgesia as the first, but for a slightly longer duration of 5 months.[53]

In another case report, Vu and Chhatre described the outcome of C-RFA of GON in a 35-year-old female with chronic bilateral greater occipital neuralgia, refractory to conservative treatment and continuous RFA. She received partial, short-term relief with P-RFA. Thus, the patient underwent C-RFA and received 100% pain relief immediately. Seven hours following the procedure, she had 100% relief of pain in the suboccipital and occipital regions but felt a similar presenting tingling, pulsating pain near the vertex of her head. There were no complications after the procedure. She continued to have 75% pain relief.[54]

Future directions

Though P-RFA has demonstrated excellent safety and effectiveness in patients with occipital neuralgia, refractory to conservative treatment, further RCTs and MA are required to provide high-quality evidence. Moreover, in this cohort, future studies should compare the efficacy and safety of P-RFA with C-RFA.

Statement 3

In patients with TN, refractory to conservative therapy, RFA of the Gasserian ganglion is an effective treatment modality.

Recommendation

In patients with TN, refractory to conservative therapy, ISSP recommends that RFA (Conventional/thermal RFA) of the Gasserian ganglion is an effective treatment modality.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 100%; mostly agree: 0%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In a randomized, observer-blinded, clinical trial, Bharti *et al*. compared the efficacy and safety of RFTA of the peripheral branches of the trigeminal nerve (study group; $N = 20$) with RFTA of the Gasserian ganglion (control group; $N = 20$) in patients with idiopathic TN. Following the procedure, both groups had a significant reduction in pain scores which continued until the end of 3 months. Effective pain relief for up to 3 months was observed in 19 patients in the control group and 18 patients in the study group. At 3 months, the pain reduction was 67% in the control group and 63% in the study group. Pain intensity estimated on the Barrow Neurological

Institute scores were comparable among groups from 1 week to 3 months, except at 2 months when it was significantly better in the control group than the study group. The number of patients having excellent pain relief without ongoing medication was 18 in the control group and 14 in the study group at 1 month, while 9 in the control group and 7 in the study group at 3 months, with no statistical significance. However, significantly more patients in the study group required medications as compared to the control group at a 2-months interval (P = 0.015). On further follow-up, the median duration of pain relief in the study group was 5.5 (4–7) months and the control group was 7 (5–9) months (P = 0.13). Minor AEs such as bruising, skin discoloration, swelling, and minor bleeding at the site of needle insertion were observed during the procedure in both groups. The patients were highly satisfied with the treatment in both groups. There was no significant difference in median satisfaction scores between the groups (8.5 and 8 in the control and study groups, respectively; P = 0.33).[55]

In a double-blind RCT, Agarwal *et al*. compared the efficacy of conventional RFA with long-duration, fixed voltage P-RFA in the treatment of idiopathic TN. On the 7th day, 1 month, and 2 months, both the groups did not differ significantly in the percentage reduction in BNI score. However, conventional RFA had a significantly greater reduction in BNI scores than P-RFA at 3 months (83.33% and 33.33%; P = 0.036) and 6 months (83.33% and 25%; P = 0.012). Similarly, conventional RFA had a significantly greater reduction in VAS scores than P-RFA at 1 month (83.33% and 33.33%; P = 0.036), 2 months (91.67% and 41.67%; P = 0.027), 3 months (83.33% and 33.33%; P = 0.036; and 6-months (83.33% and 25%; P = 0.012). With conventional RFA, mild hypoesthesia was observed in three patients at 7 days which improved by 1 month. While no AE was observed with P-RFA. Thus, conventional RFA is a more effective procedure to decrease pain than the long-duration, fixed voltage PRF for the treatment of idiopathic TGN.[56]

In a retrospective study, Li *et al*. compared the therapeutic effects and short-term outcomes of coblation (N = 75) vs. RFTC (N = 110) in patients with primary TN. On 1-day and 3-months, the two groups did not differ in pain relief (coblation group (74.7%) vs. RFTC group (85.5%); P = 0.066; and 94.7% vs. 88.2%; P = 0.0134). While, on day 3, the pain relief rate was significantly higher in the RFTC group than in the coblation group (97.3% vs. 85.3%; P = 0.003). At 3 months, a significantly greater number of patients in the coblation group were free of pain (69.3% vs. 42.7%; P < 0.001). Moreover, 3 months following the surgery, no recurrence was found in either of the group. In both groups, the mean pain score on the 1 day after surgery was significantly lower than the baseline (P < 0.001). In the coblation group, the mean pain score at 3 months was significantly lower than on the 3-day (P < 0.001). In the RFTC group, the mean pain score on the 3 day after surgery was significantly lower than on the 1 day (P < 0.001). Compared with the RFTC group, the pain was higher in the coblation on 3 day but lower at 3 months. The failure rate in coblation and RFTC was 2.7% and 4.5%, respectively (P = 0.703). There were no differences between the two groups regarding hypoesthesia, amyotrophia, and chewing weakness, but the frequency of numbness was significantly less in the coblation group than in the RFTC group (44.0% vs. 70.9%; P < 0.001).[57]

In a retrospective study, Ali *et al*. evaluated the efficacy and duration of pain relief with combined continuous RFA and P-RFA of the Gasserian ganglion in the treatment of 21 patients with idiopathic TN. Compared to baseline, there was a significant decrease in VAS score at 1-day, 1-week, 1-month, and 6-months follow-up. Excellent pain relief (>80%) was reported for 15 patients after 1 week, and 1 and 6 months; however, satisfactory pain relief (50%–80%) was reported for one of these after 12 months. Satisfactory pain relief was reported for 4 patients after 1 week, 1, 6, and 12 months. Unsatisfactory pain relief (<50%) was reported in 2 patients after 1 week, and 1, 6, and 12 months. According to the PGIC scale, at 12 months, very much improvement was observed for 15 patients, much improvement for 3 patients, minimum improvement for 1 patient, and no change for 2 patients 12 months after the procedure. P-RFA followed by conventional RF results in excellent pain relief for more than 70% of patients with idiopathic TN.[58]

In a retrospective study, Ding *et al*. compared the efficacy of peripheral nerves P-RFA (N = 45) with Gasserian ganglion P-RFA (N = 45) in 90 patients with trigeminal postherpetic neuralgia, refractory to conservative treatment. In both the groups, the mean VAS pain scores decreased significantly at each follow-up visit (1 week, 1 month, 3 months, 6 months, and 1 year; all P < 0.05). The Gasserian ganglion PRF group had a significantly lower mean VAS score at each follow-up visit (all P < 0.05). In both the groups, the physical component summary (PCS) and mental component summary (MCS) values increased significantly at each follow-up visit (all P < 0.05). Compared with peripheral nerves P-RFA group, PCS and MCS increased significantly in the Gasserian ganglion PRF group (P < 0.05).[59]

In a retrospective study, Kim *et al*. compared the effectiveness and complications of P-RFA (N = 26) with conventional RFA (N = 28) in patients with symptomatic TN following dental treatment. At 1 week (6.4 ± 2.7 vs. 3.0 ± 2.7), 1 month (5.9 ± 2.6 vs. 2.5 ± 2.8), 3-months (5.5 ± 2.4 vs. 2.6 ± 2.3), 6-months (7.1 ± 2.1 vs. 3.1 ± 2.4), and 1-year (7.2 ± 2.0 vs. 4.8 ± 2.2), the mean VAS scores were significantly greater in the P-RFA group than the conventional RFA group (all P < 0.05). At 1-month, conventional RFA group, 75.0% and 89.3% of patients had ≥50% and ≥30% pain reduction without medication, respectively. While no patient had pain reduction over 50% without medication in the P-RFA group. Although 30.8% of patients had over 50% decrease in pain, and 46.2% had >30% pain reduction during the same period, no patient could stop the medication in the P-RFA group. The number of patients whose pain decreased by >50% without medication in the conventional RFA group was greater than the corresponding

number in the P-RFA group. The duration of pain relief was longer in the conventional RFA group than in the P-RFA group (10.8 vs. 0 months). At 6 months, a greater proportion of patients in the conventional RFA group than the P-RFA group had successful pain relief without medication (67.9% vs. 0%). At 1-year and 2-year, 39.3% and 17.9% of patients in the conventional RFA group had successful pain control without medication. Moreover, the mean satisfaction scale score was significantly greater in the conventional RFA group than in the P-RFA group (3.86 vs. 2.19; $P = 0.000$).[60]

In a case series, Lan *et al*. reported the outcomes of computed tomography-guided percutaneous P-RFA of the Gasserian ganglion in 28 patients with idiopathic TN, refractory to conservative therapy. Following P-RFA, the mean NRS score decreased gradually. Twenty-four (85.7%) patients obtained effective pain relief (≥50% decrease in NRS) at 1-, 3-, and 6 months (response rate was 85.7% up to 6 months). Two of these patients had pain recurrence at 8 and 10 months, respectively. At 1 and 2 years, the response rate was 78.6%. Two patients suffered from mild postoperative dizziness, nausea, and vomiting, and two patients felt only mild dizziness after the treatment. These side effects resolved spontaneously within 1-2 h. One patient suffered from facial varicella-zoster virus infection on the affected side 3 days after treatment, which had a 10-day course.[61]

In a case series, Van Zundert *et al*. reported the outcome of P-RFA of Gasserian ganglion in 5 patients with idiopathic TN, refractory to conservative therapy. The onset of pain relief was reported within 10 days after the intervention. Three patients had an excellent (90%–100%) reduction in pain and required no additional pharmacological or interventional treatment. One patient had partial pain relief and needed a second treatment after 15 months to become asymptomatic. One patient had only short-term pain relief, which was not improved after an additional conventional thermocoagulation treatment. At long-term follow-up, 10–26 months, patients were completely pain-free. No complications or AEs were reported.[62]

Future directions

RFTC and RFTA have demonstrated excellent effectiveness, but it does not apply to P-RFA. However, future RCTs are required to compare these treatment modalities.

Table 5 depicts the summary of recommendations for patients with headache disorders and facial pain.

Lumbar Facet Joint Pain

Statement 1

Before radiofrequency neurotomy (RFA) for LFJ pain, diagnostic MIPSI, i.e., lumbar MBB, has a superior predictive value than IA injections.

Recommendation

In adult patients with LFJ pain planned for RFA, the ISSP recommends the use of diagnostic MIPSI i.e., lumbar MBB, over IA injections.

Degree of recommendation: B

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 90%; mostly agree: 10%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

Published studies have directly compared the predictive values of MBB and IA injections before RF denervation and have reported that MBB may be associated with a higher success rate than IA injections. In an RCT, Birkenmaier *et al*. assigned 26 patients equally to receive either pericapsular blocks or MBB. At 6 weeks and 3 months, patients diagnosed with MBB had significantly greater pain relief than did patients diagnosed by use of pericapsular blocks (2.2 vs. 4.2 and 2.3 vs. 4.2; both $P < 0.05$, respectively).[63] In a single-blind, RCT (Facet Treatment Study [FACTS]), Cohen *et al*. determined the therapeutic efficacy of lumbar MBB, IA injections, and saline injection, and compared their predictive value before RFA. Although both MBB and IA injections resulted in significantly greater pain relief than saline injections during the postblock period, and at 1- and 3-month follow-ups, there was no significant difference between MBB and IA injections at all time intervals.[64] In a multi-center, case − control study, Cohen *et al*. compared either MBB ($n = 212$) with IA

Table 5: Summary of recommendations in patients with headache disorders and facial pain

Recommendations	Grade of recommendation	Level of evidence	Strength of consensus	References
In patients with chronic headache disorders associated with pericranial neuralgias, ISSP recommends that RFA is safe and should be used for significantly improved analgesia and decreased disability	A	I	Strong	[45-47]
In patients with occipital neuralgia, refractory to conservative treatment, ISSP recommends that P-RFA of the occipital nerve may be used as an alternative	A	I	Strong	[48-54]
In patients with TN, refractory to conservative therapy, ISSP recommends that RFA (conventional/thermal RFA) of the Gasserian ganglion is an effective treatment modality	A	I	Strong	[55-62]

ISSP: Indian Society for the Study of Pain; RFA: Radiofrequency ablation; TN: Trigeminal neuralgia; P-RFA: Pulse RFA

injections (n = 212) who received RFA after either IA blocks, MBBs or both blocks. A significantly greater proportion of patients experienced ≥50% pain relief at the 3-month follow-up with MBB than IA injections (70.3% vs. 60.8%; P = 0.041). On multivariable analysis, the use of MBB was associated with RF success (odds ratio [OR]: 1.57; 95% CI: 1.0–2.39; P = 0.036), while opioid use (OR: 0.52; 95% CI: 0.34–0.79; P = 0.002) and previous back surgery (OR: 0.60; 95% CI: 0.38–0.95; P = 0.028) were associated with treatment failure. No significant differences were noted between MBB alone and combination treatment or single versus multiple blocks.[65]

Future direction

FACTS trial concluded that facet blocks might provide prognostic value before RFA.[66] However, it was a single-blind trial and was not powered enough to evaluate the difference in efficacy between MBB and IA injections. The study by Birkenmaier *et al*. was not well designed and used pericapsular injections that lack diagnostic specificity and face validity.[63] Thus, multicentric, double-blind, RCTs are required to demonstrate the superior predictive value of MBB over IA injections.

Statement 2

In patients with high degrees of LFJ pain relief following MBBs, "parallel to medial nerve" electrode placement during LMB with conventional RFA results in superior outcomes than "perpendicular to medial nerve" electrode placement.

Recommendation

In patients with high degrees of LFJ pain relief following MBBs, ISSP recommends that "parallel to medial nerve" electrode placement should be preferred over "perpendicular to medial nerve" electrode placement LMB with conventional RFA.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 100%; mostly agree: 0%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In a pooled-data of studies, Schneider *et al*. evaluated the perpendicular and parallel placement of the electrode. At 6 months, 26% of patients selected via single MBB with 50% pain relief and treated via perpendicular electrode placement experienced a minimum of 50% pain relief; 49% of patients selected via dual MBBs with 50% pain relief and treated via parallel electrode placement experienced a minimum of 50% pain relief. Moreover, the use of dual diagnostic MBBs with 100% pain relief and parallel electrode placement produced 100% pain relief in 56% of patients at 6 months.[66] In a retrospective chart review, Loh *et al*. compared the efficacy of the electrode-placement technique in 323 patients that underwent LMB RFA (perpendicular electrode-placement [N = 241] vs. near-parallel electrode-placement [N = 82]. The authors observed that patients with near-parallel electrode placement had lower pain scores (mean 3.64 vs. 4.27; P = 0.06) at 1-month postprocedure and a longer duration of relief (median duration 4-vs. 1.5 months; P = 0.02).[67] In A cadaver study, Lau *et al*. demonstrated that an electrode placed parallelly to a target nerve is expected to produce a lesion. However, if an electrode is placed perpendicularly, the target nerve may be partially lesioned or escape the lesioning.[68] In an experimental study, Bogduk *et al*. demonstrated that RF electrodes during conventional/thermal RFA result in minimal to no heat lesions distal to their tip and the lesion are generated circumferentially around the uninsulated shaft of the electrode. If electrodes are placed perpendicular to the target nerve, the nerve may not be affected by the heat lesion generated. Thus, the target nerve can be easily affected by circumferentially spread to the heat lesion, if electrodes are placed parallel to the target nerve.[69]

Future direction

A well-designed RCT comparing the perpendicular and parallel electrode placement and involving a large sample size with an estimation of a longer duration of pain-relief needs to be performed.

Statement 3

While performing diagnostic MBB, if pain relief is ≥80%, lumbar medial branch (LMB) RFA is an effective and durable long-term treatment for a patient with LFJP. When pain relief is <50%, the diagnosis should be re-evaluated, and when pain relief is between 50% and 80%, a dual diagnostic block should be performed.

Recommendation

In adult patients with chronic LFJ pain, the ISSP recommends that LMB RFA should be used as an effective and durable long-term treatment when diagnostic MBB is positive.

Grade of recommendation: A

Level of evidence: II-2

Strength of consensus

Strong.

Consensus

Completely agree: 90%; mostly agree: 10%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

Available long-term studies suggest that LMB RFA results in pain relief that persists for at least 6 months from the onset and a majority of the patients remain stable for up to 12 months. In an SR, Gautam *et al*. reported that the evidence for the efficacy of thermal RF lesioning in the treatment

of lumbar facet joint-mediated pain is quite promising. There is Level I evidence for both short- (<6 months) and long-term (≥6 months) effectiveness for thermal RF lesioning. They also observed that C-RFA was as effective as thermal RFA.[70] In a prospective, single-center study, Dreyfuss *et al*. used LMB RFA to treat 15 patients with LFJ pain. At 12 months, around 60% of patients experienced 90% pain relief and 87% experienced at least 60% pain relief. Two-thirds of the patients scored ≤1.1 on the VAS, and 6 of 15 scored 0.0 or 0.1.[71] MacVicar *et al*., in a prospective audit involving 106 patients with chronic LFJ pain treated at two practice sites, reported that 53%–58% of patients achieved complete pain relief at 6 months. Pain relief persisted for 15 months following the initial LMB RFA and 13 months following the repeat RFA. Due to repeat RFA, pain relief persisted for a median duration of 17-33 months, with nearly 70% of patients still pain-free at follow-up.[72] In a retrospective, cohort study, Conger *et al*. reviewed medical records of 85 patients with LFJ pain of ≥3 months who were subjected to dual comparative MBBs before RFA. Following RFA, a significant reduction in NRS scores was observed (3.0 ± 2.3, t = 12.43, P < 0.001). At a minimum duration of 6 months, 48 (56.5%, 95% CI = 45.6%–66.7%) of the patients had a ≥50% pain reduction, including 19 (22.4%, 95% CI = 14.6%–32.6%) and 11 (12.9%, 95% CI = 7.3%–22.0%) patients reporting ≥80% and 100% reduction in pain, respectively. The majority of the patients (N = 60 or 70.6%, 95% CI = 59.9–79.4%) had an improvement in NRS score of at least two points and thus surpassed the minimally clinically important change for LBP. At 6–12-months, 12–24 months, and >24 months, 63.2%, 65.6%, and 44.1% of patients reported ≥50% pain reductions (P = 0.170), respectively. A mean post-RFA PGIC was 5.5 ± 1.3, with 46 patients (54.11%, 95% CI = 43.3%–64.5%) reporting a PGIC score of ≥6, indicating being at least "much improved" from baseline. Moreover, no serious AEs or complications related to lumbar MBB or RFA were reported.[73] None of these studies reported any long-term AEs or complications due to RFA.

Future direction

Though the findings of these studies are promising and demonstrate long-term pain relief with LMB RFA, none of them is RCT and has a small sample size. Thus, further studies with RCT design and involving a large number of patients are required to confirm the findings.

Table 6 depicts the summary of recommendations for patients with LFJ pain.

Sacro-Iliac Joint Pain

Statement 1

In patients with SIJ-associated LBP, RFA is a safe and effective treatment measure.

Recommendation

In patients with SIJ-associated LBP, ISSP recommends that RFA techniques should be used in cases of recurrent pain after SIJ MIPSI (IA LA and steroids) due to its better safety profile and effective pain control.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong

Consensus

Completely agree: 80%; mostly agree: 20%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In an early SR, Rupert *et al*. evaluated the utility of therapeutic SIJ interventions and reported that RF neurotomy has limited evidence for short- and long-term pain relief.[74] In another SR, Gautam *et al*. reported the availability of Level II evidence for both short- and long-term efficacy of conventional RFA and C-RFA in the management of SIJ pain. They further found evidence supporting the role of P-RFA lesioning for SIJ pain.[70] In a MA, Aydin *et al*. assessed the effectiveness of SIJ RFA for pain relief at 3 and 6 months following the index procedure. At 3 and 6 months, 60.1% and 49.9% of patients had ≥50% pain relief, respectively. The diminished outcomes at 6 months may be attributed to the natural course of nerve regeneration and regrowth. However, the findings were limited by the presence of significant heterogeneity and lack of >1 published RCT.[75]

Table 6: Summary of recommendations in patients with lumbar facet joint pain

Recommendations	Grade of recommendation	Level of evidence	Strength of consensus	References
In adult patients with LFJ pain planned for RFA, the ISSP recommends the use of diagnostic MIPSI *i.e*., lumbar MBB, over IA injections	B	I	Strong	[63-65]
In patients with high degrees of LFJ pain relief following MBBs, ISSP recommends that "parallel to medial nerve" electrode placement should be preferred over "perpendicular to medial nerve" electrode placement during LMB RFA	A	I	Strong	[66-69]
In adult patients with chronic LFJ pain, the ISSP recommends that LMB RFA should be used as an effective and durable long-term treatment.	A	II-2	Strong	[70-73]

MBBs: Medial branch blocks; LFJ: Lumbar facet joint; ISSP: Indian Society for the Study of Pain; RFA: Radiofrequency ablation; MIPSI: Minimally invasive pain and spine intervention; IA: Intra-articular; LMB: Lumbar medial branch

In a retrospective study, Kapural *et al*. evaluated the acute safety of denervating lateral branches of the posterior primary rami at S1–S3, and the L5 dorsal ramus (DR) using C-RFA in patients with SIJ pain. Of 82 procedures, 24 were reported to be of high difficulty, and 19 with poor visualization (bowel gas). The reported complications were minor and consistent with lumbar/sacral neurotomy. Four patients reported increased pain: two from the conventional RFA of the L5DR group and two from the C-RFA group. All of the pains were transient and resolved within 6 weeks. Two patients were experiencing localized numbness over the upper medial quadrant of the buttock, both in the C-RFA group. Two patients complained of increased LBP and two of prolonged itching. Those patients who received repeated and/or bilateral RF denervation did not have more of any of the complications.[76]

Future direction

The MA involving only the RCTs is required to provide a better quality of evidence.

Statement 2

In patients with SIJ-associated LBP, both conventional RFA and C-RFA provide long-term pain relief of up to 2 years.

Recommendation

In patients with SIJ-associated LBP, ISSP recommends that conventional RFA or C-RFA should be used for long-term pain relief of up to 2 years.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 100%; mostly agree: 0%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In a 12-month follow-up of a randomized, cross-over, sham-controlled trial,[77] Patel reported the long-term outcomes of lateral sacral branch C-RFA (N = 34) and compared it with the sham group (N = 17), as a treatment for SI region pain. After 3 months, 16 patients of the sham group were crossed-over to the C-RFA group. Compared to baseline, patients in the C-RFA group had a statistically significant improvement in mean NRS ($P < 0.0001$), Oswestry Disability Index (ODI, $P = 0.0003$), SF-36 bodily pain (BP) ($P = 0.006$), and SF-36 physical functioning (PF) ($P < 0.0001$) scores at 12 months. However, no significant change was observed in any of the outcome measures at 12 months relative to 3 months. At 12 months, 40% of patients in the C-RFA group had treatment success (≥50% decrease in NRS and 10-point decrease in ODI). Moreover, 52% of patients had at least a 50% reduction in the NRS score. Compared to baseline, patients in the cross-over group had a statistically significant improvement in mean NRS ($P = 0.0003$), ODI ($P = 0.05$), SF-36 BP ($P = 0.05$), and SF-36 PF ($P = 0.05$) scores at 6-months. At 6 months, 44% of cross-over patients had treatment success. Moreover, 38% and 31% of these patients were treatment successful, based on the NRS + ODI or the NRS + SF-36-BP scores, respectively.[78]

In a prospective longitudinal cohort study, Romero *et al*. reported the long-term efficacy of SIJ RFA at 6, 12, and 18 months in 32 patients with SIJ-associated LBP. Compared to baseline (7.7 ± 1.8) values, the mean NRS pain score decreased significantly at 1 (2.8 ± 1.2), 6 (3.1 ± 1.9), 12 (3.4 ± 2.1), and 18 months (4.0 ± 2.7) (all $P < 0.001$). In general, patients felt that pain was improved, and the mean PGIC score was 1.3 ± 1.1. The GPE for patient satisfaction was positive in 84.38% (27/32) of patients. The procedure was generally well-tolerated and no complications or AEs were observed.[79]

In a retrospective study, Ferrante *et al*. reported the findings of 50 SIJ RFA (in 33 patients) for SIJ-associated LBP. Following RFA, 32% (16/50) joints were treated successfully (36.4% (12/33) patients), with ≥50% reduction in VAS score for at least 6 months. A positive response was associated with a significant decrease in SIJ pain and the distribution of referred pain ($P < 0.04$), a reversal of pain provocation tests ($P < 0.04$), and a reduction in the use of opioids ($P < 0.03$). Moreover, the responders had a significantly prolonged duration of response than the nonresponders (12.0 ± 1.2 vs. 0.9 ± 0.2 months, $P < 0.0001$).[80]

In a retrospective study, Stelzer *et al*. evaluated the general outcome following RFA of the LMB and posterior ramus of the SIJ in 160 patients with chronic LBP. Patients were divided into 3 groups: Group 1 ($N = 43$; RFA of MB lumbar facet joint L4/5 and L5/S1, MB L3-4, and L5DR); Group 2 ($N = 109$; C-RFA of the SIJ, SIJ lateral branch of the posterior rami S1–S3, and rami dorsalis of L5DR); and Group 3 ($N = 8$; other regions treated as appropriate for their disease process). At 1-, 6-, and 12 months, all groups had a reduction of the VAS pain score and a small increase between 6 and 12 months. Statistical analysis was then performed.[81]

In another retrospective study, Stelzer *et al*. evaluated the use of L5DR and lateral S1-3 branch C-RFA to treat 105 patients with chronic SIJ-associated LBP. Compared to baseline, there was a statistically significant decrease in mean VAS pain score in the 4–6-, 6–12-, and >12-months follow-up group (all $P < 0.001$). In 4–6, 6–12, and >12 months follow-up groups, 86%, 71%, and 48% of patients had ≥50% decrease in VAS pain scores. Moreover, 92%, 84%, and 74% in the groups 4–6, 6–12, and >12 months, respectively achieved at least a 2-point reduction in VAS pain scores. In the 4–6, 6–12, and >12 months follow-up groups, respectively, 79%, 70%, and 69% rated their QoL as much improved; 17%, 23%, and 16% rated their QoL as improved; and 4%, 7%, and 16% rated their QoL as the same, respectively. No subjects in any group reported a worsening in QoL. No serious complications were encountered during the study.[82]

In a case series, Ho *et al*. evaluated the efficacy of lateral sacral branches C-RFA in 20 patients with SIJ-associated LBP. Compared to preprocedure (7.4 ± 1.4) values, the mean NRS pain score decreased significantly at 1-(4.3 ± 2.4), 3-(2.5 ± 2.3), 6-(2.9 ± 2.5), 12-(3.0 ± 2.4), and 24-months (3.1 ± 2.5) (all $P < 0.001$). At 24 months, 75% of patients had at least a 3-point decrease in NRS pain score, with a statistically significant reduction in mean NRS pain scores. Overall, patients felt improved pain relief, with a mean PGIC score of 1.4 ± 1.5. Moreover, 80% (16/20) of patients had positive satisfaction with GPE. Throughout the study duration, no major complications were observed, with postoperative soreness at the injection site for up to 1 week being the most common complaint.[83]

Future direction

RCTs with large sample sizes and longer follow-ups should be performed to further validate the long-term efficacy of RFA techniques, especially C-RFA.

Statement 3

In patients with SIJ-associated LBP, C-RFA is safe and provides significantly greater and more durable pain relief than conventional RFA.

Recommendation

In patients with SIJ-associated LBP, ISSP recommends that C-RFA is safe and may be preferred over conventional RFA for greater and more durable pain relief.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 80%; mostly agree: 20%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In an SR, Hansen *et al*. reported superior efficacy of C-RFA than the conventional RFA or P-RFA in treating SIJ-associated pain.[84] In an SR and MA, Shih *et al*. compared the efficacy of different RF techniques (thermal, P-RFA, and C-RFA) for treating SIJ pain. At 1-month, both C-RFA and thermal RFA (T-RFA) led to significant improvement in pain relative to the baseline levels (both $P < 0.00001$); however, the efficacy of C-RFA was significantly better than T-RFA ($P = 0.02$). At 3 months, all three RFA techniques resulted in a statistically significant improvement in pain relative to the baseline levels (all $P < 0.00001$); however, the efficacy of all three techniques did not differ significantly ($P = 0.21$). At 6 and 12 months, both C-RFA and T-RFA led to significant improvement in pain relative to the baseline levels (both $P < 0.00001$); however, their efficacy did not differ significantly ($P = 0.85$, and 0.82, respectively). No serious complications were reported following all 3 RFA techniques, and only minor complications including pain, hemorrhage, and infection were reported. Both C-RFA and T-RFA produced similar pain relief for up to 12 months.[85]

In a retrospective study, Tinnirello *et al*. compared the safety and efficacy of conventional RFA ($N = 21$) with C-RFA ($N = 22$) in patients with SIJ-associated chronic LBP. While both groups demonstrated similar patterns of initial reductions in mean NRS and ODI scores at 1 month, each also demonstrated a rise in mean NRS scores at each succeeding follow-up. However, throughout the study period and at 6 and 12 months, the mean NRS and ODI scores in the C-RFA group were consistently less than those in the conventional RFA ($P < 0.01$). At 6 and 12 months, a significantly greater proportion of patients had treatment success (≥50% reduction in NRS score, both $P < 0.01$). In the conventional RFA group, 25% (5/20) of patients maintained treatment success from 1-to 12-month follow-up. While, during a similar period, 68% (16/22) of patients in the C-RFA group maintained treatment success. In the C-RFA group, the proportion of patients with ≥15 points decrease in ODI score was nearly 100% at 1 month and remained the same at the 6 and 12 months. While 90% of patients in the conventional RFA group had ≥15 points decrease in ODI at 1 month, this proportion consistently declined at each succeeding follow-up, with the C-RFA proportions exceeding those of the conventional RFA group by approximately 20% and 35%, respectively, at 6 and 12 months. In the C-RFA group, 1 patient had transient leg pain that could be related to postprocedure neuritis. The pain resolved after a 1-week treatment with oral steroids. No complications were reported in the conventional RFA group.[86]

In a retrospective study, Cheng *et al*. compared conventional RFA ($N = 30$) with C-RFA ($N = 58$) in patients with SIJ-associated chronic LBP. At 3 months, 50% to 60% of patients in both treatments achieved >50% pain relief. However, at 6 and 9 months, this proportion decreased to 40% and 30%, respectively. No significant complications were observed after either treatment. At any given time point, following RFA, the odds of experiencing <50% pain relief were estimated to be 2% lower among the patients receiving the C-RFA. Moreover, a significantly higher number of lesions per level in the C-RFA group did not provide a longer pain relief compared with the conventional RFA group ($P < 0.001$).[87]

Future direction

Further double-blind RCTs with a head-to-head comparison of various RFA techniques are required to demonstrate the superior efficacy of one over the other.

Statement 4

In patients with SIJ-associated LBP, C-RFA is safe and results in significant short-, intermediate-, and long-term pain relief with reduced disability and improved function.

Recommendation

In patients with SIJ-associated LBP, ISSP recommends that C-RFA may be used, especially in recurrent pain after I/A

steroid and LA, due to better safety profile and ability to provide significant short-, intermediate-, and long-term pain relief with reduced disability and improved function.

Grade of recommendation: A

Level of evidence: I

Strength of consensus

Strong.

Consensus

Completely agree: 100%; mostly agree: 0%; partially agree: 0%; mostly disagree: 0%; completely disagree: 0%; and not sure: 0%.

Rationale

In an SR, Hansen *et al*. evaluated the accuracy of therapeutic interventions for SIJ-associated LBP. Based on two double-blind RCTs, they reported fair evidence for C-RFA in providing short- and long-term pain relief associated with SIJ disorder. While, the evidence was limited or poor for IAS steroid injections, or periarticular local anesthetic and steroid or botulinum toxin injection.[84]

In a MA involving 11 studies (2 RCTs), Sun *et al*. assessed the efficacy and safety of C-RFA in the treatment of patients with SIJ-associated chronic LBP. Following C-RFA, the mean NRS and VAS pain scores decreased significantly (both $P < 0.001$). Similarly, the mean ODI scores decreased significantly ($P < 0.001$). On GPE, 72% of patients reported positive results. The overall OR was 0.01 ($P < 0.001$), indicating that patients' overall condition improved significantly. None of the evaluated studies described any severe or moderate complications pre- or post-C-RFA.[88]

In a MA, Chen *et al*. compared the effectiveness of RFA (conventional and C-RFA) with conservative medical or sham approaches for chronic LFJ-and SIJ-associated pain. The RFA group achieved significantly greater improvement in pain scores compared with controls who received sham treatment or medical treatment ($P < 0.001$). Significant improvement in pain was noted between RFA and medical treatment ($P = 0.005$). The RFA group achieved a significantly greater improvement in pain scores compared with the sham group ($P = 0.001$). For SIJ pain, the RFA group had significant improvement in pain ($P = 0.001$). The RFA group achieved a significantly greater improvement in ODI scores compared with controls who received a sham or medical treatment ($P = 0.002$). The RFA group achieved a significantly greater improvement in ODI scores compared with the sham treatment group ($P = 0.006$). For SIJ pain, the RFA group achieved a significantly greater improvement in ODI scores compared with the control group ($P = 0.020$). There was a significant improvement in QoL (measured by EQ-5D) in the RFA group compared to the medical treatment group ($P = 0.005$). Although improvements were also found for the other two scales of QoL (GPE and SF-36), the results did not reach statistical significance.[89]

In a RCT, Cohen *et al*. evaluated L4-5 primary DR and S1-3 lateral branch C-RFA ($N = 14$) and compared it with placebo-control ($N = 14$) in patients with SIJ-associated LBP. Patients who failed to respond to placebo injections were crossed-over and treated with conventional RFA. At 1 month, the RFA group had significantly lower NRS (2.4 ± 2.0 vs. 6.3 ± 2.4, $P < 0.001$, respectively) and ODI score (20.9 ± 10.9 vs. 43.6 ± 14.0 respectively, $P < 0.03$) than the placebo group. In the RFA group, compared to baseline scores, patients had significantly lower mean NRS and ODI scores at 1, 3, and 6 months (all $P < 0.001$). Contrarily, at 1 month, the mean NRS and ODI scores of patients in the placebo group were unchanged from baseline. In the placebo group, 11 patients were crossed-over to the RFA group; 9 at 1 month and 2 at 3 months. In the cross-over phase, the mean NRS and ODI scores following conventional RFA did not differ significantly from those of the original RFA group. Similar to the original RFA group, compared to the baseline, the cross-over group experienced a significant decrease in NRS scores at 1-(44%), 3-(67%), and 6 months (52%) ($P < 0.001$). However, at 1 month, the original RFA group had significantly lower ODI scores compared to the placebo/cross-over group ($P < 0.03$). In the cross-over group, following the conventional RFA, the difference between baseline and ODI scores at 3-and 6 months was statistically significant ($P < 0.02$), but not at 1 month. The proportion of patients who experienced a positive outcome was significantly higher in the original RFA than in the control group ($P < 0.001$). This success rate persisted at 3-and 6 months. In contrast, only 2 (14.3%) patients in the placebo group experienced a positive composite outcome at 1 month. In the cross-over group, patients experienced slightly lower success rates than the original RFA and this was not statistically different. In patients with a successful outcome at any time point, the mean duration of pain relief was 7.9 ± 4.7 months. Patients in the original RFA group had a mean duration of pain relief of 5.8 ± 4.2 vs. 0.7 ± 1.6 months in the placebo group. The mean duration of relief in the radiofrequency crossover group did not significantly differ from that of the initial treatment group. Two patients each in the conventional RFA and C-RFA groups continued to experience significant pain relief 1-year after treatment. There were no serious complications reported for either the 14 placebo or 25 RFA procedures. In the original C-RFA group, one patient reported transient nonpainful buttock paresthesias that resolved spontaneously.[90]

In a randomized, cross-over, sham-controlled trial, Patel *et al*. compared the efficacy of lateral sacral branch C-RFA ($N = 34$) with a sham intervention ($N = 17$) in patients with SIJ-associated LBP. All patients participated in the study until the unblinding at 3 months and 16 patients of the sham group were crossed over to the C-RFA group. No serious complications were reported for the 50 lateral branch neurotomy procedures or the 17 sham procedures. At 3 months, the C-RFA group had a statistically significant greater mean change in NRS pain ($P = 0.035$) and SF-36 PF ($P = 0.04$) scores than the sham group. At 1-and 3 months, the C-RFA group had a statistically significantly greater mean change SF-36 BP ($P = 0.006$, and 0.019, respectively) and ODI scores ($P = 0.046$, and 0.011,

respectively) than the sham group. At 3 months, a significantly greater number of patients in the C-RFA group had treatment success (≥50% decrease in NRS and 10-point increase in SF-36 BP or a 10-point decrease in ODI) than the sham group (47% vs. 12%, $P = 0.015$). At 6-and 9 months, 38% (13/34) and 59% (20/34) patients had successful outcomes, respectively. Moreover, at both 3-and 6-months, 44% (7/16) patients had treatment success in the crossed-over group. At 3 months, the improvement in mean QoL scores was significantly greater in the C-RFA group than the sham group ($P = 0.048$).[77]

In a prospective observational study, Karaman *et al*. evaluated the efficacy and safety of C-RFA on L5DR and the S1-3 lateral branches in 15 patients with SIJ-associated LBP. Compared with the baseline, the median VAS and mean ODI score decreased significantly at all follow-ups (1-, 3-, and 6-months). At 6 months, 80% of patients reported at least a 50% decrease in VAS score. During a similar period, 86.7% of patients reported improvement of at least 10 points in ODI scores. No major complications were encountered either during or after the procedure. The hip pain that was seen in nearly all of the patients and lasted about 5 days dissipated without any intervention other than simple analgesics.[91]

In an initial case series, Kapural *et al*. discussed the findings of 27 patients who presented with chronic LBP due to SIJ disorder and underwent C-RFA of S1, S2, and S3 lateral branches and L5DR following two diagnostic SIJ blocks. At 3–4-months following the procedures, mean VAS scores decreased significantly ($P < 0.001$). Similarly, the functional capacity improved, with a significant change in PDI scores ($P < 0.001$). During a similar period, 50% (13/26) of patients had at least a 50% reduction in VAS pain scores. Using GPE for patient satisfaction, 18 (67%) patients had improved or much-improved pain relief, while 8 (30%) patients claimed minimal or no improvement. Similar ratings were observed for GPE related to daily activities. The procedure did not result in any complications, and the procedure was generally well tolerated.[92]

In a retrospective study, Stolzenberg *et al*. determined the incidence of neuropathic pain following C-RFA of the sacral lateral branches for the treatment of 34 patients with chronic posterior SIJC-associated pain. A total of 48 separate procedures were performed, of which 32 (66.7%) were successful, and 16 (33.3%) were unsuccessful. There were three patients with postprocedure neuropathic pain yielding 6.3% per procedure and 8.8% per patient. In two patients, neuropathic pain resolved spontaneously and in the remaining 1 patient, treatment with gabapentin at 300 mg thrice daily and a lidocaine patch was required. Thus, the incidence of postprocedural neuropathic pain following SIJ C-RFA for denervation is low.[93]

In another retrospective study, Tinnirello evaluated the pain and disability relief produced by C-RFA in 27 patients with SIJ-associated chronic LBP, refractory to conservative treatments. Patients presented with severe pain (mean NRS score, 7.7 ± 1.0), which was significantly reduced up to 12 months ($P < 0.05$). The mean NRS score reduction at 1-, 6-, and 12 months were 5.6 ± 1.6, 4.1 ± 1.7, and 3.2 ± 1.6, respectively. The procedure was successful in 92.6% (25/27), 63.0% (17/27), and 44.4% (12/27) patients at 1-, 6-, and 12 months, respectively. None of the patients reported worsening pain at any of the follow-up visits. The severe disability at baseline (mean ODI score, 50.1 ± 9.0) was significantly reduced for up to 12 months ($P < 0.05$). Mean disability decreased by 30.7 ± 12.6 points at 1 month, while at 6-and 12-months, by 24.6 ± 12.1 and 20.2 ± 11.6 points, respectively. At 6 months, one patient reported 100% disability relief, of which 95% was sustained at 12 months.[94]

In a case report, Biswas *et al*. described a 35-year-old male with chronic bilateral SIJ dysfunction-associated LBP (NRS-9/10), refractory to conventional treatment. He had similar episodes of pain on multiple occasions in the last 5-years with a persistent presence of LBP (NRS 5-7/10). Based on the duration and severity of the pain as well as the frequency of its recurrence, he was considered a poor responder to IA steroid therapy and subjected to bilateral sacral WC-RFA. Bilateral WC-RFA was applied for the neuroablation of nerves supplying both SI joints. Postprocedure pain intensity was 5/10 and after 7 days it was 2/10. He had a pain intensity of 2/10 after 2 weeks, and it continued to be mild over the next 1 year. On the 18-month follow-up, he is pain-free except for mild pain (NRS 2/10) on occasional extreme twisting of the back.[95]

Moreover, other studies, including MA, have reported superior pain and disability relief with C-RFA in patients with SIJ-associated chronic pain, refractory to conservative treatment.[77-79,82-84,86,90,91,96,97]

Future direction

Although currently, the available evidence is sufficient to recommend the active use of C-RFA in this group of patients, further MA involving only RCTs are required in future. Moreover, RCTs comparing conventional RFA or C-RFA with various nonsurgical modalities should be performed.

Table 7 depicts the summary of recommendations for patients with SIJ pain.

Limitations

These guidelines have certain limitations. First, for four chronic pain conditions, a total of 14 statements are not exhaustive enough. Second, other chronic pain conditions, including discogenic pain, were excluded due to a lack of experience among the experts in Pain Medicine. Third, the SIG was limited in number (i.e., 10), lacked other stakeholders in pain management, and participants from other pain-practicing societies were not involved in guideline formulation. Fourth, only statements with the highest form of available evidence were chosen. Five, the findings of available evidence are summarized, and a MA of this evidence was not performed. Six, the guideline is limited to the management of chronic pain conditions with RFA and does not take into account other aspects of pain management, including diagnosis.

Table 7: Summary of recommendations in patients with sacroiliac joint pain

Recommendations	Grade of recommendation	Level of evidence	Strength of consensus	References
In patients with SIJ-associated LBP, ISSP recommends that RFA techniques should be used in cases of recurrent pain after SIJ MIPSI (IA LA and steroids) due to its better safety profile and effective pain control	A	I	Strong	[70,74-76]
In patients with SIJ-associated LBP, ISSP recommends that conventional RFA or C-RFA should be used for long-term pain relief of up to 2 years	A	I	Strong	[77-83]
In patients with SIJ-associated LBP, ISSP recommends that C-RFA is safe and may be preferred over conventional RFA for greater and more durable pain relief	A	I	Strong	[84-87]
In patients with SIJ-associated LBP, ISSP recommends that C-RFA may be used, especially in recurrent pain after IA steroid and LA, due to better safety profile and ability to provide significant short-, intermediate-, and long-term pain relief with reduced disability and improved function	A	I	Strong	[77-79,82-84,86,88-97]

SIJ: Sacro-iliac joint; ISSP: Indian Society for the Study of Pain; LBP: Low back pain; RFA: Radiofrequency ablation; MIPSI: Minimally invasive pain and spine intervention, IA: Intra-articular, LA: Local anesthetic

Conclusion

These ISSP guidelines for the management of chronic MSK pain with RFA are presented as a practical tool. They also provide recommendations for the management of patients with chronic MSK pain, refractory to conservative therapy. Due to excellent safety, effectiveness, and durability, RFA techniques should be tried at an early stage, in this cohort of patients. However, further high-quality research is required to formulate more inclusive guidelines in this evolving pain speciality.

Authorship statements

Dr. Gautam Das served as primary author, project organizer and editor; Dr. Anurag Agarwal, Dr. Pankaj Surange, Dr. Gaurav Sharma, and Dr. Uttam Siddhaye, performed literature searches; Dr. Kailash Kothari, Dr. Karthic Babu Natarajan, and Dr. V K Mohan prepared evidence tables; Dr. Neeraj Jain, Dr. Kailash Kothari, Dr. Anurag Agarwal and Dr. Pankaj Surange served as senior editors; the remaining authors acquired or interpreted data, wrote sections of the manuscript, and provided critical reviews and editing.

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Conflicts of interest

There are no conflicts of interest.

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