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NEUROPATHIC PAIN (A ABD-ELSAYED, SECTION EDITOR)

Systematic Review of Radiofrequency Ablation for Management of Knee Pain

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Abstract

Purpose of Review Chronic pain of the lower extremity remains challenging to manage. Radiofrequency ablation procedure applies heat to nerve fibers with the goal of mitigating chronic pain conditions of the knee. However, the clinical efficacy has not yet been adequately established. The goal of this review paper is to report the use of radiofrequency ablations in the treatment of osteoarthritis of the knee.

Recent Findings PubMed and the Cochrane Controlled Trials Register were searched (final search 28 February 2018) using the MeSH terms "radiofrequency ablation," "neurolysis," "radiofrequency therapy," "pain syndrome," "analgesia," and "pain" in the English literature. Bibliographies of the published papers were screened for relevance to lower extremity radiofrequency ablation therapies. The quality of selected publications was assessed using the Cochrane risk of bias instrument.

Of the 923 papers screened, 317 were further investigated for relevance. Our final search methodology yielded 19 studies that investigated the use of radiofrequency ablation at the knee. Of these 19 studies, there were four randomized control trials, two non-randomized control trials, three prospective studies, two retrospective studies, one case-control study, one technical report, and seven case reports.

Summary In summary, the data available suggests radiofrequency ablation as a promising and efficacious with all 19 studies revealing significant short- and long-term pain reductions in patients with knee pain.

Keywords RFA · Knee pain · Radiofrequency ablation · Radiofrequency therapy · Pain therapy · Neurolysis

Introduction

Osteoarthritis is one of the most common debilitating joint disorders worldwide [1]. Ten percent of patients who are 60 years and older are significantly impacted by their symptoms [2]. In particular, osteoarthritis of the knee is a leading cause of chronic disability in the developed world [3–5]. Among all adults in the USA, 37% have radiographic evidence of knee osteoarthritis and 12% report painful symptoms [6]. Osteoarthritis is a complex condition with a heterogeneous complement of clinical features and presentations. Moreover, multiple phenotypes have been identified, characterized by varying biochemical, biomechanical, and clinical pathology [7]. Though patients who experience the most significant pain have supporting radiographic evidence of knee osteoarthritis, many experience symptoms despite an absence of radiographic findings [2, 8].

Multiple factors are implicated in causing pain and subsequent activity limitation, including local tissue pathology, joint biomechanics, psychological distress, and clinical comorbidities [7]. Hyaline loss is pathognomonic for osteoarthritis; however, disease progression includes bone remodeling, fibrocartilage degeneration, chondro-osteophytes, synovial hyperplasia, and muscle atrophy. Together, these changes invoke local inflammation, triggering a nociceptive response in the peripheral nervous system [9]. Clinically, patients present with complaints of pain, effusion, crepitus, and decreased

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knee range of motion. Typically, the pain caused by osteoarthritis is related to activity: difficulty with ascending and descending stairs for instance, though some patients may also experience a dull constant ache. Together, these symptoms lead to significantly worsened mobility, mood, and sleep. Ultimately, this impacts social, recreational, and daily independent activities of living [10].

The disease course of osteoarthritis is unremitting and progressive in nature, with a predictable worsening of symptoms and pain overtime. Though there is no cure for the disease, therapeutic modalities aim to slow the progression of disease pathology focusing on conservative treatment: physical therapy, weight loss, and pharmacologic pain management. The refractory pain caused by knee osteoarthritis is difficult to adequately manage and leads to 24% of patients resorting to surgical management [11]. Though total knee arthroplasty may be an effective treatment for osteoarthritis providing long-term cost effective results, 15–20% of patients have been found to be dissatisfied with the results of their surgery [12]. Moreover, patient comorbidities including obesity and decreased physical activity have been shown to worsen surgical outcomes [13]. These patients may thus benefit most from minimally invasive techniques such as radiofrequency ablation, after failing conservative medical management and physical therapy.

Radiofrequency ablation is a commonly performed therapy for various musculoskeletal chronic pain conditions including, radicular pain, sacroiliac joint pain, post-surgical pain, and myofascial pain [13–15]. Recently, the application of radiofrequency therapy to target peripheral nerves innervating the knee joint has garnered increased attention [16–20]. Both conventional (CRF) and pulsed radiofrequency therapy (PRF) have been utilized in this application.

Conventional radiofrequency ablation (CRF) applies a continuous radiofrequency to targeted tissue, achieving a temperature of 60–80 °C. These high temperatures result in neural ablation by causing coagulative necrosis, collagen destruction, and axonal degeneration [21–23]. As per Sunderland's classification of nerve injury, third or even fourth degree peripheral nerve injury is achieved via this method. As this process does not entirely disrupt the nerve cell and preserves the fascicular arrangement of the peri and epineurium, progressive axonal regeneration ultimately results in a return of pain [22, 24].

In contrast to CRF, which relies on high temperatures to cause local tissue destruction, pulsed radiofrequency modulation creates an electromagnetic field which functionally disrupts the neuronal membrane, modulates gene expression, and affects cytokine release [23, 25, 26]. These changes are selective for small unmyelinated and lightly myelinated nerve fibers, thus eliciting a motor-sparing effect [25, 26]. Histologically, PRF results in transient endoneurial edema which may persist for up to 1 week following treatment [27]. Despite the absence of overt neurodegeneration, in some applications, clinical pain relief following PRF can last up to several years [28]. Common limitations of radiofrequency ablative or modulative techniques are failure to completely denervate the targeted nerve or disrupt nociceptive sensation. Moreover, radiofrequency therapy may worsen symptoms through aberrant neuronal regeneration resulting in adverse effects including neuroma formation, reduced motor function, deafferentation pain syndrome, neuritis, and paresthesias [24].

The use of radiofrequency therapy to target the peripheral nerves innervating the knee may be effective in the treatment of refractory chronic knee pain. Patients with chronic knee pain who may most benefit from radiofrequency ablation include those who are non-surgical candidates, have failed total knee arthroplasty, or have chronic pain following trauma to the knee. In this review, we highlight the use of radiofrequency therapy in the treatment of chronic knee pain and examine the long- and short-term efficacy of both ablative and modulative techniques.

Materials and Methods

Systematic Literature Search

Authors searched Medline, PubMed, Cochrane Database of Systematic Reviews, PROSPERO, and Cochrane Central Register of Controlled Trials for relevant publications. We also searched google scholar and the clinical trial registry (clinicaltrials.gov) for additional publications. These database search were completed on 28 February 2018. Our EMBASE and MEDLINE included both controlled terms (MeSH, EMBASE, Emtree, MEDLINE) and free text that included the following: "radiofrequency ablation," "radiofrequency," "RF," "ablation," "neurolysis," "radiofrequency therapy," "pain syndrome," "knee pain," "chronic pain," "knee osteoarthritis," "analgesia," and "pain" in the English literature. Bibliographies of the published papers were screened for various chronic pain pathologies that received lower extremity radiofrequency ablations.

Inclusion and Exclusion Criteria

We included RCTs, open non-randomized control studies, prospective studies, retrospective studied, case series, and case reports for this systematic review. We limited our search to publications that investigated patients with chronic knee pain lasting for at least 1 month or patients with a diagnosis of osteoarthritis of the knee. We also included publications that investigated the application of various RF treatments (conventional or pulsed/cooled technique), original studies, and all adult population. We excluded research that was only

available in abstract or poster forms, animal studies, non-English papers, non-radiofrequency ablation technology, and pediatric population.

Data Extraction

Our final evaluation included case reports, retrospective, prospective, and randomized controlled studies. The reference population, diagnostic group, and outcomes were extracted from these articles using a prespecified standardized extraction form. The information extracted from each study includes author's last name, publication year, study design, number of arms, sample size, ablation technique (pulse vs conventional), temperature range and duration, duration of pain relief, secondary outcomes, side effects, and conclusion. We also extracted the mean and standard deviations for the pain scores when reported. If not reported, we included the paper for thorough analysis and additional discussion purposes.

Quality of Evidence

The quality of evidence was assessed using oxford quality scoring system and GRADEpro risk of bias methodology [29, 30]. The oxford quality of evidence was classified as "high range quality score" and "low range quality score" [29]. The GRADEpro approach was used to assess for selection bias, performance bias, detection bias, attrition bias, and reporting bias for each outcome. A summary figure was constructed with the GRADEpro guideline development tool [30] (http://www.guidelinedevelopment.org/; Evidence Prime Inc., Hamilton, Ontario, Canada) [34].

Result

Search Result

Our final search methodology yielded 19 studies that investigated the use of radiofrequency ablation at the knee [19, 31–48]. The search and study selection flow chart is displayed at Fig. 1. We identified 317 publications after duplication were removed. These studies were screened based on our inclusion and exclusion criteria. The details of the 19 studies are described in Table 1. These 19 studies were made up of four RCTs [32–34, 37], two non-randomized controlled trials [35, 36], four prospective [19, 38–40], two retrospective [41, 42], two case series [43, 44], one technical [48] report, and four case reports [31, 45–47], which are summarized in Table 1. Fourteen [19, 31–37, 39–42, 44, 48] of these 19 studies were thoroughly discussed in our systematic review.

Targeted Nerves

Eighteen of the 19 publication included in this review had subjects with a diagnosis of chronic knee osteoarthritis. Only one publication included subjects with knee pain after total knee replacements [45]. The genicular nerve was the most commonly targeted nerve for with continuous or pulsed RF ablation [19, 31, 34, 40, 45–47]. Another group of nerves identified as "composite nerves" were also ablated in four of the publications included in this review [32, 37, 42, 48]. The sciatic nerve was a target in one study [38].

Quality of Evidence

Two [32, 37] of the four randomized controlled trials did not adequately blind the participants and personnel of their respective studies. The oxford quality score for Alcidi et al. and Takahashi et al. was considered low (Table 2). The remaining two RCTs were considered high quality with scores at 4/5 [33] and 5/5 [34] (Table 2). The overall risk of bias was low in studies that were considered to provide instantaneous pain relief (Fig. 2). Two [19, 35] of the studies that provided short-term pain relief were considered to be high risk for bias (Fig. 3) and five [36, 40–42, 48] of the six studies that showed evidence for long-term pain relief suggested high risk of bias (Fig. 4).

Outcome

Pain outcomes were reported as VAS or NRS by most of the publications included in this review. Simultaneously, the functional outcome measures were also reported by most publications. The most commonly reported secondary measures used to assess function of the knee include Lequesne's index [32, 37], WOMAC [36, 41, 44, 47], and oxford knee score (OKS) [34, 45], and patient satisfaction [34, 40].

Discussion

Our review of 18 publications that investigated the use of pulsed or continuous RF treatments on patients with knee osteoarthritis suggests that RF treatments can provide immediate, short-term, and long-term pain relief. This pain relief could last as long as 12 months after the RF ablation treatment. Our review also suggests that improvement in function after RF treatments can be observed without any serious adverse events.

The overall quality of evidence of the use of RF treatment in patients with knee osteoarthritis seems to have a slight improvement. A similar review conducted by Bhatia et al. [49] assigned a low quality of evidence in 2016. This was partly due to the small number of RCTs performed at that

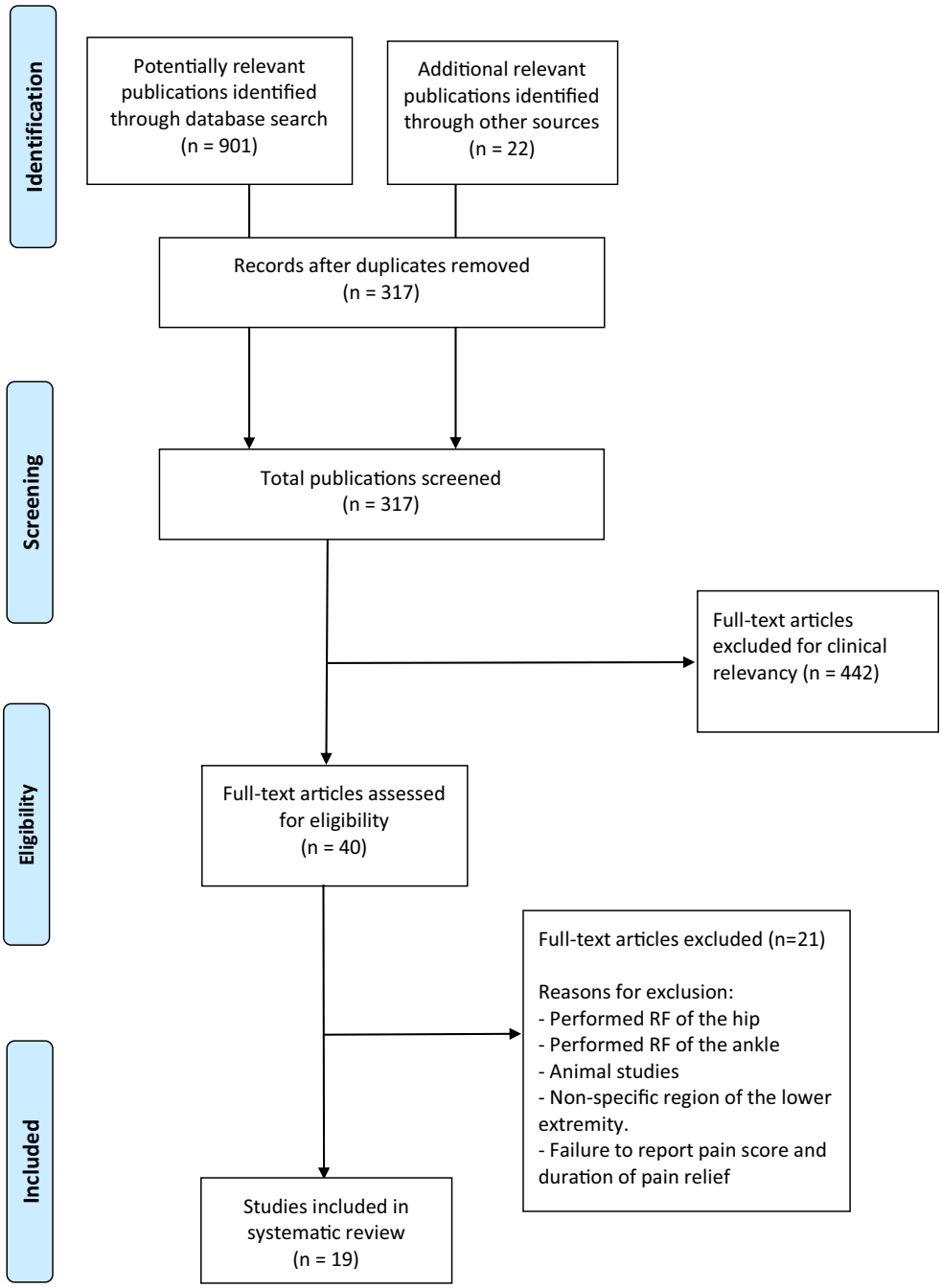

Fig. 1 Flow chart demonstrating the identification and selection of the articles for the systematic review

point in time. In our review, we were able to identify four RCTs [32–34, 37] that showed a reduction in pain after RF treatment with a low to high quality of evidence (Table 2). Two of the four studies were able to randomize and blind the participants but the remaining two studies were uncertain.

Our search methodology yielded four randomized control trials, two non-randomized control trials, three prospective studies, two retrospective studies, one case-control study, one technical report, and seven case reports investigating the efficacy of radiofrequency ablation in the treatment of knee pain. These studies suggest that radiofrequency ablation has both short- and long-term analgesic efficacies in the management of lower extremity chronic pain syndromes. We summarize the details of these findings in the following sections.

Pain Relief and Functional Outcome: Efficacy of RF Ablation in Randomized Control Trials

The randomized studies included in our review were performed by Choi et al., Taverner et al., Alcidi et al., and Takahashi et al. [32–34, 37]. The study by Choi et al. revealed that patients with chronic osteoarthritis of the knee that were

Table 1 Qualitative evaluation of the studies that assessed the efficacy of radiofrequency ablation for the treatment of knee pain

Author	Clinical diagnosis	Study size	Study design	Ablation technique	Ablated nerve	Lower extremity region	Duration of pain relief	Secondary outcome	Side effect	Conclusion
Alcidi et al. (2007)	Chronic knee osteoarthritis	40	RCT	Continuous 42 °C for 20 min	Composite nerves of the knee	Knee	Pain scores went from roughly 60/100 before the procedure to 40/100 immediately after and then 30/100 30 days after	Lequesne's index, a marker for functional impairment, showed significant improvement as well. Before treatment score was at 11/24; immediately after treatment scores went to 6/24, and then at 30 days, it was at 5/24	None	TENS (transcutaneous electrical nerve stimulation) was compared to PRF. PRF showed a significant difference in pain reduction while the TENS did not show any difference. This could be due to the fact that the TENS acts on the superficial tissue while PRF acts on the deeper tissues
Taverner et al. (2010)	Chronic knee osteoarthritis	50	RCT	Bipolar/intermittent 2-min, 20 ms, 2 pulses/s for maximum of 15 min at 80 V	5 sites around the knee	Knee	Statistically significant reduction in VAS at 1 and 4 weeks compared with baseline in the group who received active treatment. We also demonstrated what is considered a clinically significant improvement in this group that became more pronounced at week 4 compared with week 1	Clinically significant more after a 400-m walk compared with a 20-m walk in the treatment group. Maximum improvement observed in group data was 19/100 VAS	None	This is the 1st report of a controlled study of TCPRFT. This pilot study shows a benefit of the technique that justifies future research
Choi et al. (2011)	Chronic knee osteoarthritis	38	RCT	Continuous 70 °C for 90 s	Genicular	Knee	VAS: RF group showed superior improvement compared with the control group at both 4 ($p < 0.001$) and 12 ($p < 0.001$) weeks	The RF group oxford knee scores were better than control group scores at 4 ($p < 0.001$) and 12 ($p < 0.001$) weeks. The RF group patient satisfaction was better than the control group satisfaction at 4 ($p < 0.001$) and 12 ($p < 0.001$) weeks, and was highest at 4 weeks in the RF group	Temporary periosteum touch pain	RF neurotomy of genicular nerves leads to significant pain reduction and functional improvement in a subset of elderly chronic knee OA pain, and thus may be an effective treatment in such cases
Takahashi et al. (2016)	Chronic knee osteoarthritis	17	RCT	Pulsed 8 MHz and 200 W for 20 min at 1-week intervals 3×. Prior to PRF therapy,	Composite	Knee	Japanese Orthopedic Association Pain scores improved. Pain scores went from 78 at baseline to 81 1 week after the procedure and 88	Lequesne's index, a marker for functional impairment, showed improvement as well. Baseline scores were at 7/24, 1 week after they	None	PRF was compared with microwave diathermy in combination with intra-articular injection of hyaluronic acid into the knees of patients

Table 1 (continued)

Author	Clinical diagnosis	Study size	Study design	Ablation technique	Ablated nerve	Lower extremity region	Duration of pain relief	Secondary outcome	Side effect	Conclusion
				hyaluronic acid was injected intra-articularly			3 weeks after the procedure. Increased scores indicate improved pain	were at 5/24, and then at 3 weeks, they were at 4/24		with osteoarthritis. PRF showed significant decrease in pain scores and functional improvement compared with microwave diathermy
Ikeuchi et al. (2011)	Chronic knee osteoarthritis	35	Open non--randomized controlled trial	Continuous 70 °C for 90 s	Medial retinacular nerve and infrapatellar branch of the saphenous nerve	Knee	Radiofrequency treatment significantly decreased knee pain as measured by VAS for 12 weeks compared with the control group. In terms of responders, more patients in the RF group responded to the treatment than in the control group. The differences were statistically significant at 4 weeks, 8 weeks, and 12 weeks in pain VAS	8 patients (44%) treated with radiofrequency rated excellent or good but only 3 (18%) in the control group rated good, although the difference was not statistically significant		Some patients were able to benefit substantially from radiofrequency treatment. Even if its effective period is limited, radiofrequency application is a promising treatment to alleviate refractory anteromedial knee pain with osteoarthritis
Masala et al. (2014)	Chronic knee osteoarthritis	40	Non-randomized controlled trial	Pulsed, 1200 pulses at high voltage (45 V) with 20-ms duration followed by a 480-ms silent phase	Various pericapsular nerve endings	Knee	VAS scores prior to treatment were 7/10. Scores were tracked at 1 week, 1 month, 3 month, 6 months, and 12 months after with VAS scores at 2/10	WOMAC scores prior to treatment were 67/100, which reduced at 1 week, 1 month, 3 month, 6 months, and 12 months to 20–30	None	In patients with chronic pain non-responsive to conservative management, pulse-dosed radiofrequency can be used
Fucci et al. (2013)	Chronic knee pain	25	Prospective cohort study	Continuous 45 V for 480 s	Sciatic nerve	Knee	The average VAS difference before and after the procedure was 27 while walking and 11 mm at rest		10 of the procedures were ineffective. No side effects were seen at 1 month follow-up	PRF of the sciatic nerve leads to short-term pain relief. More research with longer follow-up times are necessary to delineate the exact impact
Kesikburun et al. (2016)	Chronic knee osteoarthritis	29	Single-arm prospective study	Pulsed 120 s twice at 42 °C	Genicular nerve	Knee	20/29 patients had pain relief of at least 50% reduction in VAS score to the genicular nerve block procedure for 12 weeks		13/29 patients had recurrent pain	Using ultrasound, genicular nerve PRF is effective in management of knee osteoarthritis
		54			Uncertain	Knee			None	

Table 1 (continued)

Author	Clinical diagnosis	Study size	Study design	Ablation technique	Ablated nerve	Lower extremity region	Duration of pain relief	Secondary outcome	Side effect	Conclusion
Shen et al. (2016)	Chronic knee osteoarthritis		Prospective case-control study	Continuous 70 °C for 120 s			VAS scores decreased significantly at the end of 3-month follow-up. VAS scores went from 7/10 before treatment to 3/10 immediately after and then 4/10 at the 3-month follow-up	Improved knee function and quality of life. SF-36 assessment was used, which indicated a baseline score of 58 and then improvement to 73 immediately after and then 78 at a 3-month follow-up		PRF may have better ability to relieve refractory pain and promote functional recovery in patients with knee OA compared to regular treatments
Pineda et al. (2017)	Chronic knee osteoarthritis	25	Single-arm prospective study	Continuous 90 s at 20 V to 80 °C	Genicular nerves	Knee	At 1 month, there was 22/25 (88%) with 50% improvement in pain; at 6 months 16/25 (64%) with 50% improvement in pain; and 8/25 (32%) at 12 months with 50% improvement in pain	Patient satisfaction scores at 6 months after the intervention were poor (2/25), average (1/25), good (5/25), and very good (16/25). This was associated with reduced analgesic consumption	No side effects seen at 1, 6, or 12 months follow-up	PRF of the genicular nerve leads to significant pain relief at 1 month and 6 months. It is motor-sparing treatment for knee pain
Akbas et al. (2011)	Chronic knee osteoarthritis	115	Retrospective study	Pulsed 42 °C for 120 s for 4 times	Saphenous vein	Knee	84.33% of the patients showed improvement in their VAS scores as well as in their WOMAC scores after 10 days, 3rd month, and 6 months. This was defined by a > 50% decrease in VAS and WOMAC	–		PRF of the saphenous vein can be used for treatment-resistant knee pain associated with chronic knee pain resistant to conventional care
Karaman et al. (2011)	Chronic knee osteoarthritis	31	Retrospective study	Continuous 42 °C for 15 min	Composite	Knee	VAS scores were 6/10 before procedure, 4/10 at 1st and 6th month follow-up		None	PRF is a safe and effective way to manage chronic knee pain associated with osteoarthritis. The mechanism of action is unknown but likely due to some component of immunomodulation
Sluijter et al. (2008)	Arthritis	6	Case series	Pulsed radiofrequency	Various	Various	VAS scores improved			Patients resistant to conservative pain relief techniques achieved pain relief with PRF in large joints targeting multiple nerves
Protzman et al. (2014)	Chronic knee pain	1	Case report	Continuous 80 °C for 90 s	Genicular nerves	Knee	Post-procedure VAS score was 0 at 2 weeks and 3 months, but with physical therapy pain was	Improved range of motion and strength in the extremity		Ultrasound-guided PRF of the genicular nerve can be used for pain management in

Table 1 (continued)

Author	Clinical diagnosis	Study size	Study design	Ablation technique	Ablated nerve	Lower extremity region	Duration of pain relief	Secondary outcome	Side effect	Conclusion
							at 3/10			patients who have continued pain despite a total knee replacement and removal
Bellini et al. (2015)	Chronic knee osteoarthritis	9	Case series	Cooled radiofrequency	Genicular nerve	Knee	VAS scores were 8/10 before procedure, and then thereafter at 1, 3, 6, and 12 months, scores were at 2/10	Improved WOMAC scores 1 month after treatment. Baseline WOMAC was 88, and after the procedure at 1, 3, 6, and 12 months, they were 20	None	Patients experienced significant pain relief with cooled pulsed radiofrequency up to 1 year after the procedure. It can be used in place of an invasive surgical procedure
Menzies et al. (2015)	Bilateral knee pain s/p total knee replace-ments for osteoarthritis	1	Case report	Cooled radiofrequency	Superior lateral, superior medial, and inferior medial genicular nerves	Knee	Improved oxford knee score assessment scores from on the left 24/48 to 9/48 and 30/48 to 6/48	Improved quality of life and range of motion	None	PRF can be used to improve the debilitating pain after a surgically successful total knee replacement
Wong et al. (2016)	Chronic knee pain	1	Case report	Continuous 80 °C for 90 s	Genicular nerve	Knee	Preprocedurally her pain was at 8/10 with activity and 3/10 at rest, post-procedurally her pain was 2/10 with activity and 0/10 at rest	Improved functional status and quality of life	None	In patients who are not surgical candidates and have severe knee pain due to osteoarthritis, RFA of the genicular nerves can provide relief. Ultrasound guidance can be used to assist
Rojhani et al. (2017)	Chronic knee osteoarthritis	1	Case report	Watercooled radiofrequency	Bilateral superior lateral, superior medial, and inferior medial genicular nerves	Knee	VAS scores of 8/10 preprocedure and 0/10 post-procedure	WOMAC scores of 72/100 preprocedure and 22/30 post-procedure	None	In patients with end stage osteoarthritis requesting minimally invasive pain relief techniques, watercooled radiofrequency can be used to provide pain relief
Vas et al. (2014)	Chronic knee osteoarthritis	10	Technical report	Continuous 42 C for 8 min	Composite nerves of the knee (all sensory and	Knee	PRF of these motor nerves reverse the neuromyopathy and its effect on the structural components of the joint.	Reduced pain induced sleep disturbances by the 2nd day. Improved standing and walking abilities, but	None	Persistent pain leads to an inflammation and joint damage in the knee leading to muscle spasms and stiffness.

Table 1 (continued)

Author	Clinical diagnosis	Study size	Study design	Ablation technique	Ablated nerve	Lower extremity region	Duration of pain relief	Secondary outcome	Side effect	Conclusion
					motor nerves)		Improved joint contours after PRF. It also improves pain scores significantly up to 6 months after	continued difficulty with steps		Because of the diffuse effects of the inflammation, multiple nerves must be targeted

treated with radiofrequency ablation of the genicular nerve had a significant reduction in VAS ($p < 0.001$) compared to control group [34]. Functional outcome was investigated by reporting oxford knee scores. The oxford knee scores showed that the RF group, 10/17 (59%), 11/17 (65%), and 10/17 (59%), achieved at least 50% knee pain relief. This study further concluded that RF ablation of genicular nerves can result to pain reduction and functional improvement in patients with chronic knee OA pain.

In another randomized controlled trial by Taverner et al., patients referred for total knee joint replacement were treated with transcutaneous pulsed radiofrequency ablation [33]. The VAS metric was used to evaluate pain outcome and this study showed a reduction in VAS with radiofrequency treatment when compared to baseline. These authors also noted that the reduction in VAS was more significant at week 4 compared to week 1. The maximum improvement observed in this study cohort was 19/100 VAS. There was not functional outcome assessment in this study.

Study by Alcidi et al. investigated the role of continuous ablation in reducing pain as well as improving function [32]. Pain scores were significantly reduced from 60/100 preprocedure to 40/100 after the procedure. The functional outcomes were evaluated with Lequesne's index, a marker for functional impairment. Before treatment, Lequesne's index score was at 11/2. Immediately after treatment, the scores were significantly improved and this lasted for 30 days after the procedure. Similar to Alcidi et al., another randomized control trial by Takahashi et al. found a reduction in pain score with baseline pain scores remaining lower than post-procedural pain scores [37]. They also evaluated functional outcome with Lequesne's index and found significant functional improvement at weeks 1 and 3.

Duration of Analgesic Effect: Instantaneous Pain Relief

Two studies reported instantaneous pain relief after continuous radiofrequency ablation was applied to unspecified nerves around the knee [32, 39]. In the case-control study by Shen et al., patients with chronic knee osteoarthritis had a reduction in VAS scores immediately after RF ablation [39]. VAS scores went from 7/10 before treatment to 3/10 immediately after treatment. In the randomized control study by Alcidi et al., pain scores were instantaneously reduced from roughly 60/100 before the procedure to 40/100 immediately after the procedure [32].

Duration of Analgesic Effect: Short-Term Pain Relief

Short-term pain relief was defined pain reduction lasting for as long as 12 weeks. Six of the 20 studies showed evidence of short-term pain relief after radiofrequency ablation [19,

Table 2 Quality assessment of randomized controlled trials investigating the role radiofrequency ablation in patients with chronic knee pain or osteoarthritis

Questions	Grading			
	Alcidi et al.	Taverner et al.	Choi et al.	Takahashi et al.
1. Study described as random?	1	1	1	1
2. Randomization described and appropriate?	1	1	1	1
3. Study described as double-blind?	1	1	1	0
4. Method of double blinding described?	− 1	1	1	− 1
5. Dropouts and withdrawals described?	0	0	1	0
Total	2	4	5	1

32–35, 37]. There were three studies that showed pain relief at 3–4 weeks [32, 33, 37]. The studies by Takahashi et al. [37] and Taverner et al. [33] applied pulsatile ablation technique to either a composite or unspecified nerve around the knee. These studies reported pain relief that lasted for 3 weeks [37] and 4 weeks [33]. The third study that showed short-term pain relief was performed by Alcidi et al. [32]. This study showed that patient with continuous ablation of composite nerves of the knee will result to a significant pain relief that lasted for 30 days. The functional outcome measures for all three studies suggested radiofrequency ablation could result to improvement of functional impairment at 3–4 weeks [32, 33, 37].

In addition, there were three studies that reported analgesic effect at 12 weeks [19, 34, 35]. Studies by Choi et al. and Ikeuchi et al. investigated analgesic effect after continuous radiofrequency ablation at the genicular and medial retinacular nerve, respectively [34, 35]. Both studies showed a significant reduction in VAS among patient patients with radiofrequency ablation compared to the control group. The improvement in VAS was statistically significant at 4 and 12 weeks. A single-arm prospective study by Kesikburun et al. investigated the analgesic effect of pulsatile radiofrequency ablation on the genicular nerve of patients with chronic knee osteoarthritis [19]. Similarly, this study found a reduction in VAS at 12 weeks.

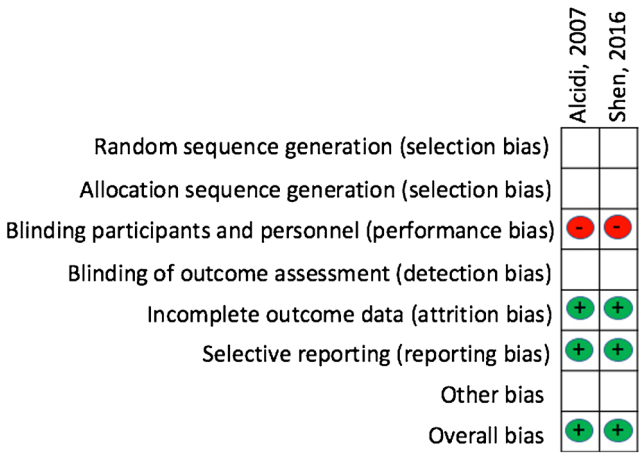

Fig. 2 Risk of bias summary for instantaneous pain relief studies. Green circles with "+" sign indicate low risk, red circles with "-" sign indicate high risk, and blank boxes indicate unclear risk

Duration of Analgesic Effect: Long-Term Pain Relief

Long-term pain relief was defined as pain reduction lasting for more than 12 weeks. Eight of the 20 studies clearly suggested that radiofrequency ablation of the knee had a long-term pain relief [31, 36, 39–42, 44, 48]. Two studies reported analgesic effect that lasted for 3 months [31, 39]. In the case-control study by Shen et al., a continuous radiofrequency ablation was applied to non-specified nerve group. VAS scores decreased significantly at the end of 3-month follow-up and functional assessment measured with SF-36 suggested improvement in quality of life at 3-month follow-up. The second study was a case report that showed an analgesic effect that lasted for 3 months after continuous ablation was applied to the genicular nerves of the knee. This study also reported improved range of motion and strength in the extremity.

Furthermore, we identified three studies that provided analgesic effect for as long as 6 months [41, 42, 48]. A retrospective study by Akbas et al. investigated the analgesic effect from using pulsatile RF ablation of the saphenous vein. This study showed that 84% of the patients showed improvement in VAS scores that lasted for as long as 6 months. Similarly, another retrospective study by Karaman et al. also looked at continuous RF ablation of composite nerve and found pain relieve that continued to last at 6 months follow-up. This evidence was also supported by a technical report by Vas et al. This study applied continuous RF ablation to composite nerves of the knee (all sensory and motor) with results showing improved pain score that lasted for 6 months.

The third category of studies that reported long-term analgesic efficacy reported pain relief lasting for as long as 12 months [36, 40, 44]. All three studies used varying methods of RF ablation to achieve the same goal. In a non-randomized controlled trial by Masala et al., pulsatile RF

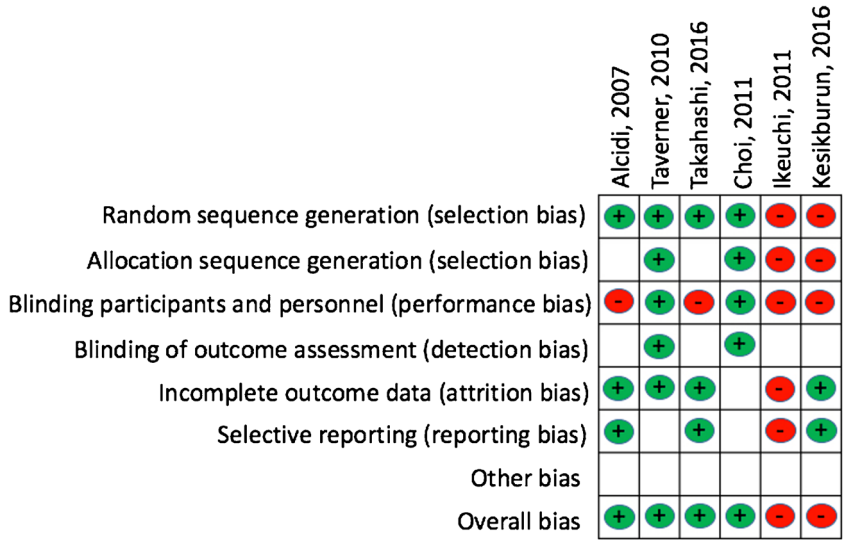

Fig. 3 Risk of bias summary for short-term pain relief studies. Green circles with "+" sign indicate low risk, red circles with "-" sign indicate high risk, and blank boxes indicate unclear risk

ablation was applied the various pericapsular nerve endings. This study showed a reduction in VAS scores that lasted for as long as 12 months. In another prospective study by Pineda et al., a continuous RF ablation was applied to the genicular nerves of the knee and significant improvement in pain was shown to last for as long as 12 months. This study also showed a reduction in analgesic consumption. The last study that showed analgesic efficacy at 12 months was performed by Bellini et al. This case series applied cooled radiofrequency to the genicular nerve and improvement in both VAS and WOMAC scores were observed at 12 months.

Safety Profile and Complications

Very few side effect was reported with the use of RF ablation of the knee. Of the 20 studies that were evaluated, only two studies reported side effect [19, 34]. Choi performed a continuous RF ablation and some of the patients complained of temporary periosteum pain that eventually resolved [34]. The second side effect was reported by Keikburun et al., who used pulsatile RF ablation. In this study, 13 of 29 patients had recurrent pain that was difficult to manage [19]. There were no reported adverse events.

Limitations

There are a few findings that arise when evaluating the data and conclusions from the selected studies. There is a lack of consistency in the procedural approach and characteristics, making difficult to make a comparison to other standard of care treatment protocols. In addition, there is also a lack of prolonged follow-up for the pain and disability scores for the patients that were treated with radiofrequency ablation.

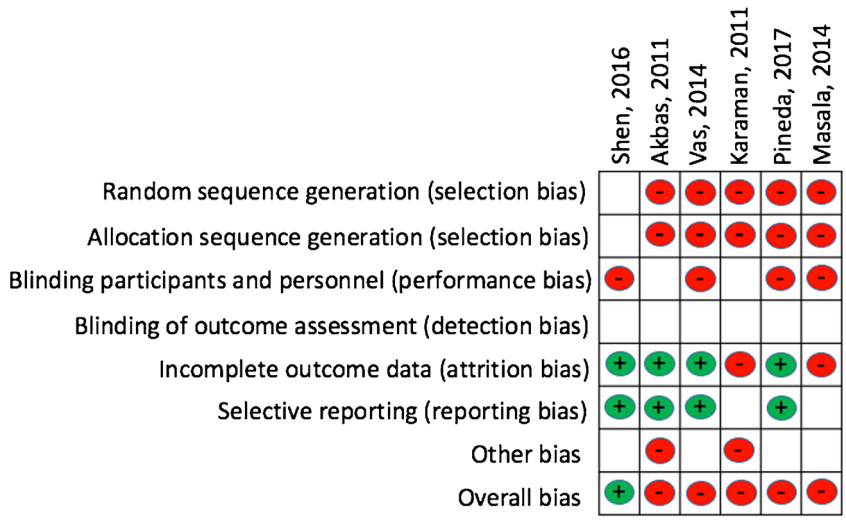

Fig. 4 Risk of bias summary for long-term pain relief studies. Green circles with "+" sign indicate low risk, red circles with "-" sign indicate high risk, and blank boxes indicate unclear risk

Conclusion

Our review reports the numerous studies that suggest the efficacy of radiofrequency ablation in the treatment of chronic knee pain. The approach (continuous vs pulsatile), temperature, and duration of administration need more thorough evaluation. Several studies report a very strong evidence for the use of RFA in treating chronic knee pain [32–34, 37] but a few need to be interpreted with caution. In addition, the majority of the studies indicate benefit of RFA or PRF over a short period of time but very few studies have investigated the long-term implications.

Contributors AA designed the study. VO, IU, and RG performed the literature search and data extraction. VO, IU, RG, and AA were involved in drafting the manuscript. All authors critically revised the manuscript, interpreted the results, and performed a critical review of the manuscript for intellectual content.

Compliance with Ethical Standards

Conflict of Interest Vwaire Orhurhu, Ivan Urits, and Ravi Grandhi declare no conflict of interest. Dr. Abd-Elsayed is a medical consultant for Medtronic, Halyard, Sollis, Axsome, and SpineLoop.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- • Of importance
- •• Of major importance

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