Systematic Review

Use of Radiofrequency Ablation for the Management of Facial Pain: A Systematic Review

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Background: Neuropathic facial pain occurs due to pathologic dysfunctions of a nerve responsible for mediating sensory fibers to the head. Surgical interventions, in cases of failed medical therapy, include microvascular decompression, radiofrequency (RF) ablation, percutaneous balloon decompression, and stereotactic radiosurgery. In this review, we focused on RF ablation as a treatment for chronic facial pain.

Objectives: The objective of this review was to summarize available evidence behind RF ablation for facial pain, including pain outcome measures, secondary outcomes, and complications.

Study Design: Systematic review.

Setting: This systematic review examined studies that applied the use of RF ablation for management of facial pain.

Methods: This systematic review was reported following the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Two reviewers independently scored the methodological quality of the selected studies. Due to heterogeneity of studies, a best-evidence synthesis of the available prognostic factors was provided.

Results: We reviewed 44 studies and assessed their short- and long-term pain relief measurements, as well as secondary outcomes including patient satisfaction, quality of life improvements, decrease in oral medication use, and recurrence rates. Maximal pain relief was achieved in treatment groups using combined continuous radiofrequency (CRF) and pulsed radiofrequency (PRF) therapies, followed by CRF therapy alone and finally PRF therapy alone. All treatment regimens improved secondary outcomes. Common complications of treatment included facial numbness, masseter weakness, cheek hematomas, diminished corneal reflex, and dry eyes.

Limitations: A large variability in definitions of trigeminal neuralgia, RF technique, and patient selection bias was observed in our selected cohort of studies. In addition, there was a paucity of strong longitudinal randomized controlled trials and prospective studies.

Conclusions: This systematic review found evidence that RF ablation is efficient in treating patients with facial pain, as well as in improving quality of life and reducing oral medication use. Maximal pain control is achieved using combined CRF and PRF therapy. Complications are uncommon and include facial numbness, masseter weakness, cheek hematomas, diminished corneal reflex, and dry eyes.

Key words: Radiofrequency, ablation, facial pain, chronic pain, trigeminal neuralgia, neuropathic pain, continuous radiofrequency, pulse radiofrequency

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Neuropathic facial pain occurs due to pathologic dysfunctions of a nerve responsible for mediating sensory fibers to the head (1). Of these conditions, trigeminal neuralgia, is the most reported diagnosis of unilateral episodic facial pain, with an incidence of approximately 4 to 5 cases per 100,000 (2). Patients may present with abrupt onset and short-lived unilateral shock-like pain over the trigeminal nerve distribution (3).

Currently used pharmacologic treatments include carbamazepine as the primary drug of choice, as well as oxcarbazepine for its relatively fewer side effects (4,5). However, nonresponders to drug therapy are as high as 25% to 50% in this population (6). Surgical interventions, in cases of nonresponsive medical therapy, include microvascular decompression, radiofrequency (RF) ablation, percutaneous balloon decompression, and stereotactic radiosurgery. RF ablation is commonly used for treatment of patients with chronic pain (7-9). In this review, we focus on RF ablation as a treatment for chronic facial pain.

Continuous radiofrequency (CRF) induces coagulative necrosis of tissue through high-frequency alternating currents, in which probe temperatures are set between 60ºC and 80ºC (10). CRF has shown to be very effective in treatment of trigeminal neuralgia, with a success rate of 90% to 100% (11,12). However, the high temperature utilized by CRF may induce neuronal injury and lead to a higher risk of complications, such as hyperalgesia, facial numbness, masticatory atonia, and corneal hypoesthesia (13). However, pulsed radiofrequency (PRF) uses short high-voltage bursts followed by a silent phase, which allows for heat elimination (10). The reduced exposure to heat may reduce likeliness of developing complications but may also restrict effectiveness of therapy (14,15). Some studies compare the effectiveness of combined CRF and PRF effectiveness and have shown promising results (15,16).

The aim of this review is to summarize available evidence behind RF ablation, including pain outcome measures, secondary outcomes, and complications.

Methods

Systematic Literature Search

We 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 searches were completed on June 25, 2019. Our EMBASE and MEDLINE searches included both controlled terms (MeSH, EMBASE, Emtree, MEDLINE) and free text that included the following: 'radiofrequency ablation', 'radio-frequency', 'RF', 'RFA', 'radiofrequency lesioning', 'ablation', 'neurolysis', 'radiofrequency therapy', 'facial pain', 'trigeminal neuralgia', 'facial pain', 'neuropathic pain', 'analgesia' and 'pain' in the English literature. Bibliographies of the published articles were screened for various chronic pain pathologies that received RF treatment of the trigeminal nerve.

Inclusion and Exclusion Criteria

We included randomized controlled trials (RCTs), open nonrandomized control studies, prospective studies, retrospective studied, case series, and case reports for this systematic review. We limited our search to publications of original studies that investigated the application of either CRF or PRF treatment in adult patients with chronic facial pain lasting for at least 1 month or in patients with a diagnosis of facial pain. We excluded research that was only available in abstract or poster forms, animal studies, non-English articles, non-RF technology, book chapters, case reports, unclear diagnosis, and pediatric population.

Data Extraction and Syntheses

Data syntheses and analyses were performed, including assessment of the risk of bias or quality of individual studies, outcomes assessment, and qualitative and quantitative analysis. 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, RF technique (pulse vs. conventional), temperature range and duration, duration of pain relief, secondary outcomes, side effects, and conclusions. We also extracted the mean and standard deviations for the pain scores when reported. If not reported, we included the article for thorough analysis and additional discussion purposes.

Quality of Evidence

The quality of each individual article used in this analysis was assessed using the Cochrane Review rating system (Table 1) and the Interventional Pain

Table 1. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Abhinav et al. (2012)	TN	70	50.3	34.3	Retrospective study	PSR	Trigeminal nerve	20/23 (87%) MS patients reported only no pain or mild pain post-PSR; 44/47 (93.6%) non-MS patients reported no pain or mild pain post-PSR	Patient satisfaction scores were good-excellent in 19/23 (82.6%) of MS patients; and in 38/47 (80.9%) of non-MS patients.	None reported	Outcome after PSR is generally good or excellent in both MS and non-MS patients with TN
Adler et al. (2009)	TN	46	78	37	Prospective observational study	CyberKnife radiosurgical rhizotomy	Trigeminal nerve	85% of patients had complete disappearance of TN; mean latency of 5.2 weeks. Pain relief began 1 week post-therapy for most patients	39/47 (83%) patients had no or mild non-bothersome facial numbness post-therapy. 61% patients became pain-free, without new development of facial numbness, and discontinued anticonvulsants.	TN recurred in 1 patient. 7/41 patients who had single RS rhizotomy had significant new ipsilateral facial numbness.	Optimized non-isocentric CyberKnife RS rhizotomy results in high rates of pain relief.
Akbas et al. (2016)	Facial pain syndromes	27	56	33	Retrospective study	PRF	Sphenopalatine ganglion	35% of patients had complete pain relief; 42%, mild-moderate pain relief; 23%, no pain relief	N/A	None reported	PRF is effective in treating intractable chronic face/head pain.
Chen et al. (2019	TN	37	59.8	35.1	Prospective observational study	RF rhizotomy; 65°C for 100s + 70°C for 100s	Trigeminal nerve	25/37 (67.6%) patients responded to therapy; VAS scores decreased ≤ 2 (post-therapy)	Trigeminal nerve volume was significantly higher in patients who did not respond to RF therapy	N/A	Majority of TN patients responded to RF rhizotomy; those that didn't have increased trigeminal nerve volume, which may be predicted using MRI.
Chen et al. (2016)	TN	43	58.8	37.2	Prospective observational study	RF rhizotomy; 60°C for 60s	Trigeminal nerve	77.8% responded to therapy, pre-procedure VAS - post-therapy VAS ≥ 6	CN V volume in affected nerve was smaller, fractional anisotropy was lower, apparent diffusion coefficiency was higher, and radial diffusivity was higher.	N/A	Majority of TN patients responded to RF rhizotomy. Demyelination and decreased CN V volume are major microstructural abnormalities in TN caused by neurovascular compression.
Ding et al. (2016)	TN	108	57.9	38	Prospective observational study	RF; 75°C for 120s	Trigeminal nerve	Pain relief was 89.8% at 1 year, 85.71% at 2 years, and 81.63% at 3 years	There were 7 procedural failures due to anatomical variations.	1 case of facial hematoma; 51.92% had extraterritorial numbness, diminished corneal reflex, or masseter weakness.	RFA relieves pain in TN regardless of approach. Mandibular angle approach delivers more pain relief, better quality of life scores, and lower recurrence rates at 3 year follow-up.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Ding et al. (2018)	TN	80	CRF; 56.4 PCRF; 55.8	CRF; 37.5 PCRF; 35	Retrospective study	CRF; 68°C for 180s PCRF; 42°C for 600s + 68°C for 180s	Trigeminal nerve	VAS scores in both groups lower than pre-intervention scores. PCRF VAS scores were significantly lower than CRF at 1 month to 2 years of follow-up	PCRF group had 5% recurrence rate. CRF group had 20% recurrence rate.	Facial numbness, facial hematoma, weakness of masticatory muscles, weakened corneal reflex, intracranial hypotension headache.	PRF combined with CRF relieves pain, increases late-stage pain remission rate, reduces complications, and reduces rate of recurrence.
Elawamy et al. (2017)	TN	43	CRF; 56 PRF; 55.7	CRF; 54.5 PRF; 50	Randomized prospective study	CRF; 75°C for 270s PRF; 42°C for 10 mins	Trigeminal nerve	VAS scores most reduced in CPRF group > CRF > PRF CPRF: 9.15+/-1.13 pre-intervention; 0 after 24 months	CPRF had highest satisfaction rates > PRF > CRF. Patients in PRF group continued to use carbamazepine after procedure; patients in CPRF and CRF groups stopped using carbamazepine by 6 months follow-up.	Numbness and weakness, paresthesia.	Pain relief was best in CPRF group, followed by CRF group, followed by PRF group.
Erdine et al. (2007)	TN	40	CRF; 60 PRF; 64.2	52	Randomized prospective study	CRF; 70°C for 60s PRF; 42°C, 2 bursts of 20ms applied for 120s	Trigeminal nerve	CRF: Median VAS was 1 at 1 day post-therapy. At 3 months, median VAS was 0.5. At 6 months, median VAS was 0.5. PRF: Only 2/20 (10%) patients had decreased VAS 1 day post-therapy; with median VAS of 8. At 3 months, median VAS was 8.5. These patients then received CRF, and median VAS at 6 months was 1	CRF; pre-therapy median patient satisfaction score (PSS) was 1.5; post-therapy day 1 PSS was 8; PRF; pre-therapy median PSS was 1; post-therapy day 1 PSS was 1. After this group received CRF, PSS was 8.	Moderate headache for 24h. In all patients who received CRF, mild hypoesthesia and paresthesia occurred after the procedure.	CRF is superior to PRF for pain management of TN.
Fang et al. (2015)	TN	60	Std V; 63.4 High V; 60.5	Std V; 46.7 High V; 43.3	Randomized prospective study	Std V; 42°C for 240s High V; max 42°C for 240s	Trigeminal nerve	Standard voltage: 11 (41%) patients had favorable outcome up to 6 months; 5 patients achieved total pain relief. 16 (59%) patients did not achieve any relief. High voltage: 18 (69%) patients had significant pain score decreases 1 year after treatment. 31% (8 patients) failed to respond to treatment. Effective rates of high voltage group were higher than that of the standard voltage	Standard voltage: 6 patients achieved numeric rating scale relief > 50% and their carbamazepine dose was reduced. High voltage: 13 of 18 patients who had significant pain score decreases stopped using carbamazepine.	In non-responders who underwent RF thermocoagulation, hypesthesia in the trigeminal area and masticatory muscle weakness was reported.	High voltage RFA is as safe as standard voltage RFA and is more effective in treating TN.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Fang et al. (2014)	TN	20	60	45	Prospective observational study	RF; 2 cycles of 42°C, 2Hz for 120s	Trigeminal nerve	7 (35%) patients experienced good effect with CT-guided PRF. Numeric rating scale of pain score was 0 starting at 2 weeks and up to 1 year. The other 65% did not experience >50% improvement, with 10 patients (50%) experiencing no pain relief. Numeric rating scale of pain score was 8 after 2 weeks and 0 after conventional RFA after 1 year	Of the 13 (65%) patients who experienced no pain relief, 10 patients needed large doses of anticonvulsants to relieve pain.	None reported	CT-guided PRF is not as effective compared to conventional RFA. However, CT-guided PRF is associated with fewer complications.
Fraioli et al. (2009)	TN	158	N/A	N/A	Retrospective study	RF; 90-95°C for 10 mins	Trigeminal nerve	Complete pain relief was obtained immediately after procedure in all patients. At average follow-up of 8.8 years, recurrences occurred in 12 (7.6%) patients. In 10 of these patients, the procedure was repeated successfully	Selective anesthesia was achieved in 3rd division of trigeminal nerve in all but 2 patients.	9 experienced cheek hematoma, 6 patients experienced hypoesthesia after the procedure, 6 experienced masseter dysfunction, 2 experienced 1st/2hd division of trigeminal nerve hypoanesthesia, 1 had transient 6th nerve palsy, 1 had orbital hematoma	RFA for pain relief of TN is immediately effective, has low rate of recurrence, and can produce selective anesthesia in 3rd division of trigeminal nerve.
Guo et al. (2016)	TN	24	64	25	Prospective observational study	RF V1; 60-65°C for 90s V2; 72°C for 90s	Trigeminal nerve	22 (91.7%) patients had decreased VAS scores from 10 to 3 within 10 days post-therapy. 2 (8.3%) patients reported decreased VAS scores from 10 to 3 by 8 weeks post-therapy. During the 12 and 24-month follow-up, 20 (83.3%) patients experienced no pain recurrence. 4 (16.7%) patients experienced pain recurrence 1-2 years after surgery	12.5% (3) patients required 2-3 punctures to target the foramen ovale	25% (6) patients experienced mild numbness post-therapy; facial numbness usually subsided within 6 months	Stereotactic approach combined with 3D CT reconstruction modeling can improve accuracy, safety, and efficiency of percutaneous RFA in TN patients for whom the foramen ovale is difficult to access.
Hamid et al. (1993)	TN	127	N/A	70	Retrospective study	N/A	Trigeminal nerve	67% of patients received excellent pain relief, 19% received "good" pain relief, 14% had poor pain relief	N/A	1 case of carotid artery puncture.	RFA is a low-cost procedure with low morbidity and no mortality to treat TN.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Huang et al. (2016)	TN	80	N/A	32.5	Prospective observational study	Pulse width 20ms, +2 degrees from 60°C to 66°C every 60s	Trigeminal nerve	Excellent pain relief achieved in 70/80 (98.8%) patients immediately after the procedure and after 3 months. 78/80 (97.5%) experienced tolerable numbness	N/A	1 patient lost corneal reflex, 14 patients experienced mildly decreased corneal reflex, 2 patients felt foreign body sensation in ipsilateral eye	Temperature controlled RFA to V1 is effective and safe in treating TN.
Kanpolat et al. (2001)	TN	1600	56.8	47.9	Retrospective study	RF; 55 to 70°C	Trigeminal nerve	Early (< 6 months) pain recurrence was observed in 123 patients (7.7%), whereas late (> 6 months) recurrence was reported in association with 278 patients (17.4%). The overall pain recurrence rate was 25.1% during an average follow-up period of 68.1 6 66.4 months (range, 12–300 months)	1216 patients (76%) were managed with a single treatment and 384 patients (24%) with multiple RF procedures	Diminished corneal reflex was observed in 91 patients (5.7%), masseter dysfunction was observed in 66 (4.1%) patients, painful dysesthesia occurred in 28 patients (1.8%)	The most important aspect in the selection of the procedure is its suitability to the patient's status, such as age and type and distribution of pain.`
Koning et al. (2014)	TN	28	68	50	Retrospective study	RF; 70°C for 60s	Trigeminal nerve	An initial treatment effect of 89% was observed, 60% sustained at 12-month follow-up	A lower sensory stimulation threshold during treatment was associated with better patient satisfaction ($P = 0.016$), improved pain relief ($P = 0.039$), and trended toward more hypesthesia ($P = 0.077$)	Major side effects were hypesthesia (56%), dry eye (20%), and masseter muscle weakness (12%)	This study supported the high efficiency of RF treatment, but there was a high level of side effects
Kosugi et al. (2015)	TN	89	69.4	33.7	Retrospective study	RF; 90°C for 180s	Trigeminal nerve	V3 TN: 80.2% at 12 months and 54.9% at 24 months. V2 TN and V2 + V3 TN: 40.5% and 49.3% at 12 months, and 19.6% and 17.1% at 24 months, respectively. The median pain-free durations for patients with V2 TN, V2 + V3 TN, and V3 TN were 9, 12, and 36 months, respectively.	Of 37 procedures for V2 TN, 28 (75.7%) patients required repeated PRT of the Gasserian ganglion or PRT of infraorbital nerve from 3 to 48 months after the initial procedure	Major complications included 10 cases of weakness of masticatory muscles (12.2%), 4 intolerable dysesthesia (4.9%), and 4 eye problems without keratitis (4.9%)	Although the immediate success rate is high, the durability of pain relief of PRT for 2nd-division TN and multiple-division TN could not be expected to be as great as for isolated trigeminal 3rd-division neuralgia

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Li et al. (2012)	TN	60	55.6	40	Randomized prospective study	Short-duration CRF: 75°C for 120-180s Long-duration CRF: 75°C for 240-300s PRF: 42oC for 10 mins	Trigeminal nerve	Short-duration CRF: pain persisted in 3 patients at 1 day, 1 patient at 7 days and 4 patients at 6 months Long-duration CRF: pain persisted in 1 patient at 1 day, 1 patient in 7 days and 3 patients at 6 months PRF: pain persisted in 5 patients at 1 day, 0 patients at 7 days and 3 patients at 6 months	There were no significant differences in quality of life at three, six, and 12 months after RF treatment between groups ($p > 0.05$).	All patients (100%) experienced facial dysesthesia on the day following the RF procedure, one patient in each group had mild discomfort in the ipsilateral eye	A shorter CRF exposure time may result in less damage to the ganglion with comparable efficacy for pain relief.
Liu et al. (2005)	TN	18	N/A	N/A	Retrospective study	RF; 60-75°C for 60-90s	Trigeminal nerve	Early (< 6 months) pain recurrence was observed in 2 patients (11.1%), whereas late (> 6 months) recurrence was reported in 3 patients (16.7%).	Five cases experienced partial pain relief, but required medication at a lower dose than in the preoperative period.	N/A	3D-CT foramen ovale locations can raise the successful rate of puncture, enhance the safety, and reduce the incidence rate of complication.
Liu et al. (2016)	TN	84	69.2	36	Retrospective study	RF; 70 to 75°C for 90s	Trigeminal nerve	The survival rates of pain free without medications at 1, 2, and 3 years after PRT were 85%, 68%, and 54%, respectively, with a nearly 80% rate for effective pain control (pain free, or pain controlled with medications) during the study period.	Fourteen of 17 patients who required retreatment selected additional PRT, resulting in 8 patients (57%) in excellent outcome and 12 (86%) in effective pain control.	The complication rate was 15%, including 6 patients with masseter weakness, 2 patients with impaired taste acuity, 4 patients with absent or decreased corneal reflex, 1 patient with oculomotor paralysis.	Percutaneous radiofrequency thermos-coagulation is a safe and efficacious therapeutic method for patients with persistent or recurrent TN after surgery.
Luo et al. (2013)	TN	28	N/A	N/A	Retrospective study	Autopulse mode with 42°C, 2 Hz and 120s	Trigeminal nerve	39% of patients achieved >50% reduction in numeric rating scale up to month 6 post-therapy, although six patients relapsed at 7–11 months	The intraoperative radiofrequency output voltage and electric field intensity were both significantly lower in the ineffective group than in the effective group	No serious intraoperative or post-therapy complications were noticed	Pulse output voltage and electric field intensity may be the most important parameters affecting the outcome of treatment

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Luo et al. (2017)	Refractory neuralgia of infraorbital nerve	60	63	12.5	Randomized prospective study	Std V group: 42°C, 2Hz, 120s, 2 times High V group: 42°C, max V, 120s, 2 times	Infraorbital nerve	In the standard voltage group, response rate was 67% at one month, 67% at 3 months, 63% at 6 months and 60% at 1 year post-therapy. In the high-voltage group, response rate was 90% after one month, 3 months, 6 months and 1 year post-therapy	Among the patients in the high voltage group who responded to the high voltage PRF, 74% had complete pain relief and thus discontinued anti-epileptic carbamazepine and did not experience recurrent pain during the one-year follow-up	Four patients (13%) in the standard voltage group and 8 patients (27%) in the high voltage group experienced mild numbness in the innervation area of the infraorbital nerve after the operation.	High voltage radiofrequency was effective and safe for patients with refractory neuralgia of the infraorbital nerve and could become a treatment option in patients who do not respond to conservative treatment.
Mathews et al. (2000)	TN	258	N/A	N/A	Prospective observational study	N/A	Trigeminal nerve	At 6 months, excellent or good pain relief occurred in 87%; Recurrence of pain required re-operation in 12%; Recurrence of pain did not require re-operation in 14%	There were no mortalities, no significant morbidity and a low rate of minor complications.	Dysesthesia developed in 20 patients (8%); corneal analgesia developed in 8 patients (3%); "Anesthesia dolorosa" developed in 5 patients (2%).	With the use of this specific diagnostic and management algorithm, patients with trigeminal neuralgia can be successfully managed with radiofrequency thermal rhizotomy.
Meng et al. (2009)	TN	26	61	34.6	Prospective observational study	VR assisted RF; 55-75°C at 0.5 min-1.0 min cycles, total of 3.5-5. mins	Trigeminal nerve	Complete pain relief was experienced throughout the whole sample. Only one patient needed a second RF trigeminal rhizotomy for pain recurrence after 16 months	Virtual reality assures accurate direction of treatment and allows real-time manipulation.	There were no noted post-therapy complications.	Accuracy and success rate of RF trigeminal rhizotomy can be improved with virtual reality
Meng et al. (2008)	TN	48	70	37.5	Prospective observational study	RF; 65, 75, 80°C for 60s, 2-3 times	Trigeminal nerve	Thirty-six (75%) patients attained 75% to 100% pain relief, 7 (14%) attained 50% to 75% pain relief, and 5 (11%) had 30% to 50% relief.	Heart rate decreased during oval foramen puncture and recovered spontaneously after pausing or ceasing the manipulation in 6 patients. Heart rate in the other 42 patients, however, increased markedly.	No relevant cardiovascular or cerebrovascular sequela was observed.	Greater anticipatory awareness should be directed toward pressor than depressor responses during percutaneous RF thermo-coagulation therapy of primary trigeminal neuralgia.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Onforio et al. (1975)	TN	135	N/A	N/A	Retrospective study	RF; Coagulating current at 80°C for 30s	Trigeminal nerve	115/135 (85.2%) patients reported good analgesia with no return of pain after the first procedure. 16/135 (11.9%) patients reported fair to good analgesia with initial pain relief but recurrence of pain 2 weeks to 14 months post-therapy	Extracranial carotid injury should be virtually impossible, and any motor weakness of the fifth cranial nerve usually subsides.	56/135 (41.5%) of patients reported some degree of weakness. One patient reported sixth-nerve palsy and it resolved in 6 months. Two patients reported neuroparalytic keratitis.	Radiofrequency coagulation of the Gasserian ganglion and posterior root to be a safe and effective mode of treatment for patients with severe facial pain, particularly trigeminal neuralgia.
Sanchez-Mejia et al. (2005)	TN	12	68.6	25	Retrospective study	N/A	Trigeminal nerve	Following RFA, 21 to 50% of patients have recurrent TN and 15% require retreatment. Mean follow-up (months) was 60 (+/- 16) if RFA was the 1st intervention and 30 (+/- 10) if RFA was the last treatment	RFA was associated with the highest rate of retreatment (41.6%)	RFA was associated with the highest rate of new trigeminal numbness after a second procedure (42%).	Lower retreatment rates were seen with patients who initially underwent radiosurgery compared with microvascular decompression or RFA.
Taha et al. (1995)	TN	154	63	35	Prospective observational study	N/A	Trigeminal nerve	153 patients (99%) had pain relief after one procedure. Pain recurrence was 25% at 14 years, 15% within 5 years, 7% within 5 to 10 years and 3% within 10 to 15 years. The median pain free survival was 32 months for patients with mild hypalgesia and more than 15 years for patients with dense hypalgesia or analgesia.	Patients with analgesia had the lowest pain recurrence rate (20%) and the highest dysesthesia rate (36%).	35 patients (23%) reported some extent of facial sensory deprivation.	PSR has a high long-term success rate in patients with trigeminal neuralgia. Pain recurs in 25% of patients within 14 years of treatment; 95% of patients are satisfied with the long-term results of the procedure.
Tang et al. (2014)	TN	33	64.1	36.4	Retrospective study	RF; 75°C for 120s	Trigeminal nerve	Of the 30 patients with immediate pain relief, 19 patients (63.4%) maintained pain relief with 'excellent' results for the duration of their follow-up (mean 44.2 months, range 13–67). The remaining 11 patients (36.6%) who achieved pain relief after the second procedure had recurrent symptoms (mean time to recurrence 17.1 months, range 5–82).	The success rate of pain relief following a second PRT procedure was 75% at 1 year, 68% at 2 years and 68% at 5 years	All patients had mild-to-moderate facial numbness which gradually alleviated in all patients. Masseter weakness was reported in 3 patients and limited mouth opening in 1 patient.	Repeated RF procedures may achieve long-term pain relief with a minimal rate of complications in patients with medication-refractory TN as effectively as an initial RF procedure.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Tang et al. (2015)	TN	1137	61.5	40.6	Prospective observational study	RF; 75°C for 120s	Trigeminal nerve	Excellent pain relief was achieved 88% at 1 year, 79% at 3 year, 72% at 5 year, 65% at 7 year, 57% at 9 years, and 52% at 11 years	The pain recurrence was observed in 9 (22% of 42 patients) patients within V1 distribution, 31 (10.8% of 289 patients) patients within V2 distribution, 51 (18.1% of 288 patients) patients within V3 distribution	983 patients (84.7%) had facial numbness after the procedure, masseter weakness was in 91 (8%) patients, corneitis was observed in 29 (2.6%) patients	From our data, all different branches division of TN achieved comparable satisfactory curative effect; V2 obtained the best excellent pain relief, after RF procedure.
Telischak et al. (2018)	Atypical facial pain	15	N/A	N/A	Prospective observational study	RF; continuous 60°C for 60s, 2 times	Glosso-pharyngeal nerve	Five of 15 (33%) had good immediate and sustained pain relief (NRS reduction > 50% up to 12 months), while the other 10 (67%) patients had a suboptimal response (NRS reduction < 50% and/or duration < 3 months).	We found that using our RF time and temperature protocol we were able to ablate the nerves enough to cause significant relief without completely damaging the nerve, causing profound numbness and complete loss of motor function.	Mild throat numbness in 50% and mild masticatory weakness in 15%.	C-arm CT and fluoroscopic-guided RFA had 100% technical success with needle guidance to previously difficult locations, specifically the foramen rotundum and the styloid process.
Tronnier et al. (2001)	TN	206	N/A	N/A	Retrospective study	N/A	Trigeminal nerve	There was a 50% risk for recurrence of pain 2 years after percutaneous RF rhizotomy.	Patients without sensory impairment after microvascular decompression were pain free significantly longer than patients who experienced post-therapy hypesthesia or partial rhizotomy.	N/A	Microvascular decompression proved to be a more effective and long-lasting procedure for patients with typical TN than RF rhizotomy.
Wang et al. (2019)	TN	38	66.8	52.6	Retrospective study	RF 60°C for 120s 65°C for 120s 70°C for 120s	Trigeminal nerve	The experiment group experienced 100% pain relief at 7 days and 3 months, 94.1% at 6 months and 88.2% at 1 year. Control group showed 100% pain relief at 7 days and 3 months, 90.5% at 6 months and 85.7% at 1 year.	Three patients experienced pain recurrence, respectively at five, six, and nine months after operation. Five patients subsequently received repeated percutaneous RF through the foramen rotundum and got satisfied post-therapy pain relief.	All patients experienced mild facial numbness in the second branch of the trigeminal nerve immediately after surgery, and this symptom gradually subsided within one to three months. There were 5 cases of facial hematomas in the control group and 1 case in the experimental group.	Computer-assisted puncture template shows great potential in enhancing the safety and accuracy ablation of RFT for isolated V2 TN.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Xu et al. (2006)	TN	54	N/A	N/A	Randomized clinical controlled trial	N/A	Trigeminal nerve	Immediate complete pain-relief rate of the navigation group was 100%, whereas it was 95% in the control. The proportion of sustained pain-relief rates at 12, 24 and 36 months after the procedure were 85%, 77%, and 62% in the navigation group, and 54%, 40%, and 35% in the control.	Annual recurrence rate in the first and second years were 15% and 23% in the navigation group, and 46%, 60% in the control group.	No side-effect and complication was noted in the navigation group except minimal facial hypesthesia	Neuronavigator-guided RF is a safe and promising method for treatment of intractable TN with better short- and long-term outcomes and lower complication rate than RF without neuronavigation
Xue et al. (2015)	TN	25	64.4	48	Prospective observational study	RF; 75°C for 4 mins	Trigeminal nerve	22 patients (88%) indicated post-therapy VAS scores of 0, indicating complete resolution of pain after the procedure. Recurrence was observed in 9 patients (36%) at follow-up (mean follow-up period 14/74 +/- 11.34 months).	All patients with recurrent symptoms were successfully managed with repeat thermos-coagulation, as of the time of publication. Thus, the total reoperation rate was 44%.	Mild persistent facial numbness was noted in 23 patients and no other complications were observed.	3D image-guided RF thermos-coagulation may help mitigate the risk of iatrogenic damage to the ophthalmic and mandibular nerves through repeated movements of the needle intra-cranially—which could result in weakened mastication and/or corneal damage.
Yang et al. (2007)	TN	12	53.8	58.3	Prospective observational study	RF; 55-75°C for 30-90s	Trigeminal nerve	Post-therapy pain was minimal and resolution of TN symptoms was achieved in all 12 patients acutely. Symptoms recurred in 2 of the 12 patients (average follow-up period = 13 weeks)	With the assistance of neuronavigation system, we were able to place RF catheter tip precisely in central part of trigeminal ganglion, which theoretically minimized the energy required to eliminate the electric stimulation elicited TN symptoms.	Facial hypesthesia occurred in all 12 patients and transient masseter weakness occurred in 2 patients	Neuronavigation system helped significantly in improving acute successful rate and avoiding major complications during RF thermos-coagulation therapy in patients with TN.
Yao et al. (2016)	TN	1354	59.2	48.6	Randomized prospective study	RF; 62, 65 or 68°C for 180s	Trigeminal nerve	The percentage of patients with BNI scores I–III (satisfactory) at discharge was 100%, with the highest percentage of BNI score I (excellent) in Group C (68°C group). At 9 years, the percentage of patients absolutely without pain was >50% in Groups B (65°C) and C (68°C) but only 40.6% in Group A (62°C).	During follow-up, TN recurrence was observed in 122 (27.35%), 91 (20.78%), and 59 (12.55%) patients within the 62, 65, and 68°C groups, respectively.	During RF, 52 (3.84%) patients experienced mouth penetration, 12 patients experienced external auditory meatus penetration with bleeding, and 4 patients experienced tympanic membrane perforation	RF at 68°C is recommended for treating V2/V3 TN, and RF at 62 to 65°C is optional for patients who wish to minimize the complications such as facial numbness.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Yao et al. (2016)	TN	62	53.2	43.5	Prospective observational study	RF; 68 or 75°C for 180s	Trigeminal nerve	The pain-free rate was 95.1% at 75°C and 93.5% at 68°C at 1 year, 84.3% and 78.1% at 3 years, and 80.7% and 74.4% at 5 years.	There were 10 and 13 cases of recurrence, respectively, and 6 cases of bilateral recurrence.	Facial numbness persisted in the 68°C group in 8 (12.9%) patients and in the 75°C group in 49 (79.0%) patients.	RF at lower temperatures may be preferable, and a temperature of 68°C can be recommended.
Yao et al. (2016)	TN	56	56.1	46.4	Randomized clinical controlled trial	CRF; 62°C for 240-360s CRF + PRF; CRF followed by 42°C for 8 mins	Trigeminal nerve	In groups A and B, a BNI score of I was found in 81.6% and 92.0% at 1 year, 68.4% and 92.0% at 2 years, and 68.4% and 83.6% at 3 years.	HRQoL scores of all the study patients were low before the thermal ablation procedures and high after the procedures	14 patients had corneal hypoesthesia (11 and 3 group A and group B patients; $P<0.05$). Facial numbness was observed in 3 (10.7%) and 2 (7.1%) groups A and B patients ($P>0.05$)	PRF can decrease the recurrence rate of TN, decrease the incidence rate and shorten the recovery time of corneal hypoesthesia, and lead to increased quality of life.
Zakrzewska et al. (1999)	TN	48	57	39.9	Prospective observational study	RF; 350mA of current at 70-80°C for 300s	Trigeminal nerve	At 3 years, 12% of patients reported that they had atypical facial pain	Three years post-therapy, there was a reported 48% reduction of depression cases and a 36% decrease in anxiety cases	8% reported problems with eating and with eye problems	Careful selection of patients for surgery using objective assessments will decrease morbidity and improve satisfaction. Psychological, sociological and patients' views must be included in evaluations.
Zhang et al. (2011)	TN	62	N/A	N/A	Retrospective study	N/A	Trigeminal nerve	Both groups attained good pain relief rate within the first two years of follow-up: 92.3%, 84.6% and 82.6%, 69.6% respectively ($P > 0.05$). After 2 years, the virtual reality or neuro-navigation assisted RTR group (group B) demonstrated higher pain relief rates of 82.5%, 76.2% and 68.8% at 3, 4 and 5 years after operation respectively, while those in group A was 57.2%, 49.6%, and 36.4% ($P < 0.05$).	N/A	None reported	RTR was effective in alleviating the pain of TN cases suffering from unsuccessful MVD management. With the help of virtual reality imaging technique or neuronavigation system, the patients could attain better long-term pain relief.

Table 1con't. *Characteristics of studies included in systematic review.*

Author (year)	Clinical Diagnosis	Sample size (N)	Age, Mean (years)	Male (%)	Study Design	Ablation Technique	Ablated Nerve	Duration of Pain Relief	Secondary Outcome	Side Effects	Conclusion
Zheng et al. (2015)	TN	27	56.3	29.6	Prospective observational study	RF; 75°C for 120s, 3 cycles	Trigeminal nerve	The immediate success rates at 3 days after procedure were 100%, and a pain-free status was still observed in 25 patients (92.6%) at 12 months.	The VAS score of facial dysesthesia was increased in the post-therapy follow-up visits compared with baseline.	Temporary masticatory dysfunction was present for a short time after the procedure, residing within 12 months.	CT-guided PATIENT-RFT for TN remains an effective and safe surgical operation.
Zheng et al. (2015)	TN	27	56.3	29.6	Prospective observational study	RF; 75°C for 120s, 3 cycles	Trigeminal nerve	The immediate success rates at 3 days after procedure were 100%, and a pain-free status was still observed in 25 patients (92.6%) at 12 months.	The VAS score of facial dysesthesia was increased in the post-therapy follow-up visits compared with baseline.	Temporary masticatory dysfunction was present for a short time after the procedure, residing within 12 months.	CT-guided PATIENT-RFT for TN remains an effective and safe surgical operation.
Zhou et al. (2016)	TN	55	49.3	63.6	Retrospective study	RF; 70°C for 100s	Trigeminal nerve	At 2-year follow-up, 11 patients (20%) had excellent pain relief, 31 patients (56.4%) had good pain relief.	N/A	N/A	RF is a satisfactory treatment strategy for patients with TN

RFA: radiofrequency ablation; HA: headache; TN: trigeminal neuralgia; MS: multiple sclerosis; PSR: partial sensory rhizotomy; PRF: pulsed radiofrequency; CRF: continuous radiofrequency; PRT: percutaneous radiofrequency thermocoagulation

Management Techniques–Quality Appraisal of Reliability and Risk of Bias Assessment Tool (IPM-QRB) for RCTs (Table 2), and Interventional Pain Management Techniques–Quality Appraisal of Reliability and Risk of Bias Assessment Tool for non-randomized or observational studies (IPM-QRBNR) (Table 3).

Utilizing the Cochrane Review criteria, studies meeting at least 9 of the 13 inclusion criteria were considered high quality. Those meeting 5 to 8 criteria were considered moderate quality, and those meeting fewer than 5 criteria were considered low quality and were excluded. Based on the IPM-QRB and IPM-QRBNR criteria, studies meeting the inclusion criteria but scoring less than 16 were considered low quality and were excluded; studies scoring from 16 to 31 were considered moderate quality, and studies scoring from 32 to 48 were considered high quality and were included. Methodologic quality assessment of each manuscript was performed by 2 review authors. The assessment was carried out independently in an unblinded, standardized manner to assess the methodologic quality and internal validity of all the studies considered for inclusion. If discrepancies occurred, a third reviewer performed an assessment, and a consensus was reached. Further remaining issues were discussed by all reviewers and were then resolved.

Results

Search Results

Our final search methodology yielded 677 studies that investigated the use of RF treatment for facial pain. The search and study selection flow chart is displayed in Fig. 1. We identified 637 publications after duplicates were removed. These studies were screened based on our inclusion and exclusion criteria. A total of 44 studies, comprised of 8 RCTs (14,15,17-22), 18 prospective (12,13,23-36), and 18 retrospective (16,18,37-53), are summarized in Table 4.

Targeted Nerves

A total of 44 of the included 44 publications had subjects with a diagnosis of facial pain. The trigeminal nerve was the most commonly targeted nerve using CRF or PRF treatment. Another group of nerves identified as sphenopalatine ganglion, infraorbital nerve, and glossopharyngeal nerve were

Table 2. *Methodological quality assessment of 8 randomized trials utilizing Cochrane review criteria.*

	Elawamy (2017)	Erdine (2007)	Fang (2015)	Li (2012)	Luo (2017)	Xu (2006)	Yao (2016)	Yao (2016)
Randomization adequate	Y	Y	Y	Y	Y	Y	Y	Y
Concealed treatment allocation	Y	Y	Y	Y	Y	Y	Y	Y
Patient blinded	Y	Y	Y	Y	Y	Y	Y	Y
Care provider-blinded	Y	Y	Y	Y	Y	Y	Y	Y
Outcome assessor blinded	Y	Y	Y	Y	Y	Y	Y	Y
Drop-out rate described	Y	N	Y	Y	Y	Y	Y	Y
All randomized participants analyzed in the group	N	Y	Y	Y	Y	Y	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	N	U	Y	Y	Y	Y	Y	Y
Co-interventions avoided or similar	Y	Y	Y	Y	Y	Y	Y	Y
Compliance acceptable in all groups	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)	Irrelevant (Procedure)
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y	Y	Y	Y
Are other sources of potential bias likely	N	U	U	U	N	U	N	N
Score	9/12	9/12	11/12	11/12	11/12	11/12	11/12	11/12

Y = Yes; N = No; U = Unclear

also ablated in 3 of the publications included in this review (19,34,38).

Quality of Evidence

Of the 44 manuscripts meeting inclusion criteria, 8 were randomized trials (14,15,17-22). Tables 1 and 2 show the methodologic quality assessment and risk of bias in each of these trials utilizing the Cochrane review criteria and the IPM-QRB criteria, respectively.

Assessment by the Cochrane review criteria showed that all of the trials were high quality. However, assessment by IPM-QRB showed only 2 trials to be of high quality (21,22), with the remaining 6 trials of moderate quality (14,15,17-20). Table 3 shows the assessment of the included nonrandomized or observational studies, including case reports, utilizing IPM-QRBNR criteria. A total of 36 studies were included in this category. However, 5 of these were shown to be of high quality. The remainders were moderate-quality studies.

Outcome

Pain outcomes were reported as Visual Analog Scale (VAS) or Numeric Rating Scale (NRS) scores 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 outcomes include patient satisfaction, quality of life improvements, decrease in oral medication use, and recurrence rates.

Table 3. *Methodological quality assessment of 8 randomized trials utilizing IPM – QRB.*

		Elawamy (2017)	Erdine (2007)	Fang (2015)	Li (2012)	Luo (2017)	Xu (2006)	Yao (2016)	Yao (2016)
I.	Trial Design And Guidance Reporting								
1	CONSORT or SPIRIT	0	0	0	0	0	0	0	0
II.	Design Factors								
2	Type and Design of Trial	2	2	2	2	2	0	2	2
3	Setting/Physician	2	2	2	2	2	1	2	2
4	Imaging	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
5	Sample Size	1	1	2	1	1	2	2	3
6	Statistical Methodology	1	1	1	1	1	1	1	1
III.	Patient Factors								
7	Inclusiveness of Population	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
8	Duration of Pain	2	2	2	2	2	2	2	2
9	Previous Treatments	0	2	0	0	0	0	1	1
10	Duration of Follow-up with Appropriate Interventions	3	1	2	2	2	1	2	3
IV.	Outcomes								
11	Outcomes Assessment Criteria for Significant Improvement	2	2	2	4	2	2	2	4
12	Analysis of all Randomized Participants in the Groups	2	2	2	2	2	2	2	2
13	Description of Drop Out Rate	0	0	1	1	1	1	1	2
14	Similarity of Groups at Baseline for Important Prognostic Indicators	0	2	2	2	2	2	2	2
15	Role of Co-Interventions	0	1	0	1	1	1	1	1
V.	Randomization								
16	Method of Randomization	2	1	2	2	2	2	2	2
VI.	Allocation Concealment								
17	Concealed Treatment Allocation	1	1	1	1	2	2	2	2
VII.	Blinding								
18	Patient Blinding	1	1	1	1	1	1	1	1
19	Care Provider Blinding	1	1	1	1	1	1	1	1
20	Outcome Assessor Blinding	1	1	1	1	1	1	1	1
VIII.	Conflicts Of Interest								
21	Funding and Sponsorship	0	0	0	1	1	0	2	2
22	Conflicts of Interest	0	0	0	0	3	0	3	3
TOTAL		21	23	24	27	29	22	32	37

Discussion

Pain Relief and Secondary Outcome: Efficacy of RF Treatment in RCTs

In the RCTs, we analyzed the trend of results between different treatment groups were fairly consistent. Pain outcome in most trials were measured using VAS and NRS. Both these measurements of pain have proven to be reliable methods of detecting changes in pain levels (54). However, NRS has been shown to be more reliable in illiterate populations when compared with VAS (54). In addition to VAS

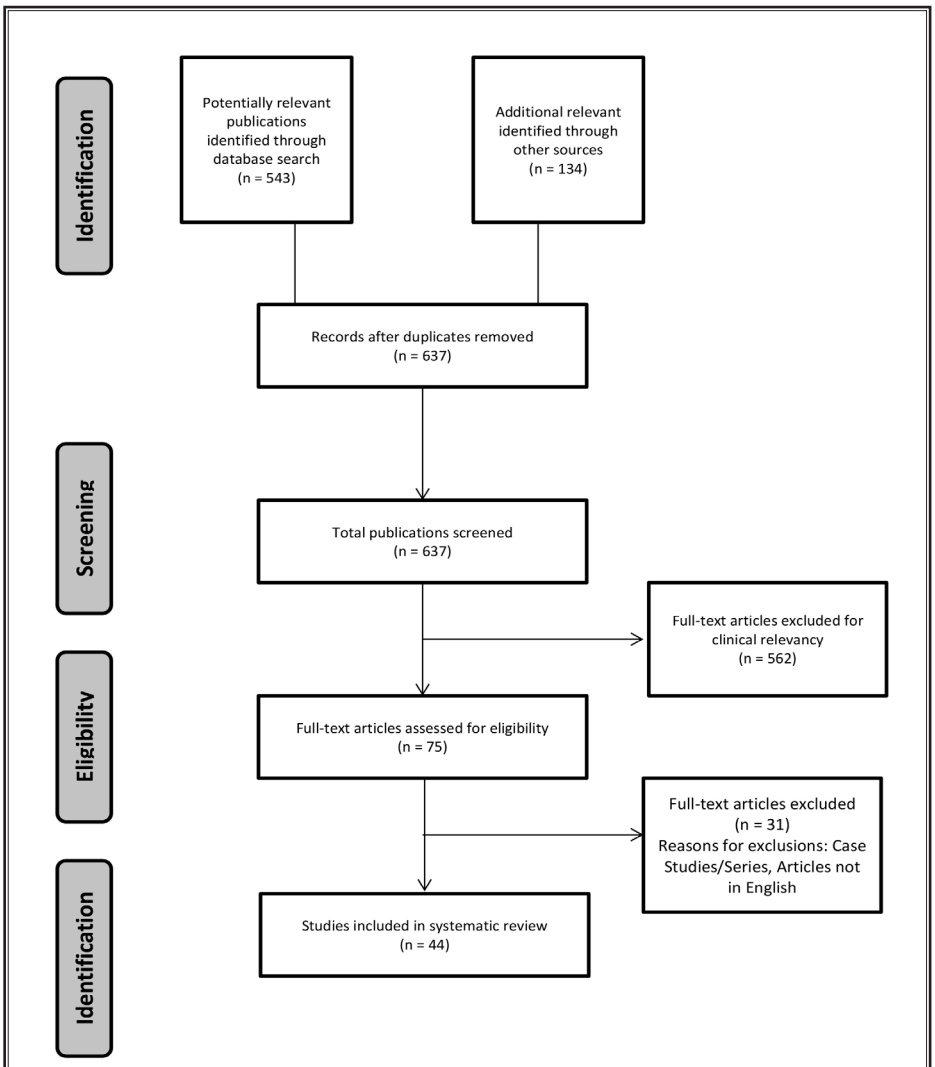

Fig 1: *Study Selection Flow Chart for Manuscripts Included in Systematic Review*

and NRS, some studies used Barrow Neurological Institute (BNI) pain intensity score, a more specialized measurement to trigeminal neuralgia, to quantify pain improvement (21,22). Of 2 clinical trials that utilized VAS to measure the primary outcome, there was a dramatic decrease of more than 90% in VAS scores between baseline and postprocedure time points of 6 months and 24 months (14,15). Most effective treatment groups in these trials show significant NRS reduction, less persistence of pain, and higher response rates in the majority of patients receiving treatment in short- and long-term outcomes (17-20). BNI scores were excellent in patients receiving high-temperature treatment regimen and combined CRF and PRF treatments (21,22). BNI scores remained high over long-term follow-up periods (21). Commonly assessed secondary outcomes included patient satisfaction, quality of life improvements, decrease in oral medication use, and recurrence rates. Satisfaction levels were consistent with CRF being more satisfactory than PRF (14,15). One study that additionally assessed combination therapy showed combined treatment to be the most satisfactory compared with CRF or PRF alone (15). Studies involving high-voltage PRF groups not only showed efficacy in decreasing pain but also showed significant reduction of oral medication use postprocedure (17,19). Quality of life improvements were significant across all treatment groups, including short- and long-duration CRF, PRF, combined CRF and PRF treatment groups (18,22). Recurrence rates postprocedure was consistently higher in treatment groups receiving lower temperature regimens (21,22).

Duration of Analgesic Effect: Short-Term Pain Relief

Short-term pain relief displayed promising results in our studies but did not necessarily correlate with good long-term outcomes. Acute resolution of symptoms immediately after the procedure was high in our studies, with values of 89%, 91%, 99%, and 100% (20,25,27,42). Other studies concluded resolution of symptoms at 100% in 3 days, 100% between 7 days and 3 months, and 85% in 5.2 weeks postprocedure (23,51,55). The presence of symptoms 6 months post-

Table 4. *Methodological quality assessment of 36 nonrandomized and observational studies utilizing IPM - QRB.*

		Abhinav et al (2012)	Adler et al (2009)	Akbas et al (2014)	Chen et al (2019)	Chen et al (2016)	Ding et al (2016)	Ding et al (2018)	Fang et al (2014)	Fraioli et al (2009)
I.	Study Design And Guidance Reporting									
1	STROBE or TREND Guidance	3	3	2	2	2	2	3	3	2
II.	Design Factors									
2	Study Design and Type	1	3	1	2	2	3	1	2	1
3	Setting/Physician	1	1	1	1	1	2	2	2	2
4	Imaging	NA	NA	3	NA	NA	2	2	2	2
5	Sample Size	0	2	0	0	0	1	0	0	1
6	Statistical Methodology	2	2	2	2	2	2	2	2	2
III.	Patient Factors									
7	Inclusiveness of Population	NA	NA	NA	NA	NA	NA	NA	NA	NA
8	Duration of Pain	2	2	2	2	2	2	2	2	2
9	Previous Treatments	2	1	2	2	1	1	2	1	1
10	Duration of Follow-up with Appropriate Interventions	1	3	1	1	1	4	4	2	2
IV.	Outcomes									
11	Outcomes Assessment Criteria for Significant Improvement	0	4	2	4	4	4	4	2	0
12	Description of Drop Out Rate	2	2	2	1	1	2	2	1	0
13	Similarity of Groups at Baseline for Important Prognostic Indicators	0	0	0	0	0	2	2	0	0
14	Role of Co-Interventions	2	2	2	2	2	2	2	2	1
V.	Randomization									
15	Method of Assignment of Participants	1	4	1	4	4	4	1	2	2
VI.	Conflicts Of Interest									
16	Funding and Sponsorship	2	0	2	2	1	1	2	1	1
TOTAL		19	29	23	25	23	34	31	24	19

procedure were 41%, 85%, and 90% across different studies (17,19,20). Short-term VAS score improvements were also proven. One study showed a VAS score of 0 immediately after the procedure in 88% of the sample (27). At 6 months, NRS scores decreased by greater than 50% in 39% of patients in one study, whereas it decreased by 33% in another study (34,46). Short-term recurrence rates were relatively low in all reporting studies, showing a rate of 7.7% and 11.1% in 6 months postprocedure (41,44). One study analyzed short-term BNI score improvement and reached a satisfactory score in 100% of the sample population immediately after the procedure (21).

Duration of Analgesic Effect: Long-Term Pain Relief

Long-term pain relief varied between different studies most likely due to various modalities of treatment regimens involving duration, temperature, and voltage. Resolution of symptoms 1 year postprocedure varied between 60% and 95.1% throughout different studies (12,17,19,22,26,51). Patients at 2-year follow-up

Table 4 con't. *Methodological quality assessment of 36 nonrandomized and observational studies utilizing IPM - QRB.*

		Guo et al (2016)	Hamid et al (1993)	Huang et al (2016)	Kanpolat et al (2001)	Koning et al (2014)	Kosugi et al (2015)	Liu et al (2005)	Liu et al (2016)	Luo et al (2013)
I.	Study Design And Guidance Reporting									
1	STROBE or TREND Guidance	2	2	3	2	3	3	3	3	2
II.	Design Factors									
2	Study Design and Type	2	1	2	1	1	1	1	1	1
3	Setting/Physician	2	1	2	1	2	1	1	1	1
4	Imaging	2	NA	NA	NA	NA	NA	2	NA	2
5	Sample Size	0	1	0	1	0	1	0	0	0
6	Statistical Methodology	2	2	2	2	2	2	2	2	2
III.	Patient Factors									
7	Inclusiveness of Population	NA	NA	NA	NA	NA	NA	NA	NA	NA
8	Duration of Pain	2	2	2	2	2	2	2	2	2
9	Previous Treatments	1	1	1	2	2	2	2	2	1
10	Duration of Follow-up with Appropriate Interventions	4	4	1	4	3	4	3	4	3
IV.	Outcomes									
11	Outcomes Assessment Criteria for Significant Improvement	4	4	2	4	4	4	4	4	2
12	Description of Drop Out Rate	2	2	1	2	1	2	1	2	1
13	Similarity of Groups at Baseline for Important Prognostic Indicators	0	0	0	0	0	0	0	0	2
14	Role of Co-Interventions	2	2	2	2	2	2	2	2	2
V.	Randomization									
15	Method of Assignment of Participants	2	1	2	3	1	3	3	3	1
VI.	Conflicts Of Interest									
16	Funding and Sponsorship	1	2	2	0	2	2	0	2	1
TOTAL		28	25	22	26	25	29	26	28	23

were more likely to be symptom-free, ranging between 83.3% and 92.3% (22,26,56). One study assessing VAS scores over 2 years resulted in a decrease from 9.15 at baseline to 0 at 2 years postprocedure (15). NRS scores followed similar trends as VAS, showing a decrease to 0 at 1-year follow-up in one study and a 33% NRS reduction in greater than 50% of the sample size at 1 year in another study (17,34). Long-term recurrence rates varied greatly between studies, ranging between 7.6% and 50% at follow-up periods between 6 months and 8.8 years (16,27,39,50). BNI results were also promising with long-term pain relief. One study showed greater than 50% of their patients having no pain at 9 years follow-up and another study categorized 92% of their patients into BNI I at 1 year postprocedure (21,22).

Outcomes with CRF Versus PRF Ablation Treatment

Studies comparing PRF and CRF with a combined treatment regimen showed the greatest efficacy in the combined treatment groups (15,22), followed by the CRF group, and finally the PRF group (15). One trial comparing CRF with PRF proved CRF to be more efficient than PRF for pain relief (14) and one trial further analyzed different duration of treatments, showing the group receiving long-term CRF treatment to be most effective, followed

Table 4 con't. *Methodological quality assessment of 36 nonrandomized and observational studies utilizing IPM - QRB.*

		Mathews et al (2000)	Meng et al (2009)	Meng et al (2008)	Onforio et al (1975)	Sanchez-Mejia et al (2005)	Taha et al (1995)	Tang et al (2014)	Tang et al (2015)	Telischak et al (2018)
I.	Study Design And Guidance Reporting									
1	STROBE or TREND Guidance	3	3	3	2	2	2	3	3	3
II.	Design Factors									
2	Study Design and Type	4	4	3	1	1	1	1	2	2
3	Setting/Physician	2	1	1	1	1	1	2	2	2
4	Imaging	NA	2	3	NA	NA	NA	2	2	3
5	Sample Size	1	0	0	1	0	1	0	1	0
6	Statistical Methodology	2	2	2	2	2	2	2	2	2
III.	Patient Factors									
7	Inclusiveness of Population	NA	NA	NA	NA	NA	NA	NA	NA	NA
8	Duration of Pain	2	2	2	2	2	2	2	2	2
9	Previous Treatments	1	2	2	1	1	2	2	2	1
10	Duration of Follow-up with Appropriate Interventions	4	3	1	3	4	4	4	4	3
IV.	Outcomes									
11	Outcomes Assessment Criteria for Significant Improvement	4	4	2	2	1	4	2	4	4
12	Description of Drop Out Rate	2	1	1	1	2	2	2	2	1
13	Similarity of Groups at Baseline for Important Prognostic Indicators	2	2	0	0	2	0	0	2	0
14	Role of Co-Interventions	2	2	2	2	2	2	2	1	2
V.	Randomization									
15	Method of Assignment of Participants	4	4	4	1	1	2	1	2	2
VI.	Conflicts Of Interest									
16	Funding and Sponsorship	1	1	1	2	2	1	2	1	0
TOTAL		34	33	27	21	23	26	27	32	27

by short-duration CRF, and concluded the PRF group to be the least effective group (18). In studies analyzing PRF treatments, high-voltage regimens were shown to be more effective when compared with standard-voltage regimens (17,19). Two trials analyzed the difference in efficacy between various temperatures and both trials demonstrated better pain relief with higher temperatures (21,22).

Targeted Nerves

Of 44 studies reviewed in this article, 41 (93.2%) target the trigeminal nerve. These studies are focused on trigeminal neuralgia. The remaining studies target the sphenopalatine ganglion (2.3%), infraorbital nerve (2.3%), and glossopharyngeal nerve (2.3%) (19,34,38).

Safety Profile and Complications

Thirty-two out of 44 articles (72.7%) reported complications following RF treatment. More common and less serious complications included facial numbness, masseter weakness, cheek hematomas, diminished corneal reflex, and dry eyes (12,15,16,19,23,28-30,41,42,49-51). Most of these reported cases were mild, temporary, and resolved spontaneously. Less common and more serious complications reported included intracranial hypotension headache, sixth nerve palsy, carotid artery puncture, and oculomotor paralysis (16,39,40). These reported cases either self-resolved or were treated. There were no reported deaths directly attributed to RF ablation treatment.

Limitations

A large variability in definitions of trigeminal neuralgia, RF technique, and patient selection bias was observed in our selected cohort of studies. In addition, there is a paucity of strong longitudinal RCTs and prospective studies.

Conclusions

This systematic review found evidence that RF ablation is efficient in treating patients with facial pain, as well as in improving quality of life and reducing oral medication use. Maximal pain control is achieved using combined CRF and PRF therapy. With studies focused on different methods of RF ablation, treatment can be more directed toward greatest efficiency by means of altering duration, temperature and frequency of therapy. Complications are uncommon and include facial numbness, masseter weakness, cheek hematomas, diminished corneal reflex and dry eyes.

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