Prospective Study

The Impact of Local Corticosteroid Administration on the Incidence of Post-Neurotomy Neuritis: A Prospective Investigation

Brody Fitzpatrick, BS, Kellen Hilton, MD, Michael Suer, MD, Michelle Poliak-Tunis, MD, and Scott Hetzel, MS

From: University of Wisconsin-Madison School of Medicine and Public Health, Madison, WI

Address Correspondence:
Brody Fitzpatrick, BS
University of Wisconsin-Madison School of Medicine and Public Health
750 Highland Avenue
Madison, WI 53705-3628
E-mail: bfitzpatric2@wisc.edu

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 07-12-2021
Revised manuscript received: 10-19-2021
Accepted for publication: 10-27-2021

Free full manuscript: www.painphysicianjournal.com

Background: Since its adoption as a treatment for neuropathic pain in the 1960s, radiofrequency ablation (RFA) has continued to gain popularity for the management of various pain etiologies. Although RFA is considered to be a safe procedure, post-neurotomy neuritis (PNN), a neuropathic-type pain, is one of the most common side effects. Due to the increasing recognition of PNN, some providers have attempted to mitigate the risk of PNN by injecting local corticosteroids at the site of RFA following the procedure. Recent studies have generally concluded that corticosteroids do not protect against the development of PNN, however, they have been limited by their retrospective study designs and the low incidence of PNN.

Objectives: We aimed to add to the growing literature regarding the role of post-RFA corticosteroid administration in preventing the development of PNN.

Study Design: We conducted a prospective study evaluating the incidence of PNN as well as the efficacy of post-RFA corticosteroid administration in preventing the development of PNN.

Setting: All RFAs were performed by the same board-certified, pain medicine fellowship-trained, attending physician at the University of Wisconsin who performed the initial patient evaluation at the pain medicine clinic.

Methods: Thirty-nine patients (47 RFAs) were included in the study. All patients were between the ages of 30 and 81; 23 (59.0%) patients were women comprising 28 (59.6%) of the RFAs performed. RFA was performed for a variety of conditions, including facet joint pain, osteoarthritic knee pain, and occipital nerve pain. The 19 patients (25 RFAs) completed prior to February 2020 received post-RFA corticosteroids; the remaining 21 patients (22 RFAs) completed after this date did not receive corticosteroids. The Numeric Rating Scale (NRS-11) and Douleur Neuropathique 4 Questions (DN4) questionnaire scores were collected before and after completion of an RFA. After their procedure, patients were either called or seen in clinic for re-evaluation of their symptoms, at which time NRS-11 and DN4 scores were collected again.

Results: There were no statistically significant differences between groups when comparing post-RFA DN4 scores. Additionally, the incidence of PNN in our study population was 0% for both treatment groups. The NRS-11 scores were similar between groups prior to completing an RFA. When comparing the post-RFA pain scores, the average NRS-11 scores in the steroid group decreased from 5.8 to 3.4, while the average NRS-11 scores in the nonsteroid group decreased from 5.4 to 3.8. However, the average NRS-11 reductions were similar between groups.

Limitations: The primary limitation of this study is small sample size, which likely limited our ability to diagnose PNN. Additionally, we utilized the 7-item DN4 and required a DN4 score of ≥ 4 to diagnose PNN, and therefore, it is likely that our protocol significantly reduced our sensitivity for diagnosing PNN.

Conclusions: Overall, our study is in agreement with prior studies that RFA is effective for the treatment of facet and osteoarthritic knee pain and that the incidence of PNN is likely small.

Key words: Post-neurotomy neuritis; radiofrequency ablation; corticosteroids post-neurotomy neuritis

Pain Physician 2022: 25:E121-E126

Radiofrequency ablation (RFA) is a technology that has gained significant popularity over the past decade for the management of various pain etiologies. First described as a treatment for neuropathic pain in the 1960s, its use has expanded since its adoption by neurosurgeon Norman Shealy in the 1970s for treatment of facet-mediated pain (1-3). RFA is a procedure wherein an RFA probe is inserted into the skin and placed along targeted nerves using fluoroscopic guidance. After successful placement, an electric current is passed through the RFA probe, subsequently generating RF energy. The resulting friction from ion movement in the tissue surrounding the probe generates heat, leading to disruption of cellular membranes and substructures as well as thermal destruction of the nerves (4-5). This ultimately degrades the nerves' ability to conduct pain signals (4-5). This procedure has demonstrated efficacy in reducing pain associated with knee osteoarthritis, facet arthropathy, and sacroiliac (SI) joint dysfunction (1,3). Patients can typically expect to achieve 6-12 months of significant pain relief after RFA (1). Therefore, this procedure may be repeated as necessary if pain were to recur.

Generally, RFA is regarded as a safe procedure with low-risk of adverse events (6). However, it is not without potential side effects, of which post-neurotomy neuritis (PNN) has been documented to be one of the most common (2). PNN is a neuropathic-type pain, often characterized by a "sunburnt" sensation (2). The severity of pain can be quite variable, ranging from transient, local symptoms in the post-procedural setting to symptoms lasting up to 6 months (2). Although denoted as the most common side effect, PNN is generally uncommon with an incidence ranging from 0.5-9.2% (6). A 2014 study (6), evaluating the incidence of PNN in patients undergoing RFA for SI joint pain, found a complication rate of 0.7% per lesion treated with RFA. This proportion increased to 6.2% and 9.4% when considering the complication rates per procedure and per patient, respectively, as patients tended to have more than one lesion treated with RFA (6).

Several ideas have been postulated regarding the mechanism of PNN development. The authors of a recent study (2) suggested the possibility of an incomplete neurotomy of the cutaneous branches of the dorsal rami during RFA. Other studies (7,8) suggest that PNN is independent of specific needle placement techniques. In a 2003 report, Govind et al (9) suggested that the pain may be due to central disinhibition of cutaneous nerves, though this idea is limited as they only evaluated patients who underwent a third occipital nerve RFA.

Due to the increasing recognition of PNN, some providers have attempted to mitigate the risk of PNN by injecting local corticosteroids at the site of RFA following the procedure (2). Retrospective analyses of their patient populations, however, have not demonstrated any benefit with the addition of corticosteroids despite one of the more commonly postulated mechanisms for the development of PNN being post-procedural inflammation (2). Additionally, animal studies have shown corticosteroid administration to be effective in decreasing post-procedural pain with some evidence suggesting corticosteroid combined with a local anesthetic prolongs the duration of nerve blockade (2). However, despite these results, these studies have generally been limited by small sample sizes and the inability to make strong conclusions due to their retrospective study designs (2).

PNN is regarded as the most common side effect of RFA (2,6). A recent study evaluating the role of post-RFA corticosteroid administration has generally concluded that corticosteroids do not protect against the development of PNN (2). This is in agreement with one other prior study (10). However, these studies have been limited by their retrospective study designs and the low incidence of PNN. In the current study, we aimed to add to the growing literature regarding the role of post-RFA corticosteroid administration in preventing the development of PNN. Additionally, given the paucity of information regarding the incidence, mechanism of development, and treatment/prevention of PNN, guidelines directing appropriate management strategies for preventing PNN are currently unavailable. Therefore, we also hope that the results of the current study will aid clinicians in the development of institutional treatment guidelines in an effort to promote standardized practices for patients undergoing RFA.

Methods

We conducted a prospective study of 47 patients who were treated with RFA by one board-certified, pain medicine fellowship-trained, attending physician at one University of Wisconsin pain medicine clinic between August 1, 2019 and October 30, 2020. RFA was performed for a variety of conditions causing neuropathic pain, including facet joint pain, osteoarthritic knee pain, and occipital nerve pain. In order to be considered for an RFA, patients had to report ≥

50% reduction in pain following 1-2 sets of diagnostic blocks using lidocaine and/or marcaine. If a patient met this criterion, they underwent an RFA. At the time of the RFA, the skin was anesthetized using a 1.5-mL mixture of 1% lidocaine and 0.25% marcaine. Once the superficial tissues were adequately anesthetized, a 17-gauge cooled RFA needle was positioned into the approximate location of the nerve using fluoroscopic guidance; the position of the needle was verified using anterior-posterior, lateral, and oblique views on fluoroscopy. In all cases, the active tip was positioned perpendicular to the nerve; for lumbar and thoracic RFA, a 4-mm active tip was used, and for cervical RFA, a 2-mm active tip was used. For each lesion site, a single ablation was delivered. In most cases, patients experienced pain in multiple locations, and thus received RFA in multiple and/or bilateral joints or spinal levels. Prior to February 2020, the treating physician would routinely administer corticosteroids (betamethasone) at each ablation site post-RFA. Following February 2020, patients did not receive corticosteroids. All procedures were performed by the same attending physician who performed the initial patient evaluation at the pain medicine clinic.

Information obtained from medical charts included patient demographics, body mass index (BMI), procedure type, laterality, date, and disability scores, including the Oswestry Disability Index (ODI), Neck Disability Index (NDI), and Numeric Rating Scale (NRS-11) scores. It should be noted that either the ODI or NDI were collected per patient. Therefore, these scores were combined into a single composite disability index for statistical analysis. In addition, we utilized the English version of the Douleur Neuropathique 4 Questions (DN4) questionnaire, an indicator for the development of PNN. The questionnaire was originally developed by a group of French physicians and was designed as a screening tool to detect between nociceptive and neuropathic pain (11). The questionnaire consists of a series of 4 questions evaluating the patient's pain characteristics and symptoms via patient interview and physical exam. Each question has a subset of yes/no questions; every question answered as "yes" is given one point, while every "no" is given zero points. In total, there are 7 patient interview questions and 3 physical exam tests comprising a total of 3 points. Therefore, the questionnaire is graded out of 10 points, and scores totaling ≥ 4 indicate neuropathic pain. Overall, the DN4 questionnaire has been reported to have a sensitivity and specificity as high as 83% and 90%, respectively. It has also been validated in multiple languages and for multiple different conditions, including painful diabetic neuropathy and low back pain (11-14).

The NRS-11 and DN4 scores were collected at procedure visits before and after completion of an RFA. For patients who reported multiple NRS-11 or DN4 scores prior to their RFA, only the score reported closest to their procedure date was collected. After their procedure, patients were either called or seen in clinic for re-evaluation of their symptoms, at which time NRS-11 and DN4 scores were collected again. These follow-up scores were collected at a median of 35 (standard deviation [SD]: 14.4, range: 15-84) days post-procedure. Patients who scored ≥ 4 on the DN4 at this follow-up evaluation were determined to have developed PNN. It should be noted that many of the patients included in the study were unable to follow-up in person. These patients were contacted for follow-up via telephone, and thus only the patient interview questions from the DN4 were able to be collected. Therefore, of the 10 total points of the DN4, only 7 points were able to be recorded. Because of the lack of data for all 10 points of the DN4 but a consistent ability to collect the 7 points from the patient interview, the analysis of the DN4 was based on a 7-point scale rather than 10 points. Therefore, for the patients who were able to answer all 7 interview questions and participate in the physical examination to complete all 10 points, only the 7 points from the patient interview were included in the analysis to ensure that the data was consistent amongst all study patients.

The primary comparison group for this study is use of corticosteroids post-RFA. This distinction is confounded with time; however, this confounding factor is mitigated by looking at a relatively small time window immediately before and after the policy change. Data were summarized between the 2 groups via mean (SD), median (interquartile range [IQR]), or n (%) when appropriate and corresponding t test, Wilcoxon rank sum test, or chi-square test was used to statistically compare the results between groups. Due to 8 patients having 2 RFA procedures each, we also tested for differences between groups using mixed-effects analysis of variance and mixed-effects logistic regression models with patient as a random effect. Both methodological results are presented. When single *P* values are presented in text, the mixed-effects *P* value is given unless otherwise stated. All analyses were conducted in R version 4 and had a 5% significance level.

Results

In summation, the 47 patients included in this study completed a total of 56 RFAs. However, only 39 patients, totaling 47 RFAs, were ultimately included in the analysis. This reduction in sample size was due to 9 instances in which the DN4 questionnaire was not completed at both time points. Additionally, 19 patients completed 25 RFAs prior to February 2020, and therefore, received post-RFA corticosteroids; the remaining 21 patients who completed 22 RFAs after this date did not receive corticosteroids.

All patients included in this study were between the ages of 30 and 81, and 23 (59.0%) patients were women comprising 28 (59.6%) of the RFAs performed. There were no statistically significant differences in the age, gender, or BMI between the steroid and nonsteroid procedure groups. There were also no statistically significant differences in the average patient disability index between procedure groups.

On preliminary analysis, there appeared to be a difference in DN4 scores recorded prior to RFA with the nonsteroid group reporting an average of 0.1 (0.3) and the steroid group reporting an average of 0.4 (0.7) (P = 0.04) (Table 1). However, after accounting for patients who underwent repeat RFA, this statistic was no longer significant (P = 0.14) (Table 1). There were no statistically significant differences between groups when comparing post-RFA DN4 scores. Additionally, none of the patients in our study reported a post-RFA DN4 score ≥ 4, and therefore, the incidence of PNN in our study population was 0% for both treatment groups.

Both the steroid and nonsteroid groups included RFA performed at each of the spinal segments (cervical, thoracic, lumbar, sacral). There were no differences in RFA site laterality (bilateral, left, right) between groups, and repeat RFA occurred at similar rates. Of the RFAs performed on the spine, 21 were performed in the steroid group and 21 were performed in the nonsteroid group. Within both groups, most RFAs were performed on the cervical and lumbar spine. When comparing between procedure groups, the steroid group performed significantly more sacral RFAs than the nonsteroid group (P < 0.001) (Table 1); however, only 2 patients were includedin this analysis. Similarly, although not statistically significant, the steroid group tended to perform more lumbar RFAs than the nonsteroid group (P = 0.09) (Table 1); the number of cervical and thoracic spine RFAs performed were similar between the groups.

Prior to completing an RFA, patients of both procedure groups reported similar NRS-11 scores (5.8 in steroid group; 5.4 in nonsteroid group). When comparing the post-RFA pain scores, there was a statistically significant decrease in average NRS-11 scores amongst all study patients (mean [SD]: -2.0 [2.6]; P < 0.001). On subgroup analysis, the average NRS-11 scores in the steroid group decreased from 5.8 to 3.4 (-2.4 [2.7]; P = 0.001), while the average NRS-11 scores in the nonsteroid group decreased from 5.4 to 3.8 (-1.6 [2.6]; P = 0.007). However, the average NRS-11 reductions were similar between groups (P = 0.24).

Discussion

The primary goals of this study were to estimate the incidence of PNN and to identify whether post-RFA corticosteroid administration reduces the incidence of PNN. However, none of the patients included in this study developed PNN. Therefore, because the incidence in both treatment groups was 0%, we were unable compare any differences between groups, nor were we able to evaluate whether corticosteroids are effective in preventing the development of PNN. Given an estimated incidence as high as 10%, it is unusual that we performed a total of 56 RFAs and, subsequently, did not identify a single patient with PNN. However, our protocol for diagnosing PNN may be accountable for this discrepancy. In previous studies evaluating the incidence of PNN (2,6), there was no standardized definition for establishing the diagnosis. Rather, PNN was diagnosed clinically when patients reported neuropathic-pain symptoms in the approximate location of the RFA site. Conversely, in our study, we utilized a validated standardized screening tool (DN4) to identify PNN (11,13). Particularly, patients were required to score ≥ 4 on the DN4 in order to be diagnosed with PNN. Thus, although 17 (43.6%) patients comprising 20 (42.6%) surgeries reported at least one neuropathic-type symptom at the approximate RFA site, those who failed to score ≥ 4 on the DN4 were not diagnosed with PNN. Likely, many of these patients would have been diagnosed with PNN in prior studies. It should also be noted that previous studies evaluating the sensitivity and specificity of the DN4 have been variable (11,13,14). A 2005 study (11) evaluating the use of screening tools for neuropathic pain found the 10-item DN4 to have a sensitivity of 83% and a specificity of 90% when using a cut-off score of 4/10. However, when using the 7-item DN4 and a cut-off score of 3/10, the sensitivity and specificity decreased to 78% and 81%, respectively (11). This statistic is of particular importance in our study as many of our patients completed follow-up via

telephone, thereby preventing us from obtaining the physical examination portion of the DN4. Therefore, because we utilized the 7-item DN4 in our statistical analyses and required a DN4 score of ≥ 4 to diagnose PNN, it is likely that our protocol significantly reduced our sensitivity for diagnosing PNN, ultimately resulting in an underestimation of the true incidence of PNN in our study population.

Despite our incongruence with prior studies in estimating the incidence of PNN, we did replicate these studies by demonstrating that RFA is an effective treatment for facet and osteoarthritic knee pain. RFA reduced NRS-11 pain scores significantly in both groups and provided pain relief lasting at least 4-6 weeks. There were no statistically significant differences between the treatment groups, suggesting that the addition of post-RFA corticosteroids does not provide any significant synergistic analgesic effects. This appears to be in agreement with one prior study (10) evaluating the addition of post-RFA corticosteroid or pentoxifylline vs RFA alone, which demonstrated significant reduction for all 3 treatment groups without any significant differences between groups.

The primary limitation of this study is small sample size. As mentioned previously, although PNN is considered the most common complication of RFA, the estimated incidence is generally < 10% (6). Additionally, when considering the fact that most of the studies evaluating the incidence of PNN had small sample sizes, only a small number of patients were required to develop PNN in order to achieve an incidence of 10%. Therefore, the actual incidence of PNN may be much lower than previously estimated. Additionally, these studies have generally found that PNN is more common after cervical spine interventions as opposed to the lumbar spine (2, 8, 9, 15). We have also found this to be true at our institution, and although 23 of the 42 spine RFAs in the present study were performed on the cervical spine, the overall sample size of the study is small. This emphasizes the notion that a large number of patients are not only needed to increase the likelihood of identifying patients who develop PNN, but also to accumulate a sufficient number of cases in order to subsequently compare differences in the incidence of PNN in patients who receive post-RFA corticosteroids vs those who do not. Therefore, larger studies will be needed in the future in order to accurately estimate the incidence of PNN and evaluate the efficacy of post-RFA corticosteroid administration in preventing PNN.

Table 1. *Composite patient demographics, procedural data, and neuritis.*

Variable	Nonsteroid (n = 25)	Steroid (n = 22)	*P* value	*P* value*
Age – Years	61.5 (8.5)	56.5 (10.0)	0.070	0.476
Gender – Men	12 (48.0%)	7 (31.8%)	0.406	0.190
BMI	31.6 (6.7)	29.2 (7.4)	0.260	0.381
Laterality			0.523	0.450
Both	10 (40.0%)	9 (40.9%)		
Left	6 (24.0%)	8 (36.4%)		
Right	9 (36.0%)	5 (22.7%)		
Number of Sites	4 (3-6)	4 (3-6)	0.999	0.410
Repeat Surgery – Yes	6 (24.0%)	4 (18.2%)	0.730	0.470
ODI/NDI	31.2 (17.5)	33.8 (16.4)	0.632	0.763
Location				
Spine	21 (84.0%)	21 (95.5%)	0.352	0.237
Cervical	13 (52.0%)	10 (45.5%)	0.876	0.691
Thoracic	2 (8.0%)	1 (4.5%)	0.999	0.636
Lumbar	6 (24.0%)	11 (50.0%)	0.122	0.090
Sacral	0 (0%)	2 (9.1%)	0.214	< 0.001
Pain Prior to Surgery – Yes	5.4 (1.8)	5.8 (2.0)	0.479	0.574
Difference in NRS-11	-1.6 (2.6)	-2.4 (2.7)	0.346	0.240
DN4 Score				
Prior to Surgery	0.1 (0.3)	0.4 (0.7)	0.040	0.140
Difference	0.7 (1.0)	0.2 (1.0)	0.138	0.174

Reported as mean (SD), median (IQR), n (%).
P value from mixed-effects analyses.
Abbreviations: BMI, body mass index; ODI, Oswestry Disability Index; NDI, Neck Disability Index; NRS-11, Numeric Rating Scale; DN4, Douleur Neuropathique 4 Questions; SD, standard deviation; IQR, interquartile range.

Conclusions

Our study is in agreement with prior studies that RFA is effective for the treatment of facet and osteoarthritic knee pain. We are in agreement with prior studies suggesting that the incidence of PNN is likely small (6); however, we recognize that our utilization of the 7-item DN4 in combination with a cut-off score of 4 likely limited our sensitivity for diagnosing PNN. Therefore, enrolling a sufficient number of patients to effectively evaluate the role of post-RFA corticosteroid administration on the prevention of PNN is challenging. Future studies seeking to provide a more insightful and definitive answer to this question will likely need to complete a large prospective trial or meta-analysis,

such that they can attain a sufficient sample size to achieve statistical significance. Upon completion of such a study, it may be possible to provide well-informed recommendations regarding institutional guidelines for post-RFA corticosteroid administration for the prevention of PNN.

References

1. Jamison D, Cohen S. Radiofrequency techniques to treat chronic knee pain: A comprehensive review of anatomy, effectiveness, treatment parameters, and patient selection. *J Pain Res* 2018; 11:1879-1888.
2. Singh JR, Miccio VF Jr, Modi DJ, Sein MT. The impact of local steroid administration on the incidence of neuritis following lumbar facet radiofrequency neurotomy. *Pain Physician* 2019; 22:69-74.
3. Leggett LE, Soril LJ, Lorenzetti DL, et al. Radiofrequency ablation for chronic low back pain: A systematic review of randomized controlled trials. *Pain Research and Management* 2014; 19:146-153.
4. Kapural L, Deering JP. A technological overview of cooled radiofrequency ablation and its effectiveness in the management of chronic knee pain. *Pain Manag* 2020; 10:133-140.
5. Cosman ER Jr, Cosman ER Sr. Electric and thermal field effects in tissue around radiofrequency electrodes. *Pain Medicine* 2005; 6:405-424.
6. Stolzenberg D, Gordin V, Vorobeychik Y. Incidence of neuropathic pain after cooled radiofrequency ablation of sacral lateral branch nerves. *Pain Medicine* 2014; 15:1857-1860.
7. Moon JY, Lee PB, Kim YC, et al. An alternative distal approach for the lumbar medial branch radiofrequency denervation. *Anesthesia & Analgesia* 2013; 116:1133-1140.
8. Kornick C, Kramarich SS, Lamer TJ, Sitzman BT. Complications of lumbar facet radiofrequency denervation. *Spine* 2004; 29:1352-1354.
9. Govind J. Radiofrequency neurotomy for the treatment of third occipital headache. Journal of Neurology, *Neurosurgery & Psychiatry* 2003; 74:88-93.
10. Dobrogowski J, Wrzosek A, Wordliczek J. Radiofrequency denervation with or without addition of pentoxifylline or methylprednisolone for chronic lumbar zygapophysial joint pain. *Pharmacological Reports* 2005; 57:475-480.
11. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). *Pain* 2005; 114:29-36.
12. Spallone V, Morganti R, D'Amato C, et al. Validation of DN4 as a screening tool for neuropathic pain in painful diabetic polyneuropathy. *Diabetic Medicine* 2012; 29:578-585.
13. Attal N, Perrot S, Fermanian J, et al. The neuropathic components of chronic low back pain: A prospective multicenter study using the DN4 questionnaire. *The J Pain* 2011; 12:1080-1087.
14. Walsh J, Rabey MI, Hall TM. Agreement and correlation between the self-report leeds assessment of neuropathic symptoms and signs and Douleur Neuropathique 4 Questions neuropathic pain screening tools in subjects with low back-related leg pain. *Journal of Manipulative and Physiological Therapeutics* 2012; 35:196-202.
15. Lord SM, Barnsley L,Wallis BJ, et al. Percutaneous radio-frequency neurotomy for chronic cervical zygapophyseal-joint pain. *New Eng J Med* 1996; 335:1721-1726.