Prospective Study

# Effectiveness of Ultrasound-Guided Pulsed Radiofrequency Treatment in Patients with Refractory Chronic Cervical Radicular Pain

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**Background:** The effect of pulsed radiofrequency (PRF) stimulation for alleviating cervical radicular pain has been demonstrated in several previous studies.

**Objectives:** We aimed to evaluate the effectiveness of PRF with ultrasound (US) guidance in patients with chronic cervical radicular pain that was refractory to repeated transforaminal epidural steroid injections (TFESIs).

**Study Design:** A prospective outcome study.

**Setting:** The outpatient clinic of a single academic medical center.

**Methods:** This study included 49 patients with chronic cervical radicular pain, unresponsive to repeated TFESIs, and who underwent PRF stimulation under US guidance. Using US, a cannula was inserted toward the cervical spinal nerve. The pain intensity was evaluated using the Numeric Rating Scale (NRS-11) for cervical radicular pain at pretreatment and 1, 3, and 6 months posttreatment; and the Neck Disability Index (NDI) was used for evaluating functional disability before treatment and 6 months posttreatment. Successful pain relief was defined as ≥ 50% reduction in the NRS-11 score as compared with the score before treatment.

**Results:** Cervical radicular pain was significantly reduced at 1, 3, and 6 months post-PRF ($P < 0.001$). At 6 months post-PRF, functional disability (NDI score) had significantly reduced, and 63.3% of the patients achieved successful pain relief.

**Limitations:** The small number of included patients and no long-term follow-up.

**Conclusions:** PRF stimulation under the guidance of US is a potentially effective treatment method for managing refractory chronic cervical radicular pain.

**Key words:** Ultrasound, pulsed radiofrequency, cervical radicular pain, chronic pain

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Chronic cervical pain is a common problem faced in clinical practice, with a prevalence of approximately 35% in the adult population (1). Cervical radicular pain is induced by herniated disc or spinal stenosis, and chemical inflammation and mechanical compression of the nerve root are main causes of radicular pain (2). Several conservative management methods are available for its management, including oral medications, modalities, and epidural steroid injection. However, some patients have shown unresponsiveness to these treatments. Persistent pain can disturb the patients' daily life activities and cause inability to work comfortably.

Continuous radiofrequency treatments have been used for over 40 years for various medical conditions, including trigeminal neuralgia, sacroiliac joint pain, facet-origin pain, shoulder pain, and radicular pain (3-5). However, it causes diffuse tissue damage due to destructive temperatures (6). To overcome this risk, pulsed radiofrequency (PRF) was developed, which has been used for alleviating several kinds of chronic pain, such as radicular pain, joint pain, myofascial pain, and headache (7-10). In PRF, the tissue temperature reaches a maximum of 42℃, which prevents the unwanted adverse effect of irreversible tissue damage (11-13). PRF may alter the pain transmission secondary to a phenomenon known as long-term depression and inhibit pain impulse propagation (14). The effect of PRF stimulation for alleviating cervical radicular pain has been demonstrated in several previous studies (15-27), and recently many clinicians are applying PRF for cervical radicular pain. Usually, PRF stimulation for cervical radicular pain is performed under fluoroscopic guidance. However, fluoroscopy cannot identify the nerve tissue or vessels; therefore performing the procedure under the guidance of fluoroscopy may potentially lead to nerve injury or hematoma following vessel puncture.

Ultrasound (US) has several advantages as it can verify nerves and vessels and obtain real-time images of body structures with great convenience, and there is no risk of exposure to radiation. For the management of cervical radicular pain, selective periradicular injection with corticosteroids and anesthesia was conducted under US guidance, and its effectiveness has been demonstrated in several previous studies (28-30). However, the effect of US-guided PRF treatment for cervical radicular pain has not yet been studied.

In this study, we prospectively performed US-guided PRF stimulation in patients with cervical radicular pain that was refractory to repeated transforaminal epidural steroid injections (TFESIs) and evaluated its effect for 6 months after PRF stimulation.

## Methods

### Patients

This prospective follow-up study included 49 consecutive patients (male:female = 30:19, age [mean ± standard deviation] = 54.3 ± 10.1 years) who presented with cervical radicular pain. The institutional review board of Yeungnam University Hospital approved the study, and all patients signed an informed consent form. The inclusion criteria for this study were presence of ≥ 6-month history of segmental pain radiating to the arm, age between 20 and 79 years, ≥ 50% temporary pain relief following a diagnostic nerve block with 1 mL of 2% lidocaine, unsatisfactory response to repeated TFESIs (segmental pain of a score of at least 5 on the Numeric Rating Scale [NRS-11] that radiated to the arm) under the guidance of fluoroscopy, no interval change of the NRS-11 score over the 4 weeks after TFESI, and imaging findings (magnetic resonance imaging and/or computed tomography) of herniated cervical disc (HCD) or cervical foraminal stenosis (CFS). We excluded patients with history of spinal surgery, cervical fusion or laminectomy, myelopathy, cervical vertebral fractures, and coagulation disorders. Out of the 49 recruited patients, 19 had HCD on imaging studies (male:female = 12:7, age = 48.0 ± 6.9 years) and 30 had CFS (male:female = 18:12, age = 58.3 ± 9.8 years) induced by hypertrophy of the Luschka or facet joint. The mean frequency of TFESI was 3.5 ± 1.1 (HCD group = 3.1 ± 1.2, CFS group = 3.6 ± 1.0), and the symptom duration was 33.6 ± 24.9 months (HCD group = 26.3 ± 12.0, CFS group = 38.2 ± 29.7). The level of PRF treatment was as follows: C5:C6:C7 = 5:28:16 (HCD group, C5:C6:C7 = 2:12:5, CFS group, C5:C6:C7 = 3:16:11).

### PRF Procedures

The patient was laid in an oblique supine decubitus with a frame support under the shoulder and hip, with the head turned about 15° to the opposite side (Fig. 1A). After aseptic skin preparation, a probe (12 MHz linear probe, Venue 40 unit; GE Healthcare, Milwaukee, WI) was placed at the symptomatic side of the neck (Fig. 1B). The probe was placed above the C7 transverse process, which was recognized by the shape of its rudimentary anterior tubercle and prominent posterior tubercle (29). The probe was then moved cephalad to identify the C6 and C5 transverse processes by their characteristic anterior and posterior tubercles that were asymmetrical and described as the "two-humped camel" sign (29). Thereafter the targeted hypoechoic nerve was identified within the intertubercular groove of the corresponding transverse process with its underlying bony acoustic shadow. A 22-gauge curved-tip cannula (SMK Pole needle 54 mm with a 4-mm active tip; Cotop International BV, Amsterdam, Netherlands) was inserted from the posterior to anterior direction, and positioned between the spinal nerve and posterior tubercle outside the intervertebral foramen using real-time US-guidance (Fig. 1C, 1D). Following this, the sensory stimulation test was carried out using a

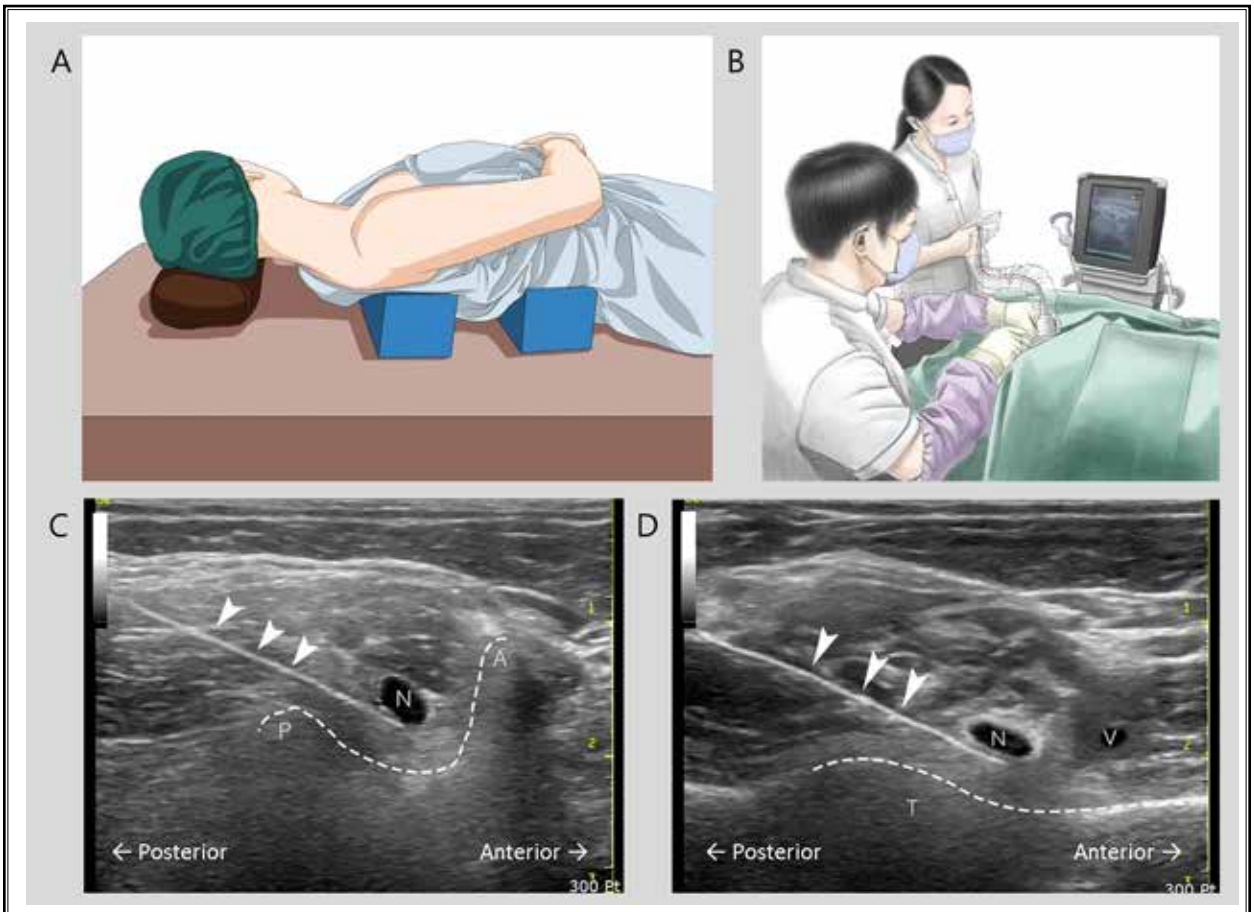


Fig. 1. *(A) The patient is positioned in an oblique supine decubitus with a frame support under the shoulder and hip, with the head turned by approximately 15° to the opposite side. (B) After aseptic skin preparation, a probe is placed at the symptomatic side of the neck. (C) PRF catheter is placed between the C6 spinal nerve and C6 posterior tubercle outside the intervertebral foramen under the guidance of US. (D) PRF catheter is placed between the C7 spinal nerve and C7 posterior tubercle.*
(Arrowheads: PRF catheter, N: spinal nerve, A: anterior tubercle, P: posterior tubercle, T: transverse process)

radiofrequency generator (Cosman G4; Cosman Medical, Burlington, MA). The catheter needle was slowly advanced until dysesthesia or pain was reported at less than 0.3 V. Finally, a catheter tip was placed on the extraforaminal spinal nerve (distal to dorsal root ganglion [DRG]). The PRF treatment was administered at 5 Hz and 5-ms pulsed width for 360 seconds at 45 V, and care was taken to ensure that the electrode tip temperature did not exceed 42°C.

The intensity of the patients' pain was measured using the NRS-11, in which 0 indicated no pain and 10 indicated the worst pain imaginable. NRS-11 scores were assessed before treatment and at 1, 3, and 6 months following treatment. The functions affected by this pain were evaluated using the Neck Disability Index (NDI). The NDI consisted of 10 items: intensity of pain, personal management (bathing and putting on clothes), raising objects, reading books, headache, concentration, working, driving, sleeping, and leisure activities. The score for each item ranged between 0 and 5 points, and the total score ranged between 0 and 50 points. An NDI score was calculated from the total of the scores for each item. A high NDI score indicated a more severe functional disability related to the cervical abnormality. The NDI scores were evaluated before treatment and at 6 months following treatment. Successful pain relief was defined as ≥ 50% reduction of pain 6 months after PRF treatment as compared with the NRS-11 score before treatment. A researcher blinded to the patients' conditions and treatment history evaluated NRS-11 and NDI.

### Statistical Analyses

Statistical Package for Social Sciences version 23.0 software (IBM Corporation, Armonk, NY) was used for statistical analyses. The characteristic variables were analyzed using descriptive statistics, with the mean ± standard deviation presented for quantitative variables and frequency (percent) for qualitative variables. Changes in NRS-11 scores over time were evaluated for each patient, including those in the HCD and CFS groups, using repeated measures one-factor analysis. Repeated measure 2-factor analysis was used to compare changes over time between the HCD and CFS groups. Multiple comparison results were obtained following a contrast under Bonferroni correction. The difference between pretreatment and 6-month follow-up NDI scores were analyzed using a paired t-test. Differences in NDI scores between the HCD and CFS groups were compared using an independent t-test. A $P$ value < 0.05 indicated statistical significance.

## Results

There were no dropouts in our study, nor were any adverse effects detected. The average NRS-11 score for cervical radicular pain declined from 7.2 ± 0.8 at baseline to 5.2 ± 1.3 at 1 month, 4.4 ± 1.7 at 3 months, and 3.8 ± 1.9 at 6 months after the PRF procedure. NRS-11 scores changed significantly over time ($P$ < 0.001) (Fig. 2). More specifically, NRS-11 scores at 1, 3, and 6 months after PRF were significantly lower than that at baseline ($P$ < 0.001) (Fig. 2).

The average NRS-11 scores of the HCD group were 7.3 ± 0.9 at baseline, 5.1 ± 1.5 at 1 month, 4.5 ± 1.8 at 3 months, and 3.8 ± 2.2 at 6 months after the PRF. Those of the CFS group were 7.8 ± 0.8 at baseline, 2.3 ± 1.2 at 1 month, 4.3 ± 1.6 at 3 months, and 3.8 ±1.7 at 6 months after PRF. The NRS-11 scores for each group changed significantly over time ($P$ < 0.001). In both groups, scores at 1, 3, and 6 months decreased significantly when compared with the pretreatment scores ($P$ < 0.001). However, changes in NRS-11 scores over time were not significantly different between the HCD and CFS groups ($P$ = 0.869). The decrease in NRS-11 score from the pretreatment stage to each evaluation time point did not demonstrate significant differences between the HCD and CFS groups (1 month: $P$ = 0.439; 3 months: $P$ = 0.910; 6 months: $P$ = 0.862).

Furthermore, the average NDI score decreased from 36.9 ± 8.9 before treatment to 20.4 ± 19.2 at 6 months after treatment. A significant reduction in the NDI score was observed after treatment ($P$ < 0.001). Additionally, the average NDI scores of the HCD and CFS groups before treatment were 36.0 ± 8.6 and 37.4 ± 9.1,

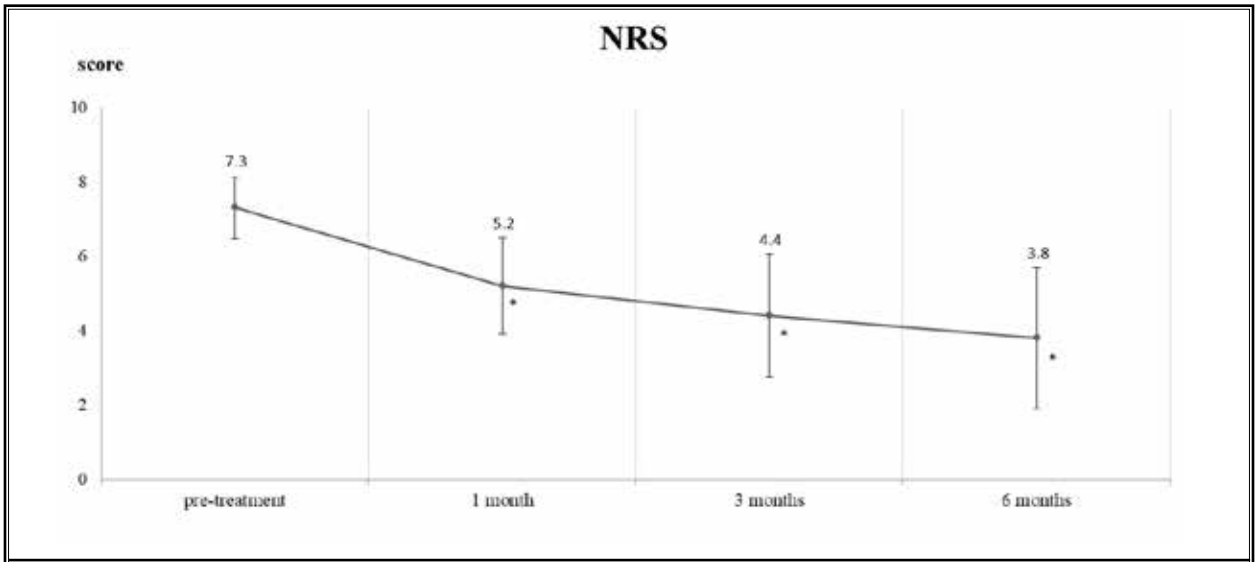


Fig. 2. *Changes in the NRS-11 scores for cervical radicular pain in the total recruited patients during the assessment period. The NRS-11 scores decrease from 7.2 before treatment to 5.2 at 1 month, 4.4 at 3 months, and 3.8 at 6 months after PRF stimulation. Significant differences were observed in the comparison between the pretreatment and posttreatment values at 1, 3, and 6 months. *Indicates significant results (P < 0.05).*

respectively. Those at 6 months after treatment were 20.7 ± 22.2 and 20.1 ± 17.3, respectively. In each group, a significant reduction in the NDI score was noted after PRF (HCD group: $P = 0.04$; CFS group: $P < 0.001$), but no significant difference was overserved between the HCD and CFS groups at pretreatment ($P = 0.596$) and 6 months after treatment ($P = 0.916$). Among the 49 patients enrolled, 31 (63.3%) reported successful pain relief (pain relief of ≥ 50%) 6 months after PRF treatment.

## Discussion

In the current study, US-guided PRF treatment was applied to patients with chronic cervical radicular pain who were unresponsive to repeated TFESIs. Pain severity scores were significantly reduced at 1, 3, and 6 months following PRF treatment. The patients' functional disability significantly decreased at 6 months posttreatment. Totally, 63.3% of the patients showed successful pain relief (≥ 50% pain reduction of initial pain) with US-guided PRF treatment. Furthermore, between the patients with HCD and those with CFS, no significant difference was observed in pain reduction and functional improvement after PRF treatment.

The mechanism of pain regulation by PRF stimulation has not yet been clearly discovered, but some mechanisms were suggested. Cosman and Cosman (31) reported that the low frequency of pulses and high voltages during PRF stimulation result in long-term depression of synaptic transmission, which inhibits the transfer of noxious signals to the brain. Higuchi et al (32) found that the PRF stimulation on the DRG increased c-fos level in the dorsal horn, which probably activated a pain-inhibitory mechanism. Cho et al (33) found that PRF stimulation decreased microglia activity in the dorsal horn. Because the activation of microglia plays an important role in the development of chronic neuropathic pain by secreting several inflammatory cytokines and chemokines that mediate pain signaling, downregulation of microglial activity by PRF seemed to prevent the progression to chronic neuropathic pain (33).

This study had the limitation of not performing a sham procedure or recruiting a control group. However, the patients' average pain duration was 33.6 months, and that of the recruited patients was ≥ 6 months. Additionally, prior to the US-guided PRF procedure, TFESIs were performed 3.6 times on an average, and all the patients underwent TFESIs more than once. Thus the reduced pain and improved function did not seem to be responsible for the natural healing process of radicular pain. Despite no sham stimulation or control group being present, we believe that the pain reduction and functional improvement in this study were induced by the US-guided PRF treatment.

To the best of our knowledge, 13 previous studies, that is, 4 randomized controlled studies (19,20,23,25), 3 prospective observational studies (17,18,22), 4 retrospective studies (16,21,26,27), and 2 case reports (15,24), evaluated the effect of PRF stimulation on cervical radicular pain (15-27). All the previous studies reported positive therapeutic effect of PRF in patients with cervical radicular pain, and all of them conducted PRF stimulation on the DRG. However, an approach to the DRG is not possible with US because the space within the cervical foramen cannot be observed. In this study, the PRF stimulation was applied on the extraforaminal spinal nerve, and not on the DRG. The positive therapeutic response of the patients seemed to indicate that PRF stimulation of areas some distance away from the DRG could affect the DRG and result in pain reduction. Furthermore, we think that the action of the electrical field on extraforaminal spinal nerve would result in reduction of chronic radicular pain.

## Conclusions

This study revealed that US-guided PRF stimulation could help to manage refractory chronic cervical radicular pain, and thus decrease functional disability. Moreover, our study showed positive therapeutic outcomes regardless of HCD or CFS. These favorable outcomes indicated that US-guided PRF is a good therapeutic option for managing cervical radicular pain. This study was the first to demonstrate the effectiveness of PRF stimulation under US guidance. However, this study had some limitations. First, as mentioned earlier, this study did not recruit a sham stimulation or control group. Second, the number of recruited patients was relatively small. Further studies in the future that address these limitations are warranted.

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