Prospective Study

Promising Outcomes of Ultrasound-Guided Pulsed Radiofrequency for the Treatment of Morton's Neuromas – A Prospective Study

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Background: Morton's neuroma is a compressive neuropathy of the common plantar digital nerve, causing significant pain and limiting patients' activities.

Objectives: This study aimed to investigate the effect of pulsed radiofrequency (PRF) on the pain, functionality, and quality of life experienced by patients with Morton's neuroma.

Study Design: This was a prospective study with pre- and post-intervention assessments after one, 3, and 6 months of treatment.

Setting: The orthopedics department of an affiliated hospital.

Methods: Patients with Morton's neuroma underwent treatment with ultrasound-guided PRF in 2 sites around the neuroma for 8 minutes. Clinical outcomes were assessed using the visual analog scale (VAS), the American Orthopedic Foot and Ankle Society (AOFAS) questionnaire for assessing foot function, and the Short Form-36 (SF-36) for quality of life.

Results: A total of 20 patients (29 feet) completed the 6-month minimum follow-up period. The VAS and face scale values at follow-up were statistically lower than the pre-procedure VAS scores ($P < 0.05$). The AOFAS and SF-36 values at follow-up were statistically higher than the pre-procedure values ($P < 0.05$). No significant adverse events were recorded during the follow-up.

Limitations: The prospective research features a limited follow-up duration and lacks an additional group, whether control or treatment, for result comparisons.

Conclusion: Applications of PRF decreased the pain and the improved functionality and quality of life experienced by patients with Morton's neuroma for a 6-month follow-up at minimum.

Key words: Compression neuropathy, Morton's neuroma, non-surgical intervention, pulsed radiofrequency, metatarsalgia, neuropathic pain, forefoot pain, neuromodulation

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Morton's neuroma is a compressive neuropathy of the common plantar digital nerve, usually in the third intermetatarsal space, associated with fibrotic changes in the nerve, microvascular degeneration, and dysregulation of sympathetic innervation (1,2). Individuals with this condition may experience acute metatarsalgia at the dorsal or plantar aspect of the forefoot, stabbing pain, numbness and/or tingling, a burning sensation, and a feeling of "walking on a stone" around the metatarsal heads (2,3).

Initial treatment of Morton's neuroma uses conservative measures, including orthotics, physical therapy, and anti-inflammatory medications (2). Alternative interventions include corticosteroid injections, alcohol injections, extracorporeal shockwave therapy, radiofrequency ablation, pulsed radiofrequency (PRF) neuromodulation, cryoablation, botulinum toxin, and YAG laser therapy (3,4).

After conservative treatment fails, minimally invasive ultrasound-guided procedures are used as second-line treatments before surgery, which is the final resort in persistently symptomatic cases (2,4). Ultrasound-guided PRF neuromodulation is a minimally invasive, safe alternative with low complication rates compared to those associated with the surgical excision of intermetatarsal neuroma (5).

Therefore, the objective of the present study was to investigate the effects of ultrasound-guided PRF on the pain, functionality, and quality of life experienced by patients with Morton's neuroma, with a 6-month follow-up.

Methods

This prospective study was carried out at the Sports Orthopedics Center outpatient clinic at the Federal University of São Paulo (CETE-UNIFESP). The study was approved by the UNIFESP Ethics Committee (CEP/UNIFESP/n:5.037.010P/2021).

Study Population

Thirty patients diagnosed with Morton's neuroma were invited to join the study, which was conducted from January 2022 to January 2023. To be included, patients had to meet the following criteria: First, they needed to be older than 18 years old. Secondly, they were required to have a clinical diagnosis of Morton's neuroma characterized by neuropathic pain localized in the intermetatarsal space and radiating toward adjacent toes. All patients reported discomfort and imaging abnormalities in the third intermetatarsal space, with pain radiating to the third and fourth toes. MRI scans revealed that Morton's neuroma was a well-defined, oval, or fusiform soft tissue mass, typically presenting intermediate-to-low-signal intensity on T1-weighted images and variably hyperintense signals on T2-weighted images. Morton's neuroma involves thickening of the interdigital nerve due to repeated trauma or compression. Pain and a clicking sensation, often reproduced through local palpation and lateral compression (Mulder's test), are characteristic findings. MRI findings offer detailed anatomical views, aiding in the differential diagnosis by distinguishing Morton's neuroma from other conditions, such as ganglion cysts, lipomas, or inflammatory lesions. Techniques like short tau inversion recovery (STIR) or fat-suppressed T2-weighted sequences, used in conjunction with physical examination, support high diagnostic accuracy. Thirdly, the patients must have had no prior interventions for their painful condition. Patients who declined participation, had a history of foot surgery, or presented with clinical comorbidities (e.g., cardiovascular, neurological, or rheumatological conditions) were excluded. Ultimately, 20 individuals who met the study requirements were included (Fig, 1).

Three patients refused to participate in the study. Because the procedure was performed at the university outpatient clinic and ensuring patient safety was essential, patients with cardiovascular comorbidities such as high blood pressure and a history of cardiovascular events were excluded. Patients with rheumatological pathologies or neurodegenerative or neuromuscular neurological diseases were also excluded.

Intervention

The AK-A304 Multichannel Radio Frequency Generator® (Apro Korea Inc.) was utilized for the procedure. The patient was placed in a supine position on a treatment table. To minimize pain, the physician anesthetized the patient's skin with 0.5 mL of 1% lidocaine administered via a 26G needle (13 x 0.45 mm). The local anesthetic was injected into the subdermal layer to avoid deactivating the nerve because the plantar pad and local fatty tissue allowed the nerve to be spared from the superficial anesthetic blockade.

Under real-time ultrasound guidance, using a linear probe (6-15 MHz) from Esaote®, the third plantar interdigital nerve was targeted precisely. This nerve branch results from the convergence of the medial and lateral plantar nerves and is located in the forefoot region between the third and fourth metatarsals. Ad-

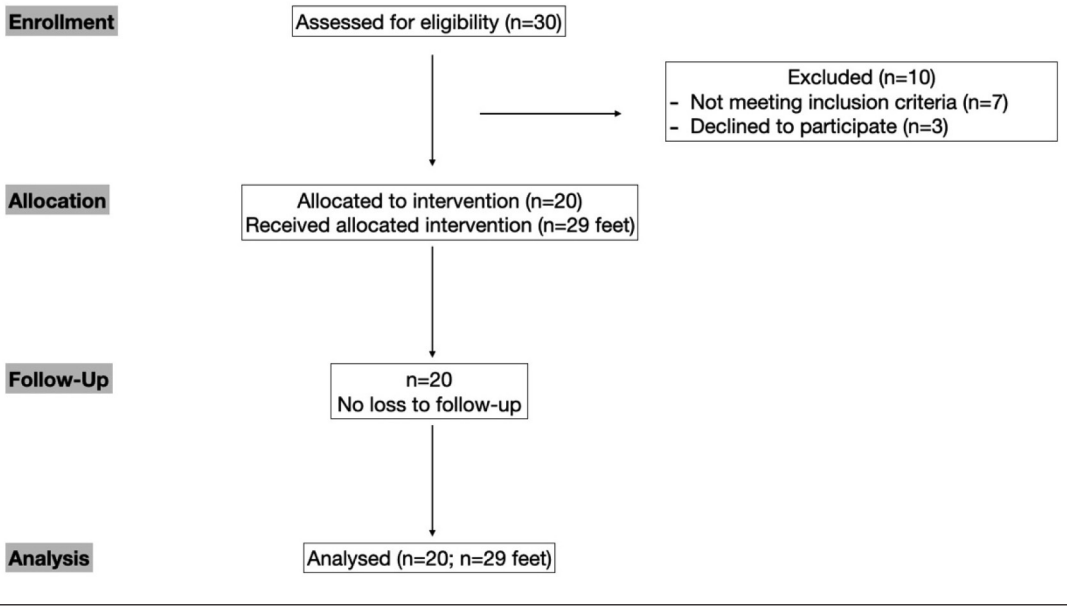

Fig. 1. *Recruitment, allocation, and data analysis of the patients.*

ditional ultrasound direction was used to place the cannula in the intermetatarsal space, at 2 points around the neuroma and parallel to each metatarsal. Each placement occurred one at a time (Fig. 1).

A Pajunk® steel cannula coated with Teflon (22G, 5 mm active tip) was inserted into the designated intermetatarsal space. Ultrasound was used to visualize the neuroma, identified as a hypoechoic mass with an oval or fusiform shape. To enhance neuroma visibility, gentle compression of the forefoot was applied before cannula insertion, causing the neuroma to protrude outward from the intermetatarsal space. Sensory stimulation was performed at 50 Hz with an intensity of 0.1 V to confirm accurate cannula placement by eliciting a sensory response without triggering motor activity. Radiofrequency application proceeded only if the patient exhibited a sensory response. The targeted nerve had no motor innervation at that point on the plantar surface of the foot. For this reason, motor stimulation was not performed and should not be expected in events such as the procedure described in this study. Even so, if motor stimulation occurs, it will be due to the proximity of the electromagnetic field of the cannula to the local intrinsic musculature.

The generator was set with the following parameters:

- Frequency: 5 Hz
- Pulse Duration: 5 ms
- Voltage: 60 V
- Temperature: 42°C

PRF was applied for 4 minutes on each side of the neuroma. In cases in which bilateral treatment was necessary, the cannula was carefully removed and reinserted under ultrasound guidance for the contralateral side to ensure precise targeting. The entire procedure was conducted in a single session by 2 physicians who worked in conjunction, specialized in foot and ankle surgery, and had extensive expertise in musculoskeletal ultrasound. This collaborative approach ensured accurate identification and treatment of the neuroma, enhancing the procedure's reliability and reproducibility.

Data Collection

Data on age, gender, and professional and sporting activities were collected. Pain, functionality, and quality of life were collected pre- and post-intervention: one, 3, and 6 months after treatment with PRF.

The visual analog scale (VAS) and Faces Pain Scale were used to assess pain intensity. The American Orthopedic Foot and Ankle Society (AOFAS) questionnaire assessed foot function, and the Short Form-36 (SF-36) assessed the quality of life (6). For VAS assessment, individuals were asked to place a vertical mark along

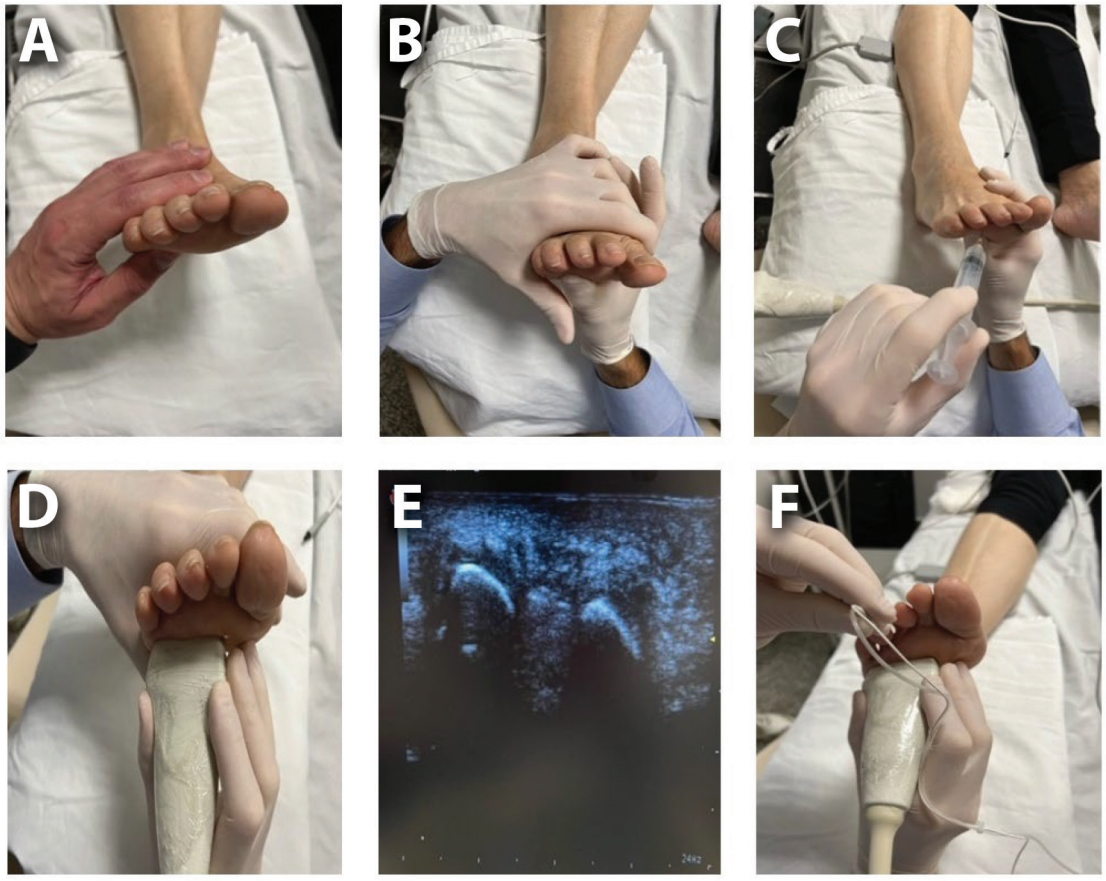

Fig. 1. *Intervention steps with PR in foot affected by Morton's neuroma. A) The patient's positioning. B) Mulder's test being applied. C) Application of anesthesia after the neuroma was located by ultrasound. D) Short axis of the ultrasound to better localize the intermetatarsal space. E) Plantar view of the transverse axis at the height of the metatarsal heads, with access to the interdigital space. F) The cannula was precisely placed at the edges of the neuroma (2 distinct points) "out of the plane." The positions were confirmed in the long axis of the foot "in the plane" (not represented).*

a horizontal line indicating the current level of pain, on which 0 points indicated "no pain" and 10 points indicated "worst pain" (6). Furthermore, the Faces Pain Scale was used, which is a pain scale that represents a series of faces ranging from a happy face (scale 0), or "no pain," to a crying face (scale 5), which represents "it hurts like the worst pain imaginable" (7).

The SF-36 scale is a quality-of-life assessment questionnaire containing 36 multidimensional items divided into 8 domains and a final score ranging from 0 to 100. The higher the final score, the better the overall quality of life (8). The domains classified as physical functioning (PF), role physical (RP), and bodily pain (BP) were measured for this study.

The AOFAS scale (9) was used to assess the functional status of the feet in the metatarsal region. The scale ranges from 100 to zero (values below 70 points are considered unsatisfactory).

In the present study, 2 orthopedists performed the procedures, strictly following the standardized technique and obtaining uniform and consistent results.

Statistical Analysis

Pre- and post-intervention data (VAS, Faces Scale, AOFAS, and SF-36 scores) were recorded. Means, SDs, and percentages were used to describe the data. First, the Shapiro-Wilk test was used to determine whether the data were normally distributed. Pre- and post-intervention differences were tested using independent samples t-tests. Statistical significance was set at a level of $P < 0.05$. For statistical analysis, Stata® software version 13.0 was used.

Results

A total of 20 patients (29 feet) completed the 6-month minimum follow-up period. Of these patients, 15 were women, and 5 were men, with a mean age of 58.4 ± 10.08 years. Three patients (15%) had Morton's neuroma on only the left foot, 8 (40%) on the right, and 9 (45%) on both feet. Five patients were lost to follow-up.

The average pain assessed by the VAS was statistically lower than it was during the pre-procedure period. After a single application of PRF, there was a progressive pain decrease in the post-treatment period at 4 weeks (P = 0.003), 12 weeks (P = 0.000), and 6 months (P = 0.000). Furthermore, the average pain levels at 12 weeks (P = 0.000) and 6 months (P = 0.000) after procedure, as assessed by the Faces Scale, were also statistically lower than the pre-procedure scores (Table 1).

Table 1. *Pain levels change in patients with Morton's neuroma after a single application of ultrasound-guided PRF.*

Variable	Pre-procedure	4 weeks	12 weeks	6 months	P-value
VAS score Mean ± SD	7.10 ± 1.79	5.4 ± 1.93	4.65 ± 2.05	3.90 ± 1.89	P1 = 0.003 P2 = 0.000 P3 = 0.000
Face scale Mean ± SD	3.34 ± 1.04	2.76 ± 1.30	2.19 ± 0.98	2.23 ± 1.09	P1 = 0.085 P2 = 0.000 P3 = 0.001
AOFAS Mean ± SD	71.55± 13.04	79.38 ± 11.75	81.1 ± 11.80	83.19 ± 11.29	P1 = 0.034 P2 = 0.010 P3 = 0.002

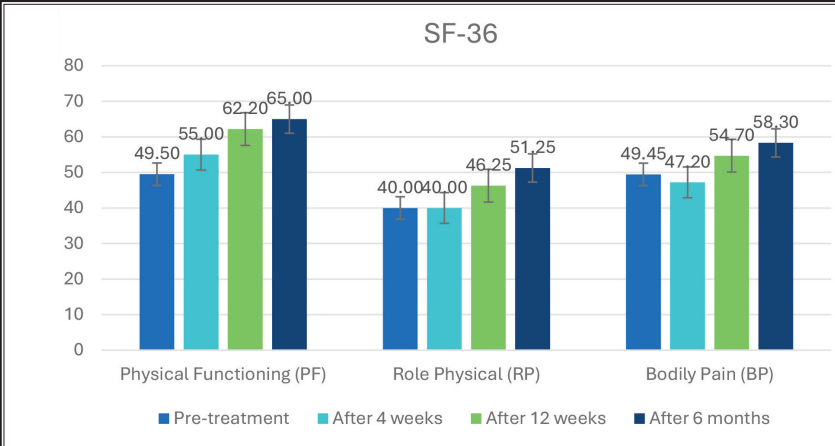

Fig. 2. *Quality of life of individuals with Morton's neuroma after ultrasound-guided PRF application.*

The average function assessed by the AOFAS scale was statistically higher in the post-procedure period at 4 weeks (P = 0.034), 12 weeks (P = 0.010), and 6 months (P = 0.002) than in the pre-procedure period. Patients' foot function improved after the application of PRF (Table 1).

The quality of life experienced by patients with Morton's neuroma after an ultrasound-guided radiofrequency application, as measured by the SF-36 questionnaire, are seen in Fig. 2. There was a significant increase in the PF domain between the pre-procedure (49.5 ± 27.13) and post-procedure periods at 4 weeks (55.00 ± 26.15, P = 0.071), 12 weeks (62.50 ± 24.30, P = 0.005) and 6 months (65.00 ± 23.50, P = 0.001). From the pre-procedure periods (40.00 ± 46.87) to the post-procedure periods at 4 weeks (40.00 ± 46.87, P < 0.0001) and 6 months (51.25 ± 44.77, P = 0.016; Fig. 2), the RP domain similarly showed an increase. There was also a significant improvement in BP from the pre-procedure (49.45 ± 18.86) to the post-procedure periods at 12 weeks (54.70 ± 14.60, P = 0.005) and after 6 months (58.30 ± 13.85, P = 0.016; Fig. 2).

There were no significant differences in physical limitations (RP) before the procedure (40 ± 46.87) and 12 weeks after it (46.25 ± 47.48, P = 0.056) or for BP during the pre-procedure period (49.45 ± 18.86) and 4 weeks after the procedure (47.20 ± 11.83, P = 0.350; Fig. 2).

Discussion

This study investigated the effects of a single ultrasound-guided PRF application on the pain, functionality, and quality of life experienced by patients with Morton's neuroma. We compared pre-procedure and post-intervention effects at 4 and 12 weeks and after 6 months. Our data demonstrated a significant reduction in pain score assessed by the VAS and Faces Pain Scale, an increase in the AOFAS questionnaire scale, and the average quality of life (SF-36 questionnaire) in the domains of physical functioning, role physical, and bodily pain. The results showed continuous improvement throughout the follow-up period.

The PRF mechanism of action for pain relief depends on a decrease in pro-inflammatory cytokines and an increase in cytosolic calcium concentration, followed by an effect on the immune system that reduces free radical molecules in the inflamed tissue (10). The PRF electrical fields are selective for small unmyelinated and lightly myelinated nerve fibers, producing a motor-sparing effect (11). Histological evaluations demonstrate that PRF promotes transient endoneural edema that persists up to one week after treatment (12). Pain relief, which is commonly observed after treatment, can last several months (13). Currently, the common pathologies treated with PRF are radicular pain, occipital and trigeminal neuralgia, and pain in the shoulders and knees (13). Recently, it has been observed that PRF has a long-term depressive effect on neuropathic pain (14). Although some mechanisms of action are well described in vitro, the electromagnetic field biophysical mechanisms generated by the active tip of the cannula for improved pain are not yet clearly elucidated.

Our study demonstrated significant pain symptom reduction after the application of PRF. Other studies have also reported the use of PRF for treating painful foot neuromas and reducing pain scores (11).

Chuter and colleagues found an overall improvement of 75% in pain symptoms after 6 months (15), and another study reported that at 8 months, 89% of treated individuals were satisfied with the outcome (16). The reduction in pain intensity was achieved after one week, and painful symptoms stabilized in the following months and after one year of treatment (17). These 3 studies described different methods using ablative radiofrequency. Brooks and colleagues also reported that radiofrequency ablation provided a high level of satisfaction for treating Morton's neuromas, with few side effects, the most common of which were thermal skin lesions. The authors reported that 3 radiofrequency cycles were better than 2 cycles (18).

Our study also significantly improved foot function, assessed by the AOFAS scale. We identified only one study that used this scale (5). These authors reported functional improvement after radiofrequency ablation during a mean follow-up period greater than 2.5 years (5).

Here, we observed improvements in quality of life using 3 SF-36 domains: PF, RP, and BP. Although many studies evaluated the effects of radiofrequency on pain (16,17,19, 20), only one study reported the effects of radiofrequency on quality of life (17). The authors reported significantly improved quality of life for all individuals (n = 52) at 6 months and one year after radiofrequency was used on the patients (17). However, our study is the only one to evaluate such improvements in association with PRF. Furthermore, to our knowledge, our study contains the largest series of uses of PRF for treating Morton's neuromas.

Like other studies (21,22), we used local anesthetic before applying radiofrequency. Using local anesthetic before the radiofrequency procedure yields a therapeutic effect and improves outcomes (5). Thus, long-term follow-up will help establish the procedure's effectiveness (5). To avoid such interference, we chose to use 0.5 mL of 1% lidocaine superficially on the plantar skin of the forefeet after checking with ultrasound.

We must highlight that we did not identify any significant adverse events. Chuter and colleagues in 2013 reported a minor temporary nerve irritation. Three neuromas (10%) progressed to surgical excision, and one patient had continuous, unchanged pain with no apparent cause (15). Other complications included difficulty wearing shoes (19) and unbearable pain in 10% of patients (20). Another study reported a patient who underwent a total of 3 procedures with no reported success and was a candidate for open excision. Additionally, of 32 patients, 6 required post-procedure cortisone injection in the 6-week follow-up due to pain (5).

Our study's strengths include using the quality-of-life SF-36 questionnaire and the functionality scale—the AOFAS scale. Few studies used both parameters. Furthermore, as far as we know, this study is currently the largest series on the topic in the literature. However, our study has a modest follow-up time and no other group, whether control or treatment, with whom to compare results. Additional studies involving long-term follow-up, other types of treatments, and sample sizes representing large populations are necessary.

Conclusion

Only one ultrasound-guided PRF session demonstrated promising results for improving the pain, foot functionality, and quality of life experienced by patients with symptomatic Morton's neuroma involving a minimum follow-up of 6 months. This treatment modality is minimally invasive and safe and can be repeated to optimize results and reduce the need for surgery.

Authors' Contributions

LFF and FGC wrote the manuscript. JTS analyzed the data with ESM and MJ. LFF and RCV performed the patients' procedures. RMB, NSM, and TSM re-

cruited individuals and scheduled them into the program. JFL, VFP, LFM, and SR revised the data and article writing. All the authors finally approved the manuscript and read and agreed to the published version thereof.

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Patient involvement statement: Study patients were not involved in the design, conduct, interpretation, or translation of the current research.

Data Availability: All data are available upon request to the corresponding author and may be reused upon request.

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