ORIGINAL RESEARCH

Cryoablation of Morton's Neuroma: An Early Clinical and Radiological Outcome Study

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Abstract

Introduction: Morton's neuroma (MN) is a common compressive neuropathy of the interdigital nerves. Nonoperative management is recommended initially, and many modalities have been described. Cryoablation (CA) has shown promising results; however, there are limited published studies in the literature. The purpose of this study was to assess the safety and efficacy of ultrasonography (US)-guided CA in patients with MN.

Methods: A retrospective analysis was completed for 20 patients (24 MN) between June 2021 and September 2022. All patients had refractory MN symptoms from previous US-guided steroid and local anesthesia injections. CA was performed under continuous US monitoring as a single outpatient procedure with one cycle for 2 minutes. Telephone follow-up with a 0–10 numerical rating scale was performed at 6 weeks and 3 months post-CA.

Results: The mean size of MN treated was 12.3 mm. Technical success was 100%. The mean preprocedure pain score was 8, which reduced to 0 at 6 weeks and 3 months follow-up in the treated MN. There were two cases of fibrosis in the webspace (12.5%) seen on magnetic resonance imaging (MRI), and 1 residual neuroma was observed (6%). There were no complications observed.

Conclusion: In this series, US-guided CA performed by musculoskeletal radiologists was deemed a safe and effective treatment for MN. Clinical advantages of the procedure are good patient tolerance, single outpatient procedure, high patient satisfaction and reduced risk of scarring or residual neuroma. Further controlled prospective studies would be beneficial.

Keywords: Cryoablation, Forefoot, Morton neuroma.

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Introduction

Morton's neuroma (MN) is a relatively common pathology presented to a foot and ankle practitioner, although the terminology can be considered controversial. Morton, in 1876 described a painful syndrome of the foot, occurring at the fourth metatarsophalangeal joint rather than a nerve problem. Other authors previously described "a neural swelling of the forefoot."[1,2] The pathogenesis most likely involves repetitive compressive trauma of the plantar nerve against the transverse intermetatarsal ligament resulting in perineural degeneration, neovascularisation and fibrosis.[3] Histological features of resected "neuromas" are not any different than those of biopsies from normal intermetatarsal space nerves in feet with no pain. The only difference is that they are larger (swollen) than that of a normal nerve and can have a significantly greater degree of demyelination.[4] Thus, the term "Morton's neuroma" can represent a clinical condition that is characterized by neuropathic pain in the forefoot that is associated with the interdigital nerve (most commonly the one in the third webspace). The symptoms of burning pain and discomfort commonly with weight bearing can be debilitating for the patients and can be associated with numbness of the toes. Ultrasound (US) can confirm the diagnosis with 98% accuracy and can be combined with injections for pain relief.[5]

Initial management is typically nonoperative. Multiple modalities have been described with physiotherapy (gastrocnemius muscle stretching protocol and use of appropriate footwear), injections (local anesthetic, steroid, and alcohol), radiofrequency ablation, shockwave therapy, and cryotherapy prior to surgical treatment. Cryoablation (CA) has been recognized as a well-tolerated procedure for analgesic therapy, especially postoperatively, with the first case report for use in MN being described in 1997.[6,7] However, there are limited published studies in the literature. Our aim in this study was to obtain early clinical and radiological results of CA for MN.

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Methods

This is a retrospective analysis of prospectively collected data for 24 patients with MN treated between June 2021 and September 2022 in a single center. Prior to starting the CA service, there was a discussion with the radiology team and the foot and ankle surgical team regarding patient selection and referral pathways. All patients underwent clinical assessment by a foot and ankle surgeon and had either musculoskeletal US or magnetic resonance imaging

(MRI) prior to the procedure to confirm the diagnosis. Diagnostic criteria, as described by Zanetti and Weishaupt, included a focal hypoechoic lesion in the intermetatarsal region on US examination or T1 and T2-hypointense lesion in the intermetatarsal space on MRI, with positive sonographic Mulder's click.[8] Partially compressible hypoechoic lesions on the US or a T2-hyperintense nonenhancing component on MRI were deemed to reflect a bursal neuroma complex with no other radiological cause for forefoot symptoms (e.g., Freiberg's disease or metatarsal phalangeal joint arthritis).

The patients were selected and consented for CA if they had transient relief for at least 1 month after US-guided steroid and local anesthetic injection into the neuroma within the previous year, with recurrence of symptoms. Options for surgical management were discussed with the patient. The presence of other potential pain generators, both radiological and clinical, was documented. Patients were excluded from CA if they preferred surgery, were pregnant, had an active infection or had previous surgery in the treatment site.

Procedure

All procedures were performed in an outpatient setting under local anesthesia in the US room by fellowship-trained consultant musculoskeletal radiologists. In our center, the IceFx (Boston Scientific, Marlborough, Massachusetts, United States of America) CA system was used. Preprocedure planning US was performed for evaluation of the lesion size and adjacent soft tissues. Using sterile aseptic technique and US guidance, the cryoprobe (IceSeed, Boston Scientific, Marlborough, Massachusetts, United States of America) was sited in the hypoechoic neuroma in the symptomatic intermetatarsal space (Fig. 1).

A single freeze cycle was performed, ranging from 60 to 100% strength, depending on operator preference. Real-time continuous US monitoring of the ice ball was performed throughout the procedure. Care was taken that the resulting ice ball covered the neuroma without extending <0.5 cm to the skin surface. The freezing cycle was terminated after 2 minutes or if the ice ball approached the plantar fat pad within 8 mm to avoid skin damage. The cryoprobe was withdrawn under monitoring, and depomedrone 40 to 80 mg was infiltrated (according to operator preference).

Data Collection

The primary outcomes for this study were clinical evaluation using numeric rating scale (NRS) pain score at 6 and 12 weeks postprocedure and radiological review using MRI.[9] Secondary outcomes included patient demographics, location and size of the MN, freeze cycle time, and percentage of freezing strength. Technical success was defined as the accurate placement of the cryoprobe within the MN as visualized in the US and the immediate postprocedure NRS score of 0. All patients were followed up by telephone consultation at 6 and 12 weeks. Questions included the primary outcome, if they were satisfied with the procedure and would have the procedure again, and if they had any new concerns. Complications were recorded as per the Clavien-Dindo complication classification.[10]

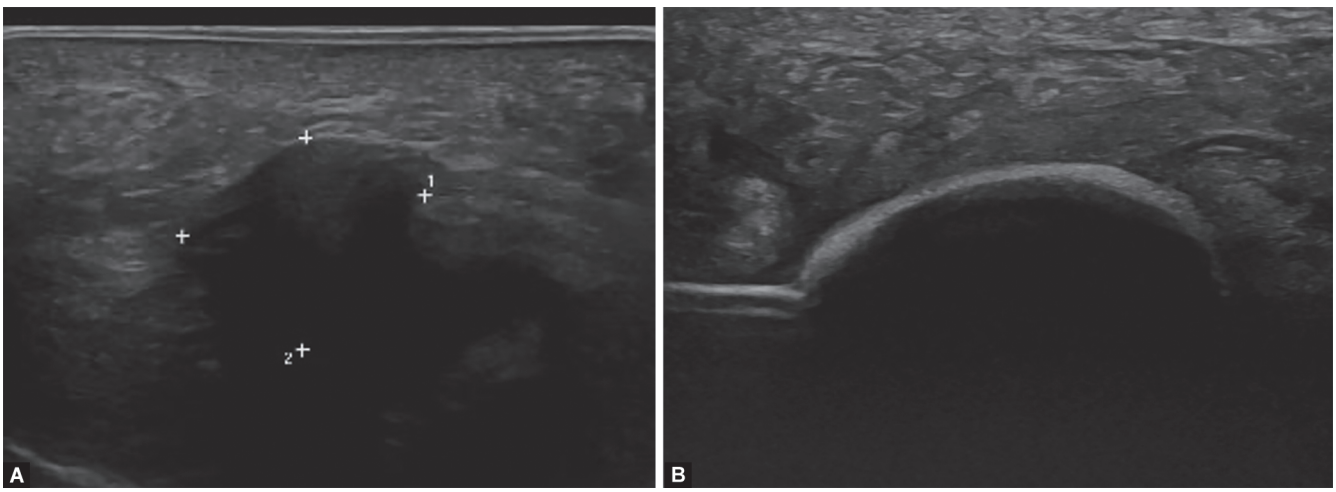
Statistics

Continuous parametric data are presented as the mean, median and 95% confidence intervals, and dichotomous data as a cross-tabulation of frequencies and percentages. Statistical analysis was performed using the student *t*-test if continuous data were tested to be normal and Mann–Whitney *U* or Fisher's exact test if tested to be independent and nonnormally distributed. Dependent, nonnormally distributed data were assessed using the Wilcoxon signed rank test. Binary data were tested using Chi-square. Significance was given to variables that reached $p < 0.05$. Statistical analysis was undertaken using Statistical Package for the Social Sciences statistics version 26 (IBM, New York, United States of America).

Results

A total of 20 patients (24 MN) underwent US-guided CA for MN (13 females and seven males) in our center from June 2021 to September 2022. Three patients had two different sites treated, and one patient had a repeat procedure for a residual neuroma.

All patients treated had failed previous US-guided steroid and lidocaine injections within the previous year. Three patients also had refractory symptoms after prior alcohol ablation. One patient had a previous nonimaging-guided CA attempt by a different operator three years prior. A total of 24 MN were treated, ranging between 8 and 20 mm in the largest dimension, with a mean size of 12.3 mm.



Figs 1A and B: (A) Ultrasound (US) image depicting the hypoechoic neuroma in the symptomatic intermetatarsal space; (B) The ice ball in the treated neuroma is monitored under US

The most common site treated was the third intermetatarsal space (14/24), followed by the second intermetatarsal space (10/24).

Technical success was 100%. All patients tolerated the procedure well under local anesthesia with a mixture of 1% lidocaine and 0.25% levobupivacaine. All patients reported complete pain relief with NRS 0 immediately postprocedure. Follow-up data for all patients except one were available. Of the patients who were available for follow-up, all were satisfied with the procedure and were willing to have CA performed again if needed.

The preprocedure, and 6 and 12-week postprocedure NRS scores are reported in Tables 1 and 2. One patient reported an increased pain score at 6 weeks and 3 months which, following a repeat procedure, had resolution of symptoms. NRS scores at 6 and 12 weeks were significantly improved as compared to preprocedure, greater than the minimal clinically important change.[11] When comparing scores between patients who had been administered corticosteroids with those who had not, there was a statistically significant improvement at 12 weeks. However, this difference was dependent on the result of one patient, and therefore the fragility index was high.[12] There was no correlation between MN size and NRS score either pre or postprocedure.

Postprocedure MRI was performed in 19 cases, on average 16.21 weeks [median 12, 95% confidence interval (CI) 10.92, 21.50] following the procedure. This showed posttreatment changes in all cases around the procedure site, most commonly osseous change corresponding to the rim of the ice ball and soft tissue edema (Fig. 2). When specifically analyzing the nerve site, 10 cases reported resolution of the neuroma, one case the neuroma had shrunk, and in six cases there was posttreatment fibrosis. In two cases, there was no change in the neuroma appearance.

There was high patient satisfaction, with 20/24 cases (83%) very satisfied with the procedure, with sustained pain relief at 3 months. In our cohort, 14 patients fell in the 12–18 month follow-up, and 11 out of 14 patients (79%) reported complete and sustained pain relief at NRS 0 postprocedure, with return to normal activity and were not taking regular analgesia. Four patients had various persistent symptoms, most commonly residual pain in the treated site with running or walking, including two with a sensation of a lump or ball that was present in the treatment site; however, all patients wanted to have CA done again.

There were no major complications recorded in this cohort. There were no cases of infection, skin necrosis or stress fracture related to the CA site. No patients in our cohort proceeded to have surgery or were found to have stump neuroma postprocedure on imaging. All patients demonstrated numbness or altered sensation in relation to the affected nerves, although this finding is an expected consequence of nerve ablation.

Discussion

Our aim in this study was to obtain early clinical and radiological results of CA for MN. In our cohort, we identified a high rate of satisfaction and significant pain relief in patients treated with CA. Although MRI findings showed osseous changes, the patient's clinical symptoms did not correlate with this as a problem. MN is a common cause of forefoot pain. Treatment remains controversial. Nonsurgical methods are always the initial management, and variable results have been described with different modalities. Surgical treatment is reserved for recalcitrant cases, but as MN is often associated with metatarsalgia and forefoot overload, all elements of the problem need to be addressed. CA is a useful second-line treatment and should be seen as an alternative to surgery.

It is important to also acknowledge that there may be other contributing factors to the patient's symptoms. Gastrocnemius tightness and forefoot osseous deformity should be assessed and dealt with as appropriate.[13] In addition, the rationale for using CA in our institution is that it induces axonal Wallerian degeneration (class III damage) with preservation of the epineurium and perineurium observed due to the resilience of collagen and fibroblasts to hypothermia.[14,15] Therefore, this theoretically allows eventual nerve regeneration to be more organized with the collagen and fibroblast scaffolding intact, without scar or stump neuroma formation.[16,17] On the contrary, the alternative, radiofrequency ablation, involves direct contact between heating elements and nerves. This is known to cause class V damage. This damage to the perineurium and epineurium results in disorganized neural regeneration which may form a posttreatment stump neuroma. There is also an increased risk of scar tissue from radiofrequency ablation or postsurgical

Table 1: Average VAS scores, preprocedure, and 6 and 12-week postprocedure

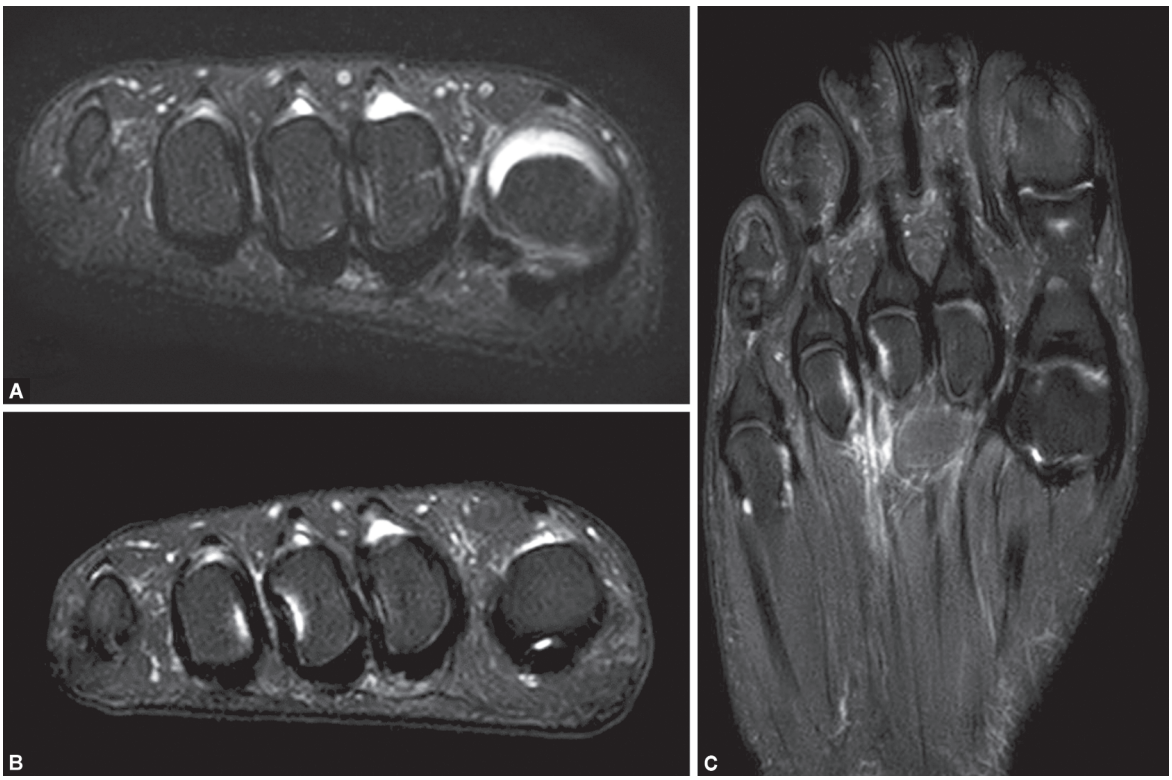
					95% CI		
	Mean	*Median*	*Min*	*Max*	*Lower*	*Upper*	*p-value*
Preprocedure VAS	7.96	8.00	5.00	10.00	7.45	8.46	
6-week VAS	1.63	0.00	0.00	8.00	0.39	2.86	<0.001
12-week VAS	2.54	0.00	0.00	8.00	1.08	4.00	0.001

CI, confidence interval of the mean; the *p*-value represents a comparison of 6 and 12-week VAS with preprocedure VAS

Table 2: Average VAS scores at 6 and 12 weeks postprocedure depending on steroid administration at the time of the procedure

						95% CI		*p-value*
		Mean	*Median*	*Min*	*Max*	*Lower*	*Upper*	
6-week VAS	No steroid	3.09	0.00	0.00	8.00	0.68	5.50	0.019
	Steroid	0.38	0.00	0.00	5.00	−0.45	1.22	
12-week VAS	No steroid	4.82	7.00	0.00	8.00	2.57	7.06	0.004
	Steroid	0.62	0.00	0.00	8.00	−0.73	1.96	

CI, confidence interval of the mean; the *p*-value represents a comparison of VAS between steroid use and not at 6 and 12-week intervals



Figs 2A to C: (A) Short-axis T2 fat suppressed (T2FS) pretreatment image on MRI; (B and C) Short- and long-axis T2FS images show T2-hyperintense osseous change corresponding to the rim of the ice ball and soft tissue posttreatment edema in the treated intermetatarsal space

fibrosis entrapping the regenerating nerve fascicles. CA can be safely repeated if necessary.

Caporusso et al., in a prospective series of 20 patients (31 MN), attained a satisfaction rate of 90%, but only 39% of patients were pain-free based on the VAS score.[18] Five patients (16%) had no pain relief at all from the procedure, but they all had previous surgical neurectomies. Their follow-up was for 1 year. They did not report any complications. In our series, 67% of patients were pain-free postprocedure, but we mainly treated primary MN, with only one revision case.

Friedman et al., in their retrospective case series, performed US-guided cryoneurolysis in 20 patients.[19] They included postsurgical and posttraumatic neuromas as well; only five patients were treated for MN. Of the MN patients, 3/5 patients reported marked treatment response, and one patient reported moderate and no response. Overall, 15 of 20 patients (75%) had a positive response to treatment, with five patients having no relief. Only 11 patients had marked pain relief, with the remaining four patients having only moderate or minor. They reported only minor bleeding at the site as a complication. They performed the procedure with a proximal nerve block for regional anesthesia. We did not perform regional anesthesia and used only local anesthesia, which can possibly decrease morbidity.

Cazzato et al., in their series, showed excellent results with 24 MN in 20 patients treated with MR-guided CA.[20] They used patient satisfaction and local pain scores to evaluate their results. Almost 80% of patients were "completely satisfied," and the overall patient satisfaction was 95% rate at a mean follow-up of 20 months. They reported only one complication (6% rate) in the form of local cellulitis. Up to 6 weeks of altered sensation was reported by some patients, but none of them required any further treatment. The use of MR-guided CA is technically more difficult than the US-guided technique and excludes patients with noncompatible implants and claustrophobia. Access to MR-guided therapy is limited in many centers, with diagnostic demand for scanner time and a lack of MR-compatible equipment.

We acknowledge the limitations of our study. This is a retrospective observational study with prospectively collected data from patients consecutively treated in a single center. The cohort of patients is small, with a relatively short follow-up with 3 months minimum in all patients. We used only the NRS score and patient satisfaction for outcomes, and there was no registration of patient-reported outcome measures (PROMs). The follow-up was limited to telephone consultations by the operators and not an independent observer. A future study on a larger scale with a control group, longer follow-up, and PROM questionnaire would be beneficial.

Conclusion

In this series, US-guided CA performed by musculoskeletal radiologists was deemed a safe and effective treatment for MN in an outpatient setting. Clinical advantages of the procedure are good patient tolerance, single outpatient procedure, high patient satisfaction and reduced risk of scarring or residual neuroma. CA also does not disrupt the epineurium or perineurium, which may allow nerve regeneration with less risk of stump neuroma. Further controlled prospective studies would be beneficial to determine the long-term outcomes of the method and placebo-controlled trials are needed to clearly define the long-term benefits and complications compared to other treatments.

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