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MUSCULOSKELETAL

Short term comparison between blind and ultrasound guided injection in morton neuroma

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Abstract

Objective The aim of this work is to compare the effectiveness of blind and ultrasound-guided injection for Morton's neuroma (MN) to determine which is more appropriate as the initial procedure in conservative treatment.

Methods This is an evaluator-blinded randomised trial. Of the 56 included patients, 27 were assigned to the blind group (A) and 29 to the ultrasound-guided group (B). Injection includes 1 ml of 2% mepivacaine and 40 mg of triamcinolone in each web space with MN. The included patients were assessed clinically by VAS score and the Manchester Foot Pain and Disability Score (MFPDS). The follow-up was performed at 15 days, 1 month, 45 days, 2 months, 3 months and 6 months after the initial injection.

Results No differences in age or clinical measurements were found at presentation between group A and group B. At the follow-up, the ultrasound-guided group showed greater symptomatic relief at several stages of the follow-up: 45 days (VAS 3.0 ± 0.5 versus 5.5 ± 0.5, $p = 0.001$; MFPDS: 32.2 ± 1.8 versus 38.8 ± 2.0, $p = 0.018$), 2 months (VAS: 3.1 ± 0.5 versus 5.6 ± 0.5, $p = 0.002$; MFPDS: 31.5 ± 1.9 versus 38.5 ± 2.1, $p = 0.020$) and 3 months (VAS: 3.1 ± 0.4 versus 5.2 ± 0.6, $p = 0.010$; MFPDS: 31.2 ± 1.9 versus 37.7 ± 2.4, $p = 0.047$).

Conclusion Injection of MN under ultrasound guidance provides a statistically significant improvement at some stages of the follow-up (45 days, 2 and 3 months), compared with blind injection.

Key Points

- *Ultrasound-guided steroid injections in Morton's neuroma provide short-term pain relief to over 60% of the patients.*
- *Ultrasound-guided injections in Morton's neuroma lead to a higher percentage of short-term pain relief than blind injections.*
- *Ultrasound-guided injections in Morton's neuroma lead to a lower percentage of skin side effects than blind injections.*

Keywords Morton neuroma · Ultrasonography interventional · Metatarsalgia

Abbreviations

MFPDS	Manchester Foot Pain and Disability Score
MN	Morton's neuroma
US	Ultrasound
VAS	Visual analogue scale

Introduction

Morton's neuroma (MN) is a frequent pathology, mainly in middle-aged females, with a female:male ratio ≥ 5:1. It arises from the common plantar digital and proper plantar digital nerves, mainly in the second and third web spaces. The location in the first and fourth web spaces is extremely rare [1].

It is considered to be secondary to mechanical stress over the nerves, leading to fibrosis in and around the neural tissue [2]. Pain is elicited under pressure of the web space, and Mulder's click may be felt by the patient and physician during forefoot squeezing [3].

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MN is not a true neuroma, but a degenerative process of the nerve characterised by epineural, perineural and endoneural fibrosis [4]. Several conservative non-surgical measures have been implemented to relieve symptoms of MN because after surgical excision the success rate rarely exceeds 80% [5] and recurrent painful neuroma after surgery is less responsive to a further surgical intervention [6]. Conservative care provides relief in most patients with MN, including footwear modifications, use of insoles and steroid injections [2]. Some authors consider footwear modifications and insoles the first step of treatment and injections the second step before considering surgery [7]. Nevertheless, better outcome has been reported with steroid injections versus footwear modifications [8].

Imaging methods are useful in confirming the diagnosis of MN and excluding other causes of forefoot pain, such as metatarsophalangeal arthritis or intermetatarsal bursitis. The available evidence suggests that ultrasound is more accurate for the diagnosis of Morton's neuroma than MRI. Considering pooled sensitivity, both ultrasound (90-91%) and MRI (90-93%) were similar and relatively high [9, 10]. Nevertheless, MRI has been reported to have an equal [9] or a relatively lower specificity than ultrasound (68% vs. 88%) in the detection of Morton's neuroma [10].

Percutaneous injection in MN may be performed blind or under ultrasound guidance as part of non-surgical conservative treatment. The hypothesis of the present study is that ultrasound-guided injections lead to greater pain relief than blind injections. If this hypothesis is demonstrated to be correct, it will be advisable to recommend that injections of MN be preferentially performed under ultrasound guidance. The main aim of this work is to compare the short-term effectiveness (15 days to 6 months) of blind versus ultrasound-guided injections for MN to determine which one is more appropriate as the initial procedure in conservative treatment.

Materials and methods

The study was approved by the local ethics committee (code: 0565-N-16), and patients gave their written informed consent to participate. It was also registered in clinicalTrials.gov (NCT03046108).

Treatment was randomised to an ultrasound-guided (group A) or non-ultrasound-guided (Group B) group. The program Epidat 4.1, Sampling module, was used to generate a series of random numbers indicating in which group each patient should be included. A researcher not involved in the diagnosis or treatment of the patients guarded the list that was generated. If a patient fulfilled the inclusion criteria, he or she was scheduled for injection by the orthopaedic surgeon (blind) or the radiologist (ultrasound guided) according only to the entrance order to the study.

Recruited patients were older than 18 years with clinical criteria of MN and symptoms lasting more than 6 months. Physical examination was performed by a > 20 year experienced orthopaedic surgeon. The inclusion criterion was ultrasound detection of MN with a sagittal length ≥ 5 mm (Fig. 1). In case of bilateral foot pain only the most symptomatic foot was included.

Ultrasound was performed by an experienced musculoskeletal radiologist, of > 20 years, using a 12-5 MHz probe in a Philips IU 22 or Philips Epic 5 ultrasound machine. First, the dorsal aspect of the forefoot was explored to detect any sign of metatarsophalangeal arthritis. Then, the plantar aspect was explored to search for MN and to exclude another causes of pain, such as flexor tenosynovitis or intermetatarsal bursitis without neuroma. Manoeuvres to explore MN included pressure on both sides of the forefoot, clasping with the hand, trying to push the neuroma toward the plantar aspect of the forefoot, known as the sonographic Mulder sign [11] (Figs. 1F and 2). If a mass-like structure was detected, a second manoeuvre was performed. It consisted of applying pressure on the dorsal aspect of the web space, trying to push forward the distal part of the neuroma and compress the bursa. MN showed a fusiform elongated shape and was not as compressible as the intermetatarsal bursa. The bursa showed a more rounded or oval shape (Fig. 3 and video 1).

Exclusion criteria were lack of willingness to enter the study, contraindication to the use of steroids or local anaesthetics, web space injection in the previous year, previous surgery in the area or the presence of other causes of foot pain, such as arthritis, intermetatarsal bursitis without neuroma, enthesitis or tendinosis.

Both the orthopaedic surgeon and the musculoskeletal radiologist used a dorsal approach to inject the intermetatarsal space introducing a 23-G needle after antiseptic cleansing of the skin. In the former case there was no internal visualisation of the injection. In the ultrasound-guided cases the needle was placed in the dorsal aspect of the neuroma and moved forward and backwards to achieve a homogeneous distribution of the injectate around and/or inside the neuroma. Care was taken to avoid the injectate crossing the limit of the overlying superficial transverse metatarsal ligament (Fig. 4). In each patient a mixture of 1 ml of 2% mepivacaine and 40 mg of triamcinolone acetonide was injected into each web space affected by Morton's neuroma.

Included patients were assessed clinically by the VAS score, 0-10 points, and the Manchester Foot Pain and Disability Score (MFPDS), 17 to 51, with higher scores indicating greater severity in both tests [12]. The 17 items of MFPDS can be classified into four components: functional limitation (7 items), activity restriction (2 items), pain intensity (6 items) and concern about appearance (2 items) [13].

To determine if differences in the scores were clinically relevant, the patients also graded the results on a four-grade

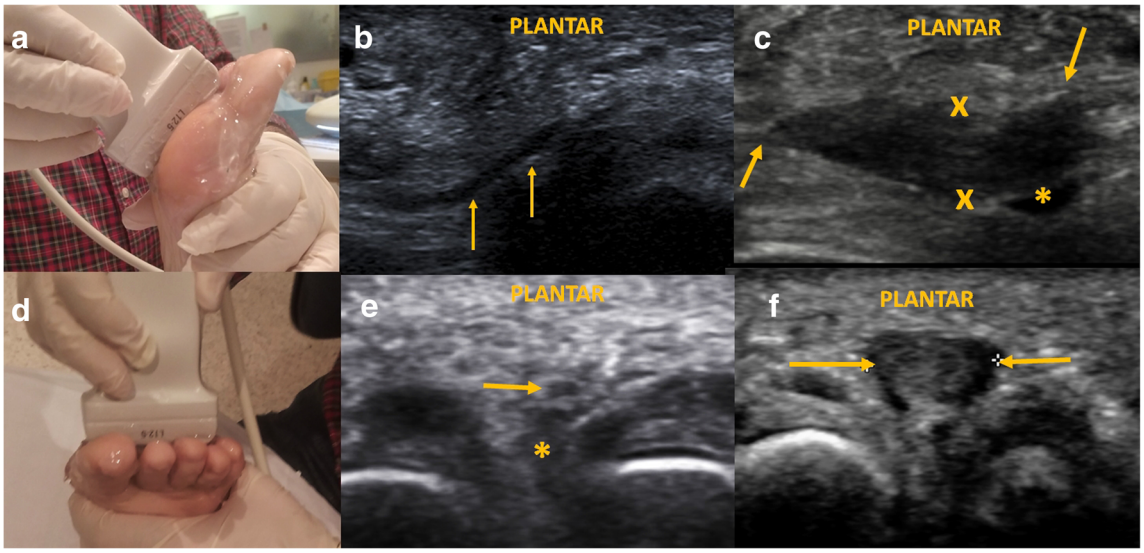

Fig. 1 **a** Long-axis US view; probe position. **b** Normal plantar digital nerve (arrows). **c** In the long axis view we measured the longitudinal (arrows) and dorsoplantar axes (X) of the neuroma. Bursa (*). **d** Short-axis US view. Probe position. **e** Normal plantar digital nerve (arrow) and intermetatarsal bursa (*). **f** In the short axis view we measured the transverse axis of the neuroma scanned while clasping the forefoot (arrows)

qualitative scale: very satisfied, satisfied, disappointed and very disappointed. For statistical analysis this scale was categorised into two groups: satisfied (very satisfied + satisfied) and disappointed (disappointed + very disappointed). The initial score was obtained at consultation by a researcher not related to diagnosis or treatment and before the diagnostic ultrasound, even if the patient did not enter the study eventually. Follow-up scores were obtained by a phone call by another researcher, always the same, and also not related to diagnosis or treatment, at 15 days, 1 month, 45 days, 2 months, 3 months and 6 months. Scores were communicated to the researchers involved in the diagnosis and treatment by e-mail to determine if the patients needed a new injection. Up to four injections, according to patients' clinical evolution, were allowed within the first 3 months.

Statistical analysis was performed using IBM SPSS software Statistics 19. Descriptive statistics included mean ± standard deviation, minimum and maximum, for numeric variables and frequency and percentages for qualitative variables. Variable normality was checked by the Shapiro-Wilk test. The bivariate analysis included the analysis of evolution for each individual group, blind and ultrasound guided, and

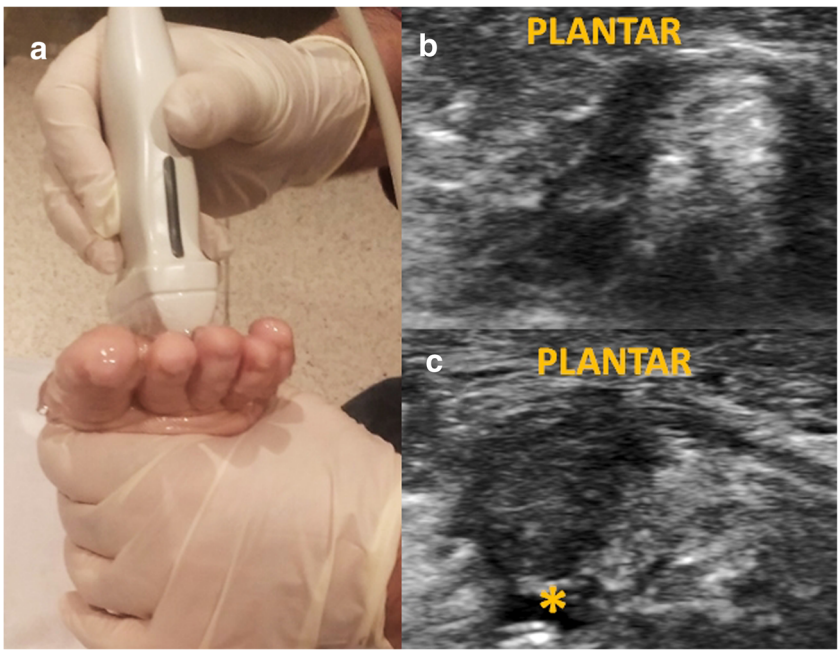

Fig. 2 **a** Sonographic Mulder sign in long-axis view. **b** No clear identification of the soft tissue structures of the web space before exerting any pressure on the forefoot (arrow). **c** Morton neuroma is clearly shown after exerting pressure on the clasped forefoot (arrow). Bursa (*)

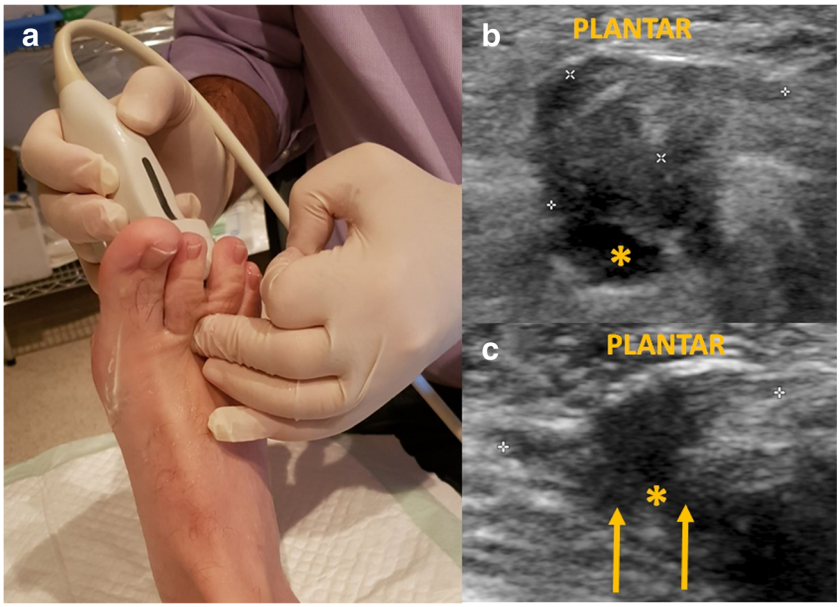

Fig. 3 and video1. **a** Pressure on the dorsal aspect of the web space in long-axis view. **b** The elongated neuroma is seen plantar regarding the rounded bursa (*) before exerting any pressure. **c** After pressure on the dorsal aspect of the web space (arrows) the bursa is compressed and the neuroma displaced distally and toward the plantar aspect of the forefoot

comparison between both groups. Evolution of individual groups at different time points of the follow-up was performed by the Friedman test of related samples and the significance between the different times was tested by the Wilcoxon test. Bivariate analysis between groups in the case of numeric variables was performed by the unpaired Student's *t* test for parametric variables and by the Mann-Whitney U test in the case of nonparametric variables. Regarding the neuroma size computation in case of two neuromas in the same patient, only the largest one was included. The effect of MN size and patients' age on the clinical outcomes was assessed by the unpaired Student's *t* test. Statistical significance was considered when $p < 0.05$.

Results

One hundred four patients were sent for ultrasound diagnosis of MN and 73 (70.1%) were confirmed to have MN. Of the 31 patients without neuroma, no soft tissue cause of pain was found in 20 of them, 5 had isolated arthritis and 6 had isolated bursitis.

Of the 73 patients with MN, 6 refused to enter the study, 5 had MN with an associated cause of foot pain (arthritis, fasciitis) that could mask the results of injection and 6 failed to attend the scheduled consultations. All of them were excluded from the study. Therefore, 56 patients were included in the final analysis (50 females and 6 males). Thirty-two of the 56

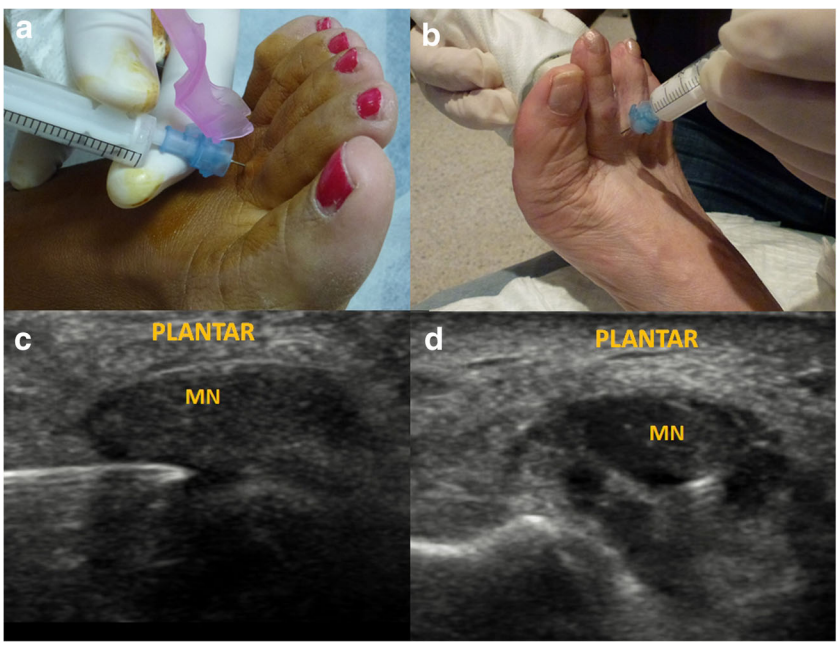

Fig. 4 **a** Blind injection in Morton's neuroma. **b** Morton's neuroma (MN) injection under ultrasound guidance. **c** In ultrasound-guided injection the tip of the needle is advanced between the MN and the bursa distributing the injectate around the MN (**d**)

patients (57.1%) presented neuroma in only one web space, 24 in the third web space and 8 in the second web space. The rest of the patients had neuromas in both the second and third web spaces (42.9%).

Of the 56 patients included, 27 were assigned to the blind group and 29 to the ultrasound-guided group. Table 1 shows the basal state and follow-up of the patients at 15 days, 1 month, 45 days, 2, 3 and 6 months. Both groups showed a significant reduction in the VAS score and the MFPDS score at every follow-up time point with regard to the initial values. The comparison between both groups showed a general trend of better results in the ultrasound-guided group, reaching statistical significance in the VAS score at 45 days, 2 and 3 months of the follow-up, and almost significant at 6 months of the follow-up ($p = 0.061$) (Table 1 and Fig. 5).

Regarding the MFPDS score, statistically significant differences were found at 45 days, 2 and 3 months of the follow-up (Table 1). Compared with the initial score, the ultrasound-guided group showed statistical improvement at all follow-up time points in all four components of the MFPDS ($p \leq 0.001$), while the blind group showed improvement in only two of the four components: pain intensity ($p = 0.007$) and concern about appearance ($p = 0.001$). Compared with both groups, the ultrasound-guided group showed a greater statistically significant improvement regarding functional limitation at 45 days ($p = 0.015$) and 2 months ($p = 0.011$), activity restriction at 2 months ($p = 0.031$), pain intensity at 45 days ($p = 0.025$) and almost significant improvement in concern about appearance at 45 days ($p = 0.057$) and 2 months ($p = 0.078$).

Table 1 Comparison between the ultrasound- and blind-guided group of basal and follow-up values. *VAS* Visual analogue scale, *MFDS* Manchester Foot Pain and Disability Score, *NS* Not statistically significant. Values expressed as mean ± standard error of the mean.

Variable	Ultrasound guided	Blind	Significance
Age	54.1 ± 2.7	50.3 ± 1.6	NS
Number of infiltrations	2.1±0.1	2.7±0.2	$p = 0.038$
Length of the neuroma	14.8 ± 0.6	13.3± 0.6	NS
Dorso-plantar axis	4.0 ± 0.2	3.4 ± 0.2	NS
Transverse axis	5.5 ± 0.4	4.2 ± 0.3	NS
VAS initial	8.5 ± 0.2	8.5 ± 0.2	NS
VAS 15 days	3.9 ± 0.5	5.2 ± 0.5	$p = 0.097$
VAS 30 days	3.7 ± 0.5	5.2 ± 0.5	$p = 0.056$
VAS 45 days	3.0 ± 0.5	5.5 ± 0.5	$p = 0.001$
VAS 2 months	3.1 ± 0.5	5.6 ± 0.5	$p = 0.002$
VAS 3 months	3.1 ± 0.4	5.2 ± 0.6	$p = 0.010$
VAS 6 months	3.4 ± 0.5	5.1 ± 0.7	$p = 0.061$
MFDS initial	43.7 ± 1.6	45.4 ± 1.3	NS
MFDS 15 days	35.9 ± 2.1	38.5 ± 2.0	NS
MFDS 30 days	34.9 ± 2.0	38.7 ± 2.1	NS
MFDS 45 days	32.2 ± 1.8	38.8 ± 2.0	$p = 0.018$
MFDS 2 months	31.5 ± 1.9	38.5 ± 2.1	$p = 0.020$
MFDS 3 months	31.2 ± 1.9	37.7 ± 2.4	$p = 0.047$
MFDS 6 months	33.6 ± 2.3	37.6 ± 2.7	NS

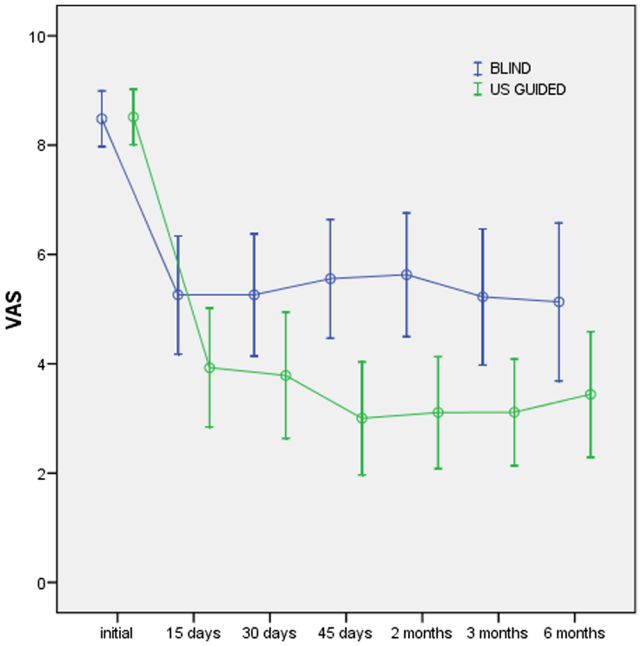

Fig. 5 Evolution of the visual analogue score (VAS) in the two groups of patients. Values are expressed as mean ± standard error of the mean

Qualitative evolution of the patients is shown in Table 2 and Fig. 6. Better results were observed within the ultrasound group at 45 days, 2 and 3 months of the follow-up and almost significant at 6 months ($p = 0.064$). Disappointed patients received a greater number of injections than satisfied patients (3.0 ± 0.2 vs. 2.2 ± 0.1, $p = 0.01$). In the same way, the blind group received a greater number of injections than the ultrasound-guided group (2.7 ± 0.2 vs. 2.1 ± 0.1, $p = 0.01$).

Regarding neuroma size no statistical differences were found compared with the degree of patient satisfaction. Age was not statistically associated with outcome.

Reported complications of the patients included six cases of local depigmentation (5 in the blind group), one case of local hypersensitivity in the ultrasound group and one case of crossover toe in the ultrasound group.

Discussion

Conservative management of MN includes modification of the foot-loading area (adapted footwear and/or insoles), anti-inflammatory drugs and percutaneous injection of medication. Injections of local anaesthetics and steroids in MN are part of the most common non-surgical treatments of this condition [14].

Table 2 Comparison of the percentage of satisfied patients in the blind- and ultrasound-guided group. *NS* Not statistically significant

Follow-up	Ultrasound guided	Blind	Significance
15 days	69.0	51.9	NS
1 month	69.0	59.3	NS
45 days	82.8	51.9	$p = 0.013$
2 months	79.3	48.1	$p = 0.015$
3 months	79.3	44.4	$p = 0.007$
6 months	69.0	44.4	$p = 0.064$

Percutaneous injection may be performed blind or under ultrasound guidance. Nevertheless, it is theorised that the use of US guidance increases the efficacy of injections because it facilitates accurate real-time placement of the injection needle into the MN complex, avoiding other soft tissue structures [15].

Studies using ultrasound-guided injections have shown superior symptomatic relief after the injection of local anaesthetic + steroids versus anaesthetics alone at 3 months of follow-up [16]. Previous nonrandomised cohort studies have shown a degree of satisfaction of about 45% in both blind and single echo-guided infiltration [4] and around 75-80% in case of multiple blind injections [7, 8, 17, 18]. These results concur with our study where the percentage of satisfaction ranged at the different stages of the follow-up from 44.4-59.3% in the blind group and 69-82.8 % in the US-guided group.

Although there is abundant literature on the effect of anaesthetics alone or combined with different types of steroids on the clinical relief of patients with MN, we only found one study comparing the echo-guided with the blind technique based on anatomical landmarks. In this study, no significant differences between both injection methods were found, but the sample size (only 36 cases) constitutes a substantial limitation [19]. In fact, the ultrasound-guided group showed a trend for greater improvement, but it is likely that the small sample size prevented those researchers from reaching statistical significance. In our cohort, such statistically significant differences were found, mainly at certain follow-up time points, namely 45 days, 2 and 3 months in the quantitative VAS score, and 45 days, 2 and 3 months in the MFPDS. Moreover, a trend for greater improvement at 6 months' follow-up was found. The need for more injections in the blind group also strengthens the case for the superiority of ultrasound-guided injections.

Although the pain VAS score and pain intensity subscale scores of the MFPDS are correlated, different factors appear to be associated with these two measurements of pain, with age negatively correlated with the pain intensity subscale and female sex positively correlated with pain VAS score. However, the pain intensity subscale is more correlated with the functional limitation subscale of the MFPDS than with the VAS score [20]. This may partially explain the discrepancies found between the VAS score and MFPDS in our study. Similarly, despite pain improvement, patients still may follow some of the precautions measured in the MFPDS to prevent foot pain recurrence and disability.

Regarding the neuroma size, our results concur with previous works that found no influence of this factor on any clinical outcome [14, 21, 19], but results are in contradiction with authors that found superior relief with treatment in neuromas < 5 mm in sagittal diameter [22]. Still, our work only included

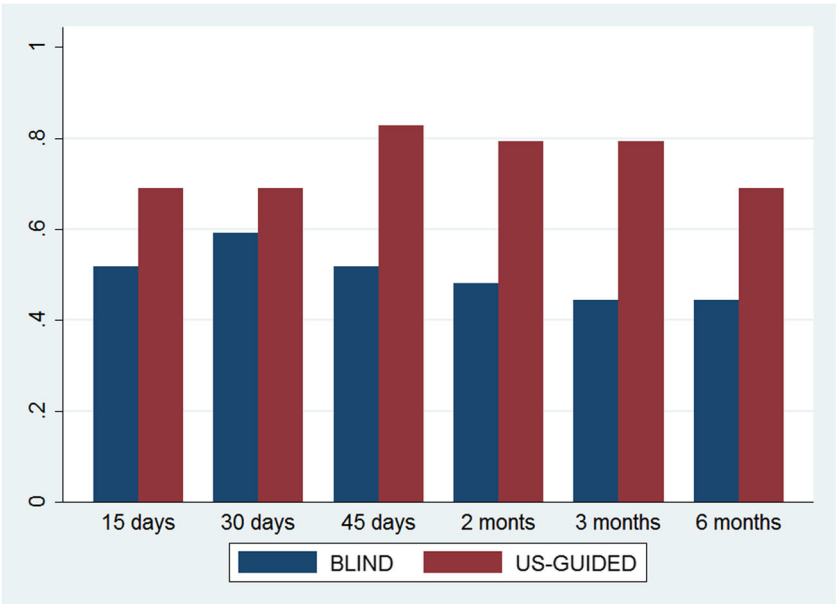

Fig. 6 Comparison of the percentage of satisfied patients: blind versus ultrasound-guided groups

neuromas > 5 mm long. It has been postulated that larger neuromas may need more volume of injectate [23]. Therefore, the smaller volume of injectate in other works or the use of different kinds of anaesthetic or steroid may have influenced these results. We used 2 ml of injectate, considered by us to be enough to cover even larger neuromas. This coverage could be checked in the ultrasound-guided group, where appropriate injections spanned the whole extension of the neuroma.

Patient age was also not associated with best or worse outcome in our study. This contradicts previous retrospective works that found poorer results in younger patients [23, 24], arguing that younger patients are more active and usually exert more pressure on their feet. In the short-term prospective follow-up of our study, these findings were not reproduced, although there was a trend of older age in satisfied patients (54.5 ± 2.3 vs. 50.0±2.5, $p = 0.297$, at 6 months' follow-up).

The incidence of two neuromas in the same foot was high in our study, 42.9%, but in the range of the figures reported in the literature, 1.5% to 65% [24, 25]. It is likely that the improvement of the ultrasound resolution contributed to the increased sensitivity in detecting MN leading to diagnosis of a higher percentage of ipsilateral concurrent MN in recent studies compared with older ones.

Steroid injections can lead to atrophy of the plantar fat pad and skin discoloration at the injection site [26]. These minor complications have been reported to occur in 5% of patients who received US-guided corticosteroid injection [16]. Our rate of skin discolouration was about 10%. This may be due to the high number of injections allowed within the first 3 months of follow-up. The blind group showed a higher incidence of this complication, probably because there was not a real control of the inner placement of the injectate.

The present study has some limitations. We acknowledge that the diagnosis of MN was not confirmed by histological examination in all our patients, but the overall accuracy of clinical and imaging diagnosis altogether has been reported to be very high, over 95% [3, 27]. Another limitation of the study is the sample size, which may have prevented differences from reaching stronger statistical significance.

In conclusion, injection of Morton's neuroma, blind or ultrasound guided, leads to symptomatic relief in a high percentage of patients. Probably, the volume injected, 2 ml, contributed to the success achieved with both methods. Yet, according to our results, injection of MN under ultrasound guidance is worthwhile because a statistically significant improvement was observed compared with blind injection at some stages of the follow-up.

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Compliance with ethical standards

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Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

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One of the authors has significant statistical expertise.

Informed consent Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- prospective
- randomised controlled trial
- performed at one institution

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