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ORIGINAL ARTICLE

Gender Correlation to the Prevalence of Pedal Neuromas in Various Interspaces

A Retrospective Study

Patrick A. DeHeer, DPM*
Artinder P. Nanrhe, DPM*
Shannon R. Michael, DPM†
Sarah N. Standish, DPM†
Christine D. Bhinder, DPM†
Todd L. Foster, PhD‡

*Hoosier Foot and Ankle, Franklin, IN.

†Department of Podiatry, St. Vincent Hospital, Indianapolis, IN.

‡Office of Research and Clinical Trials, St. Vincent Hospital, Indianapolis, IN.

Corresponding author: Patrick A. DeHeer, DPM, FASPS, FACFAS, Attending, Hoosier Foot and Ankle, 1159 W. Jefferson St. Suite 204, Franklin, IN 46131. (E-mail: padeheer@sbcglobal.net)

Background: Morton's neuromas are abnormalities of the common digital nerve branch located between the lesser metatarsal heads. Historically, interdigital (Morton's) neuromas have been characterized as being most common in the third interspace and predominantly identified in females. The principal investigator observed Morton's neuromas commonly in both the 2nd and 3rd interspaces in both genders. To the best of our knowledge, no literature exists to evaluate Morton's neuroma location with a focus on each gender independently. The present study evaluates Morton's neuroma interspace location and if there is a variation between males and females.

Methods: In this retrospective study, 582 de-identified ProScan magnetic resonance imaging reports, with a diagnosis code for Morton's neuroma (ICD Code 355.6), were obtained from their centralized database. These reports were evaluated for patients scanned from January 2015-April 2016. Incomplete records and those where the radiologist findings were not consistent with

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Morton's neuroma were eliminated. For the remaining 379 patients, data was collected on several factors such as gender, laterality, history of trauma, plantar plate tear, age and interspace location. Special focus was given to second and third interspace Morton's neuromas. Data was then evaluated statistically utilizing the Pearson Chi-Square and Independent Samples Mann-Whitney U Test with statistical significance deemed $p < 0.05$.

Results: No statistically significant distribution between gender and second and third interspace Morton's neuromas were noted. Additionally, right vs left foot, age and history of trauma did not vary between genders in a significant way. Lastly, there was a statistically significant difference between the presence of plantar plate tears between genders. Male patients with Morton's neuromas were found to have a higher rate of plantar plate tears (34/92, $p = 0.01$).

Conclusions: Our study found that there was not a statistically significant difference between female and male and Morton's neuromas location, laterality or age.

Morton's neuromas are a common finding in the general population as it is estimated that 50-87 per 100,000 people suffer from the condition.¹ Patients typically present with sharp, tingling pain from the forefoot to the toes. Often symptoms are exacerbated by shoe gear especially shoes with a narrow toe box or high heels.

On physical exam, pain would be noted with palpation of the affected interspace. There are multiple examinations that can aid in the diagnosis of a Morton's neuroma such as the Mulder's sign, Gauthier's test, Bratkowski's test and possible Tinel or Valleix phenomenon. The Mulder's and Gauthier's tests are squeeze tests of the forefoot, while the Bratkowski is a hyperextending of the toes and rolling the thumb in the area of the symptoms.² Additionally, on physical exam spreading or divergence of the digits also supports the Morton's neuroma diagnosis.³

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Morton's neuromas have many differential diagnoses such as stress fracture, arthritis, autoimmune conditions, ischemia, peripheral neuropathy, capsulitis, metatarsalgia, and predislocation syndrome. It is also necessary to differentiate symptoms from other sources of metatarsalgia such as MTPJ degeneration, Freiberg's disease, synovitis, and bursitis.⁴ Imaging can be performed to further confirm an interdigital Morton's neuroma diagnosis.

Several different imaging modalities can be utilized to evaluate for a Morton's neuroma. Grace et al. found that there was no statistically significant relationship between radiographs and clinical presence of Morton's neuromas.⁵ On ultrasound, Morton's neuromas were seen as an ovoid mass with hypoechoic signal best seen on coronal view, and Kakanala and Jain found the probability that ultrasound will confirm the presence of a plantar interdigital Morton's neuroma to be 91.67%.⁶ MRI has a high sensitivity and specificity with rates reported from 87-98% and up to 100% respectively.⁷⁻⁹

The benefit of an MRI is that it will allow the clinician to better visualize the forefoot, as a result, the clinician can identify alternative sources of pain or confirm a suspected Morton's neuroma.¹⁰ If a Morton's neuroma is present on MRI, the T1 weighted images will show a focal area of decreased signal intensity between the metatarsal heads.¹¹ Furthermore, T2 sequences are important to distinguish a Morton's neuroma from a bursitis.¹²

Despite the thickened and abnormal appearance of the nerve on imaging, the "neuroma" is not a tumor. Histological examination of a Morton's neuroma reveals extensive inflammation of the perineural tissue with no evidence of tumor formation.¹³⁻¹⁵ The process is one of a degenerative nature and not a neoplastic one, and the involved nerve histologically demonstrates demyelination, densely packed whorls of collagen (Renaut bodies), and fibrosis of the epineurium and endoneurium.¹⁶

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Researchers believe that the inflammation is due to compressive forces from the deep transverse metatarsal ligament (DTML) on the nerve. In some patients the 3rd common digital branch has a large communicating branch from the lateral plantar nerve, which passes deep to the DTML. Due to the nerve anatomy and a high incidence of 3rd interspace Morton's neuromas, many researchers believe that nerve anatomy is to blame for symptomatic Morton's neuroma.⁴

Although both males and females have the same pedal nerve anatomy, females are more likely to experience Morton's neuroma symptoms. One possible explanation is that shoe gear causes more women to have symptoms.¹⁷ However, research indicates that unilateral symptoms are most common. Studies vary drastically in their reported bilateral symptomatic patients, ranging from 2-39%.¹⁷⁻¹⁹

Past literature demonstrates a wide variation of the reported prevalence of Morton's neuromas at various interspaces. Consistently the 2nd and 3rd intermetatarsal spaces were the most common. Mann and Reynolds found similar frequency in Morton's neuromas located at the 2nd and 3rd interspaces.²⁰ On the contrary, Friscia found around 91% in the 3rd intermetatarsal space.²¹

Based on extensive literature review, it is to be noted that Morton's neuromas occur in the both the 2nd and 3rd interspaces frequently. A common flaw to Morton's neuroma studies is that the majority of the populations are comprised of female subjects (>80%).^{17,19,20,22-24} Due to this large underrepresentation in the male patient populations, it is unclear which interspace is most commonly affected in males. If males and females were evaluated separately, it is possible that Morton's neuromas in male patients occur more frequently than reported and possibly in a different interspace.

Inconsistency in the literature on the prevalence and location of pedal Morton's neuromas is widespread, despite the frequency of this common pathology. We conducted a retrospective study with use of magnetic resonance imaging (MRI) reports to evaluate the location of Morton's

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neuromas and possible correlation with gender. The authors' clinical experience did not support a clear higher frequency in a certain interspace correlating with gender, nor did an extensive literature search. However, higher frequency in the 2nd and 3rd interspaces was well supported and thus a gender was assigned to each location. For this study the authors hypothesized that our cohort would show a statistically significantly higher frequency of Morton's neuromas in the 2nd interspace among males, as well as a higher frequency in the 3rd interspace among female.

Methods

This study was approved by the institutional review board at St. Vincent Hospital Indianapolis (Study ID#R20180029). The Proscan Imaging database was utilized to obtain deidentified MRI reports with the diagnosis code for Morton's neuroma (ICD Code 355.6) from January 2, 2015 to April 19, 2016. Obtained MRI reports were void of patient's name, DOB, MRI facility and any private health information. A total of 582 MRI reports were identified. Only reports with complete records and a positive MRI finding of a neuroma were included in the study. Positive MRI findings of a Morton's neuroma were identified based on the following terminology utilized in the MRI report: neuroma and perineural fibrosis. Studies were excluded if the MRI report did not confirm a presence of a Morton's neuroma in the report. Furthermore, the following terminology noted in the MRI report were excluded as a positive neuroma diagnosis could not be inferred: possible neuroma or callus, soft tissue edema, perivascular tumor, ganglion cyst, capsulitis or other inflammatory conditions unrelated to nerve tissue.

Data was collected from the reports with the categorical and discrete variables including location of the interdigital neuroma (1st, 2nd, 3rd, and 4th interspace) and age, laterality, history of trauma, plantar plate tear, and gender. The data was then evaluated statistically with a p-value of

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<0.05 being deemed as statistically significant. Distribution of laterality, meaning right vs left foot, was evaluated using the Pearson Chi-Square test. The Pearson Chi-Square was also used to evaluate the distribution of patients with a history of trauma, plantar plate tear and Morton's neuroma location. Independent Samples Mann-Whitney U Test was used to evaluate age. Statistical tests were completed using IBM SPSS 24.0 (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.)

Results

Eighty-eight reports were immediately excluded from statistical analysis because the gender or location of Morton's neuroma was not reported. Of the remaining 494 reports, 115 were found to not have Morton's neuromas as their true diagnosis once evaluated by the radiologist. Three Morton's neuromas were found in the 1st interspace, two independently and one in conjunction with other Morton's neuromas (interspaces 2 and 3). All three 1st interspace Morton's neuromas were found in Females. Twenty-three patients were found to have Morton's neuroma in the 2nd and 3rd interspaces. One patient's report had a Morton's neuroma in the 3rd and 4th interspaces. The remaining patients had a Morton's neuroma in either the 2nd or 3rd interspace. Table 1 represents the number of individual Morton's neuromas per interspace found among our 379 positive MRI reports. There were a total of 463 Morton's neuromas identified as outlined above.

Of patients with Morton's neuroma(s) on MRI, no statistically significant difference ($p=0.89$) in the distribution between patient age and gender was observed (Table 1). Likewise, similar numbers of Morton's neuromas were found in the right and left feet in both females and males. We found that there was not a statistically significant difference ($p=0.28$) in the distribution of laterality (Table 2).

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History of trauma and associated plantar plate tears were evaluated in our patients positive for Morton's neuroma as indicated by MRI. There were 55 patients that reported a history of trauma. Among males and females, 14.1% and 14.6% of those cohorts, respectively, reported a history of trauma (Table 2). A total of 101 plantar plate tears were identified in both female and male patients (Table 3). There was a significant relationship in patients with Morton's neuromas between gender and associated plantar plate tear, with males having a higher rate of associated plantar plate tears than females with the same parameters ($\chi^2=6.60$, $p=0.01$). Among males and females, there were 37.0% and 23.3% that reported a history of trauma, respectively.

Lastly, we evaluated the presence of Morton's neuromas in the second and third interspaces and their association to patient gender ($\chi^2=0.001$, $p=0.98$) and laterality ($\chi^2=2.10$, $p=0.15$) as seen in Tables 4 and 5. No statistically significant difference was found between males and females among the 172 Morton's neuromas found in the 2nd interspace and the 173 found in the 3rd interspace. When comparing incidence of 2nd and 3rd interspace Morton's neuromas with laterality, 53.2% Morton's neuromas of the 2nd interspace were found in the Left foot and 46.5% in the right foot. For Morton's neuromas of the 3rd interspace, 46.8% were located in the left foot and 53.5% in the right foot ($p=0.15$)

Discussion

To the authors' knowledge, this article is the first report evaluating the location of Morton's neuromas and their relationship with gender. As mentioned previously, it has been reported in the literature that females have a higher prevalence of Morton's neuromas as compared with males, but the exact incidence is unknown. This study aimed at comparing differences of prevalence and location of Morton's neuromas in males vs females.

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There was not a statistically significant variation in gender and second versus third interspace Morton's neuromas. Therefore, we reject both hypotheses stating a higher frequency of Morton's neuromas in the 2nd interspace among males and a higher frequency in the 3rd interspace among female. Additionally, right vs left foot, age and history of trauma did not vary between genders in a statistically significant way. We believe this finding may be in part due to not evaluating patients in a clinical setting in combination with MRI.

Claassen et al. found accuracy of clinical assessment was greater than MRI when evaluating for Morton's neuroma even though MRI, under routine conditions, had a good detection rate.²⁵ However, clinical and imaging assessment combined lead to a better conclusion than each individually.²⁶ Sharp et al. reported that the accuracy of MRI and ultrasound was dependent on size and similar and ultrasound was inaccurate for smaller lesions. They also found that clinical assessment demonstrated the highest sensitivity and specificity compared to imaging modalities.²⁷ Pastides et al. found that there was no absolute requirement for imaging in patients who demonstrated having a Morton's neuroma clinically, unless clinical assessment was unclear or pain was present in multiple web spaces. Additionally, they reported that ultrasonography should be the choice investigative modality.²⁸

Our study, however, did have an incidental finding that was statistically significant. It revealed an association between the presence of plantar plate tears and gender. Male patients with Morton's neuromas were found to have a higher rate of plantar plate tears ($p=0.01$) in our patient population. Although some prior literature reports higher incidence of plantar plate tears for females in comparison to males,²⁹⁻³⁰ our study evaluates plantar plate tears in conjunction with a Morton's neuroma. Our results present a new observation in incidence of plantar plate tears in men utilizing advanced imaging which prompts future studies to assess for gender bias in differential

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diagnoses for metatarsalgia. Additionally, with a secular change in fashion and lifestyle we may see different stresses applied to patients' feet of both genders in association with shoe gear.

There were a few limitations to our study. First, Morton's neuromas are often diagnosed and treated based off clinical presentation and do not require advanced imaging, such as MRI evaluation. Surgical planning or efforts to confirm a diagnosis of Morton's neuroma may result in obtaining advanced imaging. Future studies conducted in the clinical setting could result in a different finding between gender and Morton's neuromas in the 2nd and 3rd interspaces, but this prediction was not confirmed in this study. Additionally, males were underrepresented in our population which is consistent with current literature. If equal amounts of male and female patients were evaluated in a clinical setting, we may have found statistically significant distribution differences among different interspaces based on gender. Additional research is needed to fully evaluate gender relationships with the second and third interspace Morton's neuromas.

Conclusions

Morton's neuromas are a common pathology, that are often treated clinically and surgically when conservative measures fail. Our study found that there was not a statistical significance between females and males in relation to Morton's neuroma location in the second and third interspaces. We also found that there was not a statistical significance in the presence of Morton's neuromas based on laterality or age. Male patients with Morton's neuromas were found to have a higher rate of plantar plate tears in our patient population, contrary to prior research findings. Additional investigation from the clinical level could allow for better evaluation of the relationship between Morton's neuroma interspace location and gender.

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Ethical Requirements

As information on patients was de-identified prior to being obtained by the research team, there was minimal risk of private health information being mismanaged. Additionally, the ethical protection of human subjects was of the utmost importance and in compliance of guidelines set by the internal review board.

Financial Disclosure

No member of the research team has a financial interest in ProScan or in regards to the content of this manuscript. No patients were offered any financial gain as this study is a de-identified retrospective evaluation.

Conflict of interest

No member of the research team has a conflict of interest to declare in regards to the content of this manuscript.

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Table 1. Location, Gender, and Age of Patients with Morton's Neuromas						
Interspace Location of Morton's Neuromas	Interspace	1	2	3	4	Total
	n	3	229	230	1	463
	%	0.6	49.5	49.7	0.2	100.0
Patient Gender And Age		n	25th Percentile	Median	75th Percentile	p*
	Female	287	49	56	65	0.89
	Male	92	50	56	63	
	*Independent Samples Mann-Whitney U Test					

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Table 2. Laterality and History of Trauma of Morton's Neuroma and Patient Gender						
			Laterality		History of Trauma	
			Left	Right	No	Yes
Patient Gender	Female	n	143	144	245	42
		% within	49.8	50.2	85.4	14.6
		% of Total	37.7	38.0	64.6	11.1
	Male	n	52	40	79	13
		% within	56.5	43.5	85.9	14.1
		% of Total	13.7	10.6	20.8	3.4
Total		n	195	184	324	55
		% within	51.5	48.5	85.5	14.5
		% of Total	51.5	48.5	85.5	14.5
<p style="text-align: center;">Laterality Pearson Chi-Square $\chi^2=1.25$ $p=0.28$ History of Trauma Pearson Chi-Square $\chi^2=0.01$ $p=0.91$</p>						

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Table 3. Occurrence of Plantar Plate Tear in Males and Females with Morton's Neuromas					
			Plantar Plate Tear		Total
			No	Yes	
Patient Sex	Female	n	220	67	287
		% within Patient Sex	76.7	23.3	100.0
		% of Total	58.0	17.7	75.7
	Male	n	58	34	92
		% within Patient Sex	63.0	37.0	100.0
		% of Total	15.3	9.0	24.3
Total		n	278	101	379
		% within Patient Sex	73.4	26.6	100.0
		% of Total	73.4	26.6	100.0
Pearson Chi-Square $\chi^2=6.60$ $p=0.01^*$					

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Table 4. Gender and Morton's Neuromas in Interspaces Two and Three				
			Interspace	
			2	3
Patient Sex	Female	n	172	173
		% within Patient Sex	49.9	50.1
		% of Total	37.5	37.7
	Male	n	57	57
		% within Patient Sex	50.0	50.0
		% of Total	12.4	12.4
Total	n	229	230	
	% within Patient Sex	49.9	50.1	
	% of Total	49.9	50.1	
Pearson Chi-Square $\chi^2=0.001$ $p=0.98$				

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Table 5. Laterality of Morton's Neuromas of Interspaces Two and Three		Interspace		
		2	3	Total
Left	n	123	108	231
	% within Laterality of the Neuroma	53.2	46.8	100.0
	% of Total	26.8	23.5	50.3
Right	n	106	122	228
	% within Laterality of the Neuroma	46.5	53.5	100.0
	% of Total	23.1	26.6	49.7
Total	n	229	230	459
	% within Laterality of the Neuroma	49.9	50.1	100.0
	% of Total	49.9	50.1	100.0
Pearson Chi-Square $\chi^2=2.10$ $p=0.15$				