

Title

Sensitivity and Specificity of a new test for Thermographic Evaluation of the Foot in the Diagnosis of Diabetic Peripheral Polyneuropathy

Introduction

Diabetic peripheral neuropathy is a major risk factor for the occurrence of foot injuries. It can cause changes in sensory and motor fibres and in the **autonomic** system. The commonest presentation is in the form of symmetrical distal polyneuropathy with a distribution of sensory loss in “gloves or socks”. This loss of protective sensation is the main factor involved in the development of ulcers and the consequent amputations.^{1,2}

Despite technological advances in the prevention and treatment of complications of the diabetic foot, ulcer incidence is still very high. The identification of high-risk individuals represents the most effective way to reduce the incidence of amputations in patients with diabetes mellitus.³ Therefore, one of the fundamental objectives of the tests that are performed on these patients should be to detect a level of peripheral neuropathy sufficient to contribute to the development of lesions (a level termed "protective sensitivity").⁴

Among the neurological complications of diabetes mellitus, there occurs significant deterioration of the short unmyelinated nerve fibres, which is preceded by damage of the long nerve fibres.^{5, 6} Indeed, 50% of people with diabetes with a threshold of vibration perception that is normal exhibit deterioration of thermal sensitivity to heat (short unmyelinated C-fibres) which is damaged before the thermal sensitivity receptors to cold (short unmyelinated nerve A δ -fibres).⁷ The decrease in sweating and increased temperature, are associated with the risk of foot ulceration,⁸ and appear to be useful to identify patients at risk. Since the neuropathic foot presents a raised temperature, it is clearly interesting to apply temperature measurements to the study of the diabetic foot.^{8,}
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There have been works that argue for the effectiveness of monitoring temperature to reduce the incidence of the occurrence of foot ulcers, and consequently of amputations, in patients at high risk.¹⁰⁻¹³ Home-based monitoring studies of foot temperature show

that the incidence of foot ulcers in the risk group can be reduced by more than 60%.¹³ The authors of the present research believe that it is necessary to study the possible inclusion of tests that evaluate thermal sensitivity in order to complete the neurological examination of patients with diabetes, and thus allow the early diagnosis of diabetic neuropathy. Therefore, the main aim of the present study was to determine the sensitivity, specificity, and predictive values of a test evaluating the thermal perception threshold to cold and heat. Such a test would allow one to assess the involvement of the type of nerve fibre that is affected at an early stage of diabetic neuropathy. Another objective was to establish a thermal threshold which can be used to detect diabetic peripheral neuropathy by means of a specific examination protocol. **This could be helpful in screening diabetic polyneuropathy contributing to the early diagnosis of diabetic peripheral neuropathy.**

Methods

Study design and sample size

The study design was descriptive, observational, and cross-sectional. The aim was to determine the sensitivity and specificity of foot thermometry as a complementary **screening** test for diabetic peripheral neuropathy of a subject's feet.

The sample size was calculated with the following formula:¹⁴

$$n = \frac{z_{\alpha/2}^2 p q}{FE^2}$$

where $p = 0.9$ and $q = 0.1$. The desired precision of the proportion ($\pm FE$) was $\pm 5\%$. The α error for a 95% confidence level was 2.5% on each tail (i.e., $\alpha/2 = 0.025$), with the normal value of z for this α error being 1.96. The result was that, to estimate the proportion or prevalence of patients with an accuracy of $\pm 5\%$ and an alpha error of 5%, it was needed to include at least 139 participants. The final sample consisted of a total of 172 participants, mean age 62.69 ± 9.54 (42 to 83) years, of which 86 were men and 86 women. **This study was approved by the University of Seville's Ethical Committee.**

Subjects

The participants were selected from patients who regularly attend the Podiatry

Clinical Area at the University of Seville (35 participants), patients from a private foot clinic in the province of Seville (60 participants) with an agreement to this end, and two diabetes associations to which this activity was proposed during the period January 2010 to February 2012 (58 participants from San Juan de Aznalfarache, Seville, Spain; 19 participants from Puente Genil, Córdoba, Spain). All the participants were informed about the explorations to be made as part of the research study, and gave their signed informed consent.

The sole criterion for inclusion was that the subject presented diabetes mellitus. The sample was divided into two groups depending on whether neuropathy was detected from the subject's failure to perceive the Semmens-Weistein Monofilament 5.07 (hereafter, SW MF 5.07) on both feet (diabetic neuropathy group) or not (diabetic group without neuropathy). Each participant's both feet were evaluated in order to ascertain whether there were differences in the results between them.^{10-12, 15, 16}

For both sample groups the following exclusion criteria were set: current foot ulceration, trauma, or infection; history of ulcers or partial amputation of the feet; non-palpable foot pulses; ankle-brachial index < 0.9; peripheral arterial disease; current or past Charcot osteoarthropathy; presence of oedema; another cause of peripheral neuropathy other than diabetes (treated with chemotherapy, etc.); chronic kidney disease; liver failure; heart failure; thyroid disease; systemic diseases whose medications may interfere with the body's temperature; cognitive function dementia; current or past drug or alcohol abuse.

Protocol

Participants remained seated 15 to 20 minutes prior to data collection in the place at which the examination was to be carried out, with an ambient temperature regulated to 23–25°C and relative humidity of 50%, and with the leg and the foot bare, in order to avoid any influence of external factors on the temperature conditions of the foot.¹¹⁻²² Also, the temperature evaluations were made in the morning to avoid the influence on the subject of diurnal temperature variations.²²

For the study, a podiatry chair that allowed the participant to be examined while seated was used.⁵ It was noted the type of diabetes, years since onset, type of treatment (diet, OAD, and/or insulin), and HbA1c level [17, 19, 20]. Then the pedis and posterior

tibial pulses of both feet were palpated, and the ankle-brachial index was determined by Doppler and sphygmomanometry.^{11, 18}

The neurological examination applied to both feet consisted of the exploration of tactile sensitivity with the 10-gram SW MF 5.07,²⁷ and the perception of vibratory sensitivity by neurothesiometry.^{2, 17, 23} The SW MF 5.07 was applied at the plantar level to the great toe and the first and fifth metatarsal heads.^{24, 25} There was taken to be a lack of protective sensitivity when there was no perception at one or more points.²⁷

The neurothesiometer was applied dorsolaterally on the first metatarsal head. Vibratory stimulation was ramped up from 0 V to 50 V, taking the state to be pathological when the voltage required to perceive the stimulus (vibration perception threshold, VPT) was greater than or equal to 25 V.^{17, 19}

For the thermal sensitivity examination, the skin temperature of the foot was measured with an instrument designed to assess thermal discrimination and sensitivity based on the Peltier principle (TermoSkin, Meteda SRL, San Benedetto del Tronto (AP), Italy). These tests are based on the ability to perceive heat and cold via the small peripheral nerve fibres.^{2, 7}

The instrument used records the skin temperature, and performs the following two tests: (i) determining the thermal discrimination threshold, used to identify the lowest noticeable temperature difference, and (ii) examining the thermal sensitivity, used to determine the absolute thermal threshold.⁷

The points chosen at which to make the local skin temperature measurements corresponded to the zones of innervation of the main nerves of the foot: the dorsal aspect of the foot, and the plantar aspects of the first and fifth metatarsals (figures 1, 2 and 3).^{18, 21} The thermometer probe was applied to the dorsal aspect of the participant's both feet to determine their temperatures (figure 4). These were registered, and one heated face of the "hammer" of the device was maintained at this basal temperature. The temperature of the other face of the hammer was ramped up or down in steps of 0.5°C until the participant indicated that they had noted a temperature other than their own, and whether it was warmer or colder. This was applied in random order to the three points, alternating warmer and colder temperatures, so as not to condition the participant and thus alter the outcome of the test.

Data analysis

Statistical analyses of the data were done using SPSS 18.0 for Windows (SPSS Science, Chicago, USA). Descriptive statistics were calculated of the number, age, sex, and laterality of the total sample and of the two groups separately, of the mean and standard deviation of age, weight, height, body mass index, temperature, and ankle-brachial index, and frequencies of the VPT and neuropathy variables. For the intergroup comparison of the means, the Mann-Whitney test was used since application of the Shapiro-Wilk test showed that the data were not normally distributed. For the intergroup comparison of the neuropathy and VPT frequencies, the chi-squared test was used. The ROC curve technique was used to calculate the sensitivity (capacity to correctly identify patients with the disorder) and specificity (capacity to correctly identify patients without the disorder) of the diagnostic test. In addition, it was calculated the positive predictive value (the probability that a subject with a positive result is indeed affected by the disorder), and the negative predictive value (the probability that a subject with a negative result is indeed not affected by the disorder). The discriminatory power of the model was determined from the area under the ROC curves, with the model being deemed accurate if this area was greater than 0.75, or at least 0.8 lay within the 95% confidence interval.

Results

Table 1 presents the descriptive statistics of the total sample demographic variables, the type of diabetes mellitus, and type of treatment being received.

The values of the area under the curve which showed the best sensitivities and specificities for the two feet are given in Table 2. The optimal values were for the warm temperatures under the first and fifth metatarsal heads. For both zones, the temperature difference needed to predict whether or not a patient was neuropathic was 2 degrees. Sensitivities were above 75%, and the positive predictive values in all cases exceeded 60%, so that the test can be considered apt for the prediction of distal symmetrical polyneuropathy in the study's participants.

All the temperature measurements gave statistically significant differences between

the participants with neuropathy and those without (Table 3), with the former requiring greater temperature differences in the perception tests for both warm and cold differences, as well as presenting higher basal temperatures.

There was no relationship between the HbA1c values and the thermal perception tests (Table 4). However, the participants with neuropathy presented higher basal temperatures the higher were their HbA1c levels (Table 4).

Discussion

The authors have described the application of a system based on the Peltier effect that measures skin temperatures, and can then modify them and apply them to specific zones of the patient's skin, in this case to specific zones of the foot, allowing one to evaluate whether the patient perceives the variation.^{9, 19, 29, 30} It has been shown that the technique enables one to quantify the degrees of colder or warmer temperature differences that participants with diabetes (with and without neuropathy) needed to be able to detect a difference. I.e., it was possible to quantify the so-called thermal discrimination threshold. The instrument used, besides being a dermal thermometer, allowed the researchers to establish thermal perception as an appropriate test in the early diagnosis of diabetic peripheral neuropathy.

Several methods are currently used to detect diabetic neuropathy. They include the nerve conduction test, the SW MF 5.07, and the perception of vibration test. Most studies dealing with the diagnosis of peripheral neuropathy have advocated the use of SW MF 5.07 either alone or in conjunction with other exploratory instruments.^{30, 31} Since many authors consider this method to be the "gold standard" for the diagnosis of diabetic peripheral neuropathy,²⁰⁻³² the authors chose it to use for comparison with the results obtained from the thermal perception test.

The basal temperature of both feet in the participants with neuropathy (as detected with the SW MF 5.07) was approximately 1.5°C higher than in those without neuropathy. Bagavathiappan et al. used a non-invasive infrared thermal imaging technique to analyse the correlation of the plantar foot temperatures with diabetic neuropathy in patients with type 2 diabetes.¹¹ They report that neuropathic patients have higher foot temperatures (32–35 degrees) than patients without neuropathy (27–30 degrees). Likewise, Papanas et al. find higher temperatures on both the plantar and

dorsal surfaces of the feet of subjects with diabetes with neuropathy relative to those with no neuropathy.²¹

Also Papanas et al. evaluated two groups of patients – one with sudomotor dysfunction and one without this anomaly.⁸ They found that the patients with sudomotor dysfunction had significantly higher foot temperatures than those without sudomotor dysfunction. However, Boyko et al. described subjects with sensory neuropathy as having lower mean temperatures of the plantar skin of the feet (28.4 degrees) than those without neuropathy (28.9 degrees).¹⁸ In the same vein, Bharara et al. also found relatively higher values in non-neuropathic subjects.³ Armstrong et al. reported no difference in skin temperature according to whether or not neuropathy was present.¹⁷

In order to make the present thermal exploration protocol more straightforward, and in view of the results obtained, the authors propose that only the thermal discrimination threshold for warmth needs to be determined, because the data obtained from the corresponding ROC curves were statistically more significant than those for the thermal discrimination of cold. The authors therefore concur with the proposal of Ijff et al. that the preferred evaluation technique for the detection of disturbances in small nerve fibre function in patients with diabetes is to determine the warmth discrimination thresholds.³³ Also Vinik et al. indicated that, in diabetic polyneuropathy, there could be abnormal perception of hot temperatures.³⁴

In the present work, it was found a threshold of 2 degrees of relative warmth under both the first and the fifth metatarsal heads to be the parameter that allowed us to detect diabetic peripheral neuropathy in the study sample. In this way, a fixed threshold of temperature which facilitates the early diagnosis of this complication could be established. These results could contribute to the prevention of skin ulcers in diabetic feet. In the authors' opinion this finding is of practical utility since the interval of 2 degrees is the same for the two metatarsal heads, as well as being a temperature difference that does not involve decimal points, thus facilitating its use in screening and clinical practice.

Chao et al. also found higher temperature differences in diabetic subjects' perception threshold for heat compared with that for cold, although in their case this is for measurements on the great toe.³⁵ Hyllienmark et al. reported significant differences for

the perception of heat on the great toe and the lower leg in relation to the findings of a neurological examination, but minimal effects for the perception of cold on those same zones.²³ Abad et al. measured warmth discrimination thresholds on the dorsolateral zone of the right foot, finding a mean value of 3.6 degrees in the diabetic group compared with 2.1 degrees in the control group.²⁸ Ziegler et al. also made measurements on the dorsolateral zone of the right foot, and found a greater thermal perception threshold for warmth (4.7 ± 2.8 degrees) than for cold (2.3 ± 3.0 degrees), also measured on the on the dorsolateral zone of the subject's right foot.³⁶

Guy et al. conducted a sensory evaluation of diabetic neuropathy on the foot of the dominant side, beneath the lateral malleolus, finding a mean threshold of 6.0 degrees ($3.6\text{--}9.8$ degrees).²⁹ They also evaluated the plantar zone under the great toe, finding a higher thermal threshold: 8.9 degrees ($5.2\text{--}15.1$ degrees). Comparing these results with those obtained on the hand, those authors found the thermal sensitivity to be lower on the foot since, on the hand, the thresholds were 2.6 degrees ($1.5\text{--}4.5$ degrees) on the thenar eminence and 4.2 degrees ($2.4\text{--}7.4$ degrees) on the index finger.

In the present results the temperature thresholds were higher, for both warmth and cold, on the plantar aspect of the foot than on the dorsal aspect. This is indicative of a greater sensitivity of the latter. The authors therefore agree with Mayfield and Sugarman that, in using the SW MF 5.07, hairy skin (e.g., the dorsal aspect of the foot) was ten times more sensitive than the sole, and that the heel was ten times less sensitive than the plantar surface of the instep.³²

A notable difference of the present results with respect to other work is that, for all the subjects in those works, the temperature from which the thermal difference was increased or decreased was 32 degrees.^{2, 23, 29} In the authors' opinion, starting from the subject's basal foot temperature at the time of measurement could improve the precision of the test because the thermal perception would not be the same for all subjects. If the aim is to determine a subject's thermal perception threshold, the methodological approach taken in this sense could influence the results, since the zero point of the measurement changes.

With respect to how the temperature is ramped up or down, Chao et al,³⁵ and Hyllienmark et al,²³ used a one-degree step. In the present work it was decided to take a

step size of 0.5 degrees so as to see if there existed smaller thermal differences. Also, the aforementioned studies reported finding that alterations of the thermal threshold to cold were the less common (in both type 1 and type 2 diabetes patients), with which the present results agree.

Hyllienmark et al. conducted a study on a sample consisting solely of type 2 diabetes subjects, comparing thermal perception explorations with alterations in motor and sensory nerve conduction.²³ They raised the temperature of the feet of their subject by means of a heating pad until reaching 32 to 35 degrees. There was a mean 2.2 degrees (1.9–2.6 degrees) deterioration of the response to cold in neuropathy, and a mean 1.6 degrees (1.4–1.7 degrees) deterioration of the response to warmth. Similarly, Abbot et al. found elevated temperature thresholds in subjects with diabetes, but the initial temperature was also 32 degrees.³⁷

Regarding other parameters that might have influenced temperature perception, it was found no relationship of age with the temperature perception values, whereas Chao et al. indicated that age was an associated risk factor that did influence the perception of foot temperatures.³⁵ Other studies on the influence of age on patients with diabetes sensitivity to cold and heat have reported different results. Levy et al. found that thermal sensitivity of the foot was weakly associated with age in patients with diabetes.³⁸ Ziegler et al., studying patients with newly diagnosed type 1 diabetes, observed both the cold and warmth thresholds to be associated with age.³⁹ Siao and Cros found age, sex, and site of the stimulus to affect sensory thresholds.⁴⁰ Sosenko et al., however, obtained no association of age with the sensitivity to hot or cold.⁴¹

The results of Ijff et al. suggest that the skin's heat sensitivity declines with age in patients with diabetes, and therefore that the evaluation of thermal thresholds in patients with diabetes is essential to detect functional alterations in shorter nerve fibres.³³ They explain this by taking into account that the connections of cold receptors are via short myelinated A δ -fibres, while heat receptors are connected by the more slowly conducting short unmyelinated C-fibres. Thus, in diabetes, measurement of the cold perception thresholds would not detect small variations in short nerve fibre function.

With the single exception of the perception of warmth under the left foot fifth metatarsal head in the neuropathic group, the authors did not find that the glycosylated

hæmoglobin values affected the perception of temperature on the foot. However, Chao et al. did find such an association.³⁵ In their study, a multiple linear regression analysis indicated that thermal thresholds of the upper and lower limbs was linearly correlated with glycosylated hæmoglobin levels ($p < 0.01$), and a multivariate logistic regression analysis showed that both glycosylated hæmoglobin and age were the most important risk factors, independently of the elevated thermal thresholds ($p < 0.01$). Also, in the present study, the basal temperature of both feet of the neuropathic subjects was higher the greater the level of glycosylated hæmoglobin. This is contrary to the results reported by Bagavathiappan et al. who found no correlation between glycosylated hæmoglobin and the mean temperature of the foot.¹¹

The perception of hot and cold under both the first and the fifth metatarsal heads was different for the group of patients with over 24 years of evolution of their diabetes, since they required a greater temperature difference to perceive cold and warmth. The results were the same for the left foot and the right foot. This also runs contrary to the literature in that Levy et al. find that thermal sensitivity on the foot was uncorrelated with the duration of diabetes,³⁸ and Ijff et al. reported that neither hot nor cold thresholds were correlated with that variable.³³

Regarding the possible influence of the subjects' height on their thermal perception and on the presence of neuropathy, our results coincide with those of Levy et al. in there being no significant association with those two variables.³⁸ This possible correlation was examined since, according to Guy et al., the nerves of the foot are more frequently affected than those of the hand,²⁹ and the distal portions of sensory nerves are affected before there is damage at a proximal level. Indeed, as also with age, Cheng et al. report an odds ratio of 1.094 for the subject's height with respect to the presence of neuropathy.¹⁵

To the authors concern, the first study to demonstrate that thermal thresholds using the peltier principle are abnormal in diabetic neuropathy was published in 1985.⁹ Since then multiple studies have confirmed this. What is novel in the present work is that, using the patient's basal temperature, a threshold of 2 degrees of relative warmth under both the first and the fifth metatarsal heads has been established as the interval which

allowed to detect the presence of diabetic peripheral neuropathy in the participants. This could be done with acceptable sensitivity, specificity and predictive values, without the need for evaluating the thermal perception threshold to cold and heat, by means of a well-defined, quick and simple protocol.

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R.G.P. did participate in data collection, data analysis, data interpretation, and writing of the manuscript; S.B. cowrote the manuscript, did participate in data collection, data analysis, and data interpretation; P.V.M. contributed to the study design, interpreted data, and reviewed the manuscript.

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Figure legends

Figure 1.- Local skin temperature measurements: dorsal aspect of the foot.

Figure 2.- Local skin temperature measurements: plantar aspect of the first metatarsal.

Figure 3.- Local skin temperature measurements: plantar aspect of the fifth metatarsal.

Figure 4.- Thermometer being applied to the dorsal aspect of a participant's both feet to determine its temperature.

Table 1. Demographics of the study's participants

Descriptive statistics of the sample							
Variable	Mean	Median	Mode	S.D.	Minimum	Maximum	
Age (yr)	62.69	62.5	60	9.54	42	83	
Weight (kg)	78.82	78	68	11.78	51	107	
Height (m)	1.67	1.66	1.78	0.1	1.46	1.94	
BMI	28.27	28.38	27.1	3.05	20.17	38.3	
Qualitative variables							
Diabetes	Type 1: 37.8%				Type 2: 62.2%		
Type of treatment	Diet: 1%	OAD: 11%	Insulin: 10%	Diet + OAD: 28%	Diet + Insulin: 17%	Diet + OAD + Insulin: 18%	OAD + Insulin: 15%

S.D. standard deviation; BMI body mass index.

Table 2. For a temperature difference of 2°C: Area under the ROC curve, sensitivity, specificity, PPV (positive predictive value), and NPV (negative predictive value).

Variable	Left foot			Right Foot		
	Area under the curve	95% confidence interval		Area under the curve	95% confidence interval	
		Lower limit	Upper limit		Lower limit	Upper limit
Warm: Dorsal	0.682	0.603	0.682	0.603	0.682	0.761
Cold: Dorsal	0.656	0.574	0.656	0.574	0.656	0.737
Warm: 1st MTH	0.735	0.662	0.735	0.662	0.735	0.809
Cold: 1st MTH	0.662	0.581	0.662	0.581	0.662	0.743
Warm: 5th MTH	0.772	0.703	0.772	0.703	0.772	0.841
Cold: 5th MTH	0.698	0.621	0.698	0.621	0.698	0.776
Thermal perception: 2°C temperature difference						
Parameter (%)	Left foot			Right Foot		
	1st MTH	5th MTH		1st MTH	5th MTH	
Sensitivity	89.5	82.6		88.4	77.9	
Specificity	45.3	59.3		54.7	61.6	
PPV	62	67		66	67	
NPV	81	77		82	74	

MTH, metatarsal head.

Table 3. Relationship between "presence of neuropathy" and thermal perception tests.

Presence of neuropathy										
Variable	Left					Right				
	No		Yes		p	No		Yes		p
	\bar{x}	σ	\bar{x}	σ		\bar{x}	σ	\bar{x}	σ	
Basal temperature	26.87	1.54	28.23	2.11	0^(a)	26.89	1.56	28.25	2.04	0^(a)
Warm: Dorsal	1.41	0.94	2.56	2.28	0^(a)	1.35	1.11	2.45	2.1	0^(a)
Cold: Dorsal	0.88	0.51	1.27	0.8	0^(a)	0.82	0.62	1.28	0.83	0^(a)
Warm: 1st MTH	2.15	1.28	3.66	2.1	0^(a)	2.03	1.26	3.69	2.2	0^(a)
Cold: 1st MTH	1.2	0.71	1.68	0.95	0^(a)	1.18	0.66	1.7	1	0^(a)
Warm: 5th MTH	1.84	1.27	3.47	2.04	0^(a)	1.82	1.27	3.43	2.07	0^(a)
Cold: 5th MTH	1.06	0.66	1.7	1.07	0^(a)	1.01	0.57	1.62	0.93	0^(a)

(a) Statistically significant at 95%. MTH, metatarsal head.

Table 4. Relationship between "glycosylated haemoglobin" and thermal perception tests

Thermal perception test Non-neuropathic Group		Glycosylated haemoglobin interval						F	p
		< 6.5		6.5 – 7.5		> 7.5			
		\bar{x}	σ	\bar{x}	σ	\bar{x}	σ		
Left foot	Basal temperature	25.64	1.44	26.87	1.56	27.24	1.38	2.179	0.120
	Warm temperature: Dorsal	1.1	0.55	1.34	0.87	1.75	1.22	1.631	0.202
	Cold temperature: Dorsal	0.6	0.22	0.9	0.51	0.92	0.58	0.82	0.444
	Warm temperature: 1st MTH	1.6	1.08	2.02	1.28	2.75	1.2	2.849	0.064
	Cold temperature: 1st MTH	0.8	0.45	1.2	0.77	1.31	0.52	0.985	0.378
	Warm temperature: 5th MTH	1.4	0.89	1.77	1.26	2.22	1.39	1.208	0.304
	Cold temperature: 5th MTH	0.8	0.67	1.08	0.69	1.08	0.55	0.42	0.658
Right foot	Basal temperature	25.7	1.66	26.93	1.57	27.11	1.43	1.679	0.193
	Warm temperature: Dorsal	0.8	0.27	1.33	1.02	1.58	1.5	1.025	0.363
	Cold temperature: Dorsal	0.5	0	0.83	0.67	0.89	0.5	0.781	0.461
	Warm temperature: 1st MTH	1	0.35	1.98	1.27	2.5	1.21	3.112	0.050
	Cold temperature: 1st MTH	0.8	0.27	1.19	0.7	1.25	0.55	0.938	0.395
	Warm temperature: 5th MTH	0.8	0.27	1.77	1.25	2.28	1.34	2.965	0.057
	Cold temperature: 5th MTH	0.6	0.22	1	0.59	1.17	0.51	2.016	0.140
Thermal perception test Neuropathic Group		Glycosylated haemoglobin interval						F	p
		< 6.5		6.5 – 7.5		> 7.5			
		\bar{x}	σ	\bar{x}	σ	\bar{x}	σ		
Left foot	Basal temperature	27.45	0.07	27.59	1.82	29.32	2.21	7.837	0.001^(a)
	Warm temperature: Dorsal	4.5	4.95	2.67	2.5	2.27	1.69	1.056	0.353
	Cold temperature: Dorsal	1.5	0.71	1.3	0.88	1.22	0.68	0.175	0.840
	Warm temperature: 1st MTH	4.25	2.47	3.53	2.28	3.83	1.79	0.279	0.757
	Cold temperature: 1st MTH	1.75	0.35	1.64	1.06	1.73	0.78	0.093	0.911
	Warm temperature: 5th MTH	2	0	3.25	2.02	3.92	2.08	1.626	0.203
	Cold temperature: 5th MTH	1.5	0.71	1.62	1.09	1.84	1.07	0.479	0.621
Right foot	Basal temperature	27.35	0.64	27.59	1.7	29.38	2.15	9.272	0.000^(a)
	Warm temperature: Dorsal	4	2.83	2.55	2.23	2.2	1.86	0.816	0.446
	Cold temperature: Dorsal	2.75	1.77	1.27	0.84	1.2	0.71	3.453	0.036^(a)
	Warm temperature: 1st MTH	5	1.41	3.62	2.24	3.72	2.21	0.381	0.684
	Cold temperature: 1st MTH	2.25	0.35	1.73	1.05	1.63	0.94	0.415	0.662

	Warm temperature: 5th MTH	3.75	0.35	3.35	2.12	3.55	2.07	0.115	0.891
	Cold temperature: 5th MTH	2	0	1.6	0.96	1.64	0.92	0.188	0.829