The identification of higher forefoot temperatures associated with peripheral arterial disease in type 2 diabetes mellitus as detected by thermography

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Abstract

Aims: The purpose of this study was to investigate whether heat emitted from the feet of patients with type 2 diabetes (DM) and peripheral arterial disease (PAD) differed from those with type 2 diabetes without complications (DM).

Methods: A non-experimental, comparative prospective study design was employed in a tertiary referral hospital. Out of 223 randomly selected participants (430 limbs) who were initially tested, 62 limbs were categorized as DM+PAD and 22 limbs as DM without PAD. Subjects with evidence of peripheral neuropathy were excluded. Participants underwent thermographic imaging. Automatic segmentation of Regions of Interest extracted the temperature data.

Results A significant difference in temperature in all the toes between the two groups was found ($p=0.005$, $p=0.033$, $p=0.015$, $p=0.038$ and $p=0.02$ for toes 1-5 respectively). The mean forefoot temperature in DM+PAD was significantly higher than that in DM ($p=.019$), with DM+PAD having a higher mean temperature ($28.3^{o}C$) compared to DM ($26.2^{o}C$). Similarly, the toes of subjects with DM+PAD were significantly warmer than those of subjects with DM only.

Conclusions Contrary to expectations the mean toe and forefoot temperatures in DM patients with PAD is higher than in those with DM only. This unexpected result could be attributed to disruption of noradrenergic vasoconstrictor thermoregulatory mechanisms with resulting increased flow through cutaneous vessels and subsequent increased heat emissivity. These results demonstrate that

thermography may have potential in detecting PAD and associated temperature differences.

Keywords: medical thermography; peripheral arterial disease; infrared imaging; diabetes mellitus

Introduction

Diabetes is a worldwide health burden which brings about many complications, amongst the most significant being those associated with diabetic foot disease [1]. One of the commonest complications is Peripheral Arterial Disease (PAD) with a prevalence of 3-10% in the general population increasing to 15-20% in individuals over 70 years of age [2]; PAD prevalence in diabetes is estimated at being 29% in people over 50years of age [3]. One method for diagnosing PAD in a clinical setting is the Ankle Brachial Pressure Index (ABPI), however it should be noted that the reliability of this technique has been questioned in literature, especially in the diabetic population presenting with arterial calcification [2]. This raises the need for investigating alternative methods that could possibly detect the presence of PAD, such as thermography, which is the infrared imaging of the human body.

Thermography has been employed in a number of medical applications, including vascular disease, breast disease [4], skin disease [5] and Raynaud Phenomenon [6], amongst others. This technology, which is noninvasive and non-contact, has the potential to measure physiological changes resulting in alteration of emitted skin temperature [7] and skin temperature distribution [8,9]. Medical infrared imaging is a real-time temperature measurement technique used to produce visualization of thermal energy emitted by the measured site at a temperature above absolute zero [10] .

Thermography and thermometry have been employed in the study of foot vascular complications and ulceration in diabetes [8,9,11–13]. Thermal changes

in the plantar aspect of the diabetic foot may be the result of ischaemia, diabetic neuropathy, infection, or a combination of these factors (22). The neuropathic foot exhibits increased skin temperature indicating increased cutaneous blood flow [14].

Temperature differences between corresponding areas on contralateral feet are clinically significant parameters [15]. It has been suggested that if one foot has a significantly higher temperature than the other, an inflammatory disease process may be suspected. Indeed, a temperature change >2.2^{o}C in one foot is an indicator of a suspected disease process [16–18].

Van Netten et al (2013) report that whilst no difference >1.5^{o}C was found between the ipsilateral and contralateral foot of participants without complications, in the affected Region of Interest (ROI) of patients with local complications a temperature of >2^{o}C was found when compared to the similar ROI of the unaffected foot. Their study, however, was characterized by very small sample sizes of 5 participants per group [19].

In normal healthy feet, temperature patterns are symmetrical in both feet. This has recently been confirmed by Gatt et al who reported the thermographic patterns of hands and feet of healthy adults [20]. The implication is that asymmetry of temperature patterns between the feet may indicate the presence of pathology [16], which is also a logical conclusion from the findings of Gatt et al, who have demonstrated symmetry in the healthy adult. While this has been shown to be the case in the presence of peripheral neuropathy, there is a lack of studies

reporting use of thermography to detect differences between healthy and ischaemic feet in diabetes. When both feet are ischaemic, the temperature difference between the two limbs may not be present, thus making detection utilizing this 'asymmetry' theory difficult.

The aim of this study was to determine whether infrared thermal imaging can detect significant differences in the thermographic images of type 2 diabetes patients with PAD (DM+PAD), compared to those diabetes patients without PAD (DM).

Methods

Ethical approval was sought and obtained from the University Research Ethics Committee. All investigations were carried out in accordance with the principles of the Declaration of Helsinki as revised in 2013 and all participants signed informed consent prior to inclusion in the study [21].

Participants with type 2 diabetes were recruited from the patient list of a vascular surgeon at a Tertiary Referral Hospital over a 3 month period. Participants underwent a thorough clinical examination that included validated tests for neuropathy and peripheral arterial disease. Participants with evidence of peripheral neuropathy were excluded for this part of the study. Subjects with active ulceration or other significant co-morbidities that could affect thermographic patterns, such as rheumatoid arthritis and other autoimmune diseases, Raynaud's Phenomenon, Charcot neuroarthrophy, venous disorders

including varicose veins and deep vein thrombosis, oedema, dermatolgical and neurological disorders were also excluded.

Prior to data collection, all participants were rested in a supine position in a room with temperature controlled at 23^{o}C since ambient temperature is known to affect thermal emissivity of the body. During this period, a detailed medical history was obtained. Following the 15-minute acclimatization period, investigations were carried out to detect or exclude the presence of PAD and neuropathy. The presence of PAD was investigated utilizing two methods: the Ankle Brachial Pressure Index (ABPI) and Spectral Doppler Waveform Analysis [2].

An ABPI was derived as described in literature [2,22,23], according to standard clinical practice. A Huntleigh (Cardiff, Wales) Dopplex Assist was utilized for this purpose. PAD was diagnosed from the ABPI results, with normal values being 0.9 -1.3. In order to include only those participants with a definite diagnosis of PAD, only participants with an ABPI <0.6 were included for data analysis.

Spectral Doppler Waveform Analysis was also employed to classify the recorded Spectral Doppler waveform as being either triphasic, biphasic or monophasic [24]. A triphasic waveform is indicative of normal arterial perfusion, whilst the other two classifications are indicative of PAD, with the monophasic waveform denoting a more severe form of the condition. Only those participants with monophasic waveforms and an ABPI <0.6 were included to ensure an unequivocal diagnosis of PAD.

Testing for neuropathy involved the use of a 10g Semmes Weinstein monofilament administered on 10 sites on each foot. In this validated method, exactly 10g of force is applied before the monofilament bends, thus ensuring that exactly the same amount of force is applied. Neuropathy was diagnosed if at least one site was not felt by the participant. Detecting neuropathy using the 10g monofilament is recommended by most international guidelines including National Institute of Clinical Excellence (NICE), the American Diabetes Association (ADA) and the International Diabetes Federation (IDF)namong others. All the above measurements were carried out by the same experienced clinician in order to ensure consistency.

The inclusion of participants for data analysis was determined by two experienced clinicians who assessed the results of the testing carried out, whilst blinded to each other's results. Their decisions were later compared and a consensus reached between the two researchers as to whom to include in the data analysis. This ensured that only participants with severe PAD (ABPI<0.6 and monophasic waveforms) and DM subjects with no vascular and neuropathic complications were included in the study (Figure 1).

Image acquisition, segmentation, data extraction and analysis

A FLIR SC7200 infrared camera with a spatial resolution of 320 x 250 pixels and a temperature resolution of 20 mK was used for the acquisition of thermal images. The protocol for obtaining thermal images followed the recommendations of the American Academy of Thermology [10]. The camera was placed on a tripod 1.5m from the subject, and perpendicular to the body part that was being photographed

[20]. Images of the plantar aspect of the feet and palms of the hands were recorded for later analysis.

Thermal images obtained were segmented automatically utilizing an algorithm that was specifically developed for this study [25]. The feet were divided into regions so that temperature data could be extracted (Figure 2).

Insert Figure 2

SPSS version 24 was used to analyze data. The one-sample Kolmogorov-Smirnov test was used to test normality of data, which was found to be normally distributed. Thus a parametric test, the Independent-Sample T-Test, was the statistical test employed to compare the temperature means between the two groups.

Results

Out of 223 participants (430 limbs) who were initially tested and imaged, 62 limbs (from 9 females, mean age 64.5 yrs (sd5.9); 37 males, mean age 72.2yrs (sd8.9)) were categorized as DM+PAD and 22 limbs (from 7 females (mean age 59.8 (sd11), 9 males, mean age 65.8yrs (sd7.1)) as subjects with DM. Table 1 presents some characteristic data of the sample population. Independent sample T-Test demonstrated a significant difference between all the toes of the two groups ($p=0.005$, $p=0.033$, $p=0.015$, $p=0.038$ and $p=0.02$ for toes 1-5 respectively). Higher mean temperatures were noted in all the toes of the DM+PAD group (Table 2) compared to the DM only group.

Mean forefoot temperature in participants with DM+ PAD was also significantly higher than in those with DM (p=.019), (DM+PAD: 28.3^{o}C; DM only: 26.2^{o}C).

Discussion

Results of this study indicate that the regions investigated had significantly higher temperatures in the PAD group when compared to the non-PAD group. These results are unexpected since the generally held view is that in the presence of PAD the affected limb tends to be cooler. To ensure that the data set was homogenous only participants with triphasic waveforms and normal ABPIs and normal sensation were included in the DM group and only subjects with an ABPI below 0.6 and monophasic waveforms and normal sensation included in the DM+PAD group. This ensured that the comparison being made was between diabetes participants with normal perfusion (and no neuropathy) and those with peripheral arterial disease (and no neuropathy). All participants with neuropathy were excluded as it is known that peripheral neuropathy tends to result in warmer feet [26].

The veracity of these findings is illustrated by a type 2 diabetes participant who presented with a warmer ischaemic right foot when compared to the normal left limb. Participant had a palpable dorsalis pedis in the left foot with biphasic waveforms while on the right she had absent pulses, monophasic continuous waveforms and heel fissuring, together with rest pain. Figure 3 illustrates this remarkable difference as detected on thermographic imaging.

Insert Figure 3

It is standard clinical practice to palpate a patient's limbs to detect temperature differences with a cooler limb normally being interpreted as possible evidence of

ischaemia in that limb. The results of this study suggest that this interpretation may be erroneous in diabetes patients and that a cooler limb may not necessarily be less well perfused than the warmer one.

There are several implications of the findings of this study. Firstly, in diabetes patients a cooler foot is not necessarily less well perfused than the contralateral limb. Secondly a warm foot does not necessarily imply that the perfusion to the foot is normal or adequate. This means that clinicians should not rely on clinical assessment of the temperature of the feet in diabetes to assess perfusion. A "warm" foot should not lead to the assumption that the limb is adequately perfused.

The early diagnosis of complications associated with diabetes mellitus is a first prerequisite for saving the lower limb [27]. Researchers have attempted to utilize temperature measurement as a means of detecting diabetic foot disease, often by comparing the difference in temperature between the two limbs. In fact, it has been shown that a temperature difference >2.2^{o}C could be indicative of diabetic foot disease [18].

This study has identified significant temperature differences between the feet of type 2 diabetes participants with PAD when compared with those without peripheral arterial disease. This suggests that thermography may prove useful both as a research and clinical tool in distinguishing between diabetics with and without peripheral arterial disease. Baseline thermal patterns of the hands and feet have already been reported [20]. The next logical step would be to establish

thermographic data for the various categories of diabetic feet (normal, ischaemic, neuropathic, neurosichaemic) to allow comparison with normative data.

Although the higher temperatures in the feet of diabetes subjects with peripheral arterial disease is counterintuitive, one possible explanation for this is a disruption of normal thermoregulatory mechanisms in the feet. It is hypothesized that local ischaemia may lead to disruption of sympathetically mediated noradrenergic vasoconstriction which leads to increased flow to the cutaneous vessels rather than through the deeper nutritive vessels which in turn leads to higher heat emissivity. Glabrous skin (soles, palms, lips) is innervated solely by sympathetic noradrenergic vasoconstrictor nerves while other skin is also innervated by sympathetic vasodilator nerves. Another important difference between glabrous and non glabrous skin is the existence of arteriovenous anastamoses (AVA) which are thick walled, low resistance conduits that allow high flow rates directly from arterioles to venules. In glabrous skin, AVA are numerous and richly innervated by sympathetic vasoconstrictor nerves. Substantial changes occur in blood flow depending on whether AVAs are closed or open [28]. Local ischaemia may result in failure of the sympathetically mediated vasoconstriction leading to increased cutaneous blood flow and therefore increased skin temperature. In diabetics with moderate peripheral arterial disease this mechanism may explain the higher foot and toe temperatures detected. Small changes in skin blood flow can lead to large changes in heat dissipation. An increase of only 8ml/100mls/min in blood flow will lead to doubling of heat transfer to the environment [29]. It is hypothesized that in critical ischaemia the perfusion to the foot is so impaired that despite vasodilatation the

foot may still be cooler. Clinically this would explain the dusky cool critically ischaemic foot typically referred to as the *sunset foot*.

Since subjects were recruited from a vascular surgery clinic population, a potential selection bias may have been inadvertently created, although it is to be acknowledged that careful categorization of subjects was conducted to ensure that only patients with the required inclusion criteria were recruited. Another possible limitation could be the lack of screening for early subclinical small fibre autonomic neuropathy which may perhaps increase thermal emissivity in diabetes. The monofilament testing for protective sensation in the feet conducted in this study evaluated large fibre somatic nerve function. However, there have been no studies to assess the impact of autonomic neuropathy on cutaneous temperature as measured by infrared thermography, thus implying the need for further research in this area.

This study has revealed novel data regarding significantly higher mean temperature in the feet and toes of diabetics with peripheral arterial disease compared to those without peripheral arterial disease.

Conclusion

The feet and toes of diabetes patients with peripheral arterial disease are significantly warmer than those patients without peripheral arterial disease. These differences can easily be detected using infrared thermography which implies that this technology holds promise as a potential clinical tool in the

diabetic foot. More research is warranted in order to develop this tool for clinical purposes.

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Tables:

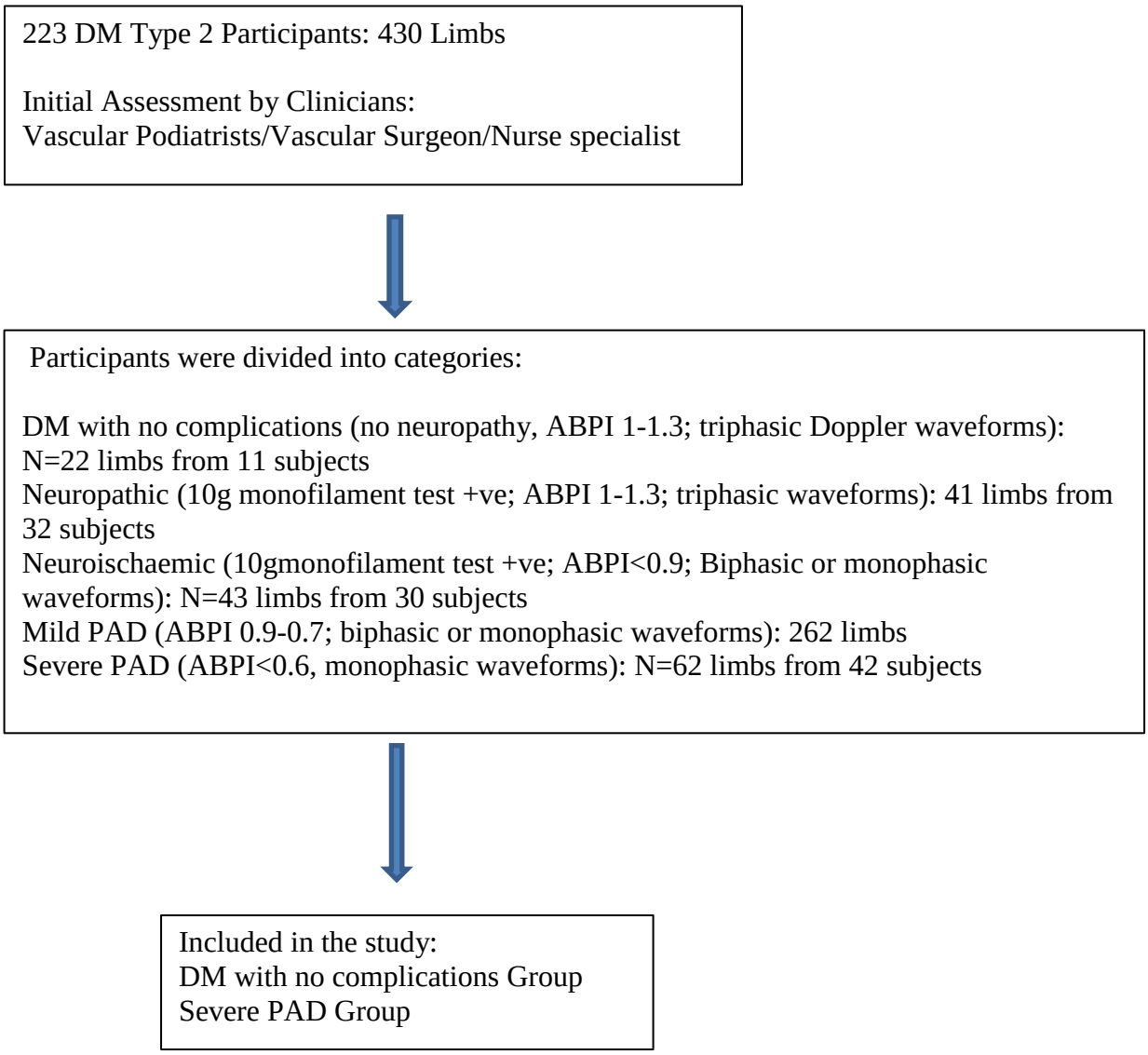
	DM+PAD	DM
Duration of Type 2 DM	14.09 years	12.17 years
HBA1c level	8.8	6.9
Smoking history	non-smokers: n=26 smokers: n=11 ex-smokers: n=10	non-smokers: n=8 smokers: n=4 ex-smokers: n=4

Table 1: Characteristics of participants

Region	Mean Temp ºC (DM+PAD)	Mean Temp ºC (DM)	p-value
Toe 1	27.85	24.81	.005
Toe 2	27.19	24.89	.033
Toe 3	27.18	25.07	.015
Toe 4	27.06	26.91	.038
Toe 5	26.98	25.07	.02
Mean Forefoot	28.33	26.23	.019

Table 2: Mean temperatures of Regions of Interest

Figures



43 neuroischaemic limbs (from 30 subjects), 41 neuropathic limbs (from 32 subjects), 58 PAD limbs (from 42 subjects), 21 DM healthy limbs (15subjects,)

Figure 1: Flow chart denoting numbers of limbs screened and excluded during the study process.

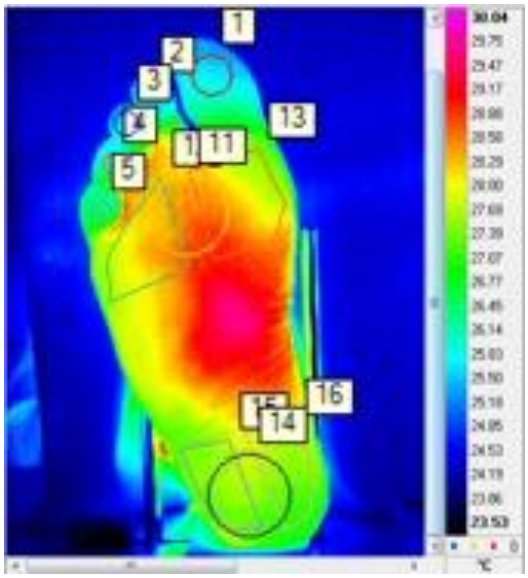


Figure 2 selected Regions of Interest in the feet

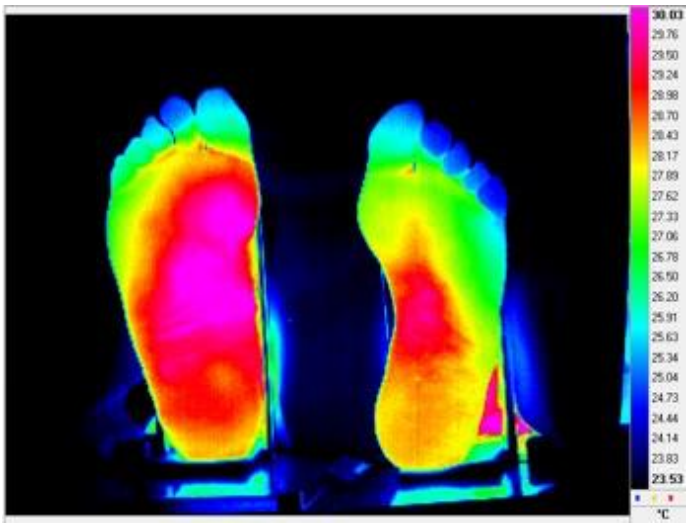


Figure 3: demonstrating remarkable difference in temperature between ischaemic Rt foot and a normal Lt foot with the ischaemic foot being warmer than the normal foot

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