Diagnostic Values for Skin Temperature Assessment to Detect Diabetes-Related Foot Complications

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Abstract

Background: Skin temperature assessment is a promising modality for early detection of diabetic foot problems, but its diagnostic value has not been studied. Our aims were to investigate the diagnostic value of different cutoff skin temperature values for detecting diabetes-related foot complications such as ulceration, infection, and Charcot foot and to determine urgency of treatment in case of diagnosed infection or a red-hot swollen foot.

Materials and Methods: The plantar foot surfaces of 54 patients with diabetes visiting the outpatient foot clinic were imaged with an infrared camera. Nine patients had complications requiring immediate treatment, 25 patients had complications requiring non-immediate treatment, and 20 patients had no complications requiring treatment. Average pixel temperature was calculated for six predefined spots and for the whole foot. We calculated the area under the receiver operating characteristic curve for different cutoff skin temperature values using clinical assessment as reference and defined the sensitivity and specificity for the most optimal cutoff temperature value. Mean temperature difference between feet was analyzed using the Kruskal–Wallis tests.

Results: The most optimal cutoff skin temperature value for detection of diabetes-related foot complications was a 2.2°C difference between contralateral spots (sensitivity, 76%; specificity, 40%). The most optimal cutoff skin temperature value for determining urgency of treatment was a 1.35°C difference between the mean temperature of the left and right foot (sensitivity, 89%; specificity, 78%).

Conclusions: Detection of diabetes-related foot complications based on local skin temperature assessment is hindered by low diagnostic values. Mean temperature difference between two feet may be an adequate marker for determining urgency of treatment.

Introduction

Foot complications, such as ulceration and infection, frequently occur in patients with diabetes and peripheral neuropathy and increase morbidity and mortality. Early detection and timely treatment of diabetes-related foot complications and their pre-signs can prevent these devastating consequences. However, early detection based on self-examination may be impeded by health impairments related to diabetes and other comorbidities or by social impairments. Frequent examination by health professionals is costly and may be too intrusive for patients. Automated telemedicine based on objective markers may overcome these disadvantages. Our ultimate objective is to develop an intelligent telemedicine system that can be deployed at patients’ homes for frequent examination of their feet to timely and automatically detect (pre-) signs of diabetes-related foot complications. Temperature assessment is a promising modality for such a system.

Inflammation precedes ulceration and infection, and this inflammation results in a temperature increase at the plantar foot surface. As inflammation is only present in the affected foot, a difference in temperature can be observed between that location and the same location on the contralateral foot. This can be accurately and reliably detected with an infrared thermometer, whereas the human hand is not an objective means for such assessment. Using a 2.2°C difference between two contralateral spots on the plantar foot surface as the cutoff value to define presence of inflammation, a fourfold decrease in the risk of developing foot ulceration was
found in a group of high-risk patients who performed skin temperature measurements twice a day compared with patients who performed structured daily foot care twice a day without skin temperature measurements.7–9 However, this cutoff value of 2.2°C has been based on data from a small group of patients,10 and diagnostic values such as sensitivity and specificity of this cutoff value have not been published to date. As low sensitivity values may mean a failure to timely detect a developing complication and low specificity values may lead to overdiagnosis, insight in diagnostic values is needed to determine optimal application of skin temperature assessment in telemedicine systems.

In the clinical studies mentioned above, an elegant and simple intervention was used that consisted of hand-held infrared thermometry.1–9 This constitutes, however, a measurement at low spatial resolution and temperature assessment at six selected spots only. Technological advancements in infrared imaging increase possibilities to quantify at high resolution the thermal pattern of the complete foot. Such advanced techniques may have the potential to differentiate between patients with complications that require immediate treatment at an emergency ward, such as with infection or a red-hot swollen foot indicative of a Charcot foot, and those that require non-immediate treatment at the outpatient clinic.9 For example, if an increase in temperature is not the result of inflammation but of infection, delay in treatment of 1 day may have devastating consequences.11,12 In a pilot study, we have recently proposed that a mean temperature difference of >3°C between the ipsilateral and contralateral foot is indicative of diabetes-related foot complications that warrant immediate treatment.5 This proposal warrants further investigation.

The aims of the current study were (1) to investigate the diagnostic values of different cutoff values for skin temperature for detecting diabetes-related foot complications such as ulceration, infection, and Charcot foot and (2) to investigate the diagnostic values of different cutoff values for skin temperature to determine urgency of treatment in case of diagnosed infection or a red-hot swollen foot.

Materials and Methods

A convenience sample of 54 patients with diabetes mellitus who visited the multidisciplinary outpatient diabetic foot clinic of Hospital Group Twente (Almelo, The Netherlands) was included in this study. The Medical Ethical Committee Twente approved the study protocol, and informed consent was obtained from each subject prior to the start of the study.

Our ultimate objective is to develop an intelligent telemedicine system that can be deployed at the patient’s home, but the current system is not yet feasible for measurements in the home situation. To imitate the home situation as closely as possible, only patients whose last visit to the outpatient clinic was more than 14 days ago were included, and measurements were performed before treatment took place. Patients with critical ischemia (no palpable pedal pulses and a toe pressure <30 mm Hg) were excluded, as critical ischemia will lower temperature values.1,13 Patients who had been hospitalized for diabetes-related foot complications within the last 6 months were also excluded, as treatment during hospitalization (such as minor amputations or prolonged treatment with antibiotics) may affect foot temperatures.

For the current study, patients were measured at one occasion at the outpatient foot clinic. Patients were seated in the supine position on a treatment bench. After shoes, socks, and (if applicable) dressings were removed, patients remained seated for a minimum of 5 min to allow equilibration of foot temperature.5 Patients were asked to place their feet on support bars just inside the experimental setup (Fig. 1), in such a way that their legs remained supported on the treatment bench. The experimental setup comprised two cameras (one for color images and one for thermal images), a light module, thermal reference elements, foot supports, a computer, and a screen. The camera for color images was a Canon (Tokyo, Japan) Eos–40D with an EF-s 17-85-mm lens, APS-C size (22.2×14.8-mm) 10.5-megapixel single-plate CMOS sensor, an angle of view comprising horizontal (68°40’–15°25’), vertical (48°–10°25’), and diagonal (78°30’–18°25’), a field of view of 420×280 mm, and a USB 2.0 Hi-Speed computer interface. The camera for thermal images was a FLIR® (Wilsonville, OR) SC305 with 16-bit resolution, 320×240 pixels, thermal sensitivity of <0.05–30°C, objective temperature range of −20 to 120°C, focal length of 18 mm, angle of view of 25°×19°, field of view of 420×315 mm, and an Ethernet IEEE 802.3 computer interface. The light module consisted of eight L1ZI-10ww05 light-emitting diodes, 4.4×4.4 mm, from LedEngin Inc. (San Jose, CA). All devices apart from the desktop computer and the screen were mounted in a wooden box with dimensions 600×600×1,900 mm, with a light shielding extension in front. The ankles and legs were covered with a sterile cloth. The entrance of the light shielding extension of the setup was covered with a black cloth, to eliminate influence of the ambient light.

During the measurement, two images were acquired: one color image with all light sources on, followed by a thermal image with all light sources off. Both cameras were driven and images were processed using custom-made MATLAB software (The MathWorks, Natick, MA). To discriminate the feet from the background, boundaries of the feet were automatically annotated in the color image and transferred to the thermal image.14 Mean temperature and SD values across pixels encapsulated by these foot boundaries were calculated. Furthermore, mean temperature across pixels was measured within circular masks 10 mm in diameter that corresponded with the six plantar spots per foot that were previously defined in clinical studies7–9: hallux, first, third, and fifth metatarsal heads, metatarsocuneiform joint, and cuboid (Fig. 2). When a spot was not available because of amputation, the contralateral spot was not measured either. Temperature differences between corresponding spots were calculated in SPSS for Windows software (version 17; SPSS Inc., Chicago, IL).

After the measurement with the imaging system, a clinical foot assessment was performed by a certified wound care consultant trained in the diabetic foot and in accordance with the diagnostic criteria described in international guidelines on the diabetic foot.1 Diabetes-related foot complications were defined as “infection, ulceration or destruction of deep tissues of the foot associated with neuropathy and/or peripheral arterial disease in the lower extremity of people with diabetes.”11 Pre-signs of these complications, such as callus and blisters, were not included in this study. Infection was diagnosed using PEDIS criteria.1,15 Diagnosis of neuropathy was based on a failed 10-g Semmes–Weinstein monofilament
Diagnosis of Charcot foot or osteomyelitis was confirmed by the findings of the radiologist on X-ray and magnetic resonance imaging. Treatment of complications after clinical assessment was recorded. All patients were followed up for 1 month via regular outpatient or inpatient clinic visits, to monitor occurrence of new diabetes-related foot complications.

Three groups of patients were defined based on the clinical foot assessment and subsequent treatment:

1. Group 1: “complication: immediate treatment.” These were patients with a diabetes-related foot complication that required immediate treatment. If such complications would be diagnosed in the home situation, patients would be referred immediately to an emergency ward. Patients were assigned to Group 1 if
   - A patient was hospitalized for further treatment (irrespective of the reason for hospitalization).
   - A patient was prescribed with antibiotics.
   - A red-hot swollen foot indicative of a Charcot foot was diagnosed.
   - A patient was referred for advanced diagnostics (X-ray or magnetic resonance imaging).

2. Group 2: “complication: non-immediate treatment.” These were patients with a diabetes-related foot
complication that required regular treatment at the outpatient foot clinic. This group consists of all patients with a diabetic foot complication but without the need for immediate treatment as defined for Group 1. These patients needed, for example, local wound care, sharp debridement, or offloading. If such a complication would be diagnosed in the home situation, these patients would be referred for multidisciplinary foot care within the next 2 days.

3. **Group 3: “no complications.”** These were patients without any diabetes-related foot complications that required treatment.

Differences between these groups for age, gender, and foot temperature were calculated with a Kruskal–Wallis test (nonparametric data).

The most optimal cutoff value for skin temperature for detecting diabetes-related foot complications was determined based on the receiver operating characteristic (ROC) curve, and the area under the ROC curve was calculated using SPSS for Windows version 17. Sensitivity, specificity, and positive and negative predictive values that determine the most optimal cutoff value were determined. For detection of a diabetes-related foot complication, cutoff values for the skin temperature difference between two contralateral spots within one patient were investigated, based on a comparison between the combined Groups 1 and 2 (i.e., presence of a diabetes-related foot complication) and Group 3 (i.e., no complication). Six contralateral spots were measured on both feet. The greatest temperature difference measured in any of the six pairs of spots was used for analysis because one spot with a temperature difference exceeding a threshold is already indicative of a diabetes-related foot complication. For determining urgency of treatment, cutoff values for the mean temperature difference measured between the whole left and right foot were investigated, based on a comparison between Group 1 (i.e., immediate treatment) and the combined Groups 2 and 3 (i.e., no need for immediate treatment). Data were analyzed using SPSS for Windows version 17. Differences between groups were determined using Kruskal–Wallis tests for nonparametric data. The value of \( \alpha \) was set at 0.05.

**Results**

Characteristics of the 54 patients included are shown in Table 1. All patients were diagnosed with peripheral neuropathy. Mean foot temperature ranged between 20.6°C and 36.2°C across patients, and no significant differences were present among Groups 1, 2, and 3 (Table 1). Mean temperature difference between the left and right foot was 2.65°C in patients who needed immediate treatment (Group 1), which was significantly greater compared with the other two groups (\( P < 0.001 \)).

The area under the ROC curve was 0.656 for detection of a diabetes-related foot complication (Fig. 3A), when patients with a diabetes-related foot complication (Groups 1 and 2) were compared with patients without a foot complication (Group 3). The most optimal cutoff skin temperature value to detect a diabetes-related foot complication was 2.2°C. Using this value, sensitivity was 76%, specificity was 40%, the
positive predictive value was 68%, and the negative predictive value was 50%.

The area under the ROC curve was 0.812 for determining urgency of treatment (Fig. 3B), when patients who needed immediate treatment (Group 1) were compared with patients who did not require immediate treatment (Groups 2 and 3). The most optimal cutoff skin temperature value to determine urgency of treatment was 1.35°C. Using this value, sensitivity was 89%, specificity 78%, the positive predictive value 44%, and the negative predictive value 97%.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Gender (male:female)</th>
<th>Group 1 (complications immediate) (n = 9)</th>
<th>Group 2 (complications regular) (n = 25)</th>
<th>Group 3 (no complications) (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7:2</td>
<td>20:5</td>
<td>12:8</td>
<td>0.311</td>
</tr>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>63 ± 7</td>
<td>64 ± 12</td>
<td>66 ± 11</td>
<td>0.595</td>
</tr>
<tr>
<td>Complication location</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hallux</td>
<td>1</td>
<td>4</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Digitus 2–5</td>
<td>4</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metatarsal heads</td>
<td>2</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midfoot or heel</td>
<td>0</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charcot foot</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected side (left:right)</td>
<td>3:6</td>
<td>10:15</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Temperature (°C)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected foot</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>31.68 ± 2.4</td>
<td>31.61 ± 2.2</td>
<td>30.25 ± 3.1</td>
<td>0.220</td>
</tr>
<tr>
<td>Range</td>
<td>26.4–35.0</td>
<td>27.3–36.2</td>
<td>20.6–35.5</td>
<td></td>
</tr>
<tr>
<td>Healthy foot</td>
<td></td>
<td></td>
<td></td>
<td>0.102</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>29.10 ± 2.1</td>
<td>30.68 ± 2.4</td>
<td>31.27 ± 3.1</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>24.4–31.6</td>
<td>26.1–34.7</td>
<td>22.4–35.6</td>
<td></td>
</tr>
<tr>
<td>Difference between feet</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>2.65 ± 1.4</td>
<td>1.36 ± 1.1</td>
<td>1.07 ± 0.9</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0.5–5.1</td>
<td>0.2–4.0</td>
<td>0.2–3.9</td>
<td></td>
</tr>
</tbody>
</table>

*aIn the group with no diabetes-related foot complications, the mean temperature of the left foot is shown.
*bIn the group with no diabetes-related foot complications, the mean temperature of the right foot is shown.
*cTo calculate the mean temperature difference, the warmest foot was taken as reference.

NA, not applicable.

FIG. 3. (A) The area under the receiver operating characteristic curve for detection of diabetes-related foot complications based on the greatest temperature difference between two contralateral spots. The most optimal cutoff value (2.2°C) is indicated with an asterisk. (B) The area under the receiver operating curve for determining urgency of treatment based on the difference in mean temperature between the left and the right foot. The most optimal cutoff value (1.35°C) is indicated with an asterisk.
Table 2. Classification of Patients for Having a Diabetes-Related Foot Complication or Requiring Urgent Treatment Based on the Most Optimal Cutoff Skin Temperature Value Calculated

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (complications immediate) (n = 9)</th>
<th>Group 2 (complications regular) (n = 25)</th>
<th>Group 3 (no complications) (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications based on skin temperature assessment(^a)</td>
<td>Present: 9; Absent: 0</td>
<td>Present: 17; Absent: 8</td>
<td>Present: 12; Absent: 8</td>
</tr>
<tr>
<td>Treatment based on skin temperature assessment(^b)</td>
<td>Immediate: 8; Non-immediate: 1</td>
<td>Immediate: 6; Non-immediate: 16</td>
<td>Immediate: 4; Non-immediate: 4</td>
</tr>
</tbody>
</table>

\(^a\)Presence or absence of diabetes-related foot complication, based on a difference \(>2.2\,^\circ\text{C}\) between one or more contralateral spots (six spots are measured: hallux, first, third, and fifth metatarsal heads, metatarsocuneiform joint, and cuboid). Patients in Groups 1 and 2 are compared with patients in Group 3 for calculating diagnostic values.

\(^b\)Immediate treatment needed, or regular or no treatment, based on a mean temperature difference of \(>1.35\,^\circ\text{C}\) between the left and the right foot of a patient. Patients in Group 1 are compared with patients in Groups 2 and 3 for calculating diagnostic values.

Classification for determining a diabetes-related foot complication or urgency of treatment of patients within the three groups based on the most optimal cutoff value is shown in Table 2. None of the patients in Group 3 (no complications) developed any complications during the 1-month follow-up.

Discussion

Preventing diabetes-related foot complications by early detection and timely treatment is important, considering the devastating consequences of these complications for morbidity and mortality.\(^1,2\) Out of a variety of possible preventative measures, evidence for the monitoring of plantar foot temperatures twice a day giving a significant risk reduction for ulceration has been found in three randomized controlled trials.\(^7-9\) However, temperature assessment has not yet found its way to daily clinical practice. Even though the efficacy has been proven in these randomized controlled trials, the effectiveness in daily practice can be impeded for various reasons. One of those reasons may be related to the diagnostic quality of temperature assessment. Low sensitivity values may mean a failure to timely detect diabetes-related foot complications, whereas low specificity values may lead to over-referral and treatment. In this study, the diagnostic values of temperature assessment for detection of diabetes-related foot complications were investigated, as these values have not been reported earlier.

The most optimal cutoff value when comparing two contralateral spots for detection of diabetes-related foot complications was found at \(2.2\,^\circ\text{C}\), which is identical to the value used in the previous clinical studies that showed efficacy of foot temperature monitoring.\(^7-9\) Despite being the most optimal cutoff value, sensitivity did not exceed 80%, and specificity was as low as 40%. This suggests that the current algorithm for temperature assessment is not yet an adequate preventative method for the detection of diabetes-related foot complications in daily clinical practice. From the low specificity values it can be concluded that many patients who were not clinically diagnosed with diabetes-related foot complications had temperature differences exceeding \(2.2\,^\circ\text{C}\) between two contralateral spots (Table 2). As none of these patients developed complications in the month following the measurement, these temperature differences are not likely to be the result of inflammation preceding ulceration. Considering the temperature equilibrium period of 5 min before infrared imaging, the extent of ambulatory activity also does not seem a possible explanation for these differences. With both peripheral neuropathy and peripheral arterial disease being related to foot temperature,\(^13,16,17\) differences in degree of peripheral neuropathy and/or peripheral arterial disease between the left and right foot of a patient may be related to differences in measured temperature. However, it is not possible to draw any conclusions on this aspect from our current study. To allow further investigation of temperature differences between the left and right foot when no inflammation is present, temperature assessment should be combined with more advanced diagnostic methods for peripheral neuropathy or peripheral arterial disease in future studies, such as the vibration perception threshold or the microcirculation of the foot.

Whereas the diagnostic values for detection of diabetes-related foot complications may not seem adequate, temperature assessment showed a more promising diagnostic value for determining the urgency of treatment. A mean temperature difference between the left and right foot exceeding \(1.35\,^\circ\text{C}\) was indicative of diabetes-related foot complications that require immediate treatment, with a sensitivity of 89% and specificity of 78%. A drawback of this algorithm is that complications requiring immediate treatment are not detected if they are present in both feet at the same time. This may be solved by combining temperature measurements with other imaging methods (e.g., photographic) or by monitoring patients over time. It should be noted, however, that the chance of having such complications in both feet at the same moment is small.

Given the results of this study, it is important to search for methods that can optimize the diagnostic value for using skin temperature measurements for detecting diabetic foot complications. A first possible option is a more detailed analysis of the temperature patterns of the plantar foot surface. In the current study, we have analyzed mean temperatures in six selected regions and in the whole foot and compared findings between left and right feet. We chose to investigate such simple parameters, as these are preferred in telemedicine systems. However, more detailed analyses at higher resolution and more complex algorithms are possible with the current advanced infrared imaging systems. These analyses or algorithms may consist of the following:

1. Detecting temperature differences between left and right feet at any spot on the foot, and not only at six selected spots
2. Analyzing the size of detected hotspots, by calculating the number of contralateral pixels that exceed the \(2.2\,^\circ\text{C}\) threshold. Within this aim, it can be hypothesized that larger hotspots are indicative of (more severe) diabetes-related foot complications, whereas smaller hotspots may be related to no or less severe complications
3. Detecting temperature differences within one foot (without the need of the contralateral foot)
Conclusions

Detection of diabetes-related foot complications based on skin temperature assessment (i.e., hotspots) using advanced infrared imaging is hindered by low diagnostic values, especially specificity, which increases chance for overdiagnosis. However, mean foot temperature difference between the left and right feet may be an adequate marker for determining urgency of treatment. Nevertheless, these results suggest that diagnostic values should be further optimized before temperature assessment can be widely implemented in telemedicine systems for use in daily clinical practice. Such optimization may potentially occur with more detailed analyses of skin temperature patterns or by combining skin temperature measurements with other diagnostic methods.

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Author Disclosure Statement

No competing financial interests exist.

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