

RESEARCH

Infrared thermography for monitoring severity and treatment of diabetic foot infections

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Abstract

Monitoring of diabetic foot infections is largely based on clinical assessment, which is limited by moderate reliability. We conducted a prospective study to explore monitoring of thermal asymmetry (difference between mean plantar temperature of the affected and unaffected foot) for the assessment of severity of diabetic foot infections. In patients with moderate or severe diabetic foot infections (International Working Group on the Diabetic Foot infection-grades 3 or 4) we measured thermal asymmetry with an advanced infrared thermography setup during the first 4–5 days of in-hospital treatment, in addition to clinical assessments and tests of serum inflammatory markers (white blood cell counts and C-reactive protein levels). We assessed the change in thermal asymmetry from baseline to final assessment, and investigated its association with infection-grades and serum inflammatory markers. In seven included patients, thermal asymmetry decreased from median 1.8°C (range: –0.6 to 8.4) at baseline to 1.5°C (range: –0.1 to 5.1) at final assessment ($P = 0.515$). In three patients who improved to infection-grade 2, thermal asymmetry at baseline (median 1.6°C (range: –0.6 to 1.6)) and final assessment (1.5°C (range: 0.4 to 5.1)) remained similar ($P = 0.302$). In four patients who did not improve to infection-grade 2, thermal asymmetry decreased from median 4.3°C (range: 1.8 to 8.4) to 1.9°C (range: –0.1 to 4.4; $P = 0.221$). No correlations were found between thermal asymmetry and infection-grades ($r = -0.347$; $P = 0.445$), CRP-levels ($r = 0.321$; $P = 0.482$) or WBC ($r = -0.250$; $P = 0.589$) during the first 4–5 days of hospitalization. Based on these explorative findings we suggest that infrared thermography is of no value for monitoring diabetic foot infections during in-hospital treatment.

Key Words

- ▶ diabetic foot infection
- ▶ infrared thermography
- ▶ monitoring
- ▶ plantar foot thermal asymmetry

Introduction

Foot disease is a major problem in people with diabetes mellitus, with a 19–34% lifetime prevalence of foot ulceration (1). When a patient has a foot ulcer, diabetic foot infection (DFI) is a common and devastating complication that occurs in approximately 60% of patients (2). DFI increases morbidity and healthcare costs and is the most common cause of diabetes-related hospitalization and lower limb amputation (3, 4, 5).

DFI is a clinical diagnosis, defined as the presence of manifestations of an inflammatory process in any tissue below the malleoli in people with diabetes (6). However, manifestations of an inflammatory process, such as swelling, induration, erythema, warmth and local tenderness, can be difficult to assess if peripheral neuropathy, peripheral artery disease (PAD) and/or immune dysfunction is present in people with diabetes (7). Mostly, DFIs occur in a site of trauma or ulceration in the presence of peripheral neuropathy, and less frequently PAD (8). Most DFIs are superficial at presentation, but microorganisms can spread via s.c. tissues, such as fascia, joints and bones (8). Progression of a DFI can occur when inflammatory processes cause tissue necrosis in compartments in the foot, after which the infection spreads from the high-pressure compartments in the foot to more proximal areas of lower pressure (8, 9). Systemic manifestations of an inflammatory process (fever, tachycardia, increased white blood cell count) are unusual, but indicate a potentially limb-threatening infection (5, 7). To define and assess DFI severity, it is recommended to use the International Working Group on the Diabetic Foot (IWGDF) classification system (6). Clinicians determine the need for treatment based on clinical assessment, serum inflammatory markers and, sometimes, additional imaging (e.g. radiographic or MRI) (6). Moderate or severe DFIs, classified as IWGDF infection-grades 3 or 4, respectively, frequently require hospitalization for parenteral antibiotic therapy and, sometimes, (surgical) debridement (6). To monitor severity of DFI during hospitalization and to guide treatment decisions, treating clinicians use clinical assessment, serum inflammatory markers and microbiological results of wound cultures. However, clinical assessment is limited by moderate validity and reliability, moderate inter-observer agreement and limited availability of competent personnel (10, 11, 12, 13). Serum inflammatory markers correlate only marginally with DFI severity (6). Microbiological results from deep tissue cultures are important to guide antibiotic treatment, however, adequate deep tissue samples are not

always obtained and it takes several days before results are known. Yet, adequate monitoring of DFI severity is important to determine which patients require continued hospitalization with parenteral administration of antibiotics or (surgical) debridement, and which patients can be safely discharged.

Although sometimes masked by the presence of peripheral neuropathy and PAD, manifestations of an inflammatory process are often accompanied by an increase in local foot temperature (13, 14). Therefore, temperature measurements might be suitable for diagnosing and monitoring DFIs. Foot temperature asymmetry has been studied for diagnosis and (home) monitoring of diabetic foot complications, including DFIs (14, 15). Van Netten *et al.* showed that patients with DFIs had a mean plantar foot thermal asymmetry (i.e. affected-unaffected foot skin temperature difference) of $>3^{\circ}\text{C}$ at presentation (15). A subsequent study found plantar foot thermal asymmetry of 1.35°C as an optimal cut-off to triage for the need of urgent treatment (e.g. hospitalization for DFI) (14). Unfortunately, patients were not followed during treatment in these studies. Only one study measured foot temperatures more than once in hospitalized patients with a DFI (16). Armstrong *et al.* measured skin temperatures of the areas closest to the DFIs and the corresponding contralateral sites at the start and discontinuation of parenteral antibiotic treatment (16). They found similar mean temperature differences between feet at baseline (1.6°C) and 12 days later (1.3°C) (16). Furthermore, they found no association with clinical assessment or serum inflammatory markers (e.g. white blood cell count (WBC) or C-reactive protein (CRP)) (16). The study by Armstrong *et al.* was part of a prospective, randomized comparison of two parenteral antibiotic regimens for DFIs (17), thus not primarily designed to assess foot temperature differences during DFI treatment (16). Also, DFI severity was expressed according to the University of Texas wound classification system which is not specifically designed for this purpose, foot temperatures were measured at one spot only, and PAD or amputations were not reported in detail (16).

Based on these studies, current guidelines advise not to use thermography for diagnosing or monitoring DFI (6). However, thermography has a variety of advantages, such as its non-invasiveness and the objectiveness of measured outcomes. Technological developments now enable high-resolution infrared thermal imaging of entire feet and (automated) thermal asymmetry analysis, which is an improvement over temperature measurements of manually selected spots with handheld low-resolution infrared devices used by Armstrong *et al.*

(14, 15, 16, 18). To this date, there are no studies investigating the monitoring of DFIs in patients using plantar foot thermal asymmetry measured by advanced infrared thermography of the entire plantar aspects of both feet. To explore the potential of measuring plantar foot thermal asymmetry for the assessment of DFI severity, we conducted a prospective study to investigate the association between plantar foot thermal asymmetry measured by an advanced infrared thermography setup and clinical assessment in patients with moderate and severe DFIs during in-hospital treatment.

Materials and methods

We conducted a prospective case series in *Hospital Group Twente*, a regional center of expertise for diabetic foot care in Almelo, the Netherlands. Our study protocol was reviewed by the medical ethical committee Twente (METC Twente, project K15-50). The medical ethical committee declared this study exempt from further ethical assessment according to Dutch law, because of its observational design. All patients provided informed consent. All study activities were performed according to the Declaration of Helsinki.

Based on our experience with patients hospitalized with DFIs in our center, we used a convenience sample of patients included during a 6-month study duration.

We included patients (age >18 years) with type 1 or 2 diabetes mellitus who were hospitalized for the treatment of a moderate to severe DFI based on the IWGDF guidelines (6). We did not include patients more than once in case of a new hospital admission for another DFI.

We excluded patients if severe PAD was present in the affected or unaffected limb, since several studies reported on the interaction of PAD with foot temperature (15, 19, 20). In our hospital, assessment of PAD by measuring the ankle-brachial pressure index (ABPI) and/or systolic toe pressure (STP) is standard practice when a patient is hospitalized with a DFI. We defined severe PAD as an ABPI ≤ 0.39 or STP <30 mmHg (21). We also excluded patients with isolated DFI of the dorsum of the foot or near the ankle joint, patients with bilateral DFIs, and patients who had a contralateral amputation proximal to the Chopart joint, since in these situations a valid assessment of plantar thermal asymmetry using our thermography setup was not possible.

At the day of inclusion, or the next morning when a patient was hospitalized in the evening or at night, we made thermographic images from the plantar surfaces

of both feet. We repeated this every morning, for 5 consecutive days or less in case of shorter hospitalization. Also, we measured core temperature ($^{\circ}\text{C}$) daily, with a digital ear thermometer. Furthermore, an experienced diabetic foot wound care consultant assessed the diabetic foot infection clinically, using IWGDF infection-grades (22). These infection-grades were based on the following manifestations of inflammatory processes: swelling or induration, erythema >0.5 cm around the ulcer, local tenderness or pain, local increased warmth, and/or purulent discharge, in absence of systemic symptoms or other causes of inflammatory responses (e.g. gout). An uninfected ulcer, indicated as infection-grade 1, was defined by absence of manifestations of inflammatory processes. A mild DFI, indicated as infection-grade 2, was defined by at least two of these manifestations of inflammatory processes, affecting the skin but not the deeper tissues with erythema <2 cm around the ulcer and without systemic symptoms. A moderate DFI, indicated as infection-grade 3, was defined as presence of at least two manifestations of inflammatory processes affecting deeper tissues (e.g. joints, tendons) or erythema reaching further than 2 cm around the wound, in absence of systemic symptoms. Severe DFI, indicated as infection-grade 4, was defined as any foot infection with associated manifestations of a systemic inflammatory response (at least two of the following: core temperature >38 or <36 $^{\circ}\text{C}$, Heart rate >90 beats/min, Respiratory rate >20 breaths/min or PaCO₂ <4.3 kPa (32 mmHg), WBC >12,000/mm³, or <4000/mm³, or >10% band neutrophils (22). In case of underlying osteomyelitis, which we diagnosed in accordance with the IWGDF-guidelines (6), we added an 'O' to the infection-grade. Also, we determined serum WBC ($\times 10^9/\text{L}$) and CRP-levels (mg/L) on the first, third and fifth day. Finally, we assessed loss of protective sensation at admission, defined as the inability to feel a 10-g monofilament (23).

We made thermographic images using a setup with an infrared thermal camera (FLIR SC 305), a digital photo camera (Canon Eos 40D), a light module and thermal reference elements that were connected to a personal computer and a screen. We covered this setup with a box-like construction to block ambient light and mounted it on a platform that was adjustable regarding location and height (Fig. 1). Previous studies have described this thermography setup in detail (14, 15, 18). Before making the thermographic images, the patients waited in supine position for 10 min after removing shoes, socks and bandages of both feet, to enable foot temperature normalization (15). Patients remained supine with the

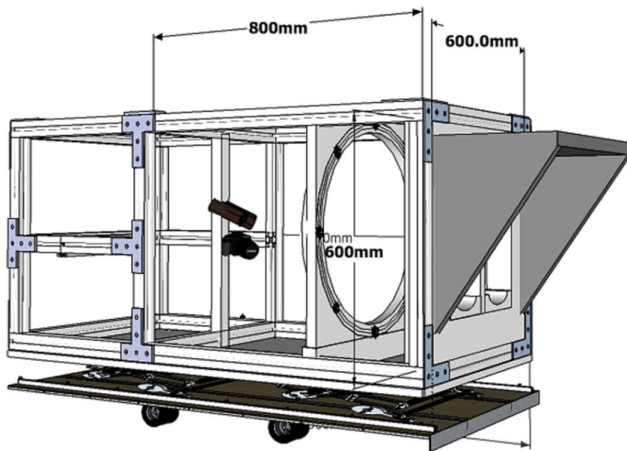


Figure 1
Schematic view of the thermography setup used in this study. The feet are positioned on the support bars below the light shield on the right side of the box-like construction. Both the infrared thermal camera and the digital photo camera are placed 800 mm from the support bar for the patient's feet. The infrared thermal camera is positioned above the digital photo camera.

setup placed at the end of the bed. Patients placed both feet on the support bars of the setup. After autofocusing the digital camera and calibrating the infrared thermal camera using the thermal reference elements, we acquired a digital photo with the light module turned on, followed by a thermographic infrared image with the light module turned off. The cameras were driven by custom-made MATLAB software (The MathWorks, Natick, MA). Subsequently, we used MATLAB software for manual annotation of the boundaries of both feet in the digital photo, inclusive of previous amputations or deformities, after which we transferred this annotation to the thermographic infrared image. With the custom-made MATLAB software, the mean temperature (°C) of all pixels enclosed within the annotated boundaries of the plantar aspects of both feet separately was automatically calculated.

The primary outcome was plantar foot thermal asymmetry, defined as the difference between the mean temperature of the plantar aspect of the affected foot and the mean temperature of the plantar aspect of the non-affected foot at baseline (day of inclusion) and at final assessment (5 days later or at hospital discharge when this was earlier). Since DFI affects mostly the whole foot, we assessed thermal asymmetry of the whole plantar surface of the foot in instead of selected contralateral spots as was done by Armstrong *et al.* (16). We calculated changes in thermal asymmetry over time (baseline to final assessment) and compared these with the improvement

of the DFI (based on clinical assessment and defined as a decrease of infection-grades 3 or 4 to infection-grade 2), and serum inflammatory markers (WBC and CRP-levels) during the same timeframe. Secondary outcome measures were: duration of hospitalization (days), change in antibiotic regime, resolution of DFI (defined as: IWGDF infection-grade 1), minor amputations (any resection distal to the ankle joint), and major amputations (any resection through or proximal to the ankle joint) during hospitalization or follow-up. We performed follow-up until resolution of DFI, amputation or last-mentioned consultation in our electronic health record system.

We expressed variables as medians with ranges. We compared the changes in thermal asymmetry from baseline to final assessment between patients with clinical improvement to infection-grade 2 and patients without clinical improvement to infection-grade 2, using a paired samples *t*-test. We used a Wilcoxon signed-rank test to assess changes in levels of serum inflammatory markers from baseline to final assessment in all patients. We assessed correlations between changes in thermal asymmetry from baseline to final assessment and changes in infection-grades and levels of serum inflammatory markers from baseline to final assessment, using Spearman's rank-order correlation analysis. All tests were performed two-sided ($\alpha=0.05$). We used SPSS software (version 24; SPSS Inc.) for statistical analysis.

Results

During a 6-month period, 37 patients with DFIs were admitted to our hospital of whom seven were included in this study (Fig. 2). All included patients were male, and age and BMI were typical for this population (Table 1).

Overall, median thermal asymmetry was 1.8°C (range: -0.6 to 8.4) at baseline and 1.5°C (range: -0.1 to 5.1) at final assessment ($P=0.515$) (Figs 3, 4A, B and Table 2).

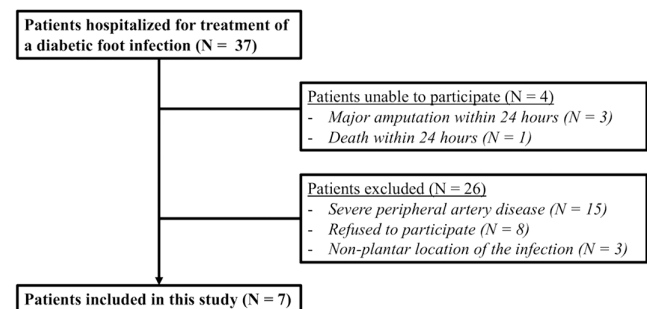


Figure 2
Flowchart of the study.

Table 1 Characteristics of the study.

No.	M/F	Age	BMI (kg/m ²)	DM	Foot	LOPS	ABPI	STP	DFI location	Aspect
1	M	45	35.0	2	Right	Yes	1.3	140	5th MTH	Planto-lateral
2	M	72	28.6	2	Left	Yes	0.8	35	Hallux	Plantar
3	M	86	23.2	2	Left	Yes	0.6	NM	5th MTH	Planto-lateral
4	M	59	29.4	2	Right	Yes	0.8	97	3rd MTH	Plantar
5	M	65	33.0	2	Right	Yes	1.3	106	1st MTH	Plantar
6	M	52	33.7	2	Left	Yes	1.2	62	Hallux	Plantar
7	M	66	26.9	2	Right	Yes	1.0	141	2nd Toe	Plantar

ABPI, ankle-brachial pressure index; DFI, diabetic foot infection; DM, diabetes mellitus type; F, female; LOPS, loss of protective sensation; M, male; MTH: metatarsal head; No., patient number; STP, systolic toe blood pressure (mm Hg, NM indicates that STP could not be measured due to non-compressible arteries).

At baseline, five patients had infection-grade 3 and two had infection-grade 4 (Fig. 4A, B and Table 2). At final assessment, DFIs had improved to infection-grade 2 in three patients (Fig. 4A and Table 2). In these patients, thermal asymmetry remained similar (median 1.6°C (range: -0.6 to 1.6) at baseline and 1.5°C (range: 0.4 to 5.1) at final assessment ($P=0.302$)) (Figs 3, 4A and Table 2). In the other four patients, thermal asymmetry decreased from median 4.3°C (range: -0.1 to 4.4) at final assessment ($P=0.221$) (Figs 3, 4B and Table 2). We found no significant correlation between changes in thermal asymmetry and changes in infection-grade from baseline to final assessment overall ($r=-0.347$; $P=0.445$).

The median serum CRP-levels at baseline (86 mg/L (range: 41 to 164)) decreased significantly to 42 mg/L (range: 15 to 88) at final assessment ($P=0.016$), while the median serum WBC of $9.5 \times 10^9/L$ (range: 6.6 to 12.6) at baseline decreased not significantly to $7.4 \times 10^9/L$ (range: 5.0 to 9.7) at final assessment ($P=0.063$) (Fig. 4A and B). We found no correlation between decrease of thermal asymmetry and decrease of serum CRP-levels ($r=0.321$; $P=0.482$) or decrease of serum WBC ($r=-0.250$; $P=0.589$).

Mean hospitalization was 7.3 days (s.d.: 5.8, range: 4 to 29) (Table 2). Patient no. 4 had a change of antibiotic regimen after 4 days based on multiple blood cultures and a wound culture with a clindamycin-resistant *Staphylococcus aureus* (Table 2). Two patients had resolution of DFIs within approximately 7–8 weeks, two patients had minor amputations during hospitalization, two patients had minor amputations after hospital discharge and one patient died three months after the study with an unresolved DFI (Table 2).

Discussion

In this pilot study, we explored the use of plantar foot thermal asymmetry in patients with DFIs, measured

with an advanced infrared thermographic setup, as a monitoring modality for the severity of DFI during in-hospital treatment. Overall, we found a non-significant difference in median thermal asymmetry between baseline (1.8°C) and final assessment (1.5°C). We hypothesized that thermal asymmetry would decrease during hospitalization in case of clinical improvement and, in contrast, that thermal asymmetry would persist or increase in case of unchanged or increased DFI severity. However, we obtained results that were contradictory to this hypothesis.

Our findings confirm the study results by Armstrong *et al.*, who measured temperature differences between contralateral spots in DFI patients at the start and discontinuation (mean 12 days later) of parenteral antibiotic therapy (16). They found a non-significant decrease of 0.30°C and no association with clinical assessment (16). In contrast to their study, in which they measured temperatures at the DFI location and the same location on the contralateral foot using a handheld infrared thermography device with 12 days in between, we used a more advanced thermography setup that enabled measurements of the mean temperature of the whole plantar surfaces of both feet. We further performed clinical assessment with a more detailed classification system, specifically developed for the assessment of infection of the diabetic foot. Despite these improvements in study design, we found comparable outcomes, suggesting that monitoring thermal asymmetry is of no additional value for monitoring the severity or treatment of DFIs.

Several factors may contribute to this lack of association between thermal asymmetry and DFI infection-grades. First, in the IWGDF classification system, infection-grade 3 and 4 DFIs include a wide variety of manifestations of inflammatory processes, ranging from 2 cm of cellulitis around the ulcer to extensive underlying osteomyelitis (24). Within this heterogeneous group of DFIs, subtle but relevant clinical improvements (e.g. decrease of erythema

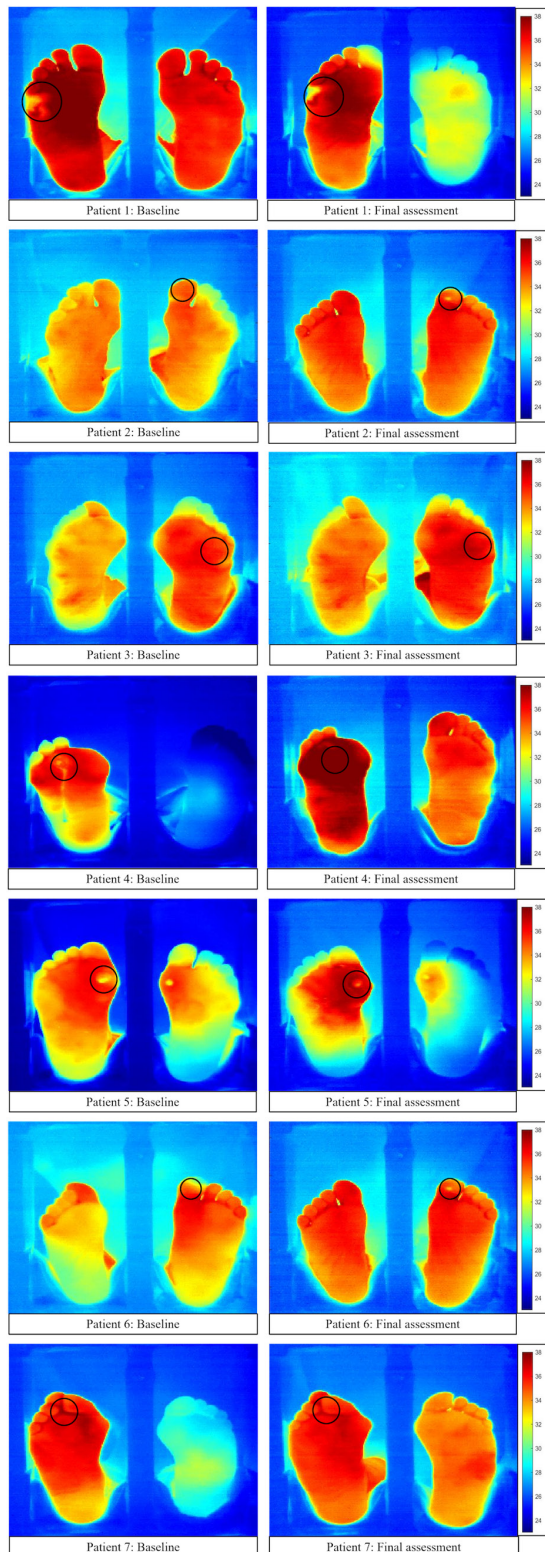


Figure 3

Infrared thermal images of the plantar aspects of both feet of each patient at baseline (left) and final assessment (right). The areas of the infected diabetic foot ulcers are indicated by the black circles. The colored reference bar represents the temperature ($^{\circ}\text{C}$).

from 10 to 5 cm around the ulcer) could influence plantar foot temperatures, but could be underreported because these would still be graded as an infection-grade 3 or 4. This limitation of the IWGDF infection-grades classification has been discussed by others as well (24). But despite this shortcoming of using IWGDF infection-grades, in our opinion its use is still indicated because it is a validated and widely used system in both patient care and research, and furthermore, in the recently developed and validated WifI classification system the same infection-grade classification is used to express the severity of an infection (6.21). Second, foot temperatures are variable across people and over time and influenced by factors such as peripheral neuropathy and PAD (19, 20, 25, 26). These can be confounding factors causing thermal asymmetry irrespective of inflammation, ulceration and/or infection. Third, the presence of increased core temperature could confound thermoregulation of the feet (e.g. in patients no. 1 and no. 4), leading to a decrease in thermal asymmetry, in an attempt of the body to cool down itself. Fourth, measuring an evident decrease in plantar foot thermal asymmetry in this study was less likely, despite clinical improvement of DFIs, due to the low plantar foot thermal asymmetry values we measured in some patients at baseline (e.g. patients no. 1, no. 2, no. 3 and no. 6).

In previous studies, CRP-levels have been reported to be useful for monitoring DFI severity or treatment in patients with DFIs complicated by osteomyelitis only (27, 28). In our group of patients, we found significantly lower CRP-levels at final assessment when compared to baseline. Regarding the WBC, we also found a decreasing trend, but no significant differences between baseline and final assessment. We suggest that these findings result from the clinical treatments. Patients were instructed to keep the infected foot elevated and at rest while they were treated with parenteral antibiotic therapy. This leads to rapid improvement of systemic manifestations of inflammatory processes (e.g. fever, highly elevated CRP and WBC), while local manifestations of inflammatory processes often remain present or improve only slightly. With a follow-up of inflammatory markers of just 5 days and uniform outcomes of the four patients with osteomyelitis (i.e. all patients were amputated) definitive conclusions could not be drawn.

Previously, van Netten *et al.* showed that plantar foot thermal asymmetry of 1.35°C can be used as a diagnostic temperature threshold, to detect diabetes-related complications that require immediate treatment such as DFIs (14). The findings of our study support this cut-off

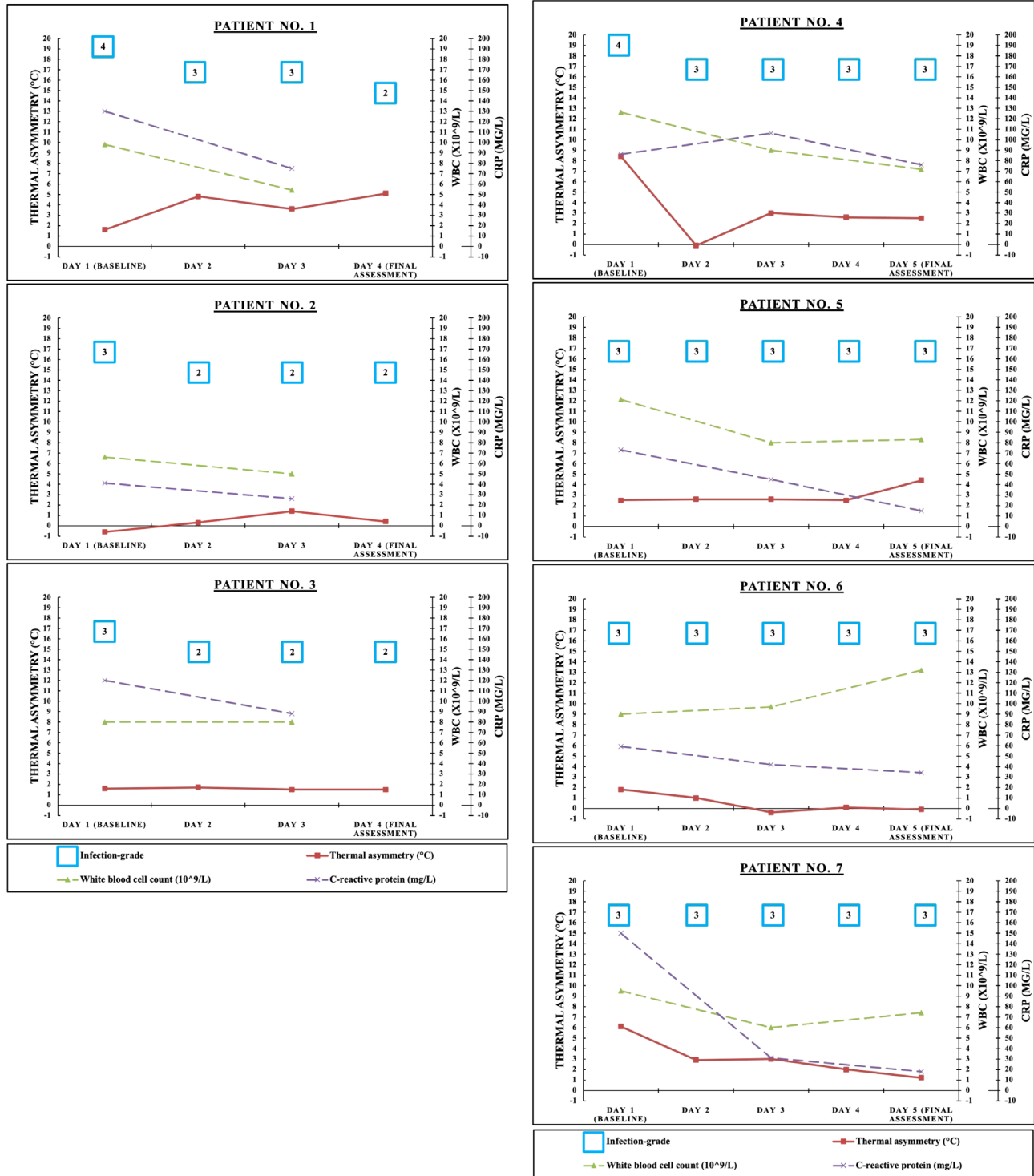


Figure 4

(A) Development of thermal asymmetry, infection-grades and serum inflammatory markers during the study for the patients that clinically improved to infection-grade 2. (B) Development of thermal asymmetry, infection-grades and serum inflammatory markers during the study for the patients that clinically did not improved to infection-grade 2.

Table 2 Clinical assessments of diabetic foot infection, temperature differences and clinical outcomes during follow-up stratified by patient.

Characteristics	Patients with clinical improvement			Patients without clinical improvement			
	1	2	3	4	5	6	7
Baseline							
Infection grade	4	3	3	4 (O)	3 (O)	3 (O)	3 (O)
Thermal asymmetry (°C)	1.6	-0.6	1.6	8.4	2.5	1.8	6.1
Core temperature (°C)	39.2	36.6	37.1	38.2	36.7	37.5	37.3
Treatment of DFI							
AB regimen	C-C	C-C	A-C	C-C	A-C	C-C	C-C
AB change	No	No	No	Yes (4)	No	No	No
Vascular procedure	No	No	No	No	No	No	No
Measurements (days)	4	4	4	5	5	5	5
Infection grade	2	2	2	3 (O)	3 (O)	3	3
Final assessment							
Core temperature (°C)	36.6	36.7	37.0	37.7	36.3	36.0	36.3
Thermal asymmetry (°C)	5.1	0.4	1.5	2.5	4.4	-0.1	1.2
Δ Thermal asymmetry (°C)	3.5	1.0	-0.1	-5.9	1.9	-1.9	-4.9
Follow-up							
Duration of hospitalization (days)	4	4	4	20	5	8	6
DFI resolution (days)	Yes (53)	No	Yes (52)	No	No	No	No
Amputation (days to)	No	Minor (85)	No	Minor (25)	No	Minor (4)	Minor (4)

The difference between plantar foot thermal asymmetry (affected–non-affected foot temperature difference) at baseline and final assessment, which was calculated by subtracting the temperature value of thermal asymmetry at baseline from the temperature value of the thermal asymmetry at final assessment. Patient no. 5 died 3 months after hospital discharge, before notion of an amputation or DFI resolution.

AB, antibiotics; C-A, amoxicillin-clavulanate; C-C, ciprofloxacin and clindamycin; DFI, diabetic foot infection; Δ, thermal asymmetry.

temperature value. We found an overall median thermal asymmetry of 1.8°C on baseline with thermal asymmetry values greater than 1.35°C in six out of seven patients. In our opinion, these findings support the potential value of thermographic assessment of plantar foot thermal asymmetry for the diagnosis of DFIs, especially in situations where experienced personnel is absent and telemedicine or home-monitoring is required.

Besides using thermal asymmetry as a diagnostic tool, it might also have prognostic value. Armstrong *et al.* found a significantly lower favorable clinical response rate (defined in their study as clinical improvement or cure of DFI) after parenteral antibiotic therapy in patients with a baseline temperature difference greater than 5.6°C (16). In our study, only two patients had baseline plantar foot thermal asymmetry greater than 5.6°C. Both had no resolution of DFI and eventually had minor amputations due to osteomyelitis. The finding of this 5.6°C cut-off temperature difference is of particular interest in the context of home monitoring as telemedicine approach, since it could indicate a cut-off temperature difference for more urgent treatment than the previously reported 1.35°C cut-off temperature difference. A higher cut-off value could, for example, be helpful to select patients for hospitalization and to guide clinicians and patients in joint decision-making for initial treatment (e.g. primary

amputation). More detailed studies in larger groups of patients are needed to assess the prognostic value of thermal asymmetry.

There are limitations to our study. First, our study is limited by the low number of included patients, which was mainly caused by the lack of available patients during the study period and the high number of excluded patients. This low number of included patients is a limitation as it makes statistically significant results unlikely. We could not increase patient inclusions by expanding our study to other hospitals, due to our large and unpractical thermography setup. Also, lengthening of our study could not be justified, since we had to overthrow our hypothesis of a positive association between plantar foot thermal asymmetry and clinical assessment of DFI severity after analyzing the initially obtained data. In retrospect, more patients could have been included if we would have used more straightforward and practical mobile phone applications for thermographic assessment in a multicenter setting (29, 30, 31), but these were not available at the time. Even though a statistical significant result was unlikely to be obtained due to the low number of included patients, the initial findings are highly indicative of our hypothesis being incorrect. Therefore, despite these limitations, our results are relevant to publish, as this may reduce waste in research by other

pursuing similar investigations. Second, the duration of measurements of 4–5 days per patient could potentially be too short for adequate assessment of thermal asymmetry during the in-hospital treatment of DFIs. However, we do not expect that measuring thermal asymmetry for a longer duration would have altered the outcomes of our study, since Armstrong *et al.* found comparable outcomes whilst they measured thermal asymmetry over approximately 12 days (16).

Conclusion

In this study, we found no association between clinical assessment of DFIs according to IWGDF infection-grades and the change in plantar foot thermal asymmetry from baseline to final assessment. We found that during the first four to five days of in-hospital treatment, plantar foot thermal asymmetry of patients with moderate to severe DFIs decreased more in patients with unimproved infection-grades than those with improved infection-grades. Also, we found that plantar foot thermal asymmetry was not correlated with serum CRP levels or WBC. We, therefore, suggest that infrared thermography assessment of plantar foot thermal asymmetry is not useful for monitoring the severity or treatment of DFIs. In our opinion, additional studies regarding thermographic assessment of thermal asymmetry for the monitoring of severity or treatments of DFIs are not indicated. Infrared thermography could potentially be of value for diagnosing and prognosing DFI, for example in a home monitoring setting, for which more research into its application is required.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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Author contribution statement

WadS and JvN conceived and designed this study. WadS performed all measurements. KH performed the statistical analysis and wrote the manuscript. WadS, JvN, RK, JvB and SB contributed to interpretation of statistical analysis. WadS, JvN, RK, JvB and SB critically reviewed and edited the manuscript. All authors have read and approved the final manuscript.

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