Prognostic value of infrared thermography in an emergency department
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**Objective** In this study, we aimed to investigate the prognostic potential of infrared thermography in a population of medical patients admitted to the emergency department. Central-to-peripheral temperature gradients were analyzed for association with 30-day mortality.

**Methods** This prospective observational study included 198 medical patients admitted to the Emergency Department, at Odense University Hospital. A standardized thermal picture was taken and temperatures of the inner canthus, the earlobe, the nose tip, and the tip of the third finger were reported. The inner canthus was chosen as a marker for central temperature and the three others as markers for peripheral temperatures, resulting in three gradients per patient. Thirty-day follow-up was performed and 30-day mortality was reported.

**Results** One hundred and ninety-eight patients were included and the number of events was nine. The gradient between the inner canthus and the nose tip (ΔN) and the gradient between the inner canthus and the fingertip (ΔF) showed a significant association with 30-day mortality (ΔN: odds ratio: 1.31; 95% confidence interval: 1.05–1.64 and ΔF: odds ratio: 1.27; 95% confidence interval: 1.02–1.57).

**Conclusion** ΔN and ΔF showed a significant association with 30-day mortality, suggesting a prognostic value. However, this was a small pilot study with few events. Larger studies are warranted for confirmation of these findings. European Journal of Emergency Medicine 00:000–000 Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction
Infrared thermography (IRT), or infrared thermal imaging, is a photographic technique based on the fact that all things above 0\textdegree{}K, or approximately –273\textdegree{}C, emit a certain degree of infrared radiation [1]. Since its introduction to the medical field in the 1960s, it has been proven to be a useful tool in a wide variety of areas such as diabetes complications, rheumatology, breast cancer, musculoskeletal disorders, neurological disorders, dermatology, and many others [1–4].

The vast majority of studies describing the use of IRT in medicine have mainly been focused on its use as a diagnostic tool and, to the knowledge of this study group, no studies have previously been carried out on the use of IRT as a prognostic tool. IRT is a fast, noninvasive, and harmless examination technique that makes it an appealing modality that should be investigated for any beneficial utilization it might provide.

Human body surface temperature changes during different physiological and pathological circumstances. For instance, the sympathetic response in the early stages of hypovolemia is an increase of peripheral vasoconstriction [5]. As a result of this, the skin temperature decreases, and the well-known clinical signs of cold and clammy skin appear, which have been proven to be independent predictors of 30-day mortality in cardiogenic shock patients [6]. In a study from 2006, Thompson \textit{et al.} [7] discovered that some of the first clinical signs of meningococcal disease and sepsis in children are cold hands and feet. These signs occurred within the first 12 h after onset of illness and appeared whether they had meningitis, sepsis, or both. A study from 2014 induced acute lung injury (ALI) in six pigs and monitored them with standard vital parameters and IRT over time as the severity of ALI progressed. They introduced the IRT obtained index: ΔT/Δx, which is a spatial temperature gradient of the hottest point next to the sternum, to the most peripheral point of the paw (ΔT), divided by the shortest distance between these two points (Δx). This index was shown to be a strong indicator of illness severity and progression [8].

All this suggests that surface temperature, and in particular, the gradient from central-to-peripheral temperature, can provide useful prognostic information, and that IRT is a fast, noninvasive, and harmless method of quantifying these temperatures.
Aim
The aim of this study was to investigate the association between 30-day mortality and an increase in the central-to-peripheral temperature gradient obtained by means of infrared thermal imaging in a mixed population of medical patients admitted to the emergency department (ED).

Methods
Study design and inclusion criteria
This was a prospective observational study that included medical patients admitted to the Emergency Department at Odense University Hospital who were 18 years or older and in a general condition well enough to be capable of signing a declaration of consent. Otherwise, there were no inclusion criteria. Odense University Hospital serves as the primary hospital for North Funen and Odense municipalities, with a combined population of 288,000. The ED handles primary care of acute patients from nearly all of the medical specialties, with the exception of cardiologic, pediatric, and obstetric patients. The study was carried out from 28 September 2015 to 30 October 2015.

Several studies on the use of IRT in a clinical setting suggest that thorough control of the ambient temperature is a necessity for the reliability of the measurements [1,3,9]. To meet these necessities, to the extent that is possible in an ED setting, only patients who were assigned with a cubicle upon admittance were included. These cubicles were controlled with a thermostat that kept the room stable at a temperature of 22 ± 2°C. The above-mentioned studies also suggest that the patients should remain under these thermally controlled conditions for at least 15–20 min before obtaining the picture. To accommodate this, and to allow for initial treatment, pictures of the patients were taken after a minimum of 30 min after arrival to their designated cubicles.

Exclusion criteria
Patients triaged as red (i.e. the highest level of triage) were excluded, partly because of their incapability to sign the consent and/or posing for the standardized picture, either because of their condition or because it would disrupt the staff treating the patient. Furthermore, patients triaged as red are already showing obvious clinical signs of a severe condition, and the aim of this study was to investigate whether or not IRT can serve as a prognostic tool and predict the progression to such a condition.

The standardized picture
After obtaining written consent, a standardized thermal image was recorded (Testo 882 handheld thermal camera; Buhl & Bønsøe A/S, Smørum, Denmark).

Comparison pictures
Standardized pictures of 13 healthy adults were also taken. The same temperature gradients were calculated for this healthy subpopulation as for the study population. These gradients were compared with the gradients in the study population to determine whether any difference in healthy individuals versus hospitalized patients could be observed. The test patients had been acclimatized by being present in the same room for 30 min before the picture was taken.

Data collection
Temperature readings were performed using the software included with the camera (Testo IRSoft, version 3.5; Testo SE & Co. KGaA, Lenzkirch, Germany). The following temperatures were reported from each patient’s image: The inner canthus, which was chosen as a marker for central temperature. Previous studies have proven IRT obtained temperature of the inner canthus to have a good correlation with conventionally used sites of measuring central temperature (i.e. tympanum, axillae, and forehead) measured with conventional thermometry [1,10]. The ipsilateral earlobe, the nose tip, and the palmar side of the third fingertip were chosen as measurement points of peripheral temperature (Fig. 1).

Analysis
Temperature differences between the inner canthus and the earlobe (ΔE), the inner canthus and the nose tip (ΔN), and the inner canthus and the fingertip (ΔF) were calculated for each patient. A 30-day follow-up was performed and information on mortality was gathered by reviewing the patients’ hospital records. Thirty-day mortality was defined as death within 30 days from picture acquisition. From the hospital records, information on age, sex, smoking status, and discharge diagnosis was also retrieved (Table 1). The 30-day follow-up was possible because of the Danish Civil Registration System, assigning every Danish citizen a unique identification number.

Fig. 1
Example of the standardized picture. HS1 and M1-M3 are the software given names for central and peripheral markers.
Table 1 Discharge diagnoses and baseline demographics of patients who died within 30 days

<table>
<thead>
<tr>
<th>Total</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD-10 code letter: A</td>
<td>0</td>
</tr>
<tr>
<td>ICD-10 code letter: F</td>
<td>1</td>
</tr>
<tr>
<td>ICD-10 code letter: I</td>
<td>2</td>
</tr>
<tr>
<td>ICD-10 code letter: J</td>
<td>1</td>
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<tr>
<td>ICD-10 code letter: K</td>
<td>1</td>
</tr>
<tr>
<td>ICD-10 code letter: N</td>
<td>1</td>
</tr>
<tr>
<td>ICD-10 code letter: R</td>
<td>2</td>
</tr>
<tr>
<td>ICD-10 code letter: Z</td>
<td>1</td>
</tr>
<tr>
<td>Male</td>
<td>6</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>87</td>
</tr>
<tr>
<td>Smokers</td>
<td>2</td>
</tr>
</tbody>
</table>

For description of ICD-10 code letters, see Table 4.

[11]. Sample size was not calculated as the study population was considered a convenience sample.

Logistic regression was performed with 30-day mortality on each of the three temperature gradients.

Receiver operating curves (ROCs) were constructed for ΔN and ΔF on 30-day mortality. Subsequently, a cut-off was chosen, and sensitivity and specificity were calculated. P-values less than 0.05 were considered significant. Statistical analysis was carried out using Stata/IC version 14.1 (StataCorp., College Station, Texas, USA).

Data collection and analysis were carried out by one investigator.

Distance, angle, and intra-reader variation
Distance and angle were factors considered to have an influence on temperature readings, but a previous study has shown them to be of negligible impact under certain conditions [12]. These conditions were deemed in agreement with the circumstances wherein the pictures for this study were taken. As reading of the temperatures was performed manually, a test of reading variation between three different readers was performed. Afterwards, the intraclass coefficient was calculated (Table 2).

Ethics
After information on the nature of this study was provided, patients were asked for consent before inclusion. The Regional Scientific Ethical Committees for Southern Denmark were consulted and found the study ‘not obliged to report’. The study was approved by the Danish Data Protection Agency.

Results
In total, 198 patients were included in the study, 48.5% of the patients were men and the median age was 66 years. Further baseline demographics of the study population are shown in Table 2. A schematic overview of the study population discharge diagnoses and a table of baseline demographics on the patients who died within 30 days are presented in Tables 3 and 4, respectively.

A significant association was found between an increase in ΔN and 30-day mortality [odds ratio: 1.31; 95% confidence interval (CI): 1.05–1.64; P = 0.02]. The same applied to ΔF (odds ratio: 1.27; 95% CI: 1.02–1.57; P = 0.03). ΔE showed no significant association with 30-day mortality.

Medians and quartiles of the temperature gradients were calculated in the healthy comparison group as well as for both the survivors and nonsurvivors of the study population. These results were visualized in boxplots. For ΔN, the boxplots show a stepwise increase in the median temperature gradient from 2.7°C in the healthy comparison group to 3.4°C in the study survivors, to 7.1°C in study nonsurvivors (Fig. 2).

Area under ROC was 0.75 for ΔN and 0.71 for ΔF. On the basis of the characteristics derived from the ROC curves, the cut-off values were chosen to be more than or equal to 5°C for ΔN and of at least 7°C for ΔF. This yielded for ΔN a sensitivity of 0.78 and a specificity of 0.65 for ΔN. For ΔF, a sensitivity of 0.67 and a specificity of 0.64 were obtained.

Discussion
In this study, we found a significant association between an increase in the temperature gradient between the inner canthus and the nose tip (ΔN), and 30-day mortality. The same applied for the temperature gradient between the inner canthus and the fingertip (ΔF). As these gradients were obtained with the use of an IRT camera, our study results indicate that IRT has potential as a prognostic tool in an ED. Furthermore, it was interesting that the ΔN gradient, with a cut-off at 5°C, yielded the highest level of sensitivity, indicating that this gradient may be the most promising from a clinical point of view.

The stepwise increase in ΔN from healthy comparison participants, to study survivors, to study nonsurvivors

Table 2 Intra-reader variations

<table>
<thead>
<tr>
<th>Temperature reading point</th>
<th>Intraclass coefficient</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye</td>
<td>0.79</td>
<td>0.61–0.91</td>
</tr>
<tr>
<td>Ear</td>
<td>0.98</td>
<td>0.96–0.99</td>
</tr>
<tr>
<td>Nose</td>
<td>0.99</td>
<td>0.99–0.99</td>
</tr>
<tr>
<td>Finger</td>
<td>0.99</td>
<td>0.99–0.99</td>
</tr>
</tbody>
</table>

Intraclass coefficients of three readers on the four temperature reading points, on 20 different standardized pictures.

Table 3 Baseline demographics of the study population

| n (%) |
|---|---|
| Total patients | 198 |
| Male | 96 (48.5) |
| Age [median (percentile; range)] (years) | 66 (5–95; 24–90) |
| Smokers | 48 (24.2) |
| Thirty-day mortality | 9 (4.6) |
| Declining participation | 5 (2.6) |
shown in Fig. 2 could indicate an increase in temperature centralization because of illness in general and that this centralization increases even further with the severity of that illness. This was in agreement with the findings of Pereira et al. [8], showing an increase in the $\Delta T/\Delta x$ index with an increase in the severity of ALI in pigs because of temperature centralization as illness progresses.

The lower values of the 95% CIs, for both of the significant findings, were close to 1. This could indicate that either the true association is of limited size or that there were too few events. With a larger study population, and subsequently more events, it is not unlikely that a higher level of association (i.e., a narrower 95% CI) could be found. A larger study with more events would also make it possible to control confounders such as age, which is a main confounder in this study, as the median age of the patients who died was 21-years older than the median age of the entire study population.

The $\Delta F$ gradient was also significantly associated with 30-day mortality. However, temperature readings of the fingers are at risk of confounding as the position of the hand, before the photography, could result in surface temperatures that are not primarily dictated by subjacent tissue perfusion, but rather by the positioning of the hand. Temperature measurements on the ear are also at risk of the same type of confounding as for the finger. Furthermore, Awad et al. [13] concluded that the ear only elicits a vague vasoconstrictive response to sympathetic stimulus. If this is an indication of the ears’ limited vasoconstrictability in general, it could indicate that the ear also elicits limited thermal changes, which again could partly explain why $\Delta E$ showed no significant association with 30-day mortality.

The choice of a time frame of 30-day mortality was predominantly made because of the small population size. It could be argued that a 10-day time frame would be more relevant for an ED setting, but with the small population size, there were too few events to carry out any reasonable statistical analysis on short-term outcomes. This leads to a risk of finding an association that, in fact, is not there, thus yielding a type 1 error. A longer study period, with a subsequently larger population, is advisable for investigating the value of IRT as a prognostic tool on such short-term outcomes.

Febrile patients were not excluded from the study as fever was considered to have little or no impact on the results as the study focused on gradients, rather than single temperature measurements. In addition, some of the patients included did not have their temperature measured by standard thermometry upon arrival to the ED, and for those who did, different measurement sites were used (i.e., rectal or tympanic).

The study was carried out on a broad population of medical patients in the ED, with the exception of the before mentioned specialties and as such, this study was not designed as an investigation of correlation between
IRT-obtained temperature gradients and 30-day mortality within specific pathologies, but rather as an investigation of the prognostic potential of IRT in a mixed population. To avoid the possible selection bias caused by the unrepresented specialties and the nonrepresented and under-represented pathologies, studies including these specialties and pathologies are needed. However, within this study population, a decrease in percentage of less than 3% (Table 3) was considered a marker of a low risk of selection bias.

It was also a feasibility study, testing whether or not IRT is a suitable instrument for use under everyday conditions prevalent in an ED. The process of obtaining the picture is definitely suitable for an ED as it is fast, easy, noninvasive, and harmless. The analysis of the pictures is equivalently easy and fast and, as our analysis of intra-reader variation showed (Table 2), it is also reliable. If future studies confirm the findings of this study, it is plausible that IRT-obtained temperature gradients could be a valuable tool in an ED, for example, for application in risk-stratification tools.

Conclusion
Both the ΔN and ΔF gradients showed a significant association with 30-day mortality. As such IRT showed potential of serving as a prognostic tool in the ED. However, this study was based on a small population size with few events, and subsequently, the statistics have limited reliability. Nevertheless, this study showed that IRT as a modality and the methods used to obtain and analyze the images are suitable for an ED environment. Further investigation, with a larger study population, is warranted for confirmation of the results obtained in this study.

Acknowledgements
Conflicts of interest
There are no conflicts of interest.

References