

Evaluation of systemic vasoconstriction and prognosis using thermography: a systematic review

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Abstract

Purpose: This systematic review investigates whether infrared thermography (IRT) can measure systemic vasoconstriction and addresses the value of IRT in assessing circulatory deficiency and prognoses.

Methods: Design was based on the PRISMA criteria and a systematic search of 6 databases was performed.

Results: Of 3,198 records, five articles were included. Three clinical studies were identified; two found significant correlations between IRT obtained temperatures and mortality. An experimental study found an association between peripheral temperature and stroke volume. An animal study found that central-peripheral temperature differences correlated with shock index, mean arterial pressure, and disease progression.

Conclusions: Data from the most valid study suggests that central-peripheral temperature differences should be investigated further, both on its own, and integrated with other variables.

Keywords

Infrared thermography; prognosis; circulation; emergency medicine; skin temperature.

Key Points

- Infrared thermography (IRT) can be used to quickly obtain a skin surface temperature and may be used to assess circulation and prognosis
- According to current literature the anatomical position of the skin temperature measurement is crucial
- Based on current literature we suggest using dynamic (several) measurements over a time span of which the ideal length is yet to be determined
- Based on current literature we suggest using differences between central and peripheral temperature measurements rather than single-points

Introduction

The identification and prevention of physiological deterioration in acutely ill patients remain a major challenge for all clinicians, and the optimal non-invasive physiological variables to measure and monitor are still hotly debated. In addition, there is no clear consensus on the reference ranges used for several physiological variables, and their association with prognosis and mortality is not clear. A recent example of this is the discussion on limits for the definition of hypotension.¹ Even though many Early Warning Scores (EWS) have been developed² the ideal non-invasive physiological variables for use to evaluate circulatory insufficiency during a pre-shock state have yet to be determined.

Since Wunderlich³ determined its normal range the measurement of body temperature has been an essential part of the clinical examination. Although, historically the central or core temperature is recommended, readings of peripheral temperature,^{4–7} as well as central-peripheral difference,^{8,9,10} have also been used in assessing a patient's condition and prognosis. While several different sites can be used to measure peripheral body temperature, the

pulmonary artery has been considered the gold standard¹⁰ for measuring core temperature. Although many clinicians consider rectal temperature a good estimation of core temperature and some studies support this,¹¹ and others report less precision¹² or inconsistent results.^{13,14} Forehead¹⁵ and oral¹⁶ measurements have been found relatively comparable to rectal values, while readings from other sites have been reported to be more prone to error.^{17,18}

Our hypothesis is that IRT can as accurately and more easily measure peripheral and core temperature. Indeed, these individual and differential measurements may even provide additional value to the assessment of a patient's condition and prognosis. The human body can normally compensate for an effective loss of circulating blood volume by evoking a sympathetic response¹⁹ that centralizes blood flow by peripheral vasoconstriction. This results in an increased central-peripheral temperature dissociation and thereby the development of cold and clammy skin, a classic symptom of hypovolemic shock.²⁰ The same clinical pictures has been observed in late septic,^{21,22} and cardiogenic²² shock. The opposite relationship with a disappearance of temperature

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Figure 1. Thermogram from IRT camera. Notice the cold nose and warm eye.
(Informed consent was obtained from the individual on the photo)

dissociation, has been observed in early septic and anaphylactic shock.²³

Skin surface temperature has been found to be a reliable indicator of total blood flow to the tissues both theoretically²⁴ and experimentally²⁵ by using venous-occlusion volume plethysmography. A significant decrease in surface temperature of the hands measured by IRT when subjects were exposed to normobaric hypoxia has also been found.²⁶ Another study from 2018 found a significant correlation between classic ankle-brachial index and the same index obtained using IRT.²⁷ It can, therefore, be argued that skin surface temperature provides a good measure of vasoconstriction, and that this is measurable using IRT. See figure 1 for an example IRT picture.

Temperature measurements from the inner canthus of the eye can be easily made using IRT and correlate well with tympanic and axillary^{28,29} temperature, both of which are acceptable estimations of core temperature.¹³ Peripheral vasoconstriction, induced by placing the hands of test subjects in iced water, has been shown to increase the temperature as measured by IRT³⁰ at the inner canthus. IRT, therefore, may be able to detect changes in central-peripheral temperature dissociation and thereby vasoconstriction, possibly before it becomes clinically obvious. This could prove useful in the early identification of severely ill patients such as those with impending cardiogenic or septic shock. Since IRT is rapid, non-invasive, contact-free and

easy to perform, it could be easily incorporated into existing clinical scoring systems.

Aim

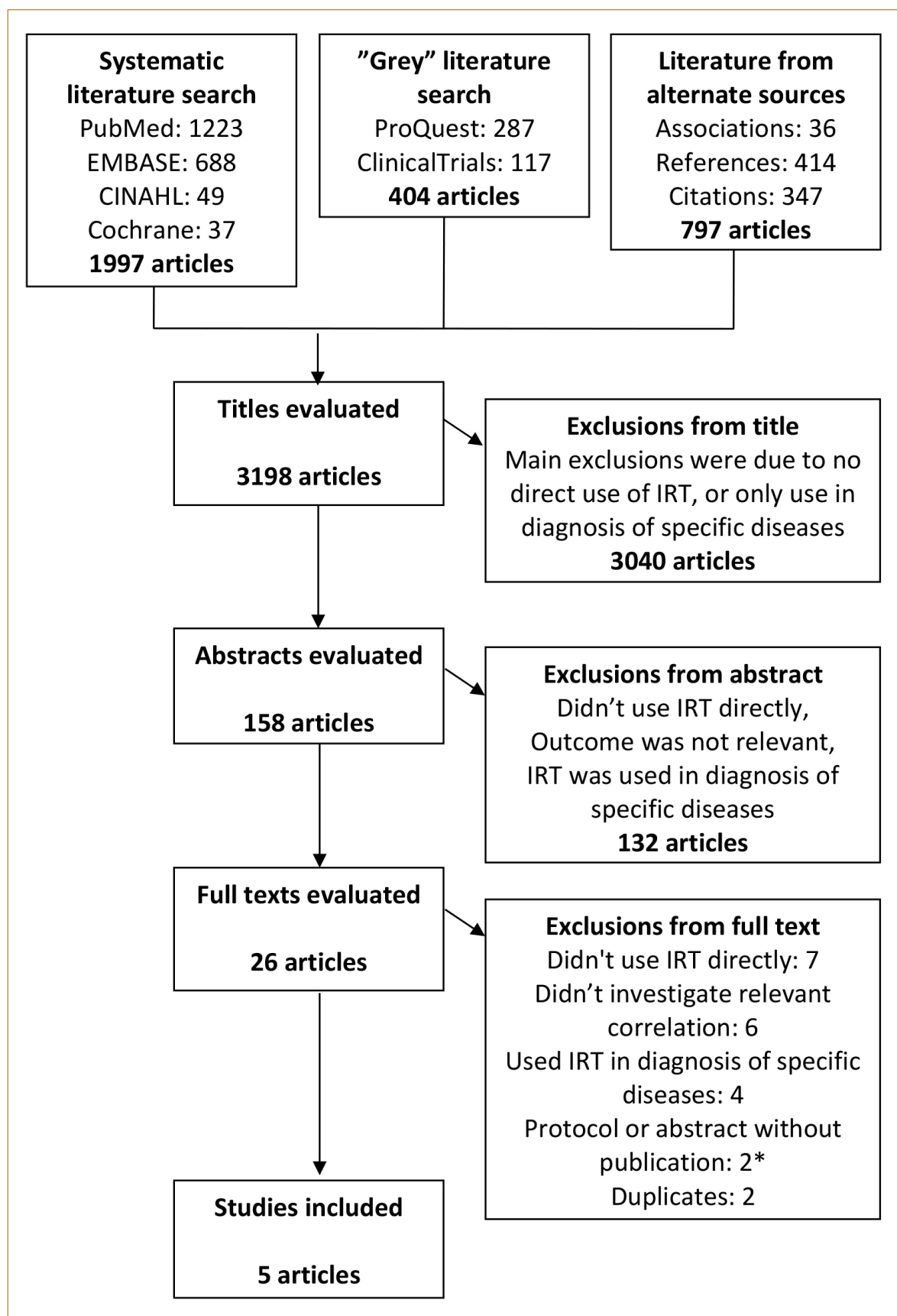
The aim of this systematic review is to investigate:

1. the evidence that IRT can be used to obtain a quantitative measurement of systemic vasoconstriction
2. the potential value of IRT in the evaluation of circulatory deficiency and predicting outcomes

Methods

The study was designed and performed in accordance with the PRISMA guidelines for systematic reviews³¹ (see Appendix 1 for a checklist). No review protocol was published. Data collection included both a systematic literature search up to 15 February 2019 using six databases (PubMed Medline, EMBASE, CINAHL, Cochrane, ProQuest, ClinicalTrials.gov), as well as searches of alternative material including relevant associations,^{32,33} local and international networks, references (using “Snowballing”³⁴), and citations (using Scopus).

The search queries were designed using database-specific syntax with criteria relevant to the study’s aim. Articles were included that contained the word “thermography” or “thermogram” and at least one of the following words: “prognosis”, “prognostic”, “mortality”, “fatality”, “shock”, “sepsis”, “SIRS”, “critically ill”, “emergency”, “trauma”, or

Evaluation of systemic vasoconstriction and prognosis using thermography: a systematic review**Figure 2.** Overview of literature search and results.

* two studies only published in abstract form were also considered relevant.

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Table 1. Included studies

Author	Year	Type of study	OCEBM-level ⁵⁶	Aim of study	n
Pereira CB, Czaplik M, Blanik N et al. ³⁵	2014	Experimental animal study	5	Investigate if IRT, in a pig model using an ALI model, could identify deteriorations in circulation and perfusion, as well as monitor progression of temperature centralization.	6 (pigs)
Cooke WH, Moralez G, Barrera CR et al. ³⁹	2011	Experimental study	4	Investigate if IRT, during a simulated uncontrollable haemorrhage, could measure RR and reveal progressive changes in skin temperature, and whether these changes correlated with changes in SV.	45 (healthy adults)
Urakov, A. L., Kasatkin, A. A., Urakova, N. A. et al. ⁴⁵	2014	Prognostic observational study in clinical setting	5	Investigate if IRT could measure finger temperature after a brachial occlusion test in haemorrhagic shock affected patients, and whether this measurement had any prognostic value in relation to 48-hour mortality.	39 (14 healthy and 25 shock-affected adults)
Holm, J., Kellett, J.G., Jensen, N.H., et al. ⁴⁷	2016	Prospective observational study in clinical setting	3	Investigate if IRT could measure a central-peripheral temperature difference and if this variable had any prognostic value in relation to 30-day mortality.	198 (mixed medical patients admitted to ED)
Ferraris, A., Bouisse, C., Mottard, N., et al. ⁴³	2018	Prospective observational study in clinical setting	4	Compare mottling score with skin temperature of the knee using IRT and evaluate correlation between these values and survival.	46 (patients admitted to an ICU for septic shock)

IRT: Infrared thermography, ALI: Acute lung injury, LBNP: Lower body negative pressure, RR: Respiratory rate, SV: Stroke volume, ED: Emergency department, ICU: Intensive care unit.

“intensive care”. The queries were used to challenge titles, abstracts, the full text, and individual database indexing (i.e. MeSH terms (PubMed) and subject headings (EMBASE)).

All results were manually reviewed. For study inclusion, two criteria had to be fulfilled. First, infrared thermography had to be used to measure either a peripheral temperature or a difference between central and peripheral temperatures. Second, the temperature measurements had to be investigated for their association with either an established variable used in circulatory evaluation or directly with prognosis. Exclusion followed if these conditions were not met following assessment of the title, abstract and then full text (in that order).

Results

All of the 3,198 articles reviewed were excluded apart from five peer reviewed papers and two studies only published in abstract form (figure 2).

Bias

Relatively few and no relevant “hits” were retrieved when searching the unpublished (i.e. grey) literature, showing similar results as the smaller databases (CINAHL and Cochrane). Therefore, no indication of publication bias was found.

Included studies

The studies that were included in our review were classified into two groups based on the variables investigated. These were categorised as the

“single” or “dynamic” group, the former involving correlations of single thermographic measurements with outcome, and the latter correlating multiple thermographic measurements, recorded over time, with outcomes. An overview is provided in Table 1, and more detailed variables, outcomes and results in Table 2.

Dynamic measurements

Temperature gradient and circulatory function

Pereira et al.³⁵ investigated two variables in an experimental animal study that used an acute lung injury model in six pigs. The standard deviation of temperatures within chosen regions and a central-peripheral temperature gradient were measured for up to 24 hours after triggering the acute lung injury or until death: both showed a significant increase during disease progression, as well as significant and strong correlations with the shock index and the mean arterial pressure. However, although there were significant differences in both IRT variables in pigs that developed acute lung injury, the corresponding changes in shock index and mean arterial pressure did not reach statistical significance.

Unfortunately the ARRIVE guidelines,³⁶ the gold standard for the design and conduct of animal experiments, were not adhered to in this study. Furthermore, the authors seem to have misinterpreted a referenced article³⁷ when describing sepsis as a leading complication of acute lung injury, when in fact acute lung injury is more

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Table 2. Outcome and results of included studies.

Author	Measurement	Variable	Outcome	Results
Pereira CB, Czaplik M, Blanik N et al. ³⁵	Dynamic	Central-peripheral temperature difference (SD, $\Delta T/\Delta x$)	Disease progression, SI, MAP, PaO ₂ , PF	Significant changes in SD and $\Delta T/\Delta x$ over time (marker of disease progression). Strong correlation (r value given in parenthesis) and p-value < 0,0005 between: SI-SD (0,593), SI- $\Delta T/\Delta x$ (0,561), MAP-SD (-0,587), MAP- $\Delta T/\Delta x$, (-0,534), MAP-SI (-0,519). Moderate correlation and p-value < 0,01 between: PaO ₂ -SD (-0,344), PaO ₂ - $\Delta T/\Delta x$ (-0,334), PaO ₂ -SI (-0,326), PF-SD (-0,315), PF- $\Delta T/\Delta x$ (-0,319), PF-SI (-0,326).
Cooke WH, Morales G, Barrera CR et al. ³⁹	Dynamic	Peripheral temperature (forehead)	Stroke volume	Quadratic correlation (R ²) between peripheral temperature and SV during both slow, moderate and fast haemorrhage (R ² Slow = 0,95; R ² Moderate = 0,89; R ² Fast = 0,99).
Urakov, A. L., Kasatkin, A. A., Urakova, N. A. et al. ⁴⁵	Single	Peripheral temperature (palm and average of finger tips)	Mortality (48-hour)	Observations were done post-occlusion: An increase in temperature to above baseline was seen in all healthy adults (n = 14). In shock affected patients an increase to baseline was correlated with survival (n = 21 of 25) while a decrease or constant temperature was correlated with death within 48 hours (n = 4 of 25). Sensitivity and specificity were 100%.
Holm, J., Kellett, J.G., Jensen, N.H., et al. ⁴⁷	Single	Central-peripheral temperature difference (IC-earlobe, IC-nose tip, IC-fingertip)	Mortality (30-day)	Significant associations with 30-day mortality was found for IC-nose tip (OR: 1.31; 95% CI: 1.05-1.64; p = 0,02) and IC-fingertip (OR: 1.27; 95% CI: 1.02-1.57; p = 0,03).
Ferraris, A., Bouisse, C., Mottard, N., et al. ⁴³	Single and dynamic	Peripheral temperature (Mottling zones at knee)	Mortality (ICU and 28-day)	Skin temperature of the knee were similar in survivors and non-survivors.

Dynamic: Multiple thermographic measurements over time, SD: Standard deviation of skin temperature, $\Delta T/\Delta x$: Temperature gradient from a central to a peripheral point, IC: Inner canthus of eye, SI: Shock index, MAP: Mean arterial pressure, PaO₂: Partial pressure of arterial oxygen, PF: PaO₂/FiO₂, FiO₂: Fraction of oxygen in inspiratory air, r: Pearson product-moment correlation, R²: Coefficient of determination, OR: Odds ratio.

commonly a complication of sepsis. The failure to demonstrate significant changes in the shock index and mean arterial pressure could imply that the model did not adequately simulate the disease under investigation and its progression. Also, as Pereira et al. acknowledged, the shock index may only be a relevant variable for sepsis and not for isolated, experimentally induced acute lung injury. The fact that it is an animal model that only tested a small number of subjects and the possibility of a substantial type II error further diminishes the study's external validity and its relevance to human populations. This study's OCEBM level of evidence³⁸ is 5 (very poor).

Peripheral temperature and stroke volume

Cooke et al.³⁹ simulated haemorrhage in 45 healthy adults and found a quadratic correlation between changes in peripheral temperature and stroke volume, as well as significant changes in peripheral temperature during the simulations. Several relevant secondary variables were also measured including

heart rate, mean arterial pressure and cardiac output. Nose temperature was mentioned in the paper, but data for it were not included in the results.

Although overall the design, methods, and documentation of this study were good, it had some minor limitations. It used lower body negative pressure to simulate haemorrhage. While this does not fully mimic a real haemorrhage, previous research⁴⁰ has demonstrated the value of this model. Inert rebreathing was used to measure cardiac output, from which the stroke volume was derived. Although the accuracy of this technique has been reported to closely approximate that of invasive monitoring,⁴¹ others have questioned its precision and accuracy.⁴² This study's OCEBM level of evidence³⁸ is 4 (poor).

Peripheral temperature and prognosis

Ferraris et al.⁴³ compared mottling score with skin temperature of the knee (primary endpoint) and investigated the correlation of both values to prognosis (intensive care unit- (ICU) and 28-day-mortality, secondary endpoints). Their sample

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included 46 patients admitted to an ICU with septic shock. Mottling score and surface temperature of the mottling zones of the knee measured by IRT were obtained twice: at ICU admission (H0) and six hours after initial resuscitation (H6). The study found no direct correlation between mottling score and skin temperature of the knee, nor any association with prognosis.

The authors also describe that “*temperature gradients from central temperature to knee temperature, and the evolution of these gradients between H0 and H6 were similar for patients with mottling*” suggesting that a central-peripheral gradient also was investigated, but no further details regarding this part is included in the article.

Inclusion and exclusion criteria were relevant and well documented. Other data points including hemodynamic parameters, lactate levels, ventilator requirements and vasopressor dose were also collected at H0 and H6, and the general characteristics included in the article. Many aspects of this study performed well according to the OCEBM’s critical appraisal guidelines for prognostic studies:⁴⁴ follow-up was sufficiently long and complete, outcomes were clearly defined, and its limitations are well described and the authors. Unfortunately, its small sample size reduced its OCEBM level of evidence³⁸ to a poor rating of 4.

Single measurements

Brachial occlusion test and prognosis

Urakov et al.⁴⁵ performed a brachial occlusion test on 25 patients suffering from hypovolemic shock and found hand temperature after occlusion to be a prognostic indication of mortality. According to the authors, their test showed perfect results with a sensitivity and specificity of 100%. However, evaluation by the OCEBMS critical appraisal guidelines for prognostic studies⁴⁴ identified several issues. First, the aim of the study is described in three different ways. Second, the authors omit several important aspects of their methodology (e.g. the number of patients screened and exclusion criteria), with no discussion of the risk of selection bias despite their inclusion of only 25 patients over a two-year period. Nevertheless, they suggest after releasing brachial occlusion an increase in finger temperature of 0.1–1.0°C, or a return to baseline values, indicated a high chance of survival from shock. Conversely, a continued decrease in temperature, or failure to return to baseline after releasing brachial occlusion, indicated a low chance of survival. However, neither confidence intervals, nor the accuracy of their infrared camera measurements are stated. The manufacturers website⁴⁶ reports an accuracy of $\pm 2\%$

of the measured value. As the camera was adjusted for a range of 25–36°C, the real temperature might vary by at least 0.5°C. Consequently, the measured temperatures do not comply with the study’s suggested test algorithm. A larger study, with an improved design and documentation is required to validate the authors’ proposed test and confirm its clinical value. This study’s OCEBM level of evidence³⁸ was a very poor rating of 5.

Central-peripheral temperature difference and prognosis

Holm et al.⁴⁷ measured central-peripheral temperature differences in 198 patients (with mixed diagnoses) admitted to an emergency department in Denmark during October 2015, and correlated them with prognoses. The central temperature was measured at the inner canthus of the eye with peripheral temperature measured in three different places (nose, ear, and fingertip). Temperature measurements were taken 30 minutes after admission making sure patients had stayed at least 15–20 minutes in a thermostat regulated cubicle ($22 \pm 2^\circ\text{C}$). The difference in temperature between the eye and nose and between the eye and fingertip showed a significant correlation with 30-day mortality.

The OCEBM’s critical appraisal guidelines for prognostic studies⁴⁴ identified only a few flaws in this study, and gave it a fair rating of 3. All the study’s deficiencies were addressed by the authors in their discussion. Since this project was a pilot study a sample size calculation was not made and only 9 deaths were observed during 30 days of follow-up. With such a low number of events there is a risk that any association identified is either coincidental or an underestimate. A higher number of events would have identified a more robust correlation. The low number of events studied is likely due to the exclusion of patients unable to sign the consent form, or patients who were triaged red (critically ill on arrival at the emergency department). The intra-class correlation coefficient for the estimation of eye temperature was 0.79, increasing to > 0.98 for all peripheral measurements. This could have led to under- or overestimation, or even selective reporting of the temperature differences. Nonetheless, the prospective nature of the study and its relatively long follow-up time argue against selective reporting.

On-going studies

Two relevant abstracts were also identified

1. Tosi et al.⁴⁸ hypothesized thermography could help in bedside evaluation of critically ill patients. In a small pilot study with 4 patients, they evaluated whether thermography could

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provide useful data during the resuscitation of septic shock. Using IRT they measured the difference between systemic and limb temperature at 0, 3, 6 and 24 hours after shock occurrence, and found a mean overall increase at 6 and 24 hours. Even though no direct association was observed, noradrenaline dose decreased, MAP increased, and lactate decreased suggesting improvement in the patient's condition during the same time-span. According to their abstract further studies will be performed.

2. Chuck et al.⁴⁹ studied the feasibility of live acquisition of clinical research variables, including both traditional and experimental sets, such as IRT obtained measurements. Whether any measurements beside core temperature was obtained using IRT is not clear from the abstract, but the protocol is currently being used in a large on-going ED cohort study.

Discussion

Applications

Although temperature measured by current technology as a single variable is not strongly associated with mortality⁵⁰ it is still included in several EWS including the National Early Warning Score (NEWS), now in widespread use in the United Kingdom and elsewhere.⁵¹ It is possible that the additional information provided by the IRT measurements of skin temperature could greatly improve its value in the clinical assessment and monitoring of acutely ill patients.^{47,45,35} It might also be of value in assessing patients' peripheral perfusion in response to treatment for sepsis and shock.⁵²

At some point in the evolution of most serious illnesses the patient may, even if only briefly, appear to be only mildly ill. Moreover, most patients will feel unwell before their vital signs become abnormal⁵³. Pereira et al.³⁵ identified significant changes in both of their IRT-obtained variables during disease progression when there were no significant equivalent changes in either mean arterial pressure or shock index. Hence IRT-obtained variables could be early indicators of circulatory deterioration, possibly superior to existing variables (e.g. shock index⁵⁴). Cooke et al.³⁹ also observed a significant change in IRT-obtained measurements prior to a significant change in heart rate, mean arterial pressure and, hence, shock index during haemorrhage. Both these studies and that of Holm et al.⁴⁷ suggest IRT might detect deterioration before traditional vital signs become abnormal, leading to the improved identification and triage of at-risk patients.

A new variable?

The “classic” approach, taken by Wunderlich³ and others in the past, to the introduction of a new variable into clinical practice is to establish the normal reference ranges for healthy individuals. Afterwards, these can be evaluated in clinical trials against specific outcomes. Holm et al.⁴⁷ and Urakov et al.⁴⁵ included control groups comprising small sample sizes ($n = 13$ and 14 respectively) of healthy individuals. Both identified small differences between the variables in healthy and ill groups, but their sample sizes were too small to conclude anything about an actual reference range. Instead, the studies took a ‘direct’ approach by looking at clinical populations and investigating the direct correlation between their chosen variables and outcome (i.e. mortality). From these investigations, cut-off values for their tests were then suggested. A ‘comparable’ approach was used by Cooke et al.³⁹ and Pereira et al.³⁵, when they investigated correlations with other well-established variables such as stroke volume, mean arterial pressure and shock index.

So far, no single study has used the ‘classic’ approach. A reference range for the central-peripheral temperature difference needs to be established, which includes the range of inter-individual and intra-individual differences. While it would be advantageous that such a study incurred no interference with clinical work, a disadvantage would be that a large sample size from a diverse population would be needed. Another option would be to extend the work of Cooke et al.³⁹ and Pereira et al.³⁵ by comparing IRT measurements with established surrogate variables in a clinical population. A study performed in an intensive care unit, where correlations with invasive variables could be investigated easily would be of significant interest.

Finally, the study by Holm et al.⁴⁷ should be repeated with a sample size large enough to reduce the risk of type 1 and 2 errors. A recent (2017), unpublished master thesis from the University of Southern Denmark, by Jensen NH and Brabrand M⁵⁵, estimated this sample size to 476 (power 80 and α 0.05), based on anticipated mortalities of 3% in patients with normal temperature gradients and 10% in patients with increased gradients. Investigating the impact of integrating IRT measurements into an existing EWS would also add value to such a study.

Both the type and anatomical position of temperature measurements should be carefully considered. The findings of Holm et al.⁴⁷ and Pereira et al.³⁵ suggest that central-peripheral temperature differences may be more useful than isolated readings of peripheral temperature. Ferraris et al.⁴³ results suggest that dynamic measurements should be for longer than 6 hours and that the knee is not an ideal site of measurement. Regarding optimal sites

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for measurements Holm et al.⁴⁷ argued that the usefulness of the ear is limited and recommended that either the fingertips or nose could be used, but the nose was their preferred site. Data reported by Urakov et al.⁴⁵ support this recommendation as they found a large inter-individual variation in finger temperature. Whether the measurement should be single or dynamic cannot be determined from the current studies. However, it could be of interest to investigate the usefulness of dynamic central-peripheral measurements in a clinical population, as this approach has, thus far, only been taken in a limited cohort using a less-than-ideal site for measurement⁴³ and in an animal model.³⁵

Limitations

A major limitation of our study was the paucity of relevant research and publications. This made it necessary to perform a broad search and use open criteria for study inclusion. Even so it was not possible to find relevant published studies with high levels of evidence. As a result studies were included that would have been excluded had there been a more extensive literature available.

Some papers may have been overlooked because of the lack of standardized nomenclature and if authors had used different terminologies. However, this is unlikely as we searched all articles containing the words “thermography” or “thermogram” and examined an extensive number of papers.

Conclusion

We found only five peer reviewed studies that fulfilled our inclusion criteria. Therefore, the current clinical usefulness of IRT remains uncertain. However, a small number of studies suggest that correlations between circulatory insufficiency detected by IRT and prognosis may exist. This topic needs to be investigated further, and if possible integrated into and compared with other prognostic signs, symptoms and scores.

Declaration of conflicting interests

No potential conflict of interest was reported by the authors.

Funding sources

No funding was received during any part of this study.

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