Prevalence of low–normal body temperatures and use of active warming in emergency department patients presenting with severe infection

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ABSTRACT

Objective: To describe the prevalence of low–normal body temperatures in emergency department (ED) patients presenting with severe infection, and to determine whether active warming is used in this setting.

Design, setting and participants: We performed a single-centre retrospective cohort study in ED patients with community-acquired infection who required admission to the intensive care unit (ICU). Temperatures recorded from presentation up until 24 hours in the ICU were extracted from the patients' clinical records. Body temperatures were then classified as low (≤ 36.4°C), normothermic (36.5–37.9°C) or fever ≥ 38°C.

Results: Over the study period, 574 patients were admitted to the ICU with infection. Of them, 151 fulfilled the inclusion criteria, and the in-hospital mortality rate for these patients was 8.6%. On presentation, 22.5% (34 patients) had a low body temperature (35–35.9°C for six patients, and < 35.0°C for three patients). In contrast, 26.5% (40 patients) had a temperature ≥ 38.0°C. Among those who presented with low temperature, the median time to reach normothermia was 7.9 hours (range, 3.3–14.0 hours). Active warming was only applied to one patient, (whose body temperature was < 35°C).

Conclusion: Among patients with community-acquired infection requiring ICU admission, about a quarter have a low temperature and active warming was essentially not applied. These findings suggest that active warming of such patients would likely achieve separation from usual care.

Crit Care Resusc 2019; 21 (2): 96-101

Sepsis is a major cause of mortality.[1,2] Fever represents an innate response to infection and is a common finding in septic critically ill patients.[3] However, it is unclear whether alterations in body temperatures simply reflect the interplay between disease severity and host response (thereby informing outcomes[4]) or represent a potentially modifiable therapeutic parameter,[5] especially in patients with severe infection.[6]

Attempts at controlling or abating the febrile response in this setting are common,[7,8] and are driven by concerns about the deleterious consequences of fever.[9] While this mostly involves the use of antipyretic medications,[10] external cooling has also been used.[11] However, the utility of this practice remains unclear.[12,13] In contrast, the opposite approach for septic patients — "active warming" (or "therapeutic warming") — has never been studied.

Many patients with infection do not develop a febrile response or are slow to do so. Such patients are frequently more unwell, and manifest inferior clinical outcomes.[14,15] In particular, registry data from Australia and New Zealand suggest that a peak body temperature of ≤ 36.4°C during the first 24 hours in an intensive care unit (ICU) is associated with a greater risk of death in those patients admitted with infection.[15] Despite this association, active warming of such patients has not been explored. Accordingly, we hypothesised that such low temperature would be common among patients presenting to the emergency department (ED) with severe community-acquired infection and that such patients would rarely be treated by active warming. We tested this hypothesis by studying a cohort of patients admitted to the ED of a tertiary hospital in Australia with severe community-acquired infection over a 2-year period.

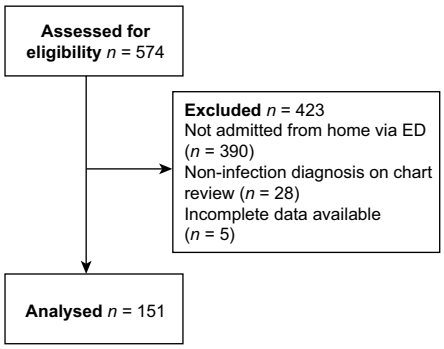
Methods

We conducted a single-centre, retrospective, observational cohort study using data collected as part of routine clinical care. Approval to undertake the study was granted by the Human Research Ethics Committee of The Alfred Hospital (Melbourne, Victoria, Australia) with a waiver for individual patient informed consent (Project No. 262/14).

Patient selection

All patients admitted to the ICU of The Alfred Hospital via the ED between 1 January 2012 and 31 December 2013 with a primary diagnosis of infection were eligible for study inclusion. Cases were identified by searching our institutional ICU database. We used the APACHE (Acute Physiology and Chronic Health Evaluation) diagnostic

Figure 1. Consort diagram describing patient selection*



ED = emergency department. ICU = intensive care unit. * Potentially eligible patients were identified by screening the hospital's ICU database (2012–2013) for infection-related APACHE (Acute Physiology and Chronic Health Evaluation) diagnostic codes.

coding system,[16] as per previous reports.[17] Patients were subsequently excluded if: they were not admitted from the community; on chart review, their primary diagnosis was not thought to be infection; or their data were incomplete.

Data extraction and definitions

All data were extracted from the ICU database and/or individual patient medical records. These included age, sex, APACHE II score, requirement for invasive mechanical ventilation, ICU length of stay, hospital length of stay, and in-hospital mortality. Diagnoses listed in the database were cross-referenced with patient records. Body temperature data were extracted from the clinical observation sheets by one of us (OTG), using specific case report forms. Initial, minimum and maximum body temperatures were recorded for the period during which the patient remained in the ED, and for the first 24 hours in the ICU. Treatment with antipyretic medications (paracetamol and non-steroidal anti-inflammatory drugs) and the use of external cooling or warming were also noted. Body temperatures were classified into one of three categories: low (≤ 36.4°C), normothermia (36.5–37.9°C), and fever (≥ 38.0°C). The use of 36.4°C as a threshold to define low body temperature was based on the increased adjusted in-hospital mortality risk (when compared with a reference category of 36.5–36.9°C) observed in an analysis of about 30 000 Australian and New Zealand patients admitted to ICU with infection.[15]

Body temperatures are typically measured in the ED using non-invasive devices, such as the TemporalScanner (Exergen Corp, Watertown, MA, USA). After admission to the ICU, measurement of body temperature routinely involves using a Foley-Temp or Mon-a-therm Thermistor temperature probe (Tyco Healthcare, Pleasanton, CA, USA) inserted into the bladder or naso-pharynx. Recordings are obtained on an hourly basis, or as clinically indicated.

Statistical analysis

Continuous variables are presented as medians with interquartile ranges. Categorical variables are presented as numbers and percentages. Univariate tests of significance were carried out using a Mann–Whitney *U* or Kruskal–Wallis test for continuous data, and a χ^2 or Fisher's exact test for categorical data, where analysis assumptions were met. A *P* value of less than 0.05 was considered statistically significant. All analyses were undertaken using IBM SPSS Statistics, version 25 (Chicago, IL, USA).

Results

Patient characteristics

Over the study period, 574 patients were admitted to the ICU with infection. Four-hundred and twenty-three patients were then excluded, as they were not admitted from the community, they were not considered to have an active infection after chart review, or their data were incomplete (Figure 1). Thus, 151 patients were included in the final analysis. Their demographic, illness severity, physiological and outcome data are shown in Table 1.

Low body temperatures

The distribution of initial body temperatures recorded on presentation to the ED is provided in Figure 2. Overall, 22.5% of patients (*n* = 34) had a low body temperature on arrival. Of these patients, six had a temperature between 35.0°C and 35.9°C, and three had a temperature < 35°C. In contrast, 26.5% of patients (*n* = 40) had a temperature ≥ 38.0°C on presentation.

For the 34 patients with a low body temperature, median time to achieve a body temperature > 36.4°C was 7.9 hours (range, 3.3–14.0 hours). In 21 of these patients, recorded temperatures remained ≤ 36.4°C for the duration of their stay in the ED, while in four patients temperatures also did not exceed 36.4°C during the first 24 hours in the ICU. Only five such patients recorded a temperature ≥ 38.0°C at any point from presentation up until 24 hours in the ICU.

Of the 77 patients who had a body temperature between 36.5°C and 37.9°C on arrival to the ED, 60 experienced a decrease in temperature to < 36.5°C and 38 experienced a decrease in temperature to < 36.0°C at least once from presentation up until 24 hours in the ICU. Similarly, of the 40 patients with fever on presentation, 30 experienced a

Table 1. Characteristics of patients included in the study (*n* = 151)

Parameter	Median (IQR) or number (%)
Age in years, median (IQR)	63 (50–75)
Male sex, number (%)	94 (62.3%)
APACHE II score, median (IQR)	17 (13–20)
APACHE diagnostic code (by system), number (%)	
Gastrointestinal	6 (4.0%)
Musculoskeletal/skin	6 (4.0%)
Neurological	3 (2.0%)
Renal/genitourinary	4 (2.6%)
Respiratory	53 (35.1%)
Sepsis	79 (52.3%)
Invasive ventilation, number (%)	34 (22.5%)
Recorded temperatures in °C, median (IQR)	
On arrival to ED	37.2 (36.5–38.0)
Maximum in ED	37.7 (36.9–38.6)
Minimum in ED	36.5 (36.1–37.0)
Maximum from presentation until 24 hours in ICU	38.1 (37.2–38.9)
Minimum from presentation until 24 hours in ICU	36.0 (35.8–36.4)
ED length of stay in hours, median (IQR)	8.1 (4.8–11.6)
ICU length of stay in days, median (IQR)	2.7 (1.5–5.0)
Hospital length of stay in days, median (IQR)	10.0 (5.8–17.4)
Hospital mortality, number (%)	13 (8.6%)

APACHE = Acute Physiology and Chronic Health Evaluation. ED = emergency department. ICU = intensive care unit. IQR = interquartile range.

decrease in temperature to < 36.5°C, and nine to < 36.0°C at least once from presentation up until 24 hours in the ICU. The median time spent with a body temperature ≤ 36.4°C overall (*n* = 124) was 11.0 hours (range, 5.0–16.8 hours). Additional detail is provided in Table 2.

Clinical outcomes

There was no significant difference in length of stay in the ED (*P* = 0.26) or the ICU (*P* = 0.60) on the basis of the temperature recorded on arrival to hospital. Similarly, there was no statistically significant difference (*P* = 0.17) for inhospital mortality (Table 2). The variation of in-hospital mortality observed for different temperature profile categories is shown in Table 3. The greatest mortality was seen in patients who had a persistently a low temperature of ≤ 36.4°C. In patients who never manifested a fever (68/151, 45%) (eg, those who arrived with low temperature or normothermia, and never recorded a temperature ≥ 38.0°C in the ED or during the first 24 hours in ICU), in-hospital mortality was about twice that of the remaining cohort (8/68 [11.8%] *v* 5/83 [6.0%]); *P* = 0.21).

Thermal manipulation

Only one patient, who had a temperature of < 35°C, was actively warmed. No patients were physically cooled. Fifty-five patients (36.4%) received antipyretics in the ED. As expected, there was an association (*P* = 0.03) between antipyretic use and higher temperature on arrival, although 22 patients received these medications despite their peak temperature being < 38.0°C. Of those patients who were persistently ≤ 36.4°C in the ED (*n* = 21), three received antipyretics.

Discussion

Key findings

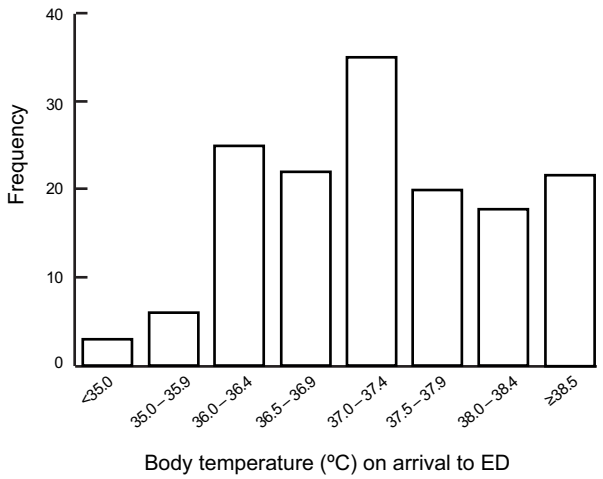
In this single-centre retrospective cohort study of patients with community-acquired infection, almost a quarter presented with a low body temperature. Not unexpectedly, a lower temperature on arrival was associated with not mounting a pyretic response. In addition, patients often had low temperatures for many hours in the ED, and only a single episode of active warming was documented. Finally, in those who were initially ≤ 36.4°C, a lack of subsequent rise in body temperature was associated with numerically greater in-hospital mortality.

Relationship with previous studies

Data concerning the epidemiology of body temperature alterations in patients presenting to the ED with community-acquired infection are sparse. In a small single-centre study, Wilson and colleagues studied a cohort of 122 patients with sepsis and reported a body temperature > 38°C in 32.0% of patients, and < 36°C in 19.7%.[18] Similarly, Kushimoto and colleagues studied the influence of early body temperature alterations in patients admitted with severe sepsis to several ICUs in Japan, reporting that 25.6% of values were ≤ 36.5°C.[14] These data are similar to our findings.

In a single-centre retrospective study, Lindvig and colleagues noted that about one-third of bacteraemic patients were normothermic (36.0–38.0°C) on arrival to

Figure 2. Distribution of body temperatures recorded on arrival to the emergency department (ED) for patients included in the study (*n* = 151)



the ED,[19] a finding consistent with other reports.[20,21] These data reinforce the limited utility of elevated temperatures in accurately diagnosing acute infection. Although our cohort was not defined on the basis of microbiological data, the observation that 45% never reached a temperature ≥ 38.0°C is in agreement with such data.

We found that patients with low temperatures had a greater in-hospital mortality. These data are consistent with those reported elsewhere,[15] in which persistently low–normal temperatures have been associated with inferior clinical outcomes in the setting of critical infection. Importantly, as hypothesised, only one of these patients received active warming.

Study implications

Our study primarily highlights the variability in the thermal response to community-acquired infection. The observation that many patients who manifest low body temperatures for lengthy periods do not receive warming, and that these patients are more likely to die, highlights that exploration of active warming may be justified. Indeed, while previous reports have described an important association between worse clinical outcomes and the absence of fever in community-acquired pneumonia,[22] bacterial peritonitis[23] and gram-negative bacteraemia,[24] it may be that clinicians are more concerned about higher, as opposed to lower, body temperatures. In line with this is the observation that active external warming was used on only one occasion, which is consistent with the limited use of physical means to manipulate temperature reported in a previous point prevalence study.[25] This may be due to a significant cognitive bias in this setting that promotes the pursuit of normothermia to deal with high but not low temperature.

Strengths and limitations

To our knowledge, the findings of our study, which demonstrate lack of warming of septic patients with low body temperature, are novel. Although sustained body temperatures ≤ 36.4°C have been associated with worse clinical outcomes using large ICU registry data,[15] our findings reinforce the utility of this threshold in identifying at-risk ED patients with community-acquired severe infection. This is particularly important as body temperatures ≤ 36.4°C are not traditionally considered to represent hypothermia, the implications of which are more widely appreciated by clinicians. Moreover, our data should help to optimise inclusion criteria for future clinical research in this setting. Finally, we validated each case by reviewing individual patient records, and identifying a specific cohort of patients with community-acquired infection, and thereby limited any confounding from previous in-hospital therapy.

Owing to the single-centre retrospective cohort study design, accurate data analysis relies on sufficient documentation in clinical records and correct data extraction. As such, our results should be viewed as hypothesis generating only. We excluded patients for whom complete data were not available, although these are likely to be missing at random, and should not have introduced significant selection bias. The majority of body temperature measurements (particularly in the ED) are likely to have been obtained by non-invasive methods, and although invasive temperature measurements are less influenced by external factors, these are uncommonly employed first-line in patients presenting to EDs. As such, our data reflect that of usual practice. Moreover, the use of physical means to modulate body temperatures overall (either cooling or warming) was low, perhaps suggesting limited resources, or a lack of equipoise about the use of such interventions in the study setting. Finally, the observed in-hospital mortality in our study cohort was low; a reflection of our inclusion of any infective process. While improvements in clinical outcomes have been noted in such patients over recent years,[17] this does limit the statistical power of our analysis to identify any meaningful associations with this endpoint.

Conclusion

In this retrospective cohort study of patients with community-acquired infection requiring ICU admission, just under a quarter presented with low temperatures on arrival to hospital. Many of them manifested such temperatures for extended periods. However, only one episode of active warming was documented. Lower initial

Table 2. Body temperature categories, treatment and in-hospital mortality

Initial body temperature	ED length of stay in hours, median (IQR)	ICU length of stay in days, median (IQR)	Time to temperature > 36.4°C from arrival in ED in hours, median (IQR)	Duration of temperature ≤ 36.4°C in hours, median (IQR)	Time to temperature ≥ 38.0°C from arrival to ED in hours, median (IQR)	Duration of temperature ≥ 38.0°C in hours, median (IQR)	Active warming in ED, number (%)	Anti-pyretic medication in ED, number (%)	In-hospital mortality, number (%)
< 36.5°C (*n* = 34)	6.4 (4.5–10.1)	3.6 (2.0–6.1)	7.9 (3.3–14.0)	13.0 (6.0–21.8)	11.9 (4.0–14.1)*	4.0 (1.5–6.0)*	1 (2.9%)	7 (20.6%)	5 (14.7%)
36.5–37.9°C (*n* = 77)	8.7 (5.0–11.5)	2.8 (1.5–5.2)	—	10.0 (4.3–15.0)†	4.9 (1.8–13.7)‡	3.0 (2.0–6.3)‡	0	28 (36.4%)	7 (9.1%)
> 37.9°C (*n* = 40)	8.2 (4.9–15.0)	2.3 (1.4–4.7)	—	9.5 (3.8–14.0)§	—	3.5 (2.0–9.0)	0	20 (50.0%)	1 (2.5%)
P¶	0.26	0.60	—	—	—	—	—	0.03	0.17

ED = emergency department. ICU = intensive care unit. IQR = interquartile range. * Includes five patients. † Includes 60 patients. ‡ Includes 38 patients. § Includes 30 patients. ¶ Comparison between groups based on initial body temperature.

Table 3. Variation in in-hospital mortality on the basis of temperature profile from presentation until 24 hours in ICU

Initial temperature	Maximum temperature	Minimum temperature	Number of patients	APACHE II score, median (IQR)*	Mortality, number (%)
< 36.5°C	< 36.5°C	< 36.5°C	4	19 (13.5–20.0)	3 (75%)
< 36.5°C	36.5–37.9°C	< 36.5°C	25	17 (11.5–20.0)	2 (8%)
< 36.5°C	> 37.9°C	< 36.5°C	5	20 (10.0–24.5)	0
P				0.76	< 0.01
36.5–37.9°C	< 38.0°C	> 36.4°C	6	13 (10.8–16.8)	2 (33.3%)
36.5–37.9°C	< 38.0°C	< 36.5°C	33	16 (13.5–19.0)	1 (3.0%)
36.5–37.9°C	> 37.9°C	> 36.4°C	11	15 (13.0–20.0)	2 (18.2%)
36.5–37.9°C	> 37.9°C	< 36.5°C	27	17 (10.0–23.0)	2 (7.4%)
P				0.69	0.07
> 37.9°C	> 37.9°C	> 37.9°C	—	—	—
> 37.9°C	> 37.9°C	36.5–37.9°C	10	15.5 (7.5–19.0)	0
> 37.9°C	> 37.9°C	< 36.5°C	30	16.5 (12.0–21.0)	1 (3.3%)
P				0.43	0.75

APACHE = Acute Physiology and Chronic Health Evaluation. IQR = interquartile range. *APACHE II score calculated without including temperature points.

body temperatures were associated with a lack of pyretic response and, if sustained, a greater risk of death. These observations provide the epidemiologic justification for pilot interventional studies of active warming of patients with low temperatures in this setting.

Acknowledgements

Andrew Udy gratefully acknowledges salary support from the National Health and Medical Research Council of Australia (Early Career Fellowship; GNT1124532).

Competing interests

None declared.

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