

COMMENTARY

# Too cold may not be so cool: spontaneous hypothermia as a marker of poor outcome after cardiac arrest

Jakobea Wörner and Mauro Oddo\*

See related research by den Hartog *et al.*, <http://ccforum.com/content/14/3/R121>

## Abstract

In a recent issue of *Critical Care*, den Hartog and colleagues show an association between spontaneous hypothermia, defined by an admission body temperature  $<35^{\circ}\text{C}$ , and poor outcome in patients with coma after cardiac arrest (CA) treated with therapeutic hypothermia (TH). Given that TH alters neurological prognostication, studies aiming to identify early markers of injury severity and outcome are welcome, since they may contribute overall to optimize the management of comatose CA patients. This study provides an important message to clinicians involved in post-resuscitation care and raises important questions that need to be taken into account in future studies.

den Hartog and colleagues prospectively analyzed data from 105 consecutive comatose patients resuscitated from cardiac arrest (CA) and treated with therapeutic hypothermia (TH) over a 2-year period [1]. They observed that the percentage of patients with unfavourable outcome (including death, vegetative state and severe disability) was significantly higher in patients with spontaneous hypothermia (69%) than in those with a body temperature  $\geq 35^{\circ}\text{C}$  on admission to the ICU (50%,  $P = 0.05$ ). Using multivariable analysis, and adjusting for age, initial arrest rhythm, and APACHE II and SOFA scores, the association between spontaneous hypothermia and outcome at 6 months was confirmed.

In this single centre prospective cohort of more than 100 patients, spontaneous hypothermia remained

significantly associated with long-term outcome, even when adjusted for APACHE II and SOFA scores. This indicates that low body temperature  $<35^{\circ}\text{C}$  on admission after CA is a strong marker of neurological recovery.

Previous studies have shown that spontaneous hypothermia is associated with increased mortality after severe trauma and haemorrhage [2]. TH has improved prognosis of hypoxic-ischemic encephalopathy [3], and might have an impact on our ability to predict final patient prognosis [4]. den Hartog and colleagues identify spontaneous hypothermia as a new prognostic marker of CA.

However, in accordance with Utstein's style registry [5], arrest conditions (that is, witnessed versus un-witnessed arrest), initial arrest rhythm (that is, ventricular fibrillation versus non-ventricular fibrillation) and duration of circulatory arrest (that is, time from collapse to return of spontaneous circulation) are other well-known predictors of prognosis [6]. These parameters, and particularly time to return of spontaneous circulation, were not entered in the logistic regression; thus, it remains to be further established whether spontaneous hypothermia is an independent predictor of outcome. Furthermore, body temperature may be difficult to measure precisely, and reasons for spontaneous hypothermia can be multiple: for example, CA occurring in cold environments may have better neurological recovery despite low admission body temperature [7]. Therefore, although admission body temperature is an important parameter and a marker of injury severity, it should not be considered alone to guide therapy.

Notwithstanding these limitations, which are well recognized by the authors, the findings by den Hartog and colleagues are important and indeed in line with previous trauma [2] and more recent post-CA [8] studies showing that spontaneous hypothermia is associated with higher mortality. Pathophysiological mechanisms may involve extended damage to specific brain areas leading to impaired thermoregulation [9], thereby establishing a plausible relationship between post-anoxic injury,

\*Correspondence: [mauro.oddo@chuv.ch](mailto:mauro.oddo@chuv.ch)  
Department of Intensive Care Medicine, Lausanne University Hospital (Centre Hospitalier Universitaire Vaudois), Rue du Bugnon 46, 1011, Lausanne, Switzerland

impaired hypothalamic thermoregulation with spontaneous hypothermia, and unfavourable outcome. Nevertheless, it should be noted that previous studies predominantly described hyperthermia, instead of spontaneous hypothermia, as a result of hypothalamic damage [10].

This study may also help explain some recent clinical observations. In particular, it was recently shown that early cooling did not seem to translate into better outcome [11]. This is in contrast with the abundant experimental literature [12] and some recent clinical evidence [13,14]. However, spontaneous hypothermia may have been a major confounding factor of these studies. While animal studies are conducted in stable conditions, this may often not be the case in humans after CA. In such conditions, time to target temperature may not be a reliable parameter, unless it is corrected for baseline demographics, including admission body temperature.

In conclusion, the findings by den Hartog and colleagues identify spontaneous hypothermia as a new prognostic marker that may have an influence on neurological recovery from CA. Together with other well-known outcome predictors [15], admission body temperature should therefore be included in the early assessment of comatose CA patients and will be an important variable to be taken into account in future studies.

#### Abbreviations

APACHE, Acute Physiology and Chronic Health Evaluation; CA, cardiac arrest; SOFA, Sequential Organ Failure Assessment; TH, therapeutic hypothermia.

#### Competing interests

The authors declare that they have no competing interests.

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