Does targeted temperature management improve neurologic outcomes in patients with nonshockable rhythms?

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Ratings: *Methods*—4/5 *Usefulness*—3/5

arrest with a nonshockable rhythm, treated with moderate therapeutic hypothermia or targeted normothermia.

Methods

Design

Randomized control trial (RCT).

Setting

Intensive Care Units (ICUs).

Subjects

Adults (≥ 18 years of age) post-cardiac arrest, with initial nonshockable rhythm and coma. Exclusion criteria included no-flow time > 10 min, low-flow time > 60 min, pregnant/breastfeeding, severe hemodynamic instability or cirrhosis.

Intervention

Targeted temperature management with moderate therapeutic hypothermia (33 ± 0.5 °C) for 24 h, then rewarming to normothermia at 0.25 – 0.5 °C per hour; or targeted normothermia (37 ± 0.5 °C) for 48 h.

Outcomes

Primary outcome was favorable neurologic outcome at day 90 using the Cerebral Performance Category (CPC) score. Secondary outcomes included 90-day mortality, length of mechanical ventilation, hospital and ICU stay.

Introduction

Background

There is uncertainty regarding the neurologic benefit of moderate therapeutic hypothermia for post-cardiac arrest patients with initial nonshockable rhythms.

Objectives

To compare survival with favorable neurologic outcome at day 90 in comatose patients post resuscitation from cardiac

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Table 1 Selective primary and secondary outcomes (from Table 2 in Lascarrou et al. 2019)

Outcome	Hypothermia (<i>N</i> = 284)	Normothermia (<i>N</i> = 297)	Hazard ratio (95% CI)
CPC score 1 or 2 on day 90–no. (%)	29 (10.2)	17 (5.7)	4.5 (0.1–8.9)
CPC score distribution on day 90–no. (%)			
CPC 1	16 (5.6)	11 (3.7)	
CPC 2	13 (4.6)	6 (2.0)	
CPC 3	22 (7.7)	31 (10.4)	
CPC 4	1 (0.4)	0	
CPC 5	231 (81.3)	247 (83.2)	
Death by day 90–no. (%)	231 (81.3)	247 (83.2)	– 1.9 (– 8.0 to 4.4)
Survival to ICU discharge–no. (%)	62 (21.8)	61 (20.5)	1.07 (0.75–1.52)
Survival to hospital discharge–no. (%)	56 (19.7)	50 (16.8)	1.19 (0.81–1.74)

Results

Results are shown in Table 1.

The hypothermia number needed to treat for favourable neurologic outcome (CPC score 1 or 2, indicating minor or moderate disability) is 22.

- Fragility index of one, signifying that outcome change in one patient would negate statistical significance
- All results within single country, limiting external validity
- Primary outcome assessed by phone, may be less accurate than in-person

Appraisal

Strengths

- Large, multicentre, blinded-outcome-assessor RCT
- Well defined population
- Similar baseline characteristics across groups
- Few patients lost to follow up
- Protocols well-described and reproducible in most ICUs
- Outcomes clearly defined and relevant
- Widely validated measure of neurologic function used (CPC score)

Limitations

- Significant confounder of higher rates of hyperthermia in normothermia group (target 37 °C), potentially contributing to adverse outcomes (versus favourable results in moderate therapeutic hypothermia group being attributable to hypothermia)
- Planned active rewarming strategy led to longer period of targeted temperature management in moderate therapeutic hypothermia group (56–64 h) versus normothermia group (48 h)
- Variability in cooling methods (invasive versus surface)

Context

The benefit of targeted temperature management in patients with initial nonshockable rhythms is unclear. A substudy of the targeted temperature management trial examining patients with out-of-hospital cardiac arrest found no difference in mortality or neurologic outcomes between patients managed at 33 °C versus 36 °C, regardless of initial rhythm [1]. The 2020 American Heart Association (AHA) Guidelines advise targeted temperature management between 32 and 36 °C for all patients not following commands after successful resuscitation from cardiac arrest, regardless of initial rhythm [2]. Nonshockable rhythms now make up the majority of cardiac arrests [3]. Trials to determine the optimal temperature to result in favorable neurologic outcomes in these patients would be helpful.

Bottom line

This study provides evidence of increased survival with favorable neurologic outcome at day 90 in a therapeutic hypothermia group (33 °C) compared to normothermia group (37 °C), in patients post-cardiac arrest from non-shockable rhythms. Current guidelines endorse the benefits

of targeting temperatures between 32 and 36 °C. However, the normothermia group experienced higher rates of hyperthermia in the first 36 h due to a temperature target of 37 °C. Hyperthermia should be avoided due to potential neurologic detriment. Further studies are needed to avoid this potential confounder and clarify whether hypothermia improves outcomes in post-arrest patients, beyond avoiding detriment from hyperthermia.

Compliance with ethical standards

Conflict of interest The authors declare they have no conflicts of interest.

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