

Systematic Review Snapshot

Clinical Synopsis

TAKE-HOME MESSAGE

Therapeutic hypothermia with conventional cooling methods improves survival and neurologic outcomes at hospital discharge for patients who have experienced a cardiac arrest.

METHODS

DATA SOURCES

The authors searched the Central Register of Controlled Trials (CENTRAL), MEDLINE (1971 to 2007), EMBASE (1987 to 2007), CINAHL (1988 to 2007), PASCAL (2000 to 2007), and BIOSIS (1989 to 2007) without language restrictions. Experts in the field were also contacted to retrieve pertinent data from ongoing, unpublished, or published trials not found in the electronic search.

STUDY SELECTION

All randomized and "quasirandomized" controlled trials were included that compared the application of any hypothermia protocol (core body temperature <35°C) within 6 hours of hospital arrival to standard care in comatose adults who were successfully resuscitated from a cardiac arrest.

DATA EXTRACTION AND SYNTHESIS

Data were extracted and quality of study methodology was assessed independently by 2 investigators. All 5 included trials were randomized or quasirandomized controlled trials. Quantitative data analyses were performed only if statistical heterogeneity was negligible.

Does Therapeutic Hypothermia Benefit Survivors of Cardiac Arrest?

EBEM Commentators

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Results

Therapeutic hypothermia after cardiac arrest

	RR (95% Confidence Interval)	Heterogeneity (I^2), %
Survival	1.35 (1.10–1.65)	0
Good neurologic outcome*	1.55 (1.22–1.96)	32

Results of pooled individual patient data from 3 trials (N=388).^{10,11}

RR, Relative risk.

*Good neurologic outcome was defined as a cerebral performance category score of 1 or 2 (5-point scale; 1=good cerebral performance; 5=brain death).

The search identified 1,353 potential studies; 5 trials met inclusion criteria, of which 3 contained individual patient data that could be pooled. These 3 trials used conventional cooling methods and reported adequate concealment of allocation, randomization, and blinded outcome assessments. One trial of the trials not included in the meta-analysis used hemofiltration, and the other trial did not report the cooling method used.

Commentary

The annual incidence of adult cardiac arrest in developing countries is approximately 0.04% to 0.19%, of which only 14% to 40% of individuals survive to hospital admission.¹⁻³ Of those who survive to hospital admission, only 7% to 30% are discharged with a good neurologic outcome.¹ Therapeutic hypothermia may improve both neurologic outcomes and overall survival.

Therapeutic hypothermia is achieved by inducing mild hypothermia to 32 to 34°C for 12 to 24 hours. This can be accomplished with simple measures such as ice packs, chilled saline solution, or commercially available devices such as cooling blankets. Most pathophysiologic mechanisms reported to explain therapeutic hypothermia's beneficial effects include a decrease in the cerebral metabolic rate and a reduction in the production of factors involved in reperfusion injury (eg, free radicals). The 3 randomized controlled trials included in this meta-analysis suggest that therapeutic hypothermia is beneficial.¹ Al-

though the majority of enrolled patients (92%) had an initial arrest rhythm of either ventricular fibrillation or nonperfusing ventricular tachycardia, limited data also suggest neurologic outcome benefit for patients whose initial cardiac rhythm was asystole or pulseless electrical activity.⁴ According to these findings, the International Liaison Committee on Resuscitation and European Resuscitation Council recommend therapeutic hypothermia in their guidelines for postresuscitation care.^{5,6}

Despite the current evidence, the use of therapeutic hypothermia in the United States is variable and considered novel.^{7,8} The authors of this Cochrane review sought to rigorously summarize and update the results of previous investigations to bridge this gap in knowledge dissemination. Although there was modest heterogeneity for the primary outcome of good neurologic outcome, there was no heterogeneity identified with respect to mortality. According to these data, for a hospital using conventional cooling methods with a baseline event rate of 20%, the number needed to treat for a good neurologic outcome would be approximately 10.⁹ For both outcomes, therapeutic hypothermia is effective, without significant adverse events identified.

This systematic review supports knowledge translation efforts to increase initiation of therapeutic hypothermia in the emergency department for comatose patients who have experienced a cardiac arrest. Therapeutic hypothermia is an inexpensive, noninvasive therapy that offers benefit with respect to patient-important outcomes for an event with devastating consequences.

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