Mild hypothermia improved neurologic outcome and reduced mortality after cardiac arrest because of ventricular arrhythmia

The Hypothermia after Cardiac Arrest Study Group. **Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest.** N Engl J Med. 2002 Feb 21;346:549-56.

QUESTION

In patients who are resuscitated after cardiac arrest because of ventricular fibrillation, is mild hypothermia more effective than standard treatment with normothermia for improving neurologic outcome?

DESIGN

Randomized {allocation concealed*}†, blinded {data collectors and clinicians assessing neurologic outcome}†,* controlled trial with 6-month follow-up.

SETTING

9 centers in Europe.

PATIENTS

275 patients seen in the emergency department, who were 18 to 75 years of age (median age 59 y, 76% men) and had spontaneous circulation restored after a witnessed cardiac arrest with ventricular fibrillation or nonperfusing ventricular tachycardia as the initial cardiac rhythm; a presumed cardiac origin of the arrest; an estimated interval of 5 to 15 minutes from the collapse to the first attempt at resuscitation by emergency medical personnel; and an interval of ≤ 60 minutes from collapse to restoration of spontaneous circulation. Exclusion criteria included a tympanic-membrane temperature < 30 °C on admission and response to verbal commands before randomization. Follow-up was 99% for neurologic outcomes and 100% for mortality.

INTERVENTION

All patients received standard intensive care that included sedation (midazolam, initially 0.125 mg/kg per h, and fentanyl, initially 0.002 mg/kg per h) and pancuronium (initially 0.1 mg/kg every 2 h, then as needed to prevent shivering) for 32 hours, with mandatory mechanical ventilation. Patients allocated to mild hypothermia (n = 137) were cooled to a target bladder temperature of 32 °C to 34 °C with an external cooling device. If cooling did not occur within 4 hours after the return of spontaneous circulation, ice packs were applied. The temperature was maintained at 32 °C to 34 °C for 24 hours from the start of cooling, after which patients were passively rewarmed. Patients allocated to normothermia (n = 138) were placed on a conventional hospital bed, and normothermia was maintained.

MAIN OUTCOME MEASURES

Favorable neurologic outcome (Pittsburgh cerebral-performance category of 1 [good recovery] or 2 [moderate disability] on a 5-category scale) and mortality.

MAIN RESULTS

Analysis was by intention to treat. The hypothermia group had a higher rate of favorable neurologic outcome and lower mortality than did the normothermia group (Table).

CONCLUSION

In patients who were resuscitated after cardiac arrest because of ventricular arrhythmia, mild hypothermia improved neurologic outcome and reduced mortality more than did standard treatment with normothermia.

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*See Glossary.

†Information provided by author.

Mild hypothermia vs normothermia after resuscitation for cardiac arrest because of ventricular fibrillation‡

Outcomes at 6 mo	Hypothermia	Normothermia	RBI (95% CI)	NNT (CI)
Favorable neurologic outcome	57%	39%	47% (9 to 82)	6 (4 to 29)
			RRR (CI)	
Mortality	34%	55%	38% (5 to 64)	5 (3 to 37)

‡Abbreviations defined in Glossary. Hypothermia event rates, RBI, RRR, NNT, and CI calculated from risk ratios (adjusted for all baseline variables) and control event rates in article.

COMMENTARY

Sudden cardiac death is a frequent cause of premature death in developed countries. Anoxic encephalopathy commonly occurs after cardiopulmonary resuscitation and results in poor neurologic outcomes and reduced long-term survival. Animal studies have suggested that mild hypothermia improves survival in comatose survivors of cardiac arrest. Although the exact mechanism by which hypothermia protects the brain is unknown, presumably it is mediated through reduced oxygen requirements and the prevention of other adverse chemical reactions.

The multicenter European study by the Hypothermia after Cardiac Arrest Study Group (HACASG) and a similar study from Australia (1) are the first controlled clinical trials to assess whether mild hypothermia improves neurologic outcomes and survival in comatose survivors of cardiac arrest. Both studies found significant improvement in neurologic outcomes with hypothermia. The study by the HACASG also found improved 6-month survival, with a number needed to treat of only 5 patients to prevent 1 additional death. The primary weakness in both studies is that caregivers could not be blinded to treatment with hypothermia and so could have provided more aggressive care overall to patients in the hypothermia group.

More studies are needed to verify these findings before hypothermia can be adopted unreservedly, but the results from these 2 studies are impressive. Physicians might consider using mild hypothermia with either a cooling device or ice packs in selected comatose survivors of cardiac arrest. When considering patients for hypothermia, it should be remembered that < 10% of assessed patients were included in this study, and so the inclusion criteria should be reviewed carefully. Patients will need to be sedated and paralyzed while receiving hypothermia. Core temperature should be maintained at not less than 32 °C, and hypothermia should not be continued for ≥ 24 hours because there may be a fine line between a temperature that provides benefit and that which increases such adverse events as malignant arrhythmias and infection.

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Reference

1. **Bernard SA, Gray TW, Buist MD, et al.** N Engl J Med. 2002;346:557-63.