

Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest (TTM2)

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The main question was to see if target temperature management (TTM) improved outcomes of patients post cardiac arrest. Prior to this study, there had only been two main trials back in 2002: HACA (Hypothermia after cardiac arrest) study and TTM (Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia) which showed a benefit (increased survival and improved neurologic outcomes) with hypothermia (33-36 degrees C) though these studies were limited due to bias + random errors and sample size. Prior to these two studies, it was mainly an observation by physicians where patients were placed in snow, found in cold environments, etc though there still is the proposed theory that fevers are thought to be a risk for unfavorable neurologic outcome.

Study Design

- Open label trial, blinded assessment
- Total of 1850 patients >18yo that suffered witnessed out-of-hospital cardiac arrest of a presumed cardiac or unknown cause (did not take into consideration of initial rhythm) that remained in a coma (unconscious and did not follow commands) and retained ROSC for at least 20 consecutive minutes.
- Exclusion criteria included unwitnessed cardiac arrest with asystole as well as >180 min from ROSC to initial assessment/screening for the study
- These were split in a 1:1 ratio to target hypothermia to 33 degrees C for 28h and then normothermia to 37.5 or less for 72h (all patients remained sedated or were comatose).
- Blinded physicians would perform a neurologic assessment 96h after randomization.
- 6 months later death and functional outcome were assessed; poor functional outcome was defined as MRS 4-6 (dichotomous scale with good vs poor outcome) then the criteria for death (from any cause) is self-explanatory.

Results

Simply put, there was no significant difference between the two groups (hypothermia and normothermia) with respect to both death and poor functional outcome at 6 months. The only difference that they found was that in the hypothermic group, there was more arrhythmia resulting in hemodynamic instability.

	Hypothermia	Normothermia
Death at 6 mo	50%	48%
Poor function outcome at 6 mo	55%	55%

To note, there were more arrhythmias resulting in hemodynamic instability in the hypothermia group (24%) compared to the normothermia group (17%) with a p value<0.001. Also, the large sample size provided a 90% power to detect a relative reduction of 15% in the risk of death in the hypothermia group.

Conclusions

This is an important study as this was the first large, randomized open label trial that showed that there was no difference in outcome in TTM (hypothermia) versus normothermia in outcome status post cardiac arrest. The randomized group in each section were very similar in co-morbid factors, type of cardiac arrest, median time to ROSC and time to randomization as well as similar neurologic exams at time of blinded exam which shows the quality of the study itself. Though something worth mentioning is the study's 50% survival rate of patients status post ROSC where the national average survival rate is more around 12-24%. There were no obvious care differences between the two groups though this was left up to physician discretion. It was noted that they were on similar sedative medications, had similar rates of PNA, sepsis, bleeding, and skin complications.

As for application of this study, it is important to keep the patient afebrile to not cause an unfavorable neurologic outcome though not necessary to be more aggressive as it may not be as beneficial and possibly cause worse outcomes (arrhythmias/hemodynamic instability) to induce hypothermia to 33 degrees C.

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