Does Intravascular Temperature Management Improve Outcomes Compared With Surface Cooling in Comatose Adults After Cardiac Arrest?

TAKE-HOME MESSAGE

Although intravascular temperature management does not improve survival compared with surface-cooling methods in post–cardiac arrest patients, it may improve neurologic outcomes.

METHODS

DATA SOURCES

MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews were searched on May 27, 2019. Additional articles were included in accordance with authors' prior knowledge of the literature.

STUDY SELECTION

Observational and interventional studies comparing intravascular temperature management with surface-cooling methods for induced hypothermia in adult patients resuscitated from cardiac arrest were eligible for inclusion. Studies also needed to report survival, neurologic outcomes, or both for each group.

DATA EXTRACTION AND SYNTHESIS

Methodological quality was assessed with the Newcastle-Ottawa Quality Assessment form for observational studies and the Cochrane Collaboration's risk of bias tool for randomized controlled trials. A random-effects model was used to pool results and heterogeneity was assessed with tau^2 and I^2 values.

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Bartlett ES, Valenzuela T, Idris A, et al. Systematic review and meta-analysis of intravascular temperature management vs surface cooling in comatose patients resuscitated from cardiac arrest. *Resuscitation.* 2020;146:82-95.**

Results

Pooled results for outcomes comparing intravascular temperature management with surface-cooling methods (positive values indicate higher likelihood in the intravascular temperature management group).

Outcome	Risk Difference, %	95% CI
Survival	2	−1 to 5
Good neurologic outcome	5	2 to 8
Arrhythmia	−6	−11 to −2

CI, Confidence interval.

Out of 248 articles identified by the search strategy, the authors included 12 in the meta-analysis, with a total of 5,581 patients. Three of these studies were randomized controlled trials, 4 were prospective cohort studies, 3 were retrospective case-control studies, and 2 were secondary analyses of randomized trials. Only one of the included studies was conducted in the United States. The quality of the observational studies was judged as moderate, whereas the risk of bias in the randomized controlled trials was also judged as moderate.

The method of surface cooling varied a great deal between studies, and included ice packs, cooling blankets, gel adhesive

pads, fans, and cold intravenous fluids. Although the majority of studies used a target temperature of 32°C to 34°C, this also varied between studies, with 2 of the randomized controlled trials using a target temperature of 36°C.

In the pooled random-effects model, the authors found no statistically significant difference in mortality between patients treated with intravascular temperature management and surface-cooling methods, but found a significant improvement in survival with a good neurologic outcome with use of intravascular temperature management. There was no reported difference regarding shivering, skin injury, clinically significant bleeding, deep venous thrombosis, pneumonia, or sepsis. Although the authors reported that there was no evidence of an effect of intravascular temperature management on survival or neurologic outcomes in randomized versus observational studies, they provided no statistical evidence of this. Specifically, they did not report a sensitivity analysis using only randomized controlled trials, which comprised a total of only 525 patients.

Commentary

Induced hypothermia and targeted temperature management have been shown to improve neurologic outcomes and survival rates after cardiac arrest.[1] There are several methods available to manage core temperature, including ice packs, cooling tents, and commercially available intravascular and surface-cooling devices. This meta-analysis sought to collate the evidence comparing surface-cooling methods with intravascular temperature management in cardiac arrest patients in whom return of spontaneous circulation was achieved. The pooled results demonstrated that intravascular temperature management led to significantly better neurologic outcomes, with little to no difference in overall survival.

Although these results are promising, this systematic review had several limitations. First, several of the authors disclosed a significant conflict of interest, including funding by one or more of the companies that produce commercial intravascular cooling devices. Specifically, there were 4 articles not identified by the search strategy that were included by the authors "based on their prior knowledge of the literature," all of which were cowritten by at least one author of this systematic review. Although this may hint at an inadequate search strategy that failed to identify these articles, it also suggests some bias in their final inclusion.

Additionally, although the authors reported that the included studies were of moderate quality, only 3 were randomized controlled trials; given the nature of the intervention being assessed, none of these were blinded. Seven of the remaining trials were observational, with a high risk for selection bias leading to high variability and subjectivity in who received intravascular temperature management or surface cooling.[2] The two remaining studies were secondary analyses of randomized controlled trials that were not originally designed to compare intravascular temperature management with surface-cooling methods,[3,4] again raising the specter of selection bias.

Finally, although the authors correctly reported that there was no statistical heterogeneity found in their analysis, there was clearly a great deal of methodological and clinical heterogeneity between the studies. Aside from the aforementioned differences in study design, the included studies also examined a variety of surface-cooling methods and target temperatures, and pooling these studies undoubtedly decreased the accuracy of the results.[5]

The authors of this meta-analysis concluded that intravascular temperature management shows greater promise than surface-cooling methods for temperature management after cardiac arrest regarding neurologic outcomes. However, given the paucity of randomized controlled data and the degree of heterogeneity between the included studies, such a conclusion may be overly optimistic.

1. Hypothermia after Cardiac Arrest Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *N Engl J Med*. 2002;346:549-556.
2. Odgaard-Jensen J, Vist GE, Timmer A, et al. Randomisation to protect against selection bias in healthcare trials. *Cochrane Database Syst Rev*. 2011;2011:MR000012.
3. Nielsen N, Wetterslev J, Cronberg, et al. TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. *N Engl J Med*. 2013;369:2197-2206.
4. Kirkegaard H, Søreide E, de Haas I, et al. Targeted temperature management for 48 vs 24 hours and neurologic outcome after out-of-hospital cardiac arrest: a randomized clinical trial. *JAMA*. 2017;318:341-350.
5. Melsen WG, Bootsma MC, Rovers MM, et al. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clin Microbiol Infect*. 2014;20:123-129.