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Citation:

Chan, Paul S., Robert A. Berg, Yuanyuan Tang, Lesley H. Curtis, and John A. Spertus. "Association Between Therapeutic Hypothermia and Survival After In-Hospital Cardiac Arrest." JAMA 316.13 (2016): 1375. Web.

Clinical Question:

Does therapeutic hypothermia improve in-hospital survival and favorable neurologic survival after in-hospital cardiac arrest compared with usual care in comatose patients?

Bottom Line Up Front:

Use of therapeutic hypothermia after in-hospital cardiac arrest may warrant reconsideration. In this potentially practice-changing study, therapeutic hypothermia compared with usual care was associated with a lower likelihood of survival to hospital discharge and a lower likelihood of favorable neurologic survival.

Introduction:

Therapeutic hypothermia, or targeted temperature management, is recommended by current ACLS guidelines for comatose patients following both out-of-hospital and in-hospital cardiac arrest. However, this treatment strategy has only been clearly proven in cases of out-of-hospital cardiac arrest due to ventricular fibrillation. Limited data has been published specifically evaluating therapeutic hypothermia following in-hospital cardiac arrest, a situation in which patient population and especially response time differ markedly from the out-of-hospital context.

Study Design:

This study was a prospective, observational study involving 26,183 adult patients identified through a national registry of in-hospital cardiac arrest patients between 2002 and 2014. Of these, 1538 underwent therapeutic hypothermia. The median lowest achieved temperature was 33.1°C, and 21% of patients achieved a lowest temperature below the originally recommended nadir of 32°C. The study used statistical software and robust propensity score matching to identify suitable controls from the registry based on a number of variables, such as initial rhythm, comorbidities, duration of CPR, and time of day. The controls received usual care without hypothermia and were selected only from hospitals capable of performing therapeutic hypothermia at the time of their cardiac arrest. Other key exclusion criteria included patients not on mechanical ventilation, patients with an initial out-of-hospital arrest, patients with missing data, and patients who died within the first 24 hours after arrest.

Results:

Survival to hospital discharge was significantly lower for the therapeutic hypothermia patients (27.4%) compared with the non-hypothermia-treated patients (29.2%), a difference that was similar for non-shockable and shockable cardiac arrest rhythms. Similar results were found for the secondary endpoint of neurologically favorable survival, with statistics favoring the non-hypothermia-treated group. Interestingly, there was a lower proportion of patients in the hypothermia-treated group (29.1%) who died during the first day than in the non-hypothermia-treated group (45.0%). Finally, the study also performed sub-group analysis, looking at one-year survival for patients who could be successfully linked to Medicare inpatient files, with no significant difference in 1-year survival identified between the two groups.

Discussion:

The study addresses an important question, given the significantly faster response times associated with in-hospital cardiac arrest compared with out-of-hospital cardiac arrest. The propensity score matching used an impressive number of variables that likely minimized confounders for this kind of study design. However, there may have been significant indication bias in the absence of randomization. Another limitation affecting the applicability of this study includes the variable hypothermia protocols across hospitals, especially in light of the relatively recent changes to temperature goals after the December 2013 Targeted Management Trial for out-of-hospital arrest was published. Other potential limitations include the use of mechanical ventilation as a surrogate for comatose status and a general lack of data on study subjects.

It is interesting that there was initially a survival benefit for the cohort group within the first 24 hours followed by a decreased survival to hospital discharge and then possibly a similar 1-year survival based on sub-group analysis showing no significant difference between the groups.

Conclusion:

Despite its limitations, this study highlights the lack of convincing proven benefit for therapeutic hypothermia after in-hospital cardiac arrest, in contrast to the published controlled trials showing benefit following out-of-hospital arrest. Given that hypothermia treatment is not without its costs, and given its potential risk for added harm, it may be worthwhile to forego this treatment for comatose patients following in-hospital cardiac arrest, pending any follow-on randomized controlled trials showing clear benefit.
