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TTM for Everyone: A Call for Tailoring Guidelines Based on Resource Availability

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Given the lack of targeted neuroprotective therapies to improve outcomes following pediatric cardiac arrest, it is imperative that we execute resuscitation and post-resuscitation care with excellence. A key pillar of post-arrest care is the use of targeted temperature management (TTM) to avoid fever ($< 38^{\circ}\text{C}$), a Class I recommendation of the American Heart Association (AHA) guidelines^{1–4}. Second, largely informed by the Therapeutic Hypothermia after Pediatric Cardiac Arrest (THAPCA) trials, the AHA recommends 5 days of therapeutic (actively controlled) normothermia (36°C to 37.5°C) or 2 days of therapeutic hypothermia (32°C to 34°C) followed by 3 days of normothermia for out-of-hospital cardiac arrest patient TTM management. For in-hospital cardiac arrest, recommendations are to actively maintain therapeutic normothermia for 5 days^{5–7}. There is no specific guidance from the AHA about how TTM should best be implemented, however.

An ideal TTM approach would offer precision temperature control, be safe for patients, and require minimal labor with adequate cost-effectiveness. Several lower-cost and commercially available TTM techniques are available, each with its own risks and benefits to be considered. Lower-cost methods such as the use of intravenous cold saline infusion, fans and external ice application are effective for hypothermia induction or treatment of fever but offer less precision during the maintenance phase in some studies, lessening enthusiasm for their use as sole methods^{8–10}. Commercially-available surface cooling devices (i.e., cooling blankets or surface pads), circulate cold fluid or air either close to or attached to patient skin. Advanced devices include servo-control mechanisms that promote less variability in blanket versus patient temperatures. However, these devices did not demonstrable superiority to devices without servo-control in a neonatal study¹¹.

Disadvantages of these devices include risk of skin irritation and burns, higher cost, and likely need for neuromuscular blockade and sedation due of shivering. The THAPCA studies provided sites with the servo-controlled Blanketrol III (Cincinnati Sub-Zero)^{6,7}. Adjunct TTM control methods were allowed but, to our knowledge, frequency of use was not reported. Reflecting the labor-intensive nature of TTM, a THAPCA survey of PICU nurses reported that 86% of respondents thought that patient care in the trial “required more work”, but protocol adherence was robust¹². Lastly, intravascular cooling systems require the placement of a central venous catheter. Benefits to these system include accuracy and precision of TTM, but risks include those known to be associated with central line insertion, including thrombosis and infection, and the device is unavailable for smaller pediatric patients¹³.

Clinical studies comparing feasibility, safety, and effectiveness of TTM techniques are less available, and thus needed, for children. In Yunge *et al*, authors used existing differences between center TTM resources to assess TTM hypothermia protocol performance in children remaining comatose following cardiac arrest.¹⁴ Centers involved in this prospective, observational study conducted in South America, Spain and Italy implemented hypothermia via either a surface cooling blanket with or without servo-control. TTM protocol targets followed THAPCA’s approach and included continuous temperature monitoring with hourly recordings and sedation with pharmacological paralysis.

The authors found that patients in both groups had similar presenting temperatures, time to target temperature (within 3 hours), and median temperatures during the maintenance phase. However, there were notable and important differences in TTM precision targets between the two cohorts. Patients in the servo-control group had more temperatures within the goal range during the hypothermia maintenance phase and less time > 38°C overall compared to the non-servo group. Given that the protocols were identical other than TTM device, we found it interesting that rewarming was twice as long in the group without servo-control compared to the servo-control group and would inquire how precisely patients were rewarmed during this risky period where rewarming too fast is to be avoided. Patients had similar occurrence of adverse events and rates of survival and neurological impairment.

While these observations are valuable and give rationale for acquisition of superior technology when possible, this study has several limitations that need to be highlighted when interpreting the results. First, the sample size is relatively small with 70 patients enrolled in a 2-year period from 5 institutions. The authors mention that the number of children in the non-servo group was small due to some centers acquiring servo-controlled devices during the study, making it difficult to analyze groups with sufficient power. Also, it was not clearly stated whether all patients completed the 120-hour TTM protocol as assigned in its entirety. Finally, data for adjunctive therapies such as anti-pyretic medications or cold saline were not reported.

The authors suggested that future development of clinical protocols be designed with implementation options-based resource availability. Going beyond equipment availability to deliver care recommended in guidelines, we would add that guidelines tailored for critically ill children in lower resource regions would best be drawn from evidence obtained from

those regions themselves until the day comes when resources are equally available for our patients¹⁵. Until then, for TTM following pediatric cardiac arrest, identifying a protocol and device that allows for both efficient and safe TTM based on available resources within an institution is imperative, as avoidance of hyperthermia as a neuroprotective strategy is an integral component of post-cardiac arrest care for all children. We challenge the field to consider resource-dependent variations for future guidelines.

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