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Commentary

Variability in Postarrest Targeted Temperature Management Practice: Implications of the 2015 Guidelines

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In 2002 postarrest care was significantly altered when multiple randomized controlled trials found that therapeutic hypothermia at a goal temperature of 32–34°C significantly improved survival and neurologic outcomes. In 2013, targeted temperature management (TTM) was reexamined via a randomized controlled trial between 33°C and 36°C in post-cardiac arrest patients and found similar outcomes in both cohorts. Before the release of the 2015 American Heart Association (AHA) Guidelines, our group found that across hospitals in the United States, and even within the same institution, TTM protocol variability existed. After the 2013 TTM trial, it was anticipated that the 2015 Guidelines would clarify which target temperature should be used during postarrest care. The AHA released their updates for post-cardiac arrest TTM recently and, based on the literature available, have recommended the use of TTM at a goal temperature between 32°C and 36°C. Whether this variability has an effect on TTM implementation or patient outcomes is unknown.

The landscape of postarrest care was significantly changed in 2002 when multiple randomized controlled trials found that therapeutic hypothermia, also known as targeted temperature management (TTM), at a goal temperature of 32–34°C for 12–24 hours significantly improved survival and neurologic outcomes, compared to an approach without controlled temperature management (Bernard *et al.*, 2002; Hypothermia After Cardiac Arrest Study Group, 2002). However, since then only one other randomized controlled trial has reexamined TTM in this population to determine if a higher target temperature might confer similar outcomes (Nielsen *et al.*, 2013). Nielsen *et al.* (2013) compared a target temperature of 33°C versus 36°C to treat coma after cardiac arrest and demonstrated equivalence at both targets. Though this study examined controlled TTM in both cohorts, some providers have questioned the use of TTM at 33°C, switching to 36°C, and even abandoning TTM all together—a practice that has been cautioned against by many experts in the field (Polderman and Varon, 2014, 2015; Clinkard *et al.*, 2015; Lopez-de-Sa, 2015).

The impact of the 2013 TTM trial on the use of TTM in the post-cardiac arrest patient population nationally is unknown. Furthermore, whether TTM variability between institutions and within institutions has a detrimental effect on patient outcomes is also unknown. The Nielsen *et al.,* 2013 study demonstrated that using 33°C is equivalent to 36°C in terms of survival and neurological outcomes, but will allowing providers the option to choose either goal temperature increase confusion and decrease implementation? It has been reported previously that post-cardiac arrest TTM has been poorly implemented in hospitals across the United States (Abella *et al.*, 2005; Merchant *et al.*, 2006). A recent study by Edelson *et al.* (2014) found that, of the hospitals in the United States responding to a nationally representative survey via mail, 58% had a post-cardiac arrest TTM protocol available but only 10% of those administered the protocol for more than 25% of their patients that met treatment inclusion criteria. This study surveyed providers before the 2013 TTM trial, when the standard target temperature goal was 33°C. Implementation of TTM may become more difficult when there is not a clearly identified, protocolized target temperature.

After the release of the 33°C versus 36°C 2013 TTM trial, the International Liaison Committee for Resuscitation (ILCOR), of which the American Heart Association (AHA) is a member organization, recommended the following updates to TTM approach (Jacobs and Nadkarni, 2013):

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> Pending formal Consensus on the optimal temperature, we suggest that clinicians provide postresuscitation care based on the current treatment recommendations (3,4). We accept that some clinicians may make a local decision to use a target temperature of 36°C pending this further guidance.

Additionally, the ILCOR update stated:

> A key message from this study is that targeted temperature management (TTM) remains an important component of the postresuscitation care of the unconscious cardiac arrest patient and that similar results were obtained when either 33°C or 36°C were selected as target temperature. As detailed by the study investigators and the authors of the accompanying editorial (2), this study does not support a treatment strategy where TTM is abandoned.

Before the release of the 2015 AHA Guidelines, our group sent a 10-question Internet-based survey to a convenience sample of healthcare providers throughout the United States (Leary *et al.*, 2015). Providers were associated with the Penn Alliance for Therapeutic Hypothermia database, Hypothermia and Resuscitation Training Institute, and other resuscitation specific e-mail lists. Participants were queried regarding their institution's TTM protocol and current practice. Between December 2014 and May 2015, 219 healthcare providers responded from 112 institutions in 35 states. Respondents were staff nurses (39%), advanced practice nurses (28%), physicians (22%), and other providers (11%). Respondents represented medical ICU (25%), cardiac ICU (21%), emergency department (15%), and other ICUs (39%).

When asked about their specific institution's TTM target temperature, 204/219 responded; 65% reported a goal temperature of 33°C, 8% reported 36°C, 25% reported either 33°C or 36°C, and 2% were unknown. When asked how the target temperature was selected, 30% stated that there were adequate data only to support 33°C, 3% stated that there were adequate data only supporting 36°C, 42% stated that they were reevaluating 33°C versus 36°C, and 25% stated unknown.

A median of 2 (interquartile range 2–3.5) clinicians from the same institution completed the survey. Of those, 5/39 (13%) of the respondents from the same institution did not agree on or were unsure whether their institution had a TTM protocol; 33% did not agree on the target temperature within their institution; 64% did not agree or did not know if data supported the institution's choice of target temperature.

Our survey results suggest that across hospitals in the United States, and even within the same institution, the target temperature for postarrest care, before the release of the 2015 AHA guidelines varied widely. The 33°C versus 36°C 2013 TTM trial found that TTM at both temperature targets was indistinguishable with regard to survival outcomes and neurological recovery. Additionally, postarrest treatment at 33°C versus 36°C resulted in a similar adverse events profile (Nielsen *et al.*, 2014; Wise *et al.*, 2014). Therefore, the decision to change target temperature in all cases from 33°C to 36°C appears to have equipoise in the literature. A recent study from the Netherlands performed a similar survey and found that 25% of Dutch ICUs used 36°C as their target temperature, whereas 73% still used 33°C. One reason found for not changing the TTM goal temperature was lack of agreement (64%) and anticipation of the updated TTM guidelines, among other reasons (Wils *et al.*, 2015).

The ILCOR and the AHA have released their updates to post-cardiac arrest TTM, and based on the literature available, the ILCOR has recommended TTM between 32°C and 36°C for 24 hours for all out-of-hospital cardiac arrest (OHCA) patients who are unresponsive after return of spontaneous circulation (ROSC) due to ventricular fibrillation/pulseless ventricular tachycardia (VF/pVT) and suggesting TTM, as opposed to no TTM, for all patients also unresponsive after OHCA due to nonshockable rhythms or in-hospital cardiac arrest (IHCA) of any rhythm (Donnino *et al.*, 2015). The AHA has made a stronger recommendation, with an endorsement of TTM for all postarrest patients regardless of presenting rhythm or location of arrest at a target temperature between 32°C and 36°C for 24 hours (Callaway *et al.*, 2015):

> We recommend that comatose (i.e, lack of meaningful response to verbal commands) adult patients with ROSC after cardiac arrest have TTM (Class I, LOE B-R for VF/pVT OHCA; Class I, LOE C-EO for non-VF/pVT (i.e, ''nonshockable'') and in-hospital cardiac arrest).

After the 2013 TTM trial, it was anticipated that the new guidelines would clarify which target temperature should be used during postarrest care; however, the studies available for review led to a wider range in the consensus of the TTM goal target temperature. One question that was clarified, however, is that the ILCOR and the AHA have maintained the recommendation of TTM for patients who are not waking up and following commands appropriately after cardiac arrest. These updated guidelines will hopefully correct the misconception that controlled TTM should be abandoned.

A recent TTM implementation study by Morrison *et al.* (2015) demonstrated that there were many factors that contributed to variability of TTM implementation, including providers being unfamiliar with the TTM protocol, lack of awareness, disagreement around supporting evidence, and lack of interdepartmental collaboration. These barriers could be the reasons that our survey showed variability in goal target temperature use and awareness around institutional TTM protocols in general. Unfortunately, the updated 2015 AHA Guidelines do not clarify the TTM goal temperature for providers and therefore may add to the growing confusion. Of added concern is the result of the large, pediatric multicenter randomized controlled trial, Therapeutic Hypothermia After Pediatric Cardiac Arrest (THAPCA). THAPCA randomized children >2 days old and <18 years who remained comatose after their cardiac arrest to receive either 33°C or 36.8°C. The trial found no difference in outcomes; however, there was a trend toward improved survival in the 33°C arm (20% vs. 12%, $p = 0.14$) (Moler *et al.*, 2015). These data could suggest a clinically relevant survival difference that should not be discounted. The 2015 AHA Guidelines suggested that it is reasonable to control normothermia (36°C–37.5°C) or maintain hypothermia (32°C–34°C) in pediatric patients who are comatose after OHCA and determined there were insufficient data to recommend TTM over normothermia for IHCA; however, they stated that fever should be treated aggressively in this population (De Caen *et al.*, 2015).

Regardless of the target temperature institutions decide upon, it is clear that adult post-cardiac arrest patients who exhibit signs of neurologic injury (e.g., coma or poor awakening) require controlled temperature management. The

HACA, Bernard, and Nielsen 2013 TTM studies have shown that these patients need to have controlled temperature management if they are to be afforded a better chance at survival and neurological recovery. The 2013 TTM trial did not conclude that providers should discontinue implementing TTM after cardiac arrest (Nielsen *et al.*, 2014) and both the ILCOR and AHA 2015 Guideline recommendations support the continued practice of TTM in this patient population. Providers who have discontinued TTM protocols based on an incorrect reading of Nielsen 2013 TTM study will need to reexamine their practice.

Across hospitals in the United States, and even within the same institution, the target temperature for postarrest patients undergoing TTM varies widely. Whether variability surrounding TTM goal temperature use will decrease or increase due to the variability in the updated recommended goal temperatures in the 2015 AHA Guidelines is unknown. More research is required to understand the choice of TTM target temperature for specific patient indications and its long-term effect on patient outcomes.

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