Program Evaluation of a Targeted Temperature Management Program at an Academic Medical Center

Hannah L. Kaylor, DNP, APRN, AGACNP-BC

University of Virginia School of Nursing

Beth Hundt, PhD and Clareen Wiencek, PhD

On my honor, I have neither given nor received aid on this assignment.

Abstract

Purpose: The purpose of the DNP project was to perform a systematic evaluation of a Targeted Temperature Management (TTM) program at an academic medical center; the focus was on timing components of TTM.

Methods: A systematic review of the literature was performed to assess ideal timing to achieve target temperature following ROSC for optimal survival and neurologic function. A program evaluation was performed at one academic medical center utilizing the Centers for Disease Control 6-step framework. Following a stakeholder assessment, nine questions were answered through chart review of patients admitted to a Coronary Care Unit (CCU) who underwent TTM from 2018 to 2019.

Results*:* A review of the literature showed mixed results for shorter versus longer duration to initiation of TTM and time to target temperature from ROSC. Twenty-seven patient charts were reviewed. The results indicated that the practice site is meeting its current standards for time from arrest to the initiation of intravascular TTM, as well as time from TTM catheter placement to target temperature. However, the results from the stakeholder assessment and chart review revealed a delay in timely admission to CCU, as well as opportunities to reduce the time from arrest to target temperature. A stakeholder assessment revealed CCU nurse and physician knowledge and familiarity of protocols was a facilitator of timely TTM initiation.

Implications: Recommendations were made to improve timeliness and efficiency in initiating TTM and achieving target temperature.

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Introduction and Background

Cardiac arrest remains a public health problem in the United States and beyond. Globally, mortality from cardiac arrest is higher than colorectal cancer, breast cancer, prostate cancer, influenza, pneumonia, auto accidents, HIV, firearms, and house fires combined (Meaney et al., 2013). In the United States, more than 350,000 out-of-hospital cardiac arrests (OHCA) occur annually. Survival from an OHCA ranges from 2% to 11% (Meaney et al., 2013).

Cardiac arrest occurs when there is an abrupt loss of heart function. There are a multitude of risk factors for cardiac arrest, including cardiomyopathies, coronary artery disease, severe electrolyte abnormalities, medications, and recreational drug use. The intrinsic loss of cardiac electrical activity results in cessation of the mechanical "pumping" of the heart; this is the normal process for delivering oxygen-rich blood throughout the body. The loss of perfusion to vital organs, including the heart, brain, and lungs, occurs instantaneously.

There has been an increased emphasis on public health education surrounding the importance of early bystander cardiopulmonary resuscitation (CPR). The treatment goals of an OHCA remain initiation of the emergency help chain by calling 9-1-1, defibrillation with an automated external defibrillator (AED), if available and if indicated by the presenting rhythm, and high-quality chest compressions. Many factors related to intra-arrest care impact the prognosis for those who experience a cardiac arrest. These factors include time from collapse to the start of CPR/defibrillation, quality of the CPR/defibrillation, and whether the person has responsiveness, indicating neurologic function, during or immediately after CPR (American Heart Association, 2017).

Post-arrest management following return of spontaneous circulation (ROSC) is aimed at hemodynamic stabilization, determining why the individual arrested and taking corrective

measures to help prevent another arrest, and assessing and preserving neurologic function. Post-anoxic brain injury is the most dramatic complication of cardiac arrest. About 80% of patients who have had an OHCA will be comatose following ROSC. Moreover, about two-thirds of these patients will die from the complications of the hypoxic-ischemic brain injury that ensues during cardiac arrest (Sandroni, D'Arrigo, & Nolan, 2018). Current guidelines recommend performing neuroprognostication no earlier than 72 hours following ROSC in those who do not receive therapeutic temperature management and no earlier than 72 hours following rewarming in those who do receive targeted temperature management (American Heart Association, 2015). Elimination of confounding factors when assessing in-the-moment and projected long-term neurologic function is of the utmost importance (Sandroni, D'Arrigo, & Nolan, 2018).

While determining a cardiac arrest survivor's prognosis, especially when considering withdrawal of life-sustaining treatments, is complex, certain variables can help guide care decisions. The American Heart Association (AHA) describes prognosis in terms of the individual's before-, during-, and after-arrest factors (American Heart Association, 2017). Individual factors before cardiac arrest that impact prognosis include age, ethnicity, and comorbidities (chronic kidney disease, heart failure, etc.). Intra-arrest factors include arrest rhythm (shockable versus non-shockable), time from collapse to start of CPR/defibrillation, the quality of CPR/defibrillation, and what the person's neurologic function is during or immediately following CPR (American Heart Association, 2017). In those patients who undergo Targeted Temperature Management following a cardiac arrest, a validated scoring system for early stratification of neurologic outcome exists. The scoring system, called C-GRApH, uses objective patient data available at hospital presentation to predict neurologic outcome. The C-GRApH score ranges from 0 to 5 using equally weighted variables: (C): coronary artery disease, known

pre-arrest; (G): glucose >/= 200 mg/dL; (R): rhythm of arrest not ventricular tachycardia/fibrillation; (A): age > 45 years; (pH): </= 7.0 (Kiehl et al., 2017). A high score is associated with worse neurologic outcomes, whereas, a lower score is associated with favorable neurologic outcomes. This scoring system brings variables from the different stages of the peri-arrest period together to predict neurologic outcome.

Targeted Temperature Management (TTM), previously referred to as induced hypothermia, is the only neuroprotective measure recommended following OHCA (Taccone, Picetti, & Vincent, 2020). While TTM is a complex intervention, the overarching goal of TTM is to reduce anoxic brain injury thereby improving neurologic function following cardiac arrest. Cerebral perfusion is driven by the cerebral metabolic rate. For every 1-degree Celsius drop in body temperature, the cerebral metabolic rate decreases by about 6% to 7%, thereby reducing oxygen demand. Moreover, the hypothermia-induced reduction in cerebral oxygen demand leads to a preservation of autoregulation. Hypothermia is known to decrease the release of reactive oxygen species (ROS), nitric oxide, and excitatory amino acids and glutamate, all of which are toxic to neurons and can lead to neuronal injury or death (Karnatovskaia, Wartenberg, & Freeman, 2014).

In the sub-acute phase of neuronal injury, one of the major protective effects of hypothermia on cerebral blood flow and oxygen demand appears to be a decrease in hyperemia following reperfusion. As is the case with cardiac myocytes, reperfusion injury and subsequent inflammation following an insult to brain tissue can lead to neuronal death and/or cell stunning. Hypothermia helps attenuate reperfusion injury, inflammation, edema, and neuronal apoptosis (Karnatovskaia, Wartenberg, & Freeman, 2014).

In 2002, two landmark TTM trials were published that greatly influenced management of the post-arrest patient. Bernard et al. (2002) showed that treatment with moderate hypothermia (33-degrees Celsius), compared with normothermia (37-degrees Celsius), improved outcomes in patients with coma after resuscitation from out-of-hospital arrest. In 2002, the Hypothermia after Cardiac Arrest Group conducted a multi-center, randomized, controlled trial. This group showed patients who were successfully resuscitated after cardiac arrest due to ventricular fibrillation and underwent mild hypothermia had an increased rate of favorable neurologic outcomes and reduced mortality compared to those who remained normothermic after cardiac arrest (Holzer, 2002). In each of these studies, external cooling methods by either ice packs or cooling blankets were used to achieve and maintain hypothermia.

Nielsen et al. (2013) published findings from an international, multicenter, randomized trial which compared mortality and neurologic outcomes in OHCA survivors. The results from the trial created skepticism surrounding the utility of TTM, as the authors reported no benefit was conferred when hypothermia at 33-degrees Celsius versus 36-degrees Celsius was implemented. Mortality was the primary endpoint, and neurologic function, as measured by the Cerebral Performance Category (CPC) scale (Appendix B, page 9) and modified Rankin scale, were secondary outcome measures. TTM "supporters" argued that the results reported by Nielsen et al. may have been impacted, in part, due to the high heterogeneity of the study sample, the short resuscitation time, and the rapid rewarming period (Taccone, Picetti, & Vincent, 2020).

TTM continues to be supported as the standard of care for post-cardiac arrest patients who do not regain consciousness after ROSC by the AHA and the Society for Critical Care Medicine (SCCM). In 2015, the AHA published updated guidelines for the management of the post-cardiac arrest patient. In these guidelines, the authors assert that TTM does seem to confer

benefit. However, the guidelines widened the goal target temperature range of 32-degrees Celsius to 36-degrees Celsius. Patients should be maintained at a constant temperature in this range, which would largely be based on clinician preference, for at least 24-hours (American Heart Association, 2015).

In 2009, five professional societies issued a consensus statement recommending that "targeted temperature management" replace what had previously been referred to as "therapeutic hypothermia" (Nunnally et al., 2011). The overarching reason for this change in terminology was an acknowledgement that TTM encompasses more than just the period of hypothermia. TTM acknowledges that other components, such as induction of cooling, mode of cooling, and rate of rewarming, may have a great impact on patient outcomes. Thus, the concept of high quality TTM has evolved in the last decade. Today, while evidence surrounding certain components related to the quality of TTM remains insufficient, programs employ methods based on what is known from the available evidence.

While there is a lack of good-quality evidence on the matter of precise timing of TTM, it is generally regarded that induction of hypothermia should be as soon as possible thereby minimizing long-term neurologic injury following ROSC. Several studies have shown no improvement in outcomes in those treated with cooled saline delivered intravascularly during CPR or during pre-hospital transport (Taccone, Picetti, & Vincent, 2020). Based on the available evidence, the 2015 AHA guidelines recommend against pre-hospital cooling of patients with rapid infusion of cold IV fluids. The AHA does not, however, include a goal time for induction of hypothermia in the most recent guidelines (2015).

Following at least a 24-hour period of "goal temperature," rewarming should be slow and controlled. To achieve this slow, controlled rewarming, a TTM device that allows for precise and

accurate temperature management may be ideal. Often this involves using either an intravascular catheter or an external device that can achieve central cooling to goal temperature quickly and then be used to gradually rewarm the patient at a preset rate of 0.15 to 0.25 degrees Celsius per hour (Taccone, Picetti, & Vincent, 2020).

Given the global impact of and the significant morbidity and mortality associated with cardiac arrests, TTM exists as an intervention to improve neurologic outcomes in some patients. There has been debate in the last two decades regarding whether normothermia is just as effective as hypothermia at preserving neurologic function in the post-arrest patient (Taccone, Picetti, & Vincent, 2020). However, the use of TTM continues to be supported by the AHA and SCCM as evidence-based therapy following cardiac arrest. As such, many academic medical centers and community hospitals offer this therapy.

The TTM program at the doctoral student's practice site began in 2007 and has been the clinical standard of care for comatose patients with ROSC after a cardiac arrest event. However, no systematic program evaluation has been conducted since the program was implemented in 2007. Thus, the purpose of this DNP project was to complete a program evaluation of the TTM program with a focus on the timing components of TTM. While the focus of the program evaluation was on the various timing components of TTM, successes and opportunities for improvement, with stakeholder input, were also evaluated.

Review of Literature

The purpose of this evidence-based review of the literature was to answer the nursing practice question: In comatose adult survivors of cardiac arrest undergoing TTM, what is the ideal timing to achieve target temperature following ROSC to yield optimal survival and/or neurologic function?

Search Methods

A systematic literature review of peer-reviewed academic journal articles published was conducted to explore the impact of timing to goal temperature in cardiac arrest patients undergoing targeted temperature management. Following consultation with the School of Nursing Librarian, four databases were searched: PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, and the Cochrane Library. The search key words included *cardiac arrest, timing, temperature, and ROSC,* and were combined with the AND Boolean operator in each database search: *cardiac arrest* AND *timing* AND *temperature* AND *ROSC.* In CINAHL, the search terms and parameters above yielded 5 results. In Web of Science, a "Topic" search utilizing the search terms and parameters above yielded 112 results. In PubMed, the aforementioned search terms yielded 13 results. Finally, a "Title, Abstract, Keyword" search in the Cochrane Library yielded 50 results using the search terms and parameters.

Then, titles and abstracts were reviewed based on the relevance to the nursing practice question. In CINAHL, four articles were excluded due to a lack of relevance to the primary nursing practice question. For example, two articles discussed the optimal timing of measuring optic nerve sheath diameter as a prognostic measure following cardiac arrest. Another article focused primarily on timing of TTM in pediatric survivors of cardiac arrest. In Web of Science,

eighty-five articles were excluded due to lack of relevance to the nursing practice question. For example, articles based on testing in animal models were excluded. In Cochrane Library, forty-one articles were excluded. Reasons for exclusion included duplicate articles within the database, abstracts from presentation to which access to the presentation was not possible, and primary measures other than those pertaining to the nursing practice question (e.g. goal cooling temperature as the primary intervention). In PubMed, ten articles were excluded because they lacked relevance to the nursing practice question. For example, seven of the excluded articles focused on prognostic tools and/or parameters other than timing that impact patient outcomes.

The total number of articles retrieved from the four databases was 180. After the title and abstract reviews, the 140 articles that were found to be irrelevant to the nursing practice question as described above were removed, resulting in 40 remaining articles. After removing all duplicates, 33 articles remained. After a full-text review, 19 articles were removed. One article could not be accessed, though attempts were made to retrieve it through multiple databases. Nine articles were removed because they assessed feasibility and/or safety of a specific cooling device and/or implementation of a new program or protocol. One article was removed because it was a preliminary report with the same sample from another trial included in this review of literature. One article was excluded because the article did not specify whether patients received high quality TTM with rapid cooling and a controlled rewarming phase. Additional excluded articles assessed impact of body mass index on time to target temperature (1), time to defibrillation on functional outcome (1), time from cardiac arrest to ROSC on functional outcome (2), factors delaying cooling (1), and temperature on arrival as a correlate with mortality (1). An additional article comparing normothermia versus hypothermia was excluded. As a result, 14 articles were

retained for analysis. Figure 1 shows the search process, using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Analysis

The fourteen articles retained for review showed mixed results for shorter versus longer duration to initiation of TTM and time to target temperature from ROSC. A variety of designs were reviewed, including four randomized controlled trials (RCT), one meta-analysis, two quasi-experimental studies, and multiple non-experimental studies. Utilizing the Johns Hopkins Evidence Based Practice evidence appraisal tools, each article was rated for quality and level of evidence. This review included four Level I articles, three Level II articles, and seven Level III articles. Quality was appraised and yielded two "A" ratings, six "B" ratings, and six "C" ratings. Overall, there was an adequate representation of higher and lower levels and quality of evidence in the present review.

Of the articles included in this review, timing related to TTM was evaluated using several outcome measures (Table 1: Sources of Evidence), including survival to discharge and neurologic function, which was most often categorized by the Pittsburgh Cerebral Performance Category (CPC) score. Of note, the CPC score ranges from good cerebral performance (1) to brain death (5). Favorable neurologic outcome is most often defined as a CPC score of 1 or 2 (Grossestreuer et al, 2016). While several articles reported additional outcome measures, this review focused on timing's impact on survival, mortality, and neurologic function. Aside from the outcome measures, several key themes appeared through review of the search articles. A thematic analysis was performed based on two key themes that included time to target temperature and time to initiation of TTM.

Impact of Time to Initiation of TTM

Kim et al. (2014) conducted a RCT in adults with cardiac arrest to assess the effect of pre-hospital induction of mild hypothermia on survival and neurologic status. The authors showed that those receiving chilled saline in the pre-hospital setting had significantly lower core temperatures by hospital arrival. Additionally, these patients also had a reduction in time to reach target temperature (34-degrees Celsius) of about one hour from those who only received in-hospital cooling. However, the group receiving pre-hospital cooling did not have improvement in survival and neurologic function at discharge. The authors noted that those in the intervention group experienced more pre-hospital re-arrest events and required more diuretic use in the first 24 hours of hospital admission. One notable limitation of this study was that those receiving the pre-hospital iced saline also received sedatives and paralytics as a rule by emergency medicinal personnel. The administration of sedatives and paralytic agents may have impacted the time to goal temperature in the intervention group. Additionally, the authors did not describe the in-hospital cooling protocol that was utilized.

Another RCT utilizing pre-hospital, intra-arrest cooling via a trans-nasal evaporative device was conducted in adults following a witnessed out-of-hospital cardiac arrest. The authors showed that while time to reach a core temperature of 34-degrees Celsius was significantly reduced, the intra-arrest cooling, compared to usual care, did not result in a statistically significant improvement in survival with good neurologic outcome at 90-days post-arrest (Nordberg et al., 2019). The time from collapse to target temperature was 105 minutes in the intra-arrest cooling group versus 182 minutes in the control group. The authors note that the study may have been underpowered, and as such, a larger sample size may have been able to detect significant between-group differences. Similarly, Castren et al. (2010) reported comparable findings from their analysis of part of the same sample as Nordberg et al. (2019).

Castren et al. also showed a significant reduction in median time to target temperature with the use of the intra-nasal, intra-arrest cooling device. However, there were no significant differences in early nasal cooling and survival or neurologic outcomes.

In an RCT, Scales et al. (2017) evaluated the impact of pre-hospital cooling initiated five minutes after ROSC on the time to reach the target temperature range (32-to-34-degrees Celsius). The pre-hospital cooling group did not have significantly higher rates of achieving the target temperature range within the 6-hour goal time; however, the authors noted that pre-hospital cooling was associated with increased application of in-hospital TTM. One important limitation was that not all patients received TTM in the hospital. This has serious implications for the nursing question at hand, as the lack of in-hospital TTM would be very likely to impact survival with good neurological outcome based on the available evidence. Additionally, 16% of eligible participants were not included due to a lack of willingness of some paramedics to participate, which may have created selection bias. Scales et al. notes they did not achieve the goal sample size and that the study may have been underpowered to detect small, but clinically significant differences between the groups.

Uray et al. (2015) conducted a retrospective, single center cohort study to test the long-term outcomes associated with using a surface cooling device applied in the pre-hospital setting. The control group was cooled with the same device following hospital admission. Between-group hospital admission temperatures differed significantly, with those in the pre-hospital cooling group arriving with a mean temperature of 35.2-degrees Celsius versus 35.8-degrees Celsius in those who received cooling following emergency department (ED) arrival. Favorable outcomes, defined as CPC score of 1 or 2 at 12-months post-arrest, were 26.8% (pre-hospital) and 37% (in-hospital), but these differences were not significant. Similar to Scales et al. (2017),

selection bias was evident in the pre-hospital group, as only about15% of ambulances that served the catchment region were equipped with the surface cooling devices (Uray et al, 2015).

Yochum and Utley (2017) looked at survival to discharge and time to initiation of TTM as outcome measures. Their sample was small, with a sample size of 20. However, they showed that creation and implementation of an ED protocol for TTM significantly decreased the time from ROSC to initiation of cooling. These shorter induction times of TTM in the ED were not associated with significant improvements in better rates of survival at discharge. There were multiple limitations with this study, namely the small sample size and limited generalizability. Additionally, measurements of temperature at the time of ED arrival and time of ICU admission were not reported.

Perman et al. (2015) reported that shorter induction times using chilled IV fluids, defined as initiation of TTM to goal temperature, were associated with significantly poorer neurologic status. The author also found that age at time of cardiac arrest, initial shockable rhythm, and downtime in minutes were significantly associated with neurologic outcome. This was a retrospective analysis, and as such, one limitation is that there is no way to control the independent variable (induction time). Additionally, the authors reported that data was obtained from chart review and there were gaps in data when it could not be sufficiently accessed.

Ruivo et al. (2016) showed that in a small sample (n = 15) of adults experiencing out-of-hospital cardiac arrest, the time from collapse to initiation of TTM was not significantly different between non-survivors and those who survived with good neurologic function. Given the sample size and that the study was conducted at a single center, generalizability is low.

Impact of Time to Target Temperature

Schock et al. (2016) conducted a meta-analysis that resulted in the inclusion of 13

randomized and observational studies looking at the use of TTM in adults. The authors showed that early, rapid cooling without the use of cold intravascular infusions was associated with superior outcomes as compared with delayed cooling or cooling with cold saline. Interestingly, this meta-analysis showed that neurologic outcomes were similar over the 4-to-8-hour range of time delay from ROSC to target temperature. The authors suggested a stepwise improvement in outcomes for times to target temperature below 3 hours, supporting the theory that there is an improved activation of neuroprotective mechanisms if induction of cooling is completed within this window (Schock et al., 2016). The limitations were reported to include the presence of potential significant uncontrolled and unidentified confounders.

Benz-Woermer et al. (2012) examined admission body temperature in survivors versus non-survivors. Non-survivors had significantly lower spontaneous body temperatures than did survivors. Given this finding, time to target temperature was significantly shorter among the non-survivors. While time to target temperature was shorter in non-survivors, no association between the rate of cooling and survival at discharge was found. Similarly, there was no association between CPC score at discharge or at 3 months. The generalizability of this study is limited given that only 22% of the sample were women.

Holm et al. (2020) sought to evaluate the impact of pre-ICU cooling using cool IV fluids on the time to target temperature. The median time to target temperature from ROSC was 318 minutes in the pre-ICU cold intravenous fluids (IVF) group versus 281 minutes in the cold IVF not given group. This finding, however, was not statistically significant. There were no significant differences in incidence of harmful side effects in the cold IVF group. There were significant limitations including that the amount of IVF given to the intervention group was not standardized.

Sendelbach et al. (2012) assessed differences in CPC scores in patients who received therapeutic hypothermia post-cardiac arrest by time to initiation, time to target temperatures, and duration of therapeutic hypothermia. CPC scores were gathered at three time points: transfer from ICU, discharge from hospital, and post discharge. This study demonstrated that a delay in initiation of therapeutic hypothermia and a delay in reaching target temperature were consistently associated with a poorer CPC score (3-5). Upon initiating cooling, a delay in reaching target temperature of 30 minutes was associated with worse outcomes.

In contrast, Lyon et al. (2010) showed that mean time from ROSC to target temperature was significantly longer (320 minutes) in those who survived to discharge versus those who did not survive to discharge (219 minutes). One of the major limitations of this observational study was that approximately 64 percent of those patients enrolled, and for whom data was reported, were pronounced dead prior to TTM being initiated in the ICU. This, alone, distorts the data related to neurologic outcome and mortality because not all patients actually underwent TTM.

Finally, a 2020 article by Choi et al. looked at the impact of inter-hospital transfers on patient outcomes given the delay in initiation of TTM that a transfer could result in. The authors found that time to initiation of TTM did not differ significantly between those with a good or poor neurologic outcome. Despite finding that inter-hospital transfer did result in a delay to initiation of TTM, neurologic outcomes at 6-months post-OHCA were not associated with time to initiation. Additionally, Choi, et al. found that time to target temperature was longer in the good neurological outcome group than in the poor neurologic outcome group. One limitation of this study was that standardization of TTM protocols across the various hospitals of this multi-center study was not detailed. Variation among TTM protocols could have been associated with neurologic outcomes and survival.

Publication Bias Check

To address the possibility of publication bias, a search of the gray literature was performed by searching: *cardiac arrest* AND *timing* AND *temperature* AND *ROSC* in Google and looking at the first 20 results. There was no evidence of significant publication bias based on the gray literature, and findings were consistent with the themes in this systemic review. Several themes in the gray literature included: management of post-cardiac arrest syndrome, specific TTM protocols by institutions, and pre-hospital initiation of cooling. Several articles from the evidence search discussed above were among the results of the gray literature search.

Limitations of the Literature Review

In post-arrest care there can be significant gaps in the available data and standardization of care due to the nature of the circumstances that surround a cardiac arrest. For example, timelines are often blurry at best, most especially if the patient has suffered an unwitnessed arrest. In this case, it is difficult to quantify "downtime." Secondly, due to variations in EMS transport time, as well as hospital-specific resources and protocols, timing to initiation and target temperature can differ greatly among patients undergoing TTM.

Additionally, the articles represented in this review of the literature used similar outcome measures; however, time at which CPC scores were measured did vary among these articles. TTM protocols, which drive target temperature and method of cooling, differ among hospitals. Several articles were underpowered to detect meaningful differences in outcomes. Lastly, no RCTs were identified that specifically tested time to initiation of hypothermia or time to target temperature as the independent variable. This meant that the primary outcomes of timing were associative in many of these articles.

Conclusion

In comatose adult survivors of cardiac arrest undergoing TTM, data surrounding the nursing practice question, ‘What is the ideal timing to achieve target temperature to yield optimal survival and neurological function following ROSC?’ remains equivocal. In contrast with traditional thoughts and accepted practices (Stanger et al., 2019), many of the articles supported that longer times to initiation of cooling and time to target temperature were associated with better neurologic outcomes at hospital discharge and beyond. However, several studies supported that shorter times to initiation and target temperature were associated with improved survival and neurologic outcomes. Further randomized controlled trials testing timing as the independent variable may be warranted in the future to clarify this important nursing practice question.

Methods

Project Purpose

The purpose of this project was to perform a systematic evaluation of a TTM program at an academic medical center. Following initial conversations with a key stakeholder, the proposed program evaluation focused on the timing components of cooling and considered other major evaluation components that emerged from a systematic stakeholder assessment. A formal program evaluation of the TTM program at the student's practice site had not previously been conducted. The results of this program evaluation will be utilized to inform practice and potentiate practice changes.

CDC 6-Step Program Evaluation

The CDC provides a Framework for Program Evaluation in Public Health. The purpose of this program evaluation tool is to improve outcomes and detect the impact of a given program, or of a particular component of a given program. This method calls for ongoing, practical evaluation that involves stakeholders and partners of all levels, not just subject area experts. There are four standards for an effective evaluation: utility, feasibility, propriety, and accuracy. There are six key steps in the CDC framework: 1) engage stakeholders; 2) describe the program; 3) focus the evaluation design; 4) gather credible evidence; 5) justify conclusions; and, 6) ensure use and share lessons learned (Centers for Disease Control, 1999).

Step 1: Engage Stakeholders

The evaluation of the TTM program at the student's practice site began by engaging stakeholders. Those stakeholders who were interested and invested in the program, and who could enact change were engaged. Post-cardiac arrest patients who require TTM are most often admitted through the Emergency Department (ED) for stabilization and then transferred to the

Coronary Care Unit (CCU) for ongoing management. Stakeholders from across the care continuum, from the ED to the CCU, and from various disciplines, from registered nurses (RN) to medical trainees to attending physicians, were included in the stakeholder assessment to capture the lived experiences of a range of professionals who routinely engage with TTM therapy. In total, ten stakeholders were interviewed, and their roles are described below.

The program coordinator of the TTM program, who is also the Nurse Manager for the Coronary Care Unit (CCU), oversees the data collection for each patient who undergoes TTM. The TTM program coordinator also teaches a course on TTM to nurses and is the major resource for clinical queries related to TTM.

The Quality Director for the Heart and Vascular Center is an attending physician who oversees the TTM program, in collaboration with the TTM program coordinator, and who is specifically interested in the quality metrics. The CCU Medical Director is an attending physician who is responsible for the oversight of care in the CCU, as well as serving as a link between physicians, nurses, and other services in the CCU. Moreover, both the Quality Director and the CCU Medical Director are attending interventional cardiologists, who drive in-the-moment decisions regarding whether post-arrest patients should go to the cardiac catheterization lab and whether the patients meet inclusion criteria for TTM.

Cardiology fellows, with the assistance of cardiology attendings, coordinate admissions for patients requiring TTM. The cardiology fellows also help direct residents and other medical trainees, who are ultimately responsible for TTM order entry and the day-to-day management of patient care. Two current cardiology fellows, the Chief Fellow and a previous internal medicine resident at the practice site, were interviewed.

CCU RNs receive formal and informal training on TTM. As the TTM protocol is largely nurse-managed, the nurses are responsible for much of the clinical management of these patients and are often the first to advocate for TTM therapy in post-arrest patients. Additionally, CCU shift managers, who are also RNs, help to coordinate timely transfer of the patients from the ED, or outside hospital, to the CCU. Three CCU RNs were interviewed, each working various shifts (i.e. weekends, nights, weekdays), where available resources are notably different. Additionally, each of the RNs who were interviewed have varying years of experience in CCU and with TTM therapy to capture the experience of each.

Emergency department physicians and nurses are the first point of contact with patients who present to the hospital following an OHCA. They obtain initial information from the emergency medical personnel, stabilize the patient, and obtain baseline data that includes vital signs, laboratory data, and radiologic imaging. One ED RN, who served as the primary ED RN Education Coordinator during the period from which patient data was pooled from chart review (2018-2019), was interviewed. No ED physician was included in the stakeholder assessment, though multiple attempts at connecting were made.

Each stakeholder was given the choice of a verbal interview (face-to-face or via phone call) or interview questions delivered by e-mail. Each question was asked systematically to each stakeholder and careful attention was given to avoid undue influence in the manner the questions were presented. Stakeholders were given the ability to clarify the meaning of each of the questions asked. Stakeholder responses to each of the questions were analyzed for themes to identify additional necessary elements and outcomes in need of evaluation for the program evaluation at present. The following questions were asked of each stakeholder.

What are barriers to optimal timing of TTM? The major themes identified were: determining whether a patient meets the criteria for TTM therapy; limited resources available to effectively cool patients in the ED; where and when the intravascular cooling catheter is placed; differences in protocols and decisions to cool among critical care units or services; time required for transfer of a patient presenting to an outside hospital; and, coordination of tests and imaging prior to CCU admission.

What are facilitators to optimal timing of TTM? The major themes identified were: staff familiar with and knowledgeable of TTM protocols; utilization of a protocol; tests and imaging performed prior to CCU admission; early decision making regarding whether to cool a patient; and, early deployment of alternative cooling methods in the pre-hospital and ED settings.

Based on question 1 and question 2, an additional question was added for systematic review in the EMR to assess how often patients underwent intracranial CT imaging prior to initiation of TTM with the intravascular catheter.

What elements and outcomes of the program are currently being systematically recorded and routinely reviewed? The major themes identified were: cGRAPH scores; survival and disposition at discharge; [stakeholder] uncertainty regarding elements and outcomes being routinely reviewed; and, elements of timing (i.e. time at target temperature, time to goal temperature, etc.).

Based on stakeholder feedback to this question, survival to hospital discharge was reviewed for each patient in the EMR to assess outcomes in patients having received TTM therapy.

Are there any elements or outcomes of the TTM program in need of systematic evaluation? The major themes identified were: use of paralytics during TTM therapy;

coordination and timing of patient transfer from the ED to CCU; time [from admission] to cooling; and, whether standard work and protocols are being adhered to.

Based on stakeholder feedback to this question, additional information in the EMR was reviewed to assess for the frequency of the use of continuous paralytic use concurrent with intravascular TTM.

Step 2: Describe the Program

The program description communicates the mission and objectives of the program being evaluated (Centers for Disease Control, 1999). The Donabedian Method, a conceptual model to evaluate the interconnectedness of a program's structure, processes, and outcomes, was used to describe the TTM program at the student's practice site. There are three main components: structure, processes, and outcomes.

Structure. The structure of a program includes patients, equipment, supplies, training, and guidelines. The student's practice site is a 612-bed, level 1 trauma center. The Emergency Department (ED) at the practice site is a 70-bed center and functions to stabilize life-threatening conditions. There were 64, 237 patient visits to the ED in 2019 (UVA Health, 2020).

The CCU provides comprehensive interdisciplinary team care to critically ill adult and geriatric patients, aged 13 to 100+, with a focus on acute and chronic cardiology needs (Kaylor & Templeton, 2016). The CCU is home to the TTM program; however, any of the other four adult intensive care units may care for patients undergoing TTM if the patient's primary reason for arrest was not suspected to be primarily cardiac in nature or if the patient has other, competing care needs that would be more appropriately managed in another unit.

The TTM program at the practice site began in 2007 and has been the clinical standard of care for comatose patients presenting following ROSC after a cardiac arrest event since that

time. Approximately 20 to 40 patients receive TTM on an annual basis. The objective of the TTM program is to decrease the severity of anoxic brain damage and to improve neurological outcomes in patients who have suffered from a cardiac arrest, present with ROSC, and who have no purposeful movements post-arrest (Therapeutic Hypothermia following Cardiac Arrest, 2015). The majority of patients presenting to the CCU for TTM therapies present with OHCA to the ED.

Most of the supplies needed to initiate TTM are stocked in the CCU. Iced saline and iced packs, one Thermogard XP cooling console, the Quattro intravascular cooling catheter, and most of the medications needed for induction of TTM, except for some controlled substances, are stored in the CCU. There are additional consoles are available in other ICUs if needed.

RNs in the CCU are formally trained on the management of TTM through a 1-hour course taught by the program coordinator. This course is required of all CCU nurses and is available to nurses and physicians in other intensive care units (ICU) at the practice site. Nurse champions of TTM are chosen for each ICU and receive additional education. In the CCU, each nurse receives the opportunity to be assigned to care for a patient undergoing TTM during their orientation phase, so the training nurse is paired with an experienced nurse.

Fellows in cardiology, as well as fellows in Pulmonary and Critical Care, Surgery, and Neurosciences, have the opportunity to take a course that incorporates current evidence for hypothermia, current clinical practice guidelines, and order set review. This course is offered at least one time annually; however, data surrounding the number of individuals completing this course on an annual basis could not be obtained. Resident education is available via Podcasts and informal in-service education sessions by attending physicians and the program coordinator.

There is a Clinical Decision Tool for Therapeutic Hypothermia (see Appendix B) available on the practice site's web page by searching for "hypothermia." This tool defines roles, responsibilities, and considerations for each team member who might provide direct clinical care for a patient undergoing TTM. Additionally, the decision tool defines inclusion and exclusion criteria when considering if it is appropriate for a patient to receive TTM. The tool also discusses each phase of care for patients undergoing TTM. This tool is frequently referenced by CCU physicians and nurses when considering whether a patient is eligible for TTM based on hemodynamic stability and timing from ROSC.

Processes. The processes of a program involve interactions, investigation, and examination and treatment plans. Currently, patients who have experienced an OHCA present to the ED, where they are stabilized and evaluated. A host of initial testing is completed, including serum chemistries, complete blood counts, coagulation markers, serum lactate, a blood gas, cardiac enzymes, a STAT chest x-ray, and 12-lead electrocardiogram (ECG). Once the patient is stabilized, the ED physician consults the CCU Fellow for consideration of admission to the CCU. Upon examining the patient in the ED, the CCU Fellow determines if the likely underlying cause of cardiac arrest is due to an ST-segment elevation myocardial infarction (STEMI). If the answer is 'yes,' the patient will proceed to the Cardiac Cath Lab emergently depending on their hemodynamic status and attending input. If no evidence of a STEMI is present on the ECG and the patient is deemed an appropriate admission to CCU, a bed is reserved in the CCU.

The current standard practice is for the patient to be transported to the radiology suite for a CT of the head to rule out intracranial hemorrhage prior to, or concurrent, with transport to CCU due to the close proximity of the radiology suite to the ED. Moreover, once cooling is

initiated via the Thermogard XP cooling console and Quattro intravascular catheter, the patient cannot be transported with the cooling console due to its lack of battery-power back-up.

Prior to transport of the patient to the CCU, the CCU Charge Nurse is notified by the CCU Fellow of the patient's diagnosis and reason for admission. The CCU nurses ready the cooling console so that it is prepped and ready to be connected to the patient once the intravascular cooling catheter is placed. In recognition of the urgent need to begin TTM as soon as possible, a CCU nurse is "singled," without having responsibility to care for another patient, for at least the first 6 hours of the patient's admission to CCU. While the CCU fellow is inserting the Quattro central venous cooling catheter, the CCU nurse rapidly infuses 2 liters of cold saline intravascularly to begin decreasing the patient's temperature if there are no contraindications. The nurse obtains two continuous temperature sources and prompts the resident team to place TTM-specific orders.

Once the patient is connected to the cooling console, iced saline circulates throughout the system with the goal of rapidly cooling the patient to a goal temperature of 33-degrees Celsius, or a range of 32- to- 34-degrees Celsius. Each hour, the RN documents and assures the patient's temperature is responding appropriately to the TTM therapy. The patient's Glasgow Coma Score (GCS), a measure of neurologic status, is recorded every 4-to-12 hours in the EMR by the nurse, unless there are interval changes in the patient's assessment. Vital signs are documented every hour unless, again, there are interval changes in the patient's status. Temperatures are documented upon arrival to the emergency department, admission to the CCU, and then every hour from the time of TTM initiation from two independent temperature sources.

Physician and nurse huddles take place every two hours until the patient reaches goal temperature per the practice site's TTM Clinical Decision Tool (Appendix B). However, in

everyday practice, these huddles often take place informally and more frequently than every two hours. A bedside shivering assessment is performed every hour by the nurse, given the deleterious impact shivering can have on overall metabolic demand and temperature management. Sedation and anti-shivering therapies are adjusted to aid in achieving the goal temperature. Per the practice site guidelines, ideal time to goal temperature is within two hours of initiation of TTM. A detailed timeline for cooling, controlled rewarming, and maintenance of normothermia is available in Appendix A.

In 2019, the TTM program site was selected to be one of approximately fifty sites to participate in a multi-center randomized, adaptive allocation clinical trial called ICECAP (Influence of Cooling duration on Efficacy in Cardiac Arrest Patients). The major variable to be examined through this clinical trial is the "dose" of hypothermia therapy, namely by duration of maintained hypothermia. Patients will be randomly allocated to either 12-, 24-, or 48-hours of sustained hypothermia at 33-degrees Celsius. In order to be included in the study, patients must be at or below 34-degree Celsius within 240 minutes of cardiac arrest (Adams, 2020).

The practice site's participation in the ICECAP trial will warrant stricter timing and careful consideration of current practices at the student's practice site. At present, the TTM protocol states that cooling via the intravascular cooling system must commence within 6 hours of the patient's cardiac arrest. Furthermore, the ideal timeframe from initiation of cooling to goal temperature is 2 hours under the current TTM policy (2015). However, for a patient to be eligible for enrollment in the ICECAP study, time to hypothermia (34-degrees Celsius) from cardiac arrest must be 4 hours. As such, questions regarding which pre-TTM testing and interventions are necessary and where the Quattro cooling catheter should be placed (ED versus CCU) have

arisen. Thus, a formal evaluation of the current timing practices was of great utility to key stakeholders in the CCU, ED, and the practice site.

Outcomes. According to the Donabedian Model for Quality, the outcome(s) often reflect the impact of a healthcare intervention. Each time a patient is admitted for TTM therapy, a paper form and flowsheet in the EMR are completed by the nurse, noting arrest time (if known), time of ROSC, and patient demographic information. The paper forms are held and filed by the TTM program coordinator.

Data from a previous retrospective analysis of neurologic outcomes showed that in 2018, 21 patients admitted to the CCU underwent TTM. Fifteen of the twenty-one patients survived to discharge neurologically intact which was defined as a CPC score of 1 or 2 (Adams, 2020). At present, patient outcome data for survival or neurologic function is not available beyond discharge.

At present, some TTM data is collected, but not routinely reviewed or processed. The data previously collected included patient demographics, time of cooling initiation, and barriers to therapy. Moving forward, there are additional outcomes that would be useful to track. Patient outcomes that could be tracked include survival to hospital discharge, neurologic status, defined by CPC score, at ICU discharge, neurologic status at hospital discharge, whether PCI was performed, and length of stay. Program level outcomes and feedback that could be tracked include time from ED arrival to consultation of the ICU team, staff experience with TTM protocols, variation in patient management and protocol utilization between ICUs, and staff education.

Step 3: Focus the Evaluation Design & Step 4: Gather Credible Evidence

Building from the previous two steps, the third step of the CDC framework involves focusing the evaluation to concentrate on the issues of greatest concern to stakeholders. Given that resources are limited, the evaluation must use the allotted resources as efficiently as possible (Centers for Disease Control, 1999). The focus was limited to a key set of variables; the doctoral student verified the variables of greatest utility through the stakeholder assessment. In Step 4, gathering credible evidence involves defining the key outcome indicators, identifying the source(s) for evidence, evaluating the quality and quantity of the evidence gathered, and specifying the logistics of how evidence will be collected and handled (Centers for Disease Control, 1999). Steps 3 and 4 are discussed together, given their interrelated nature and for reader clarity.

The setting and DNP project were approved by the program coordinator of the TTM program. This proposal was submitted to the Institutional Review Board – Health Sciences Research (IRB-HSR) at the student's practice site for determination of the need for human subject protection. The IRB-HSR Quality Improvement Committee determined this project did not meet criteria for Human Subject Research (Appendix C).

The identified questions (Step 3) were answered through systematic review (Step 4) of the EMR and TTM-specific data related to timing of TTM at the doctoral student's practice site from January 2018 to December 2019. Following validation through a systematic stakeholder evaluation, five of the six questions were retained for review. One of the questions, "In patients admitted with OHCA undergoing TTM therapy, what was the average time from ROSC to initiation of TTM via the intravascular cooling catheter?" was eliminated because the information yielded was not of great use to the stakeholders. The questions retained centered around timing aspects of TTM. The question, "In patients admitted with OHCA undergoing

TTM therapy, what was the average time from the time of arrest to the upper limit of the goal hypothermia range (34-degrees Celsius)?" was added given its direct implications to clinical practice, especially in the setting of the practice site's involvement in the clinical trial. Three additional questions (questions 7 -9) were identified through the stakeholder assessment. These questions were identified based on repetition of themes among stakeholders.

The doctoral student's data collection processes met patient safety and privacy standards set forth by the Corporate Compliance and Privacy Office. The 2018 and 2019 CCU Admission Databases, which are Excel spreadsheets saved to a protected storage site on health system computers, were reviewed to identify patients admitted to the CCU who underwent TTM therapy during that time period. Medical record numbers (MRNs), date and time of admission to CCU, admitting diagnosis, and patient disposition upon discharge from the CCU were recorded for each patient.

Next, the EMR, including flowsheet notes, H&P notes, and the Therapeutic Hypothermia and Vital Sign Complex flowsheets, was reviewed for each patient who received TTM therapy. The following data was retrieved: ED admission date and time, details about the presenting rhythm and time of arrest, time that cooling was initiated by any method, time that cooling was initiated via intravascular cooling catheter, and the first recorded temperature at or below 34-degrees Celsius. Additionally, the medication administration history was reviewed to ascertain whether continuous paralytics were used concurrent with TTM therapy and imaging history was reviewed to identify those patients who had undergone a CT head prior to the initiation of intravascular TTM therapy.

From January 2018 through December 2019, thirty patients underwent TTM therapy. Three of the thirty patients were excluded from the analysis due to in-hospital cardiac arrest (2)

and the inability to place an intravascular cooling catheter (1). Of the twenty-seven remaining patients who underwent TTM therapy via the intravascular cooling catheter, the average age was 59 (36-81) years, and they were predominantly males (78%). Twenty-two (81%) patients presented to the ED via Emergency Medical Services (EMS); whereas the remaining five (19%) were transferred from an outside hospital.

Question 1. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of arrest to initiation of TTM via the intravascular cooling catheter?

Six patients were not included in the analysis due to unavailable data. Of the 21 patients undergoing TTM therapy for which data was available, the average time from arrest to the initiation of TTM via the intravascular cooling catheter was 239 (139 - 463) minutes.

Question 2. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of arrest to the upper limit of the goal hypothermia range (34-degrees Celsius)?

Five patients were not included in the analysis due to unavailable data. Of the 22 patients undergoing TTM therapy for which data was available, the average time from arrest to the upper limit of goal hypothermia (34-degrees Celsius) was 339 (84 – 750) minutes.

Question 3. How often are attempts by any method of cooling (iced NS infusion, ice bags, cooling blankets, etc.) initiated prior to placement of the intravascular cooling catheter?

Of the 27 patients undergoing TTM therapy, nineteen (70%) received attempts at cooling (iced NS infusion, ice bags, cooling blankets, etc.) prior to the placement of the intravascular cooling catheter.

Question 4. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of initiation of TTM via the intravascular cooling catheter to the upper limit of the goal hypothermia temperature range (34-degrees Celsius)?

One patient was not included in the analysis due to unavailable data. Of the 26 patients undergoing TTM therapy for which data was available, the average time from initiation of TTM via the intravascular cooling catheter to the upper limit of the goal hypothermia temperature range (34-degrees Celsius) was 102 (14 – 287) minutes.

Question 5. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of initiation of TTM via any cooling method (iced normal saline infusion, ice bags, cooling blanket, intravascular cooling catheter, etc.) to the upper limit of the goal hypothermia temperature range (34-degrees Celsius)?

Two patients were not included in the analysis due to unavailable data. Of the 25 patients undergoing TTM therapy for which data was available, the average time from initiation of TTM via any cooling method to the upper limit of the goal hypothermia temperature range (34-degrees Celsius) was 196 (14 – 360) minutes.

Question 6. In patients admitted with OHCA undergoing TTM therapy, what was the average time from ED or outside hospital (OSH) admission to CCU admission?

Three patients were not included in the analysis due to unavailable data; each of these patients for which data was unavailable were admitted from an outside hospital. Of the 24 patients undergoing TTM therapy for which data was available, the average time from ED or OSH admission to CCU admission was 121 (44 – 317) minutes.

In patients who first arrived in the ED at the student's practice site, the average time from ED arrival to CCU admission was 114 (44-210) minutes. For those patients who were first treated at an OSH, average time from OSH arrival to CCU admission was 196 (75-317) minutes.

Question 7. In patients admitted with OHCA undergoing TTM therapy, how many patients survived to hospital discharge?

One patient was not included in the analysis due to unavailable data. Of the 26 patients undergoing TTM therapy for which data was available, 17 (65%) patients survived to hospital discharge. Assessments and data surrounding individual patient neurologic function, functional capacity, and quality of life indicators were not available for review.

Question 8. In patients admitted with OHCA undergoing TTM therapy, how many underwent intracranial imaging with a CT of the head prior to TTM initiation via the intravascular cooling catheter?

Of the 27 patients undergoing TTM therapy, seventeen (63%) underwent intracranial imaging with a CT of the head prior to the initiation of TTM with the intravascular cooling catheter.

Question 9. In patients admitted with OHCA undergoing TTM therapy, how often were continuous chemical paralytics utilized?

Continuous chemical paralytics were utilized concurrent with TTM therapy in six (22%) of the 27 patients included in this review.

Step 5: Justify Conclusions

To justify conclusions, the evidence collected was linked to and reviewed against the metrics in the evaluation design. This step involved a complete analysis and synthesis of the information gained from the evaluation. Finally, recommendations were made based on what

actions are indicated as a result of the evaluation. Recommendations were a separate component that required giving context to the "what's next?" of the program evaluation (Centers for Disease Control, 1999).

Analysis of TTM Timing Components and Significance. The average time from arrest to the initiation of TTM via the intravascular cooling catheter was 239 minutes. At present, the TTM protocol holds that cooling via the intravascular cooling system should commence within six hours of the patient's cardiac arrest; this metric is being achieved. Moreover, the time from initiation of TTM with the intravascular cooling catheter to 34-degrees Celsius was 102 minutes, which is also meeting the site's goal of less than 120 minutes.

The impact of time from arrest to initiation of cooling has not been well elucidated; this was supported by a systematic review of the literature. However, there is limited data to suggest that the risk of death increases for every hour initiation of cooling is delayed (Mooney et al., 2011; Wolff et al., 2009). Furthermore, many clinicians who engage with TTM operate under the notion that rapidity of cooling is of great importance to the preservation of neurologic function, even with the equivocal evidence in the literature. Though the practice site is meeting its defined standards for timing, the site's involvement in the ICECAP trial is of value to advance the scientific knowledge surrounding TTM. Thus, attempts at shortening the window from time of arrest to goal temperature must be considered.

There are many variables that can impact the time from arrest to the implementation of TTM. Altogether, the variables that occur within the practice site are easier to impact than those that occur in the field or at the transferring hospital. Therefore, recommendations for future consideration should be aimed at streamlining processes from the time of ED arrival to the time when the intravascular catheter is placed, when cooling is initiated, and when target temperature

is achieved. The time from ED arrival to CCU admission, which averaged 114 minutes in this evaluation, represents a time span that stakeholders can most reasonably impact and reduce.

Recommendations. Based on the evidence analyzed in this program evaluation, five main recommendations are supported:

1. Utilize surface cooling blankets in the ED for more rapid cooling initiation
2. Develop an algorithmic approach to determine which patients would benefit from intracranial CT imaging prior to initiation of TTM
3. Place TTM catheters in the CCU where trained medical and nursing personnel optimize protocol adherence
4. Identify an accountable person to conduct regular evaluations of TTM program outcomes
5. Provide annual standardized education for CCU nurses and physicians

Utilize Surface Cooling Blankets in the ED for More Rapid Cooling Initiation. There are opportunities to decrease the time it takes to move the patient from the ED to the CCU and continue the standard of care of placing the cooling catheter and initiating intravascular cooling in the CCU. Upon arrival to the ED and concurrent with the other routine tasks that take place in the ED, a surface cooling blanket, can be applied to the patient's core area. These machines and the blankets are already available at the practice site. While long-term surface cooling has disadvantages, notably the potential for skin breakdown, surface cooling has been shown in some studies to be an effective way to reduce body temperature. Tomte et al. (2011) showed that there were no significant differences in time from arrest to 34-degrees Celsius with the use of intravascular cooling versus a surface cooling device. However, despite equal efficiency in hypothermia induction, intravascular cooling is significantly more reliable to any other method

of cooling in the maintenance of target temperature. Hoedemaekers et al. (2007) demonstrated that once target temperature was reached, patients cooled with an intravascular device were out of range 3.2 +/- 4.8% of the time compared to 50.5 +/- 35.9% with a water-circulating cooling system. A systematic review and meta-analysis by Calabro et al. (2019) found that there was a lower probability of unfavorable outcomes in those who underwent TTM with an invasive (i.e. intravascular) cooling device. Moreover, the authors found that there was a lower probability of unfavorable outcomes in those who were treated with a TTM device with temperature feedback technology (Calabro et al., 2019). Still, surface cooling can provide a way to reduce the patient's body temperature during the initial stabilization process and keep the emphasis on quick transfer of the patient to the CCU where TTM with the intravascular catheter can be initiated.

Develop and Utilize an Algorithmic Approach to Determine Which Patients Would Benefit from Intracranial CT Imaging Prior to TTM. The current process at the practice site used to identify which patients meet eligibility for intracranial imaging with head CT should be evaluated to determine the necessity of obtaining imaging on all, or even the majority of, post-arrest patients prior to TTM initiation. The major indication for a non-contrasted head CT following cardiac arrest is to rule out intracranial hemorrhage as the cause of the arrest or as a result of the arrest. Sixty-three percent of patients in this evaluation underwent intracranial imaging with a head CT prior to the initiation of TTM, which is comparable to other institutions that utilize clinician discretion to determine whether imaging is performed prior to intravascular cooling (Donnino et al., 2011). For example, Pennsylvania Hospital cites presenting rhythms of asystole and PEA, as well as unwitnessed arrests, as indications to pursue intracranial imaging. However, at other institutions, all patients undergo intracranial imaging (Donnino et al., 2011).

To date, there is no consensus statement on performing a head CT prior to TTM therapy. Reynolds et al. (2017) noted that 67% of the CTs performed within the first 24 hours showed intracranial abnormalities, such as generalized edema or loss of gray-white matter ratio, and that patient management was often impacted by the findings of the CT. However, in an expert commentary, Lindberg (2017) stated that the management changes, such as the addition of seizure prophylaxis, that came as a result of the imaging did not clearly lead to improved care or patient outcomes. Furthermore, Lindberg concluded that the current evidence did not provide a compelling case for the routine expanded use of CT scans unless pre-arrest symptoms or the neurological exam suggests a neurologic cause for arrest.

Hong et al. (2019) determined that loss of gray-white matter ratio on early CT imaging (< 2 hours post-ROSC) was not an independent predictive factor for poor neurologic outcomes. Furthermore, the most recent AHA guidelines suggest that neuro-prognostication take place no sooner than 72 hours following return to normothermia after TTM (American Heart Association, 2015). Since the goal of TTM is to preserve neurologic function and is time sensitive, taken with that there is currently no standard protocol used to support the use of head CTs in cardiac arrest patients prior to TTM, the site may benefit from a multidisciplinary workgroup that would develop an evidence-based algorithm or protocol to guide the use of CT imaging. Such a tool and collaborative effort may reduce the time interval from ED arrival to CCU admission and initiation of cooling.

Initiate All TTM with Intravascular Catheters in the CCU Where Trained Medical and Nursing Personnel Ensure Protocol Adherence. Interdisciplinary collaboration was found to be one of the strongest contributors to the success of the TTM program. Cardiology fellows and attendings, as well as Internal Medicine residents, cited CCU nurses' knowledge of TTM

protocols, nurse familiarity with where supplies are kept, and nurse advocacy for the rapid initiation TTM were all facilitators of the timely TTM therapy. The mandatory TTM course that all CCU nurses take within the first months of employment, in addition to a strong focus on TTM protocols during nurse orientation, leaves CCU nurses prepared to care for the post-arrest patient. Moreover, the CCU nurse manager is the longstanding TTM program coordinator who serves as a valuable and accessible resource for CCU nurses. It is a strong recommendation that priority should be given to quickly moving the patient to the CCU for placement of the intravascular cooling catheter.

One solution that has been proposed by stakeholders is to place the catheter and begin intravascular cooling in the ED. If intravascular cooling is started in the ED, several conditions would likely need to be met so that protocol adherence optimal. First, ED nursing staff would need to be trained on TTM to a similar degree as CCU RNs. Emergency medicine residents would have to be familiar with TTM protocols and order entry. It would also need to be established at which time point patients would be transported to CCU, as there will naturally be a pause in therapy during transport. Outcomes should be monitored closely to ensure that this solution to decrease time from arrest to goal temperature is working.

Identify an Accountable Person to Conduct Regular Evaluations of TTM Program Outcomes.

Some of the well-established post-arrest centers cited in the study by Donnino et al. (2011) found that the perception of poor outcomes in the OHCA population does not warrant the allocation of resources that TTM requires. This belief is present among some clinicians at the student's practice site (M. Adams, personal communication, 2020). Donnino et al. (2011) cite establishment of pathways, gaining top-down support from hospital administration, and

developing partnerships with stakeholders in the ED and ICUs as potential methods to overcome these obstacles. Increasing data collection and feedback to stakeholders offers one way to evaluate and maintain the quality of the program. Furthermore, increasing staff and stakeholder awareness surrounding patient outcomes and adherence to protocols can help to build "buy-in," thus reducing skepticism and the related propensity to veer from the protocol. Lastly, it is the continual re-evaluation and sharing of lessons learned upon which the sixth step of the CDC Framework is built; knowledge and data sharing drive practice and practice changes for the improvement of patient outcomes.

Provide Annual Standardized Education for Nurses and Physicians. CCU nurses who participated in the stakeholder assessment reported that physician familiarity with the TTM protocol was both a facilitator and a barrier to optimal timing of TTM therapy. Cardiology fellows often drive the timeliness of CCU admissions and transfers from outside hospitals, place the intravascular catheter, and oversee resident management of patients. To this end, it is recommended that cardiology fellows be required to participate in an annual training that includes information on the necessity of timely induction of TTM, the TTM protocol, and strategies to improve care coordination to yield shorter durations to target cooling temperatures. This training should take place prior to the first-year fellows' initial rotation in CCU, ideally in the early fall months. Additionally, it is recommended that this annual TTM class be considered mandatory for Emergency Medicine residents and nurses, who drive the initial management of patients in the ED and who are responsible for timely consultation and communication with the ICUs.

Additional Areas of Stakeholder Interest. Stakeholder interest in patient survival data and the use of neuromuscular blocking agents (NMBA) led to additional data being collected in the EMR and synthesis of the results.

Patient Survival to Hospital Discharge. At the practice site, sixty-five percent of patients admitted to the CCU who underwent TTM therapy survived to hospital discharge. While assessments and data surrounding individual patients' neurologic function, functional capacity, and quality of life indicators were not available for review, this survival to discharge rate is notably higher than comparative data. The Advanced Resuscitation Cooling Therapeutics and Intensive Care (ARCTIC) program, which is a model comprehensive post-arrest program, is used at an academic medical center and Level I Trauma Center located in the same region as the student's practice site. That site reported that for patients who were treated under the ARCTIC protocol consisting of cooling techniques, survival to hospital discharge for patients was 49% in 2008-2009 (Kuttenkuler et al., 2009). Additionally, 2019 data from Cardiac Arrest Registry to Enhance Survival (CARES) showed that for patients admitted to the hospital following a cardiac arrest with an initial rhythm that was shockable and who underwent TTM, approximately 59% of patients were alive at discharge.

Use of Neuromuscular Blocking Agents. One use of NMBAs, or chemical paralytics, in the ICU setting is to stop shivering during TTM, as shivering is deleterious to the cooling process, in addition to the metabolic and neuroprotective benefits of TTM. Patients in whom shivering during hypothermia is refractory to titration of sedation, use of surface counter-warming with external forced warming blankets, and other pharmacologic agents (i.e. buspirone, meperidine, magnesium sulfate) may require the use of NMBAs. However, the use of NMBAs is not without significant risks and have been linked to potential adverse effects such as venous

thrombosis, patient awareness during paralysis, development of critical illness myopathy, autonomic interactions, and even residual paralysis following discontinuation of the NMBA use (Renew et al., 2020).

The Society of Critical Care Medicine (SCCM) clinical practice guidelines make no recommendation on the routine use of NMBAs in patients undergoing therapeutic hypothermia citing insufficient evidence as the reason; however, both the SCCM and AHA suggest that NMBAs may be used for the management of overt shivering in conjunction with analgesics and sedatives (Renew et al., 2020). It is not surprising, given the relative risk and lack of sufficient evidence for the routine use of NMBAs, that the stakeholder assessment yielded interest in the use of NMBAs. Since the use of chemical paralytics concurrent with TTM therapy in this evaluation was low at 22% of patients, this therapy should be tracked, due to the potential adverse effects, but does not appear to warrant any immediate change in practice.

Step 6: Ensure Use and Share Lessons Learned

The overarching focus of this step is for the evaluator and stakeholders to be prepared to disseminate the information, to continue the evaluation process in the midst of feedback and changes, and to follow-up by supporting others that may be involved in this ongoing evaluation process (Centers for Disease Control, 1999). Following complete data analysis, the doctoral student submitted the full paper, including an executive summary, to the doctoral advisor and practice mentor. The executive summary was shared with the TTM program coordinator, the CCU Medical Director, cardiology fellows, and CCU nursing staff with major findings and recommendations for improvement of the current state. Additionally, the executive summary and data was shared with the Chief of Emergency Medicine for dissemination to the Resuscitation Committee.

Strengths and Weaknesses of the Evaluation

This program evaluation has several notable strengths but is not without its weaknesses. First, the feedback from ten stakeholders was obtained. Stakeholders included training physicians, nurses with varying degrees of experience with TTM, attending physicians, and other TTM leaders to provide a wholistic representation of the lived experiences of those who engage with TTM most frequently. While a former nurse education coordinator for the ED was interviewed in the stakeholder assessment, there was no emergency medicine physician included in the stakeholder assessment. Emergency medicine physicians play a critical role in the initial stabilization of cardiac arrest patients and in consulting the intensive care unit(s), making them important stakeholders in the TTM process.

Chart review for each patient undergoing TTM at the practice site was performed in a systematic manner by one doctoral student reviewer; this provided for consistency in data extraction and management. For each of the questions answered through chart review, there were missing data points due to incomplete data in the electronic medical record for some patients. This is likely, at least in part, related to the difficulty of obtaining complete data for unwitnessed arrests and through bystander recall. The aim of this program evaluation was to review data and processes for patients admitted to the CCU; however, the practice site would benefit from future review of all patients managed with the TTM protocol admitted to the practice site, which include those admitted to the medical intensive care unit (MICU).

Nursing Practice Implications

The stakeholder assessment in this program evaluation revealed that nurse-driven, evidence-based protocols can lead to optimal patient outcomes in this low frequency, high impact therapy. Additionally, nurse champions involved in ongoing evaluation of practice-

related processes and patient outcomes will inform future practice site needs and will contribute to improved efficiency of TTM therapy at the practice site. Standardized, ongoing education for nurses and physicians offers one method to reduce TTM timing variability and increase adherence to the TTM protocol. Finally, interdisciplinary collaboration is an important aspect of TTM. Nurses and physicians must have open and ongoing discussions about barriers to optimal patient management. The development of guidelines by an interdisciplinary workgroup to drive initial diagnostic procedures and imaging offers one way to reduce the time to target temperature.

Conclusions

This program evaluation revealed that for patients admitted to the CCU at the practice site, current timing standards are being achieved. However, there are opportunities for improvement given the prevailing view that shorter durations to target temperature lead to improved outcomes, as well as the practice site's participation in a multisite clinical trial. The ED arrival-to-CCU admission provides a window of opportunity to improve process efficiency and reduce time to TTM initiation and time to target temperature. The familiarity of CCU nurses with the TTM protocols was cited as a significant facilitator to the optimal timing of TTM. Finally, stakeholders would benefit from regular review of outcomes to improve stakeholder buy-in and to support ongoing process improvement.

PRISMA Flow Diagram

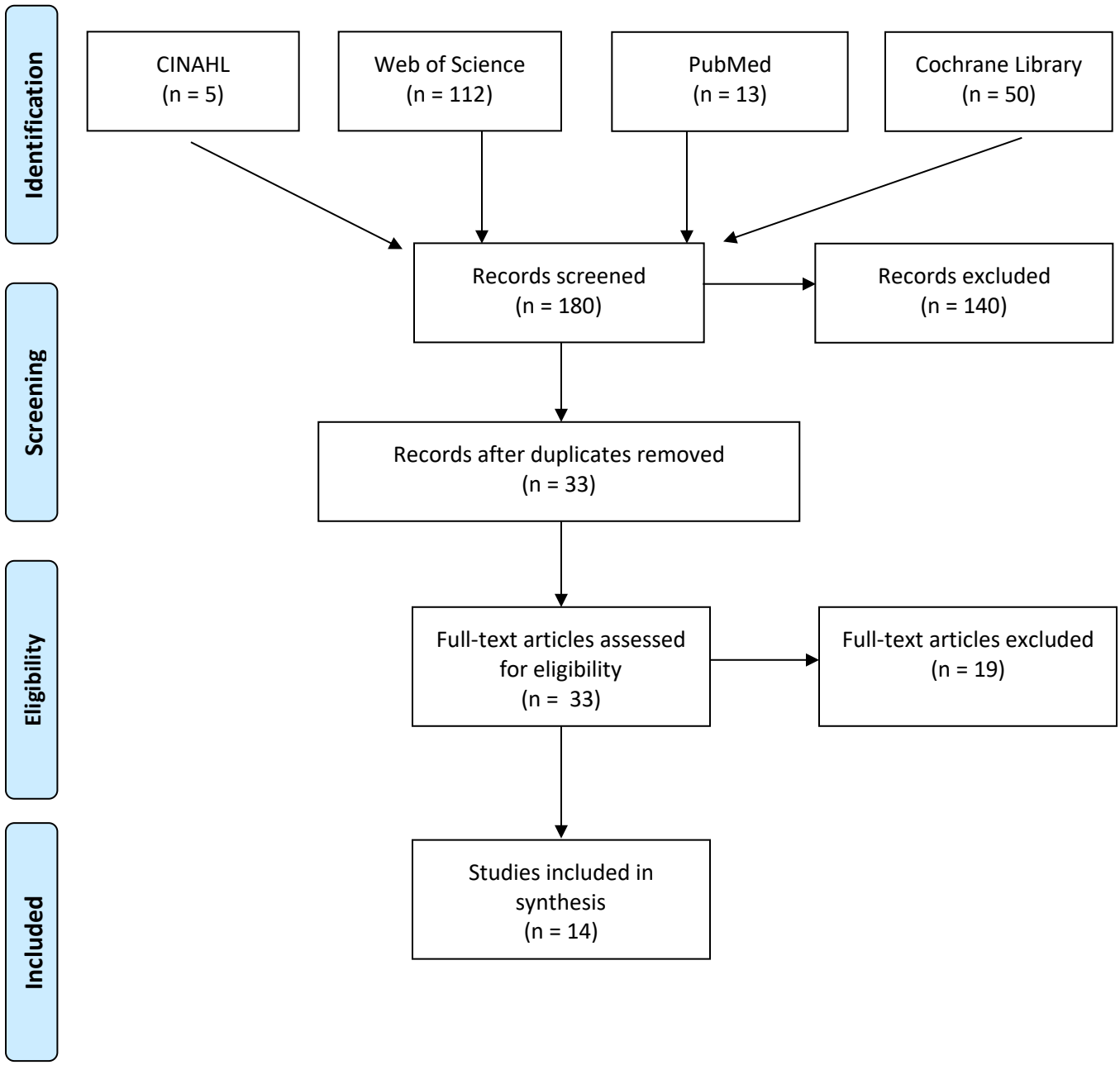

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for the systematic literature search process. CINAHL = Cumulative Index to Nursing and Allied Health Literature

Table 1

Table of Evidence

Author and Date	Evidence Type	Sample, Sample Size	Findings that help answer the nursing practice question	Outcome measures	Limitations	Evidence Level, Quality, Theme
Kim et al. (2014)	Randomized controlled trial	Adults experiencing an OHCA, n = 1359	Although use of prehospital cooling reduced core temperature by hospital arrival and reduced the time to reach a temperature of 34°C (by about 1 hour), it did not improve survival or neurological status among patients resuscitated from prehospital VF or those without VF.	Survival to hospital discharge, neurological status at discharge	1) Method of pre-hospital cooling (IV iced saline) may have had negative impact on survival, 2) Intervention group not only received iced saline, but also sedative and paralytic by EMS, 3) No mention of which systemic cooling method used beyond the initial iced saline	I, A; I
Nordberg et al. (2019)	Randomized controlled trial	Adults experiencing a witnessed OHCA, n = 677	Among patients with out-of-hospital cardiac arrest, although time to a core temperature of 34-degrees was significantly reduced, trans-nasal evaporative intra-arrest cooling compared with usual care did not result in a statistically significant improvement in survival with good neurologic outcome at 90 days.	Survival with good neurologic outcome at 90-days, survival at 90-days, time to reach goal temperature (34-degrees C)	1) Blinding of pre-hospital and hospital personnel was not achievable due to the intervention, 2) Many eligible patients were not included, and this may have introduced bias, 3) The study may have been underpowered, and a larger sample size may have been able to detect a statistically significant difference in the intervention vs control group.	I, B; I
Scales et al. (2017)	Randomized controlled trial	Adults experiencing an OHCA, n = 585	Pre-hospital cooling initiated 5 minutes after ROSC did not increase rates of achieving a target temperature of 32- to- 34-degrees C within 6 hours of hospital arrival but was safe and increased application of TTM in-hospital. Temperature at time of ED arrival was not significantly different between the intervention and control groups.	Rates of "successful TTM" defined as achieving goal temperature (32-to- 34- degrees C) within 6 hours of hospital admission/ED arrival; secondary outcome, survival with good neurological outcome	1) Not all patients received TTM in-hospital, 2) various methods of pre-hospital cooling used (ice packs, IV iced saline, wrist reminders), 3) Did not achieve goal sample size which may have caused it to be underpowered to detect small, but clinically significant differences between the two groups, 3) 16% of eligible patients were not included due to some paramedics declining	I, B; I

					participation in the study, 4)	
Schock et al. (2016)	Meta-analysis	13 randomized and observational studies on the use of TTM in adults were included; n = 4700 (among all studies combined)	The meta-analysis examined the time dependency of cooling in 4700 patients suggested that early and rapid cooling without the use of cold infusions is associated with superior outcomes as compared with delayed cooling or cold saline volume resuscitation. Rapid cooling to 32-34-degrees C is associated with superior outcomes as compared with delayed cooling to any temperature.	Favorable neurologic status as defined by CPC score of 1 or 2, time from ROSC to target temperature	1) As reported by the authors, the presence of significant uncontrolled and unidentified confounders cannot be excluded. 2) There is a lack of large rapid cooling investigations that may result in overstatement of the impact of rapid cooling.	II, A; I
Benz-Woermer et al. (2012)	Non-experimental	Adults experiencing an OHCA, n = 177	Time to target temperature was significantly shorter among non-survivors (200 min) vs. survivors (270 min). The time to target temperature was shorter in non-survivors, however no associations between outcome and the cooling rate was found.	Survival to discharge, CPC score at discharge and at 3 months	1) When adjusted for other known outcome predictors (time to ROSC, initial arrest rhythm), the authors found spontaneous admission BT was not independently associated with in-hospital mortality. 2) Only 22% of the sample were women.	III, B; II
Holm et al. (2020)	Quasi-experimental	Adult patients admitted to ICU following OHCA, n = 352	The initiation of TTM with cold IV fluids before ICU arrival did not decrease the TTT. We detected no significant between-group difference in mortality or the incidence of side effects according to the administration or not of pre-ICU cold IV fluids.	Incidence of side effects, survival	1) amount/volume of cold IV fluids not controlled, relied on clinician judgment, 2) Sample was taken from a RCT in which post-hoc analysis revealed current findings; the trial from which the data comes from examined the differences between 24- and 48-hours of cooling. This paper did not comment on how duration of hypothermia impacted outcomes in the pre-ICU fluids vs no pre-ICU fluids. 3) not described whether patients in the pre-ICU IVF not given group received IVF upon admission to ICU	II, B; II

Sendelbach et al. (2012)	Non-experimental	Adults experiencing a cardiac arrest , n = 172	This study demonstrated that delay in initiation of TH and 30 min delay in reaching target temperature were consistently associated with a CPC 3–5 (poor or deceased) versus CPC 1 (good) neurological outcome.	Neurologic function, reported as CPC score	1) Nearly 75% of those enrolled were males. 2) In some, but not all, cases cooling was initiated with ice packs prior to hospital arrival. 3) Multiple personnel reviewing charts to infer CPC scores from available data - interrater reliability unknown.	III, C; II
Lyon et al. (2010)	Non-experimental	Adults experiencing an OHCA, n = 164	Mean time to target temperature from ROSC was significantly longer (320 minutes) in those who survived to discharge versus time to target temperature (219 minutes) in those who did not survive to discharge. Mean time from ICU admission to target temperature was also significantly longer in those who survived to hospital discharge than those who did not.	Survival to hospital discharge, time to target temperature (<34 degrees C)	1) Major limitation was that patients who did not survive to ICU/did not undergo TTM protocol are included in the analysis. 2) Small "n" of patients that underwent TTM. Of the 183 included in the analysis, only 59 were admitted to the ICU for cooling.	III, C; II
Yochum and Utley (2017)	Quasi-experimental	Adults experiencing an OHCA, n = 20	Shorter induction times in the group that received TTM initiated in the ED was not associated with better rates of survival to discharge. Those in the postimplementation group who survived to discharge had a significantly shorter time from ROSC to initiation of TH than those who did not survive to discharge.	Survival to discharge, time to initiation of TTM	1) Short evaluation time and small sample size limit generalizability, 2) Measurements of temperature at time of ED arrival, time of ICU admission not reported - begs the question, how cool did the patients get in the ED vs those who were not cooled? 3) Multiple confounding variables/findings, including shorter arrest-to-ROSC times in those who survived to discharge	II, C; I
Choi et al. (2020)	Non-experimental	Adults experiencing an OHCA, n = 1326	The time to initiation of TTM did not differ significantly between those with good and poor neurological outcomes. The authors found that inter-hospital transfer after achieving ROSC showed no association with neurologic outcomes at 6 months in post-OHCA patients treated with TTM, even though	Neurologic function (CPC score) at 6-months post-arrest	1) Multicenter study, and article did not mention if TTM treatment protocols were standardized at the sites.	III, C; II

			TTM induction was delayed in transferred patients.			
Castren et al. (2010)	Randomized controlled trial	Adults experiencing an OHCA, n = 194	Median time to target temperature (core) of 34°C in the treatment group was 155 minutes (interquartile range 124 to 315 minutes) versus 284 minutes (interquartile range 172 to 471 minutes) in control patients	Survival to discharge, neurologic status (CPC score) at discharge	1) The present study was not powered to detect outcome differences. 2) Multicenter trial, where the in-hospital cooling and post resuscitation protocol was not standardized, and in-hospital temperatures were not recorded systematically, 3) Blinding to treatment group was not guaranteed in individual performing the discharge neurologic assessment	I, C; I
Ruivo et al. (2016)	Non-experimental	Adults experiencing an OHCA, n = 15	Time from collapse (CA) to initiation of TH was not significantly different between non-survivors and those who survived with good neurologic function.	Survival to discharge, neurologic status (CPC score) at discharge	1) Small sample, underpowered to detect differences in outcomes, 2) single-center, limited generalizability	III, C; I
Uray et al. (2015)	Non-experimental	Adults undergoing TTM following OHCA, n = 234	Target temperature was reached in 85 (66–117) min (prehospital) and in 135 (102–192) min (IH) after ROSC ($p < 0.001$). Favorable outcome was reached in 26.8% (prehospital) and in 37.0% (IH) of the patients ($p = 0.17$).	Good neurologic outcome at 12-months post-arrest, defined as a CPC score of 1 or 2, survival	1) Selection bias was evident in the pre-hospital cooling group, as only about 15% of ambulances transporting OHCA patients were equipped with surface cooling devices. 2) No data available about when external cooling devices were applied in the pre-hospital setting. 3) Pre-hospital esophageal temperature was not measured in the IH cooling group.	III, B; I
Perman et al. (2015)	Non-experimental	Adults experiencing a cardiac arrest , n = 322	Shorter induction times (defined as initiation of TTM to goal temperature) of TTM were associated with poorer neurologic status. Pre-induction time (time from ROSC to start of cooling) did not differ significantly	Good neurologic outcome with CPC score 1 or 2.	1) Retrospective analysis, no way to control the independent variable (induction time), 2) relied on data from chart and there was reportedly missing data, which included initial temperature	III, B; I

			from those with good neurologic outcomes and those with poor neurologic outcomes.		prior to iced saline administration	

Themes: 1= Impact of Time to Initiation of TTM; 2 = Impact of Time to Target Temperature of TTM

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[redacted] Therapeutic Hypothermia Clinical Timeline & Huddle Points

Cooling started **By any method**	**2-hour cooling huddle (Repeated every 2hr until goal temp reached)**	**Cooling Phase *** • Shivering managed • Electrolytes monitored every 4hr • Lactate monitored every 4hr x 4 • Sedation maintained until goal temp is reached. Then reduce sedation 50% per TTM order set.	**Controlled Rewarming Phase** • Electrolytes monitored every 4hr • Sedation maintained (no sedation interruption)	**Pt reaches 36.5° ** Thermogard XP™ remains on** *to actively maintain normothermia* • If applicable, stop paralytic. • Continue sedation wean.	**Thermogard XP™ placed in "standby"** to monitor patient temperature. If temp rises, consider 'Fever mode' immediately
24 hours from start of cooling*			**Approximately 14 hours**	**24 Hours****	**12 hours plus**
0:00	**02:00**	**24:00:00**	**38:00:00**	**62:00:00**	

* Cooling phase 'clock' starts with initial attempts to cool (pre-hospital, ED, ICU) by ANY method (iced NS infusion, ice bags, cooling blankets, etc.), not from the time the ICY catheter is inserted or goal temperature is reached. **However, clock may be 'reset' due to extenuating circumstances after team discussion.**

** Once patient is rewarmed to 36.5°, **DO NOT** change Thermogard XP™ console settings for **24 hours.** The patient is **actively** maintained for at least **24 hours** at this temperature.

2-Hour Cooling Huddle Guide

Goal Temperature Reached? (32-34°C)

YES → ☐ Document 2 temperatures
☐ Notify physician
☐ Continue following clinical timeline

NO →
☐ **Notify physician immediately**
☐ **DOCUMENT** (2 temperatures, 2 hour huddle, and physician notification)
☐ **Equipment troubleshooting**
- Ensure all input/output cables are connected properly and console is not in 'Standby'
- Ensure Thermogard™ is on 'Max' setting and that the visual flow indicator is spinning

☐ **Evaluate for other mechanical/technical issues**
- Call CCU (4-2582) with questions or page TTM Coordinator (PIC 3745)

☐ **Consider more aggressive cooling interventions; obtain appropriate orders**
- Additional chilled IVF
- Iced OG/NG tube lavage

☐ **Continue 2 hour huddles until goal temp is reached**

Created August 2013 by MICU TTM champions
Revised April 2015 [redacted]

Appendix B
Practice Site Clinical Decision Tool for Therapeutic Hypothermia

[redacted]

Clinical Decision Tool for Therapeutic Hypothermia

TITLE: Therapeutic Hypothermia following Cardiac Arrest

This is a:
✓ **Guideline** (recommended best practice)

OBJECTIVE:

Reducing brain temperature during the first 24 hours following resuscitation from cardiac arrest and closely managing temperature for 48 or more hours has a significant effect on survival and neurological recovery. The use of targeted temperature management (TTM) by inducing mild therapeutic hypothermia (TH) early after ischemic insult has been shown to decrease the severity of anoxic brain damage and to improve neurological outcomes. The patients who qualify for TH have suffered from a cardiac arrest, have had a return of spontaneous circulation (ROSC), and have no purposeful movements post arrest.

PATIENT POPULATION:

✓ Adult Critical Care
✓ Emergency Dept

PATIENT ASSESSMENT (and DOCUMENTATION)

Inclusion Criteria:

1. ROSC from cardiac arrest with ability to initiate therapy within 6 hours
2. No purposeful movements after ROSC
3. Age >18 years
4. Mechanically ventilated
5. Blood pressure can be maintained at ≥90 mm Hg systolic spontaneously or with fluid and/or a maximum of two vasoactive agents

Exclusion Criteria:

1. Alternative clinical conditions causing the patient to be comatose (i.e. drugs, sepsis, head trauma, stroke, overt status epilepticus)
2. Major trauma or <72 hours after major surgery*
3. Pregnancy in third trimester
4. Temperature of <30° C following arrest
5. Unstable blood pressure (MAP<60mm Hg for >30 minutes on vasopressor therapy) or ventricular rhythm unresponsive to therapy. The addition of a 3rd pressor or a 2nd pressor with mechanical circulatory support is generally considered too unstable to initiate therapy.
6. Known or preexisting coagulopathy (PTT >1.5 times upper limit of normal or active bleeding)
7. Cryoglobulinemia

*May consider therapy with a goal temperature **of** 35-36° C with attending physician approval

TREATMENT & MONITORING (and DOCUMENTATION)

Preparation:

1. MD/RN: Ensure use of this clinical guideline and the hypothermia order set in the EMR

2. RN: Obtain baseline labs (per hypothermia order set): BMP, Mg, Phos, CBC, PT/PTT, lactate

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6. Team: Cooling should continue for 24 hours from the **initiation of therapy**. This is a guideline, and can therefore be adjusted depending on patient circumstances such as prolonged time to goal temperature or significant interruption of therapy resulting in temperature rise. "Resetting the clock" requires a team decision and attending physician approval, as well as explanation in a progress note.

B. Medication: Shivering Prophylaxis (refer to Appendix C)
MD/RN: Initiate fentanyl and midazolam for synergistic shivering prophylaxis as follows:
   1. Fentanyl: 50 mcg IV bolus followed by a maintenance infusion of 25-100 mcg/hr
   2. Midazolam: 2 mg IV bolus followed by a maintenance infusion of 2 to 8 mg/hr

C. Shivering Management : refer to Appendix D
Team: Regular monitoring and aggressive treatment of shivering is vital. Besides the negative effects of heat generation, uncontrolled shivering can have significant, detrimental metabolic effects. Surface counterwarming (forced warm air) should be employed as soon as any shivering is noted.

Phase II-Rewarming/Maintenance: (Appendix B- UVAHS Therapeutic Hypothermia Clinical Timeline)

A. Begin rewarming once 24 total hours of cooling has occurred
   1. Use a slow rewarming approach of **0.25◦ C/hour** until the patient **reaches 36.5◦ C,** then…
   2. Maintain patient at 36.5◦ C with the intravascular temperature management (IVTM) system for at least 24 hours, then…
   3. Discontinue active temperature maintenance (place IVTM system in "standby") but continue monitoring temperature until stable for 48 hours. The ICY and Quattro catheters have an FDA-approved 4 day dwell time and can be used for fever management. Other physical and pharmaceutical measures may also be used to maintain normothermia.

B. Medication management (Appendix D)
   1. Discontinue neuromuscular blocking agent infusion (if used) at start of rewarming.
   2. Pharmacologic intervention may be necessary for shivering during the rewarming phase of therapy to prevent rapid rewarming and its sequelae (see Appendix D).
   3. Titrate analgesics and sedatives for patient comfort until patient is rewarmed to 36.5◦ C .

Monitoring/Documentation:

- RN: **Continuous temperature monitoring from two sources is required for the duration of therapy, including rewarming.** Display both temperatures on the bedside monitor (via the hospital monitor interface accessory) for any patient receiving therapy with an IVTM system.
- RN: Documentation of peri-arrest information, hourly BSAS values, and therapies must be entered in the TTM flowsheet.
- MD: Obtain neurology consultation and EEG monitoring when neuromuscular blockade is utilized or if status epilepticus is suspected.
- RN: Obtain labs q4 h during active cooling and rewarming (see order set in EMR)

Therapy Considerations:

- Therapeutic hypothermia is an urgent treatment priority post-cardiac arrest. Therefore, the benefits of any off-unit procedure or imaging should be carefully weighed against the interruption of cooling. If warranted, CT scan should be obtained prior to transfer to ICU.

[redacted]
Clinical Decision Tool for Therapeutic Hypothermia

- The management of electrolyte and acid base disturbances is essential. Serum potassium levels are monitored closely as the serum level will decrease during the cooling phase of management and increase during the rewarming period. A mild increase in lactic acid should also be expected.
- Glucose management: hypothermia causes increased insulin resistance, leading to elevated glucose levels. Follow ICU glucose management protocols.

PATIENT & FAMILY EDUCATION (and DOCUMENTATION)

Family education is located in the UVA Repository PE 01094.

POTENTIAL COMPLICATIONS (and DOCUMENTATION)

- Electrolyte shifts are expected and must be monitored per the process set forth earlier.
- Dysrhythmias possible:
  - -PR, QRS and QT interval prolongation
  - -Tachycardia (expected upon initiation)
  - -Bradycardia (expected as cooling progresses)
  - -Atrial fibrillation
  - -Very, very low risk of VT/VF with mild hypothermia (avoid overcooling)

.

HAND-OFF OF CARE / DISCHARGE / FOLLOW-UP CARE (and DOCUMENTATION)

- Patients will be transferred out of the ICU or discharged home dictated by clinical progression and overall health status as appropriate by clinical team
- Key information must be recorded in the EMR on the TTM flow sheet

OUTCOMES MEASURES

The goal of TTM is to discharge patients with neurological function equivalent to a CPC score of 1 or 2.

CLINICIAN EDUCATION PLAN:

*Nursing Education: New staff will attend a mandatory class presented by UVA TTM trainers. Trainers are selected by the TTM program coordinator.
*TTM nurse champions will be chosen and educated for each ICU. Those champions will serve as unit experts and provide updates to staff as new information is made available.
*Fellows-Cardiology/Pulmonary-Critical Care/Surgical/Neurosciences Education: TTM coordinator and/or TTM trainers will offer annual classes incorporating current evidence for hypothermia, clinical practice guideline and order set.
*Resident Education: Podcasts are available; in services done upon request.

ADDITIONAL INFORMATION:

DEFINITIONS:

TH: Therapeutic hypothermia is the induction and maintenance of a core body temperature between 32°-34° Celsius for the purpose of mitigating the neurologic sequelae of cardiac arrest
TTM: Therapeutic Temperature Management- collective term for several therapies, including TH
ROSC: Return of Spontaneous Circulation (ROSC)-return of perfusing rhythm following resuscitation from cardiac arrest

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RASS: Richmond Agitation Sedation Scale-used to evaluate presence of delirium and sedation level in ICU patients.
BSAS: Bedside Shivering Assessment Scale-used for hypothermic patients to assess shivering intensity (Appendix C).
CPC Scale: Cerebral Performance Category Scale-a scale in neurological medicine that grades a patient's functional capacity response on a scale of 1-5, 1 being a return to normal cerebral function and 5 is brain death. (Appendix B)

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DISCLAIMER:
Protocols contain a specific, established set of actions expected to be followed by clinicians. Guidelines provide evidence-based recommendations to assist practitioners in making decisions for patient care. However, guidelines and protocols are general and cannot take into account all of the circumstances of a particular patient. Judgment regarding the propriety of using a specific protocol or guideline with a particular patient remains with the patient's physician, nurse, or other health care professional, taking into account the individual circumstances presented by the patient. Care providers should document any deviations from protocol / guideline in the patient's electronic medical record, including the rationale for deviation.

REVISION HISTORY					
Date	Version	Description	Owner(s) Name, Credentials, Title	Committee Approval*	Date of Approval
12/2015			Mark Adams	Patient Care Committee	12/2015

***Adults-** Patient Care Committee approval is required if the guideline will be used in multiple areas or if the local area does not have a practice committee to approve the guideline. If approval is required through other committees (such as patient safety, infection control, etc), please list those committees and dates of approval as well.

***Pediatrics-** Children's Hospital Clinical Practice approval is required if the guideline will be used in multiple areas or if the local area does not have a practice committee to approve the guideline. If approval is required through other committees (such as patient safety, infection control, etc), please list those committees and dates of approval as well.

[redacted]

Clinical Decision Tool for Therapeutic Hypothermia

APPENDIX A: Clinical Timeline

Cooling started (by any method)	**Cooling Phase*** Shivering managed Electrolytes monitored q4hr Lactate monitored q4hr x4 Sedation maintained (no holiday)	**Controlled rewarming phase** Electrolytes monitored q 4hr Sedation maintained (no holiday)	Patient reaches 36.5 **	ThermoGard remains **on** to actively maintain normothermia Stop paralytic; begin sedation wean	ThermoGard placed in '**Standby**' to monitor patient temperature
24 hours from start of cooling*		Approx. 14 hours	**24** hours		12 hours +
0:00	24:00:00	38:00:00		62:00:00	

* Cooling phase 'clock' starts with initial attempts to cool (prehospital, ED, ICU) by any method (iced NS infusion, ice bags, etc.), NOT from time the IVTM catheter is inserted or goal temperature is reached.

** Once patient is rewarmed to 36.5, **DO NOT** change anything with ThermoGard console settings for **24** hours. The patient is actively maintained for at least **24** hours at this temperature.

[redacted]
Clinical Decision Tool for Therapeutic Hypothermia

APPENDIX B: SHIVERING MANAGEMENT

Bedside Shivering Assessment Scale (BSAS)

SCORE	*TYPE OF SHIVERING*	*LOCATION*
0	None	No shivering is detected on palpation of the masseter, neck, or chest muscles
1	Mild	Shivering localized to the neck and thorax only
2	Moderate	Shivering involves gross movement of the upper extremities (in addition to neck and thorax)
3	Severe	Shivering involves gross movements of the trunk and upper and lower extremities

[redacted]

Clinical Decision Tool for Therapeutic Hypothermia

Appendix C:

Cerebral Performance Categories Scale

CPC Scale

Note: If patient is anesthetized, paralyzed, or intubated, use "as is" clinical condition to calculate scores.
CPC 1. Good cerebral performance: conscious, alert, able to work, might have mild neurologic or psychologic deficit.
CPC 2. Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.
CPC 3. Severe cerebral disability: conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.
CPC 4. Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep/awake cycles. Cerebral unresponsiveness.
CPC 5. Brain death: apnea, areflexia, EEG silence, etc.

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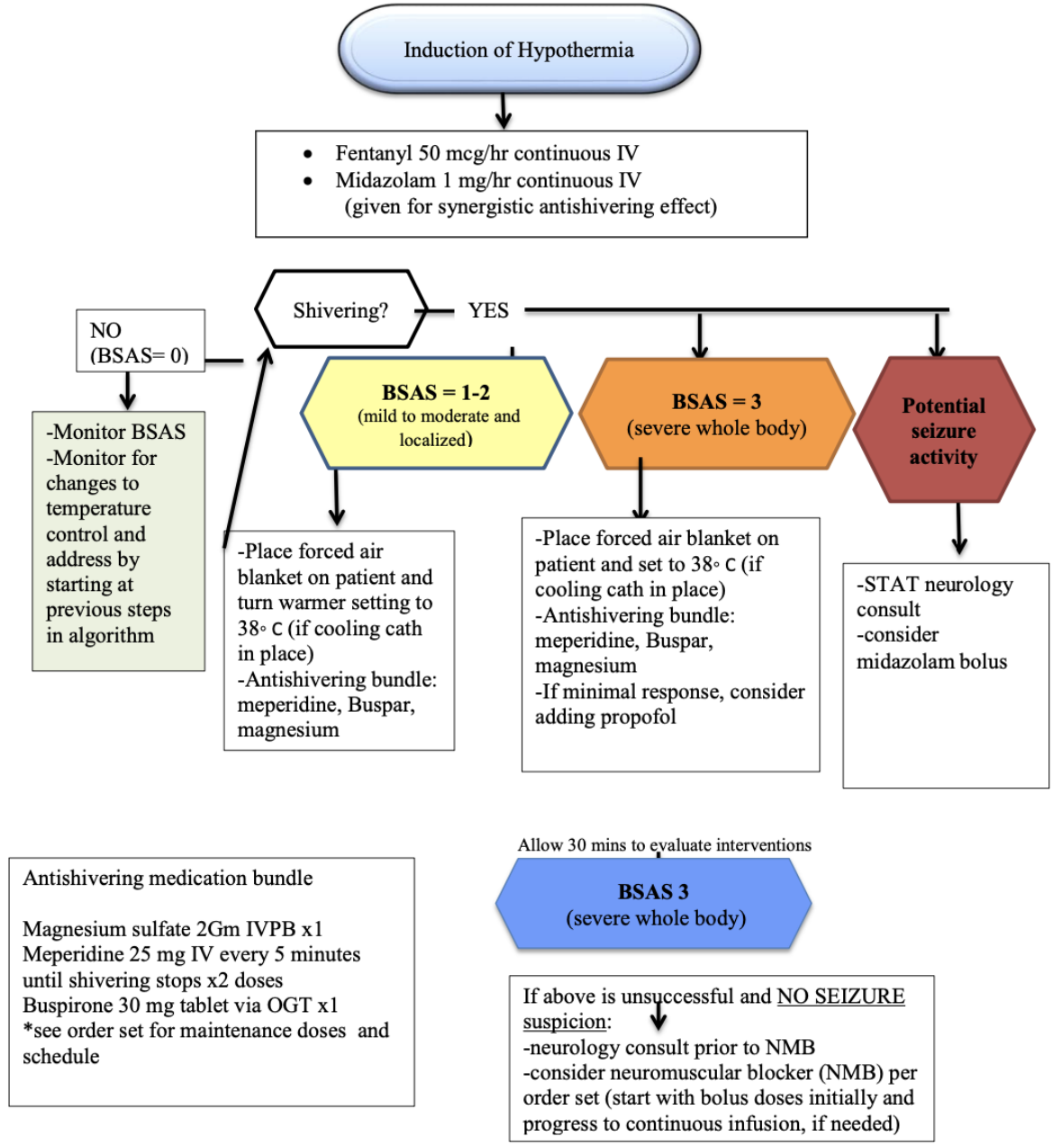
[redacted]
Clinical Decision Tool for Therapeutic Hypothermia

Appendix D: Shivering Prophylaxis / Pharmacological Management of Shivering



Appendix C
Institutional Review Board – Health Sciences Research (IRB-HSR) Determination Form

☒ **Project is determined to NOT meet the criteria of Research with Human Subjects or a Clinical Investigation and therefore is not subject to IRB-HSR Review.**

All project team personnel are required to follow all requirements described in this form and follow:

- *Procurement requirements if participants will be compensated for their time*
- [redacted]*Information Security policies to protect the data: See Appendix B: Privacy Plan.*
-

Pick One

☐ No health information/specimens are to be collected or used for this project

☒ Health information/specimens to be collected or used for this project meet the criteria of Deidentified under HIPAA (No identifiers as noted in Appendix A may be collected/ used.) If data/specimens are from dbGaP, keep Appendix C on file with your project documents and contact School of Medicine Office of Grants and Contracts to obtain an Agreement and a dbGaP Data Request Form/Institutional Certification.

☐ Health information collected meets the criteria of identifiable. Follow the Privacy Plan Appendix B.

☐ Health Information meets the criteria of Limited Dataset. HIPAA Data Use Agreement is required to share data outside of [redacted]. Complete Appendix E.

☐ Data/Specimens used in this project are coded: Complete Appendix D.

☒ Your project was determined to be non human subject research. If you decide to publish results of this project you must describe the project in the publication as non-human subject research and NOT as human subject research.

IF SENDING OR RECEIVING DATA/SPECIMENS

☐ Provide this signed form to School of Medicine Office of Grants and Contracts and/or Medical Center Procurement if your project has external funding or plans to share data/specimens outside of [redacted].

Contact the IRB if anything concerning this project changes that might affect the non-human subject determination.

☐ **Project is determined to be Human Subjects Research or a Clinical Investigation** and must be submitted to the IRB-HSR for review and approval prior to implementation. Please go the Protocol Builder to create your submission. [redacted]

Name of IRB Staff: _____	***Date:*** 10-06-20

Appendix D
A Program Evaluation of a Targeted Temperature Management Program at an Academic Medical Center
Executive Summary

A systematic program evaluation of the Targeted Temperature Management (TTM) program in the Coronary Care Unit (CCU) was performed utilizing the CDC 6-step framework; the focus was on the timing components of TTM. Following a stakeholder assessment, nine questions were answered through chart review of patients admitted to the CCU from 2018 to 2019. A total of 27 patients received TTM and were included in this evaluation.

A systematic review of the literature showed mixed results for shorter versus longer duration to initiation of TTM and time to target temperature from return of spontaneous circulation (ROSC). However, there is a prevailing view that shorter durations to target temperature lead to improved survival and neurologic function. Of note, the CCU team is participating in a multi-center RCT, called ICECAP, which tests the dose of cooling. This study protocol requires the time from arrest to target temperature to be less than 4 hours. Thus, there is a need to streamline processes and shorten times to target temperature following arrest.

Major Findings:

- Meets the current practice site standard of less than 6 hours from arrest to initiation of TTM (239 minutes)
- Average time from the time of arrest to the upper limit of the goal hypothermia range (34°C) is 339 minutes; this is significantly higher than the 240 minutes needed for inclusion in the ICECAP study
- Meets the current practice site standard of achieving goal temperature within 2 hours from initiation with the intravascular catheter (102 minutes)
- Average time from ED arrival to CCU admission is 114 minutes
- Majority of patients (65%) survive to hospital discharge
    - CDC/Emory 2019 data showed 59% survival at discharge
- Majority of patients (63%) undergo intracranial CT imaging prior to TTM
    - Comparable to other institutions
- Minimal use of continuous chemical paralytics at 22%
- Stakeholders report that CCU nurse and physician familiarity with the TTM protocol is a facilitator to optimal TTM timing

Recommendations:

6. Utilize surface cooling blankets in the ED for more rapid cooling initiation
7. Develop an algorithmic approach to determine which patients would benefit from intracranial CT imaging prior to initiation of TTM
8. Place TTM catheters in the CCU where trained medical and nursing personnel optimize protocol adherence
9. Identify an accountable person to conduct regular evaluations of TTM program outcomes
10. Provide annual standardized education for CCU nurses and physicians

April 21, 2021

Appendix E
Publishable Manuscript

Title: Targeted Temperature Management: Evidence and Evaluation of Timing

Corresponding Author: Hannah L. Kaylor, DNP, APRN, AGACNP-BC, Doctor of Nursing Practice Student, University of Virginia School of Nursing, 304.952.6337, hlk7v@virginia.edu

Author: Clareen Wiencek, PhD, RN, ACNP, Professor of Nursing, University of Virginia School of Nursing, 434.982.2890, caw2pa@virginia.edu

Author: Elizabeth Hundt, PhD, APRN, NP-C, ACNS-BC, Assistant Professor of Nursing, University of Virginia School of Nursing, 434.924.0130, eah8yc@virginia.edu

Acknowledgments: Special thanks to Mark Adams, MHA, RN for his dedication to the Targeted Temperature Management program and mentorship with this project.

Disclosures: There are no financial disclosures or conflicts of interest to report.

Abstract

In the United States, more than 350,000 cardiac arrests occur annually. Survival following an out-of-hospital cardiac arrest remains low. The majority of those who have return of spontaneous circulation will die due to complications of hypoxic-ischemic brain injury. Targeted Temperature Management (TTM) is the only recommended neuroprotective measure for those who do not regain consciousness following return of spontaneous circulation (ROSC). Many clinicians who engage with TTM operate under the notion that rapidity of cooling is of great importance to the preservation of neurologic function. Despite current practices, a review of the literature revealed that evidence surrounding the ideal time to achieve target temperature following ROSC remains equivocal. A systematic program evaluation of a TTM program at an academic center was performed; the focus was on timing components of TTM.

Keywords: cardiac arrest; timing; temperature; ROSC; evaluation

Introduction and Background

Cardiac arrest remains a public health problem in the United States and beyond. Globally, mortality from cardiac arrest is higher than colorectal cancer, breast cancer, prostate cancer, influenza, pneumonia, auto accidents, HIV, firearms, and house fires combined.[1] In the United States, more than 350,000 out-of-hospital cardiac arrests (OHCA) occur annually. Survival from an OHCA ranges from 2% to 11%.[1]

Cardiac arrest occurs when there is an abrupt loss of heart function. There are a multitude of risk factors for cardiac arrest, including cardiomyopathies, coronary artery disease, severe electrolyte abnormalities, medications, and recreational drug use. The intrinsic loss of cardiac electrical activity results in cessation of the mechanical "pumping" of the heart; this is the normal process for delivering oxygen-rich blood throughout the body. The loss of perfusion to vital organs, including the heart, brain, and lungs, occurs instantaneously.

There has been an increased emphasis on public health education surrounding the importance of early bystander cardiopulmonary resuscitation (CPR). The treatment goals of an OHCA remain initiation of the emergency help chain by calling 9-1-1, defibrillation with an automated external defibrillator (AED), if available and if indicated by the presenting rhythm, and high-quality chest compressions. Many factors related to intra-arrest care impact the prognosis for those who experience a cardiac arrest. These factors include time from collapse to the start of CPR/defibrillation, quality of the CPR/defibrillation, and whether the person has responsiveness, indicating neurologic function, during or immediately after CPR.[2]

Post-arrest management following return of spontaneous circulation (ROSC) is aimed at hemodynamic stabilization, determining why the individual arrested and taking corrective measures to help prevent another arrest, and assessing and preserving neurologic function. Post-

anoxic brain injury is the most dramatic complication of cardiac arrest. About 80% of patients who have had an OHCA will be comatose following ROSC. Moreover, about two-thirds of these patients will die from the complications of the hypoxic-ischemic brain injury that ensues during cardiac arrest.[3] Current guidelines recommend performing neuroprognostication no earlier than 72 hours following ROSC in those who do not receive therapeutic temperature management and no earlier than 72 hours following rewarming in those who do receive targeted temperature management.[4] Elimination of confounding factors when assessing in-the-moment and projected long-term neurologic function is of the utmost importance.[3]

While determining a cardiac arrest survivor's prognosis, especially when considering withdrawal of life-sustaining treatments, is complex, certain variables can help guide care decisions. The American Heart Association (AHA) describes prognosis in terms of the individual's before-, during-, and after-arrest factors.[2] Individual factors before cardiac arrest that impact prognosis include age, ethnicity, and comorbidities (chronic kidney disease, heart failure, etc.). Intra-arrest factors include arrest rhythm (shockable versus non-shockable), time from collapse to start of CPR/defibrillation, the quality of CPR/defibrillation, and what the person's neurologic function is during or immediately following CPR.[2] In those patients who undergo Targeted Temperature Management following a cardiac arrest, a validated scoring system for early stratification of neurologic outcome exists. The scoring system, called C-GRApH, uses objective patient data available at hospital presentation to predict neurologic outcome. The C-GRApH score ranges from 0 to 5 using equally weighted variables: (C): coronary artery disease, known pre-arrest; (G): glucose >/= 200 mg/dL; (R): rhythm of arrest not ventricular tachycardia/fibrillation; (A): age > 45 years; (pH): </= 7.0.[5] A high score is associated with worse neurologic outcomes, whereas a lower score is associated with favorable neurologic

outcomes. This scoring system brings variables from the different stages of the peri-arrest period together to predict neurologic outcome.

Targeted Temperature Management (TTM), previously referred to as induced hypothermia, is the only neuroprotective measure recommended following OHCA.[6] While TTM is a complex intervention, the overarching goal of TTM is to reduce anoxic brain injury thereby improving neurologic function following cardiac arrest. Cerebral perfusion is driven by the cerebral metabolic rate. For every 1-degree Celsius drop in body temperature, the cerebral metabolic rate decreases by about 6% to 7%, thereby reducing oxygen demand. Moreover, the hypothermia-induced reduction in cerebral oxygen demand leads to a preservation of autoregulation. Hypothermia is known to decrease the release of reactive oxygen species (ROS), nitric oxide, and excitatory amino acids and glutamate, all of which are toxic to neurons and can lead to neuronal injury or death.[7]

In the sub-acute phase of neuronal injury, one of the major protective effects of hypothermia on cerebral blood flow and oxygen demand appears to be a decrease in hyperemia following reperfusion. As is the case with cardiac myocytes, reperfusion injury and subsequent inflammation following an insult to brain tissue can lead to neuronal death and/or cell stunning. Hypothermia helps attenuate reperfusion injury, inflammation, edema, and neuronal apoptosis.[7]

In 2002, two landmark TTM trials were published that greatly influenced management of the post-arrest patient. Bernard et al. showed that treatment with moderate hypothermia (33-degrees Celsius), compared with normothermia (37-degrees Celsius), improved outcomes in patients with coma after resuscitation from out-of-hospital arrest.[8] The Hypothermia after Cardiac Arrest Group conducted a multi-center, randomized, controlled trial which showed patients who were successfully resuscitated after cardiac arrest due to ventricular fibrillation and

underwent mild hypothermia had an increased rate of favorable neurologic outcomes and reduced mortality compared to those who remained normothermic after cardiac arrest.[9] In each of these studies, external cooling methods by either ice packs or cooling blankets were used to achieve and maintain hypothermia.

Nielsen et al. published findings from an international, multicenter, randomized trial which compared mortality and neurologic outcomes in OHCA survivors.[10] The results from the trial created skepticism surrounding the utility of TTM, as the authors reported no benefit was conferred when hypothermia at 33-degrees Celsius versus 36-degrees Celsius was implemented. Mortality was the primary endpoint, and neurologic function, as measured by the Cerebral Performance Category (CPC) scale and modified Rankin scale, were secondary outcome measures. TTM "supporters" argued that the results reported by Nielsen et al. may have been impacted, in part, due to the high heterogeneity of the study sample, the short resuscitation time, and the rapid rewarming period.[6]

TTM continues to be supported as the standard of care for post-cardiac arrest patients who do not regain consciousness after ROSC by the AHA and the Society for Critical Care Medicine (SCCM). In 2015, the AHA published updated guidelines for the management of the post-cardiac arrest patient. In these guidelines, the authors assert that TTM does seem to confer benefit. However, the guidelines widened the goal target temperature range of 32-degrees Celsius to 36-degrees Celsius. Patients should be maintained at a constant temperature in this range, which would largely be based on clinician preference, for at least 24-hours.[4]

In 2009, five professional societies issued a consensus statement recommending that "targeted temperature management" replace what had previously been referred to as "therapeutic hypothermia."[11] The overarching reason for this change in terminology was an acknowledgement

that TTM encompasses more than just the period of hypothermia. TTM acknowledges that other components, such as induction of cooling, mode of cooling, and rate of rewarming, may have a great impact on patient outcomes. Thus, the concept of high quality TTM has evolved in the last decade. Today, while evidence surrounding certain components related to the quality of TTM remains insufficient, programs employ methods based on what is known from the available evidence.

While there is a lack of good-quality evidence on the matter of precise timing of TTM, it is generally regarded that induction of hypothermia should be as soon as possible thereby minimizing long-term neurologic injury following ROSC. Several studies have shown no improvement in outcomes in those treated with cooled saline delivered intravascularly during CPR or during pre-hospital transport.[6] Based on the available evidence, the 2015 AHA guidelines recommend against pre-hospital cooling of patients with rapid infusion of cold IV fluids. The AHA does not, however, include a goal time for induction of hypothermia in the most recent guidelines.[4]

Following at least a 24-hour period of "goal temperature," rewarming should be slow and controlled. To achieve this slow, controlled rewarming, a TTM device that allows for precise and accurate temperature management may be ideal. Often this involves using either an intravascular catheter or an external device that can achieve central cooling to goal temperature quickly and then be used to gradually rewarm the patient at a preset rate of 0.15 to 0.25 degrees Celsius per hour.[6]

Given the global impact of and the significant morbidity and mortality associated with cardiac arrests, TTM exists as an intervention to improve neurologic outcomes in some patients. There has been debate in the last two decades regarding whether normothermia is just as

effective as hypothermia at preserving neurologic function in the post-arrest patient.[6] However, the use of TTM continues to be supported by the AHA and SCCM as evidence-based therapy following cardiac arrest. As such, many academic medical centers and community hospitals offer this therapy.

The TTM program at the doctoral student's practice site began in 2007 and has been the clinical standard of care for comatose patients with ROSC after a cardiac arrest event. However, no systematic program evaluation has been conducted since the program was implemented in 2007. Thus, the purpose of this DNP project was to complete a program evaluation of the TTM program with a focus on the timing components of TTM. While the focus of the program evaluation was on the various timing components of TTM, successes and opportunities for improvement, with stakeholder input, were also evaluated.

Review of Literature

The purpose of this evidence-based review of the literature was to answer the nursing practice question: In comatose adult survivors of cardiac arrest undergoing TTM, what is the ideal timing to achieve target temperature following ROSC to yield optimal survival and/or neurologic function?

Search Methods

A systematic literature review of peer-reviewed academic journal articles published was conducted to explore the impact of timing to goal temperature in cardiac arrest patients undergoing targeted temperature management. Four databases were searched: PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, and the Cochrane Library. The search key words included *cardiac arrest, timing, temperature, and*

ROSC, and were combined with the AND Boolean operator in each database search: *cardiac arrest* AND *timing* AND *temperature* AND *ROSC.* Fourteen articles were retained for analysis. Figure 1 shows the search process, using a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Analysis

The articles retained for review showed mixed results for shorter versus longer duration to initiation of TTM and time to target temperature from ROSC. A variety of designs were reviewed, including four randomized controlled trials (RCT), one meta-analysis, two quasi-experimental studies, and multiple non-experimental studies. Utilizing the Johns Hopkins Evidence Based Practice evidence appraisal tools, each article was rated for quality and level of evidence. Overall, there was an adequate representation of higher and lower levels and quality of evidence in the present review.

Of the articles included in this review, timing related to TTM was evaluated using several outcome measures, including survival to discharge and neurologic function, which was most often categorized by the Pittsburgh Cerebral Performance Category (CPC) score. Of note, CPC scores range from good cerebral performance (1) to brain death (5). Favorable neurologic outcome is most often defined as a CPC score of 1 or 2.[12] While several articles reported additional outcome measures, this review focused on timing's impact on survival, mortality, and neurologic function. Aside from the outcome measures, several key themes appeared through review of the search articles. A thematic analysis was performed based on two key themes that included time to target temperature and time to initiation of TTM.

Impact of Time to Initiation of TTM

Kim et al. conducted a RCT in adults with cardiac arrest to assess the effect of pre-hospital induction of mild hypothermia on survival and neurologic status.[13] The authors showed that those receiving chilled saline in the pre-hospital setting had significantly lower core temperatures by hospital arrival. Additionally, these patients also had a reduction in time to reach target temperature (34-degrees Celsius) of about one hour from those who only received in-hospital cooling. However, the group receiving pre-hospital cooling did not have improvement in survival and neurologic function at discharge. The authors noted that those in the intervention group experienced more pre-hospital re-arrest events and required more diuretic use in the first 24 hours of hospital admission. One notable limitation of this study was that those receiving the pre-hospital iced saline also received sedatives and paralytics as a rule by emergency medicinal personnel. The administration of sedatives and paralytic agents may have impacted the time to goal temperature in the intervention group. Additionally, the authors did not describe the in-hospital cooling protocol that was utilized.

Another RCT utilizing pre-hospital, intra-arrest cooling via a trans-nasal evaporative device was conducted in adults following a witnessed out-of-hospital cardiac arrest. The authors showed that while time to reach a core temperature of 34-degrees Celsius was significantly reduced, the intra-arrest cooling, compared to usual care, did not result in a statistically significant improvement in survival with good neurologic outcome at 90-days post-arrest.[14] The time from collapse to target temperature was 105 minutes in the intra-arrest cooling group versus 182 minutes in the control group. The authors note that the study may have been underpowered, and as such, a larger sample size may have been able to detect significant between-group differences. Similarly, Castren et al. reported comparable findings from their analysis of part of the same sample as Nordberg et al.[14, 15] Castren et al. also showed a significant reduction in

median time to target temperature with the use of the intra-nasal, intra-arrest cooling device. However, there were no significant differences in early nasal cooling and survival or neurologic outcomes.[15]

In an RCT, Scales et al. evaluated the impact of pre-hospital cooling initiated five minutes after ROSC on the time to reach the target temperature range (32-to-34-degrees Celsius).[16] The pre-hospital cooling group did not have significantly higher rates of achieving the target temperature range within the 6-hour goal time; however, the authors noted that pre-hospital cooling was associated with increased application of in-hospital TTM. One important limitation was that not all patients received TTM in the hospital. This has serious implications for the nursing question at hand, as the lack of in-hospital TTM would be very likely to impact survival with good neurological outcome based on the available evidence. Additionally, 16% of eligible participants were not included due to a lack of willingness of some paramedics to participate, which may have created selection bias. Scales et al. notes they did not achieve the goal sample size and that the study may have been underpowered to detect small, but clinically significant differences between the groups.[16]

Uray et al. conducted a retrospective, single center cohort study to test the long-term outcomes associated with using a surface cooling device applied in the pre-hospital setting.[17] The control group was cooled with the same device following hospital admission. Between-group hospital admission temperatures differed significantly, with those in the pre-hospital cooling group arriving with a mean temperature of 35.2-degrees Celsius versus 35.8-degrees Celsius in those who received cooling following emergency department (ED) arrival. Favorable outcomes, defined as CPC score of 1 or 2 at 12-months post-arrest, were 26.8% (pre-hospital) and 37% (in-hospital), but these differences were not significant. Similar to Scales et al., selection bias was

evident in the pre-hospital group, as only about15% of ambulances that served the catchment region were equipped with the surface cooling devices.[16, 17]

Yochum and Utley looked at survival to discharge and time to initiation of TTM as outcome measures.[18] Their sample was small, with a sample size of 20. However, they showed that creation and implementation of an ED protocol for TTM significantly decreased the time from ROSC to initiation of cooling. These shorter induction times of TTM in the ED were not associated with significant improvements in better rates of survival at discharge. There were multiple limitations with this study, namely the small sample size and limited generalizability. Additionally, measurements of temperature at the time of ED arrival and time of ICU admission were not reported.

Perman et al. reported that shorter induction times using chilled IV fluids, defined as initiation of TTM to goal temperature, were associated with significantly poorer neurologic status.[19] The author also found that age at time of cardiac arrest, initial shockable rhythm, and downtime in minutes were significantly associated with neurologic outcome. This was a retrospective analysis, and as such, one limitation is that there is no way to control the independent variable (induction time). Additionally, the authors reported that data was obtained from chart review and there were gaps in data when it could not be sufficiently accessed.

Ruivo et al. showed that in a small sample (n = 15) of adults experiencing out-of-hospital cardiac arrest, the time from collapse to initiation of TTM was not significantly different between non-survivors and those who survived with good neurologic function.[20] Given the sample size and that the study was conducted at a single center, generalizability is low.

Impact of Time to Target Temperature

Schock et al. conducted a meta-analysis that resulted in the inclusion of 13 randomized

and observational studies looking at the use of TTM in adults.[21] The authors showed that early, rapid cooling without the use of cold intravascular infusions was associated with superior outcomes as compared with delayed cooling or cooling with cold saline. Interestingly, this meta-analysis showed that neurologic outcomes were similar over the 4-to-8-hour range of time delay from ROSC to target temperature. The authors suggested a stepwise improvement in outcomes for times to target temperature below 3 hours, supporting the theory that there is an improved activation of neuroprotective mechanisms if induction of cooling is completed within this window.[21] The limitations were reported to include the presence of potential significant uncontrolled and unidentified confounders.

Benz-Woermer et al. examined admission body temperature in survivors versus non-survivors.[22] Non-survivors had significantly lower spontaneous body temperatures than did survivors. Given this finding, time to target temperature was significantly shorter among the non-survivors. While time to target temperature was shorter in non-survivors, no association between the rate of cooling and survival at discharge was found. Similarly, there was no association between CPC score at discharge or at 3 months. The generalizability of this study is limited given that only 22% of the sample were women.

Holm et al. sought to evaluate the impact of pre-ICU cooling using cool IV fluids on the time to target temperature.[23] The median time to target temperature from ROSC was 318 minutes in the pre-ICU cold intravenous fluids (IVF) group versus 281 minutes in the cold IVF not given group. This finding, however, was not statistically significant. There were no significant differences in incidence of harmful side effects in the cold IVF group. There were significant limitations including that the amount of IVF given to the intervention group was not standardized.

Sendelbach et al. assessed differences in CPC scores in patients who received therapeutic hypothermia post-cardiac arrest by time to initiation, time to target temperatures, and duration of therapeutic hypothermia.[24] CPC scores were gathered at three time points: transfer from ICU, discharge from hospital, and post discharge. This study demonstrated that a delay in initiation of therapeutic hypothermia and a delay in reaching target temperature were consistently associated with a poorer CPC score (3-5). Upon initiating cooling, a delay in reaching target temperature of 30 minutes was associated with worse outcomes.

In contrast, Lyon et al. showed that mean time from ROSC to target temperature was significantly longer (320 minutes) in those who survived to discharge versus those who did not survive to discharge (219 minutes).[25] One of the major limitations of this observational study was that approximately 64 percent of those patients enrolled, and for whom data was reported, were pronounced dead prior to TTM being initiated in the ICU. This, alone, distorts the data related to neurologic outcome and mortality because not all patients actually underwent TTM.

Finally, a 2020 article by Choi et al. looked at the impact of inter-hospital transfers on patient outcomes given the delay in initiation of TTM that a transfer could result in.[26] The authors found that time to initiation of TTM did not differ significantly between those with a good or poor neurologic outcome. Despite finding that inter-hospital transfer did result in a delay to initiation of TTM, neurologic outcomes at 6-months post-OHCA were not associated with time to initiation. Additionally, Choi, et al. found that time to target temperature was longer in the good neurological outcome group than in the poor neurologic outcome group.[26] One limitation of this study was that standardization of TTM protocols across the various hospitals of this multi-center study was not detailed. Variation among TTM protocols could have been associated with neurologic outcomes and survival.

Publication Bias Check

There was no evidence of significant publication bias based on the gray literature, and findings were consistent with the themes in this systemic review.

Limitations of the Literature Review

In post-arrest care there can be significant gaps in the available data and standardization of care due to the nature of the circumstances that surround a cardiac arrest. For example, timelines are often blurry at best, most especially if the patient has suffered an unwitnessed arrest. In this case, it is difficult to quantify "downtime." Secondly, due to variations in EMS transport time, as well as hospital-specific resources and protocols, timing to initiation and target temperature can differ greatly among patients undergoing TTM.

Additionally, the articles represented in this review of the literature used similar outcome measures; however, time at which CPC scores were measured did vary among these articles. TTM protocols, which drive target temperature and method of cooling, differ among hospitals. Several articles were underpowered to detect meaningful differences in outcomes. Lastly, no RCTs were identified that specifically tested time to initiation of hypothermia or time to target temperature as the independent variable. This meant that the primary outcomes of timing were associative in many of these articles.

Conclusion

In comatose adult survivors of cardiac arrest undergoing TTM, data surrounding the nursing practice question, 'What is the ideal timing to achieve target temperature to yield optimal survival and neurological function following ROSC?' remains equivocal. In contrast with traditional thoughts and accepted practices, many of the articles supported that longer times to initiation of cooling and time to target temperature were associated with better neurologic

outcomes at hospital discharge and beyond.[27] However, several studies supported that shorter times to initiation and target temperature were associated with improved survival and neurologic outcomes. Further randomized controlled trials testing timing as the independent variable may be warranted in the future to clarify this important nursing practice question.

Project Purpose

The purpose of this project was to perform a systematic evaluation of a TTM program at an academic medical center. The results of this program evaluation will be utilized to inform practice and potentiate practice changes. The CDC provides a Framework for Program Evaluation in Public Health which was utilized in the present evaluation. There are six key steps in the CDC framework: 1) engage stakeholders; 2) describe the program; 3) focus the evaluation design; 4) gather credible evidence; 5) justify conclusions; and 6) ensure use and share lessons learned.[28]

Step 1: Engage Stakeholders

Post-cardiac arrest patients who require TTM are most often admitted through the Emergency Department (ED) for stabilization and then transferred to the Coronary Care Unit (CCU) for ongoing management. Stakeholders from across the care continuum, from the ED to the CCU, and from various disciplines, from registered nurses (RN) to medical trainees to attending physicians, were included in the stakeholder assessment to capture the lived experiences of a range of professionals who routinely engage with TTM therapy. In total, ten stakeholders were interviewed. The following questions were asked of each stakeholder.

What are barriers to optimal timing of TTM? The major themes identified were: determining whether a patient meets the criteria for TTM therapy; limited resources available to

effectively cool patients in the ED; where and when the intravascular cooling catheter is placed; differences in protocols and decisions to cool among critical care units or services; time required for transfer of a patient presenting to an outside hospital; and, coordination of tests and imaging prior to CCU admission.

What are facilitators to optimal timing of TTM? The major themes identified were: staff familiar with and knowledgeable of TTM protocols; utilization of a protocol; tests and imaging performed prior to CCU admission; early decision making regarding whether to cool a patient; and, early deployment of alternative cooling methods in the pre-hospital and ED settings. Based on question 1 and question 2, an additional question was added for systematic review in the EMR to assess how often patients underwent intracranial CT imaging prior to initiation of TTM with the intravascular catheter.

What elements and outcomes of the program are currently being systematically recorded and routinely reviewed*?* The major themes identified were: cGRAPH scores; survival and disposition at discharge; [stakeholder] uncertainty regarding elements and outcomes being routinely reviewed; and, elements of timing (i.e. time at target temperature, time to goal temperature, etc.). Based on stakeholder feedback to this question, survival to hospital discharge was reviewed for each patient in the EMR to assess outcomes in patients having received TTM therapy.

Are there any elements or outcomes of the TTM program in need of systematic evaluation? The major themes identified were: use of paralytics during TTM therapy; coordination and timing of patient transfer from the ED to CCU; time [from admission] to cooling; and, whether standard work and protocols are being adhered to. Based on stakeholder

feedback to this question, additional information in the EMR was reviewed to assess for the frequency of the use of continuous paralytic use concurrent with intravascular TTM.

Step 2: Describe the Program

The Donabedian Method, a conceptual model to evaluate the interconnectedness of a program's structure, processes, and outcomes, was used to describe the TTM program at the practice site.

Step 3: Focus the Evaluation Design & Step 4: Gather Credible Evidence

The identified questions (Step 3) were answered through systematic review (Step 4) of the EMR and TTM-specific data related to timing of TTM at the doctoral student's practice site from January 2018 to December 2019. During this time period, thirty patients underwent TTM therapy. Three of the thirty patients were excluded from the analysis due to in-hospital cardiac arrest (2) and the inability to place an intravascular cooling catheter (1). Of the twenty-seven remaining patients who underwent TTM therapy via the intravascular cooling catheter, the average age was 59 (36-81) years, and they were predominantly males (78%). Twenty-two (81%) patients presented to the ED via Emergency Medical Services (EMS); whereas the remaining five (19%) were transferred from an outside hospital.

Question 1. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of arrest to initiation of TTM via the intravascular cooling catheter?

Of the 21 patients undergoing TTM therapy for which data was available, the average time from arrest to the initiation of TTM via the intravascular cooling catheter was 239 (139 - 463) minutes.

Question 2. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of arrest to the upper limit of the goal hypothermia range (34-degrees Celsius)?

Of the 22 patients undergoing TTM therapy for which data was available, the average time from arrest to the upper limit of goal hypothermia (34-degrees Celsius) was 339 (84 – 750) minutes.

Question 3. How often are attempts by any method of cooling (iced NS infusion, ice bags, cooling blankets, etc.) initiated prior to placement of the intravascular cooling catheter?

Nineteen (70%) received attempts at cooling (iced NS infusion, ice bags, cooling blankets, etc.) prior to the placement of the intravascular cooling catheter.

Question 4. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of initiation of TTM via the intravascular cooling catheter to the upper limit of the goal hypothermia temperature range (34-degrees Celsius)?

Of the 26 patients undergoing TTM therapy for which data was available, the average time from initiation of TTM via the intravascular cooling catheter to the upper limit of the goal hypothermia temperature range (34-degrees Celsius) was 102 (14 – 287) minutes.

Question 5. In patients admitted with OHCA undergoing TTM therapy, what was the average time from the time of initiation of TTM via any cooling method (iced normal saline infusion, ice bags, cooling blanket, intravascular cooling catheter, etc.) to the upper limit of the goal hypothermia temperature range (34-degrees Celsius)?

Of the 25 patients undergoing TTM therapy for which data was available, the average time from initiation of TTM via any cooling method to the upper limit of the goal hypothermia temperature range (34-degrees Celsius) was 196 (14 – 360) minutes.

Question 6. In patients admitted with OHCA undergoing TTM therapy, what was the average time from ED or outside hospital (OSH) admission to CCU admission?

Of the 24 patients undergoing TTM therapy for which data was available, the average time from ED or OSH admission to CCU admission was 121 (44 – 317) minutes.

In patients who first arrived at the ED at the student's practice site, the average time from ED arrival to CCU admission was 114 (44-210) minutes. For those patients who were first treated at an OSH, average time from OSH arrival to CCU admission was 196 (75-317) minutes.

Question 7. In patients admitted with OHCA undergoing TTM therapy, how many patients survived to hospital discharge?

Of the 26 patients undergoing TTM therapy for which data was available, 17 (65%) patients survived to hospital discharge.

Question 8. In patients admitted with OHCA undergoing TTM therapy, how many underwent intracranial imaging with a CT of the head prior to TTM initiation via the intravascular cooling catheter?

Of the 27 patients undergoing TTM therapy, seventeen (63%) underwent intracranial imaging with a CT of the head prior to the initiation of TTM with the intravascular cooling catheter.

Question 9. In patients admitted with OHCA undergoing TTM therapy, how often were continuous chemical paralytics utilized?

Continuous chemical paralytics were utilized concurrent with TTM therapy in six (22%) of the 27 patients included in this review.

Step 5: Justify Conclusions

The average time from arrest to the initiation of TTM via the intravascular cooling catheter was 239 minutes. At present, the TTM protocol holds that cooling via the intravascular cooling system should commence within six hours of the patient's cardiac arrest; this metric is being achieved. Moreover, the time from initiation of TTM with the intravascular cooling catheter to 34-degrees Celsius was 102 minutes, which is also meeting the site's goal of less than 120 minutes.

The impact of time from arrest to initiation of cooling has not been well elucidated; this was supported by a systematic review of the literature. However, there is limited data to suggest that the risk of death increases for every hour initiation of cooling is delayed.[29, 30] Furthermore, many clinicians who engage with TTM operate under the notion that rapidity of cooling is of great importance to the preservation of neurologic function, even with the equivocal evidence in the literature. Though the practice site is meeting its defined standards for timing, the site's involvement in a clinical trial, whose protocol requires patients achieve target temperature within 4 hours of arrest, is of value to advance the scientific knowledge surrounding TTM. Thus, attempts at shortening the window from time of arrest to goal temperature must be considered.

There are many variables that can impact the time from arrest to the implementation of TTM. Altogether, the variables that occur within the practice site are easier to impact than those that occur in the field or at the transferring hospital. Therefore, recommendations for future consideration should be aimed at streamlining processes from the time of ED arrival to the time when the intravascular catheter is placed, when cooling is initiated, and when target temperature is achieved. The time from ED arrival to CCU admission, which averaged 114 minutes in this evaluation, represents a time span that stakeholders can most reasonably impact and reduce.

Recommendations. Based on the evidence analyzed in this program evaluation, five main recommendations were supported:

1. Utilize surface cooling blankets in the ED for more rapid cooling initiation
2. Develop an algorithmic approach to determine which patients would benefit from intracranial CT imaging prior to initiation of TTM
3. Place TTM catheters in the CCU where trained medical and nursing personnel optimize protocol adherence
4. Identify an accountable person to conduct regular evaluations of TTM program outcomes
5. Provide annual standardized education for CCU nurses and physicians

Step 6: Ensure Use and Share Lessons Learned

The executive summary was shared with the TTM program coordinator, the CCU Medical Director, cardiology fellows, and CCU nursing staff with major findings and recommendations for improvement of the current state. Additionally, the executive summary and data was shared with the Chief of Emergency Medicine for dissemination to the Resuscitation Committee.

Nursing Practice Implications

The stakeholder assessment in this program evaluation revealed that nurse-driven, evidence-based protocols can lead to optimal patient outcomes in this low frequency, high impact therapy. Additionally, nurse champions involved in ongoing evaluation of practice-related processes and patient outcomes will inform future practice site needs and will contribute to improved efficiency of TTM therapy at the practice site. Standardized, ongoing education for nurses and physicians offers one method to reduce TTM timing variability and increase

adherence to the TTM protocol. Finally, interdisciplinary collaboration is an important aspect of TTM. Nurses and physicians must have open and ongoing discussions about barriers to optimal patient management. The development of guidelines by an interdisciplinary workgroup to drive initial diagnostic procedures and imaging offers one way to reduce the time to target temperature.

Conclusions

This program evaluation revealed that for patients admitted to the CCU at the practice site, current timing standards are being achieved. However, there are opportunities for improvement given the prevailing view that shorter durations to target temperature lead to improved outcomes, as well as the practice site's participation in a multisite clinical trial. ED arrival to CCU admission provides a window of opportunity to improve process efficiency and reduce time to TTM initiation and time to target temperature. The familiarity of CCU nurses with the TTM protocols was cited as a significant facilitator to the optimal timing of TTM. Finally, stakeholders would benefit from regular review of outcomes to improve stakeholder buy-in and to support ongoing process improvement.

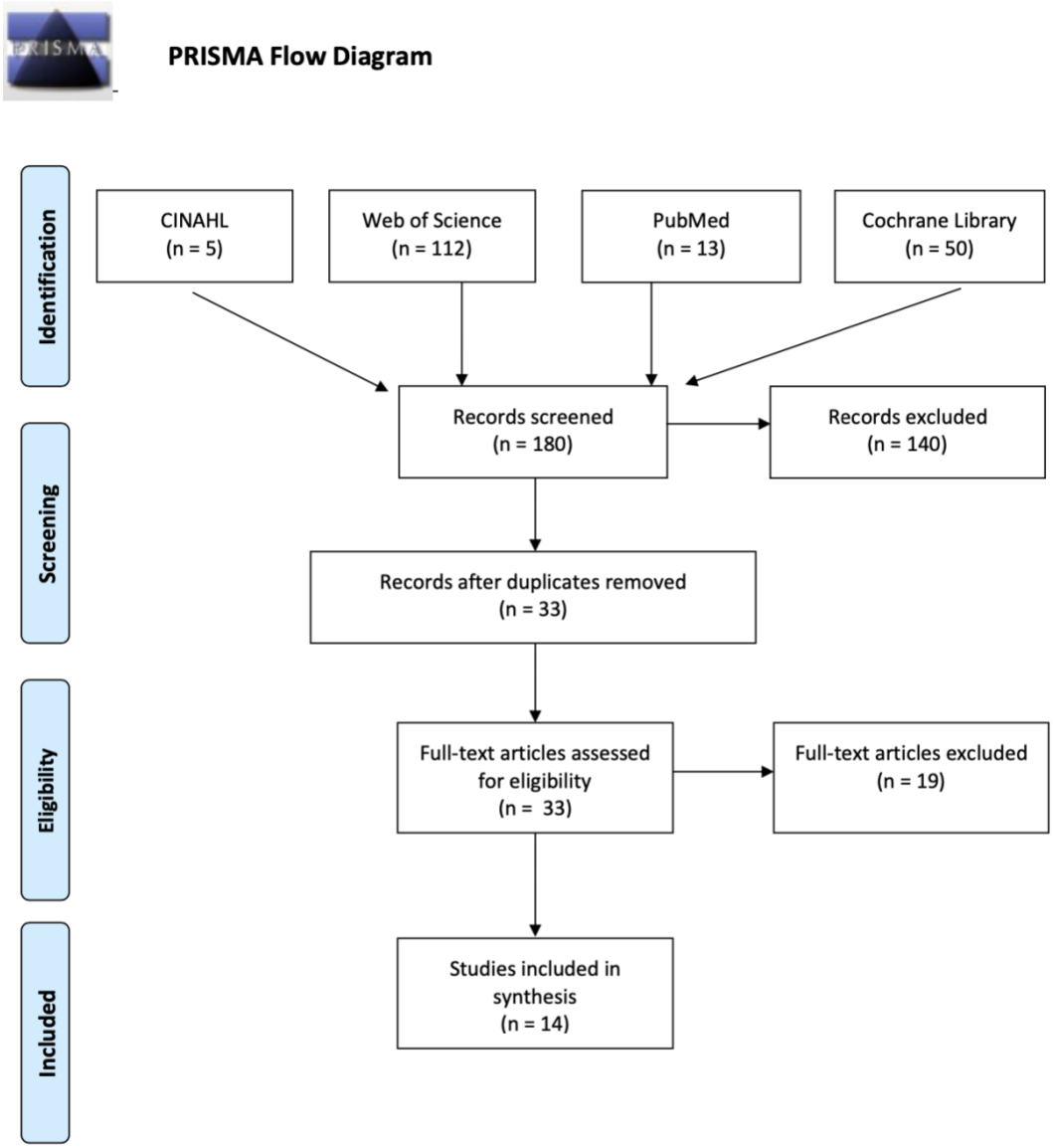


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for the systematic literature search process. CINAHL = Cumulative Index to Nursing and Allied Health Literature

Resources

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