

THE USE OF HIGH FIDELITY SIMULATION IN TRAINING NURSES ON THE
DELIVERY OF TARGETED TEMPERATURE MANAGEMENT
AFTER CARDIAC ARREST

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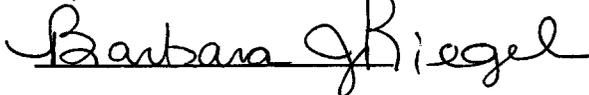
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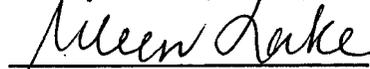
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ARREST

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Dedication

In loving memory of my Grandmother, Anna Bilyk (1928 - 2013).

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ABSTRACT

THE USE OF HIGH-FIDELITY SIMULATION IN TRAINING NURSES ON THE DELIVERY OF TARGETED TEMPERATURE MANAGEMENT AFTER CARDIAC ARREST

Roksolana Starodub

Barbara J. Riegel

The delivery of targeted temperature management (TTM) is recommended for cardiac arrest patients with specific initial rhythms after the return of spontaneous circulation. Some hospitals have established institutional TTM protocols based on national guidelines. Yet, successful implementation of an institutional TTM protocol depends on the nurses' knowledge and skills.

The study's purpose was to compare the level of post-training knowledge, psychomotor skills, confidence and satisfaction among nurses taught the delivery of TTM with video lecture versus high fidelity simulation. The effectiveness of the two different training programs was compared with multiple choice and psychomotor skills testing prior to, immediately after, and 6 weeks after training. Confidence and satisfaction were assessed using a questionnaire immediately after training and 6 weeks later. Mixed effects model and independent t-tests were used to investigate the study aims.

The results from the mixed effects model, repeated measures analysis of variance, simple regressions and paired t-tests were all consistent. Fifty-two nurses were recruited; all completed baseline and immediate post-intervention testing, while 48/52

(92.3%) completed follow-up evaluation at 6 weeks. The knowledge test scores did not differ between the groups immediately after the training (beta = 3.80, SE = 3.47, $p = .27$), but there was a strong trend 6 weeks after training, with higher scores in the simulation group (beta = 7.93, SE = 3.88, $p = .04$). In the simulation group, skills were significantly better immediately after the training, however, there was no significant difference between the groups 6 weeks later. No difference in confidence was found between the groups at either post-test point. Training satisfaction was significantly higher in the simulation group at both post-testing points.

Nurses trained with high-fidelity simulation may benefit from such training by maintaining their TTM knowledge longer. Frequent “booster” sessions may help to maintain their competency in the use of cooling equipment. Further research should focus on the assessment of the effect of different TTM education interventions on the transfer of the knowledge/skills to bedside and subsequent patient outcomes.

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CHAPTER 1: INTRODUCTION

According to the American Heart Association (AHA) (2015), approximately 326,200 individuals suffer an out-of-hospital cardiac arrest (CA) and 209,000 patients suffer an in-hospital CA annually with 10.4% to 31.4% and 57.8% survivor rates, respectively (Mozaffarian et al., 2015). Prior to a more widespread use of therapeutic hypothermia (TH) or targeted temperature management (TTM) in the hospitals, the overall survival for an out-of-hospital CA in the early 2000s was between 7% to 8%, where only a third of the patients who regained spontaneous circulation survived to discharge (Nichol et al., 2008). Favorable (Cerebral Performance Category 1 and 2, Appendix 1) neurologic outcomes after an out-of-hospital CA vary, but can be as high as 70%-90% in patients who regained spontaneous circulation in the hospital setting (Rittenberger & Callaway, 2013; Nielsen et al., 2013; Elliot, Rodgers, & Brett, 2011; Peberdy et al., 2003). Over the past decade, survival and neurologic outcomes improved at some settings due to the use of TTM and aggressive critical care management (Rittenberger & Callaway, 2013; Nielsen et al., 2013; Peberdy et al., 2003).

In the early 2000s, TTM at 32°C - 34°C was shown to improve patient outcomes by almost doubling patient survival and favorable neurological outcomes in certain patient populations (Bernard et al. 2002; HACA, 2002; Hachimi-Idrissi, Corne, Ebinger, Michotte, & Huyghens, 2001). In 2010, the AHA and International Liaison Committee on Resuscitation (ILCOR) recommended the use of TTM at 32°C - 34°C for 12 to 24 hours in comatose out-of-hospital CA patients with an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia (Peberdy et al., 2010). A slightly weaker recommendation was made for the use of TTM at 32°C - 34°C in comatose out-of-hospital

CA patients with an initial rhythm of pulseless electrical activity or asystole and for in-hospital CA patients with any initial rhythm (Peberdy et al., 2010). In 2013, a large Temperature Management Trial demonstrated an improvement in survival, ranging between 48% and 50% after investigating the benefits of two different target temperatures (i.e., 33°C versus 36°C) in post-CA patients (Nielsen et al., 2013). In the Nielsen et al. (2013) trial, the authors coined the term “targeted temperature management” based on the similar outcomes of comparing the treatment of two “doses” of temperature. The Nielsen et al. (2013) trial will be discussed in more detail in Chapter 2.

Recently, the AHA and ILCOR have released the updated 2015 guidelines on the use of TTM, defined as “an active therapy to achieve and maintain a specific target temperature for a defined duration” (Callaway et al., 2015; Donnino et al., 2015). In comparison to the 2010 guidelines, the AHA and ILCOR relaxed the temperature frame for the TTM delivery (Callaway et al., 2015; Donnino et al., 2015; Peberdy et al., 2010). It is now recommended that TTM be delivered at a constant temperature between 32°C and 36°C for at least 24 hours for out-of-hospital unresponsive CA patients with an initial shockable rhythm (i.e., ventricular fibrillation, pulseless ventricular tachycardia) (Callaway et al., 2015; Donnino et al., 2015). Similarly to the 2010 AHA guidelines, the delivery of TTM should also be considered in comatose out-of-hospital CA patients with an initial non-shockable rhythm (i.e., pulseless electrical activity, asystole) as well as for in-hospital CA with any initial rhythm (Callaway et al., 2015; Donnino et al., 2015). The 2010 guidelines specified that rewarming should be performed slowly at approximately .25°C to .50°C per hour regardless of the CA location or initial rhythm (Peberdy et al., 2010). The use of gradual return to normothermia continues to be recommended at approximately .25°C/hour (Callaway et al., 2015).

The new 2015 AHA and ILCOR guidelines were released after the study completion. As the participants in this study were educated according to the 2010 AHA guidelines, the term “therapeutic hypothermia” was used in the study’s educational materials in order to eliminate any confusion associated with the prescribed “dose” of TH. The most updated term of TTM will be used for the remainder of this document.

The delivery of TTM is labor-intensive. During the preparation for cooling and throughout the four stages of TTM (i.e., induction, maintenance, rewarming, post-rewarming), bedside nurses are responsible for: 1) providing support and education for the patient’s family on what to expect during TTM; 2) knowing how to operate cooling and monitoring equipment; 3) monitoring/requesting specific laboratory/diagnostic tests; 4) assessing the patient for TTM-associated risks; 5) initiating/titrating and monitoring the response to vasoactive medications via hemodynamic parameters; and 6) identifying and responding quickly to abnormalities. Nurses are expected to work as part of a team and some hospitals allow for a 2:1 nurse to patient ratio, especially during TTM induction with a target goal of 32°C - 34°C. Very limited literature exists on the best strategies for improving individual knowledge and corresponding clinical skills during the delivery of TTM by the bedside nurses (Blewer, Delfin, Leary, Gaieski, & Abella, 2013). There is a lack of published guidance on this topic.

The delivery of effective care relies on high-quality education of providers (Mullan, Kessler, & Cheng, 2015; McGaghie, Draycott, Dunn, Lopez, & Stefanidis, 2011; Gaba, 2004; Issenberg et al., 2002). Although observation in the workplace is a valid method for evaluating knowledge and clinical performance, it is limited when the therapy of interest (e.g., TTM after CA) occurs infrequently. Nurses need to be ready to respond quickly and competently to these infrequent events. The proposed study will examine how nurses can obtain and retain knowledge and skills needed for an infrequent but risky procedure.

Simulation has presented an opportunity for preparing nurses and teams of healthcare staff with tailored scenarios that review the occurrence of such rare events (Cheng et al., 2015; Chang, 2013; Orledge, Phillips, Murray, & Lerant, 2012). High fidelity simulation, which includes the use of programmed mannequins discussed further below, can be used as the best opportunity, outside of actual observation of performance, to not only learn but evaluate if learning has occurred (Cheng et al., 2015; McGaghie et al., 2011; Gaba, 2004; Issenberg et al., 2002). Simulation-based educational intervention and testing offers a safe teaching and practice environment that can be scheduled, standardized and repeated for data collection (Cook et al., 2011; Cavanaugh, 1997). Simulation-based education mimics real life clinical encounters and facilitates the integration of knowledge and skills through the process of post-simulation reflection, known as debriefing (Fanning & Gaba, 2002). Simulation facilitators serve as debriefing catalysts by creating a situation where the learner draws his/her own conclusions and prescriptions for change.

The Problem of Lack of Standardized TH Training

A recent analysis of 83 U.S. hospitals' TTM protocols revealed varied practice patterns (Starodub, Abella, Leary, & Riegel, 2014). As a result, nursing practices on implementing TTM on post-CA patients may significantly vary at different hospitals. The best method for training nurses on TTM delivery after CA has not been identified in the research literature. Many nursing schools and university-affiliated hospitals have invested in simulation centers and associated technologies in order to provide a controlled learning environment without putting patients at risk. However, the effectiveness and design of

specific simulation resuscitation training approaches for interventions such as TTM delivery by nurses, remains unknown.

Study Purpose, Specific Aims & Hypotheses

The purpose of the study was to compare the level of post-training knowledge, psychomotor skills, confidence and satisfaction among the critical care and emergency room nurses, who care for a population at high risk for cardiopulmonary resuscitation, taught the delivery of TTM with video lecture versus high fidelity simulation.

The primary aim of this study was to assess whether teaching the delivery of TTM therapy via high fidelity simulation will lead to a greater increase in knowledge compared to teaching with video lecture only. The secondary aim of the study was to assess whether experienced critical care and/or Emergency Room (ER) nurses who have been trained and de-briefed on the delivery of TTM via high fidelity simulation versus traditional lecture format will perform better on the psychomotor skills of using cooling equipment and report higher confidence and satisfaction after the simulation training. The following hypotheses were tested:

Critical care and/or ER nurses who have been trained and de-briefed on the delivery of TTM via high fidelity simulation compared to those trained using a video lecture format will:

H1: Achieve higher TTM knowledge immediately after training and after 6 weeks;

H2: Achieve higher psychomotor skills of cooling equipment use immediately after training and after 6 weeks;

H3: Report higher confidence immediately after the simulation training program and after 6 weeks;

H4: Report higher satisfaction with training immediately after the simulation training program and after 6 weeks.

Definition of Terms

The operational definition for TTM in this study followed the 2010 AHA recommendations on TTM delivery after CA. During the delivery of TTM to post-CA patients with an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia, the body temperature is decreased as quickly as possible to 32°C - 34°C, maintained for 12 to 24 hours, rewarmed at a suggested rewarming rate between .25°C and .50°C per hour, and post-rewarming fever identified and treated (Peberdy et al., 2010). In this study, *simulation* was defined as a “technique, not a technology, to replace or amplify real experiences with guided experiences that evoke or replicate substantial aspects of the real world in a fully interactive manner” (Gaba, 2004). *Simulator* was defined as “a device that presents a simulated patient (or part of patient) and interacts appropriately with the actions taken by the simulation participant” (Gaba, 2004).

Simulators can be grouped either into low- or high-fidelity devices. The *low fidelity simulators* include partial-task trainers, virtual patient simulation and standardized patients (Jeffries, 2005). These simulators offer a limited degree of clinical realism as they focus on specific skills and/or a chosen part of human anatomy (Jeffries, 2005). Conversely, *high fidelity simulators* are “computer-controlled, human-sized simulation mannequins that are programmed to mimic human physiology” and to respond to different interventions (Ko, Scott, Mihai, & Grant, 2011). These simulators are able to “speak” on their own with the operator’s voice, exhibit vital signs, hemodynamic changes and physical

signs/symptoms. The clinical scenarios can be pre-programmed into a computer algorithm or can be manipulated by a trained simulation instructor.

In this study, resuscitation was defined as “the response to a sudden deterioration in physiologic state in adult populations, including basic cardiac life support; advanced cardiac life support; advanced trauma life support; and shock/sepsis/rapid response” (Mundell, Kennedy, Szostek, & Cook, 2013).

In Chapter 2, these definitions are explained in more detail.

Study Significance

TTM at 32°C - 34°C has been shown to double patient survival and favorable neurological outcomes in certain patient populations (Peberdy et al., 2010). Therefore, TTM has become a recommended part of post-resuscitation care in Emergency Departments and Intensive Care Units. In order to help to improve patient outcomes from CA, systems for training healthcare staff in advanced resuscitation skills, such as TTM therapy, are much needed (Perkins, 2007).

Simulation training provides health care professionals with an opportunity to gain the necessary knowledge, skills and confidence in order to manage post-CA care in a structured and organized manner (Mundell et al., 2013). Simulation offers an opportunity to learn without jeopardizing patient safety due to suboptimal care. Nevertheless, the best strategy for such training has not been identified in the literature.

Although simulation can provide a high degree of realism, simulation technology is expensive and requires investment into training individuals to run the simulators and facilitate the training (Perkins, 2007). The approach to such training needs to be efficacious in building individual knowledge and skills. It needs to be time-efficient and

resource-efficient. The results of this study will inform nursing educators about the most effective best approach to use when educating nurses on the delivery of TTM to post-CA patient. The results of this study will also inform future clinical trials evaluating the efficacy of simulation versus video lecture TTM training in transferring the nurses' knowledge to clinical practice and evaluating the effects of these two training methods on patient outcomes.

CHAPTER 2: BACKGROUND AND REVIEW OF LITERATURE

A comprehensive review of literature is provided in this chapter on the background of TTM, teaching via high fidelity simulation and evaluations of those training programs. This chapter outlines gaps in the literature and describes how this study will begin to address those gaps. In addition, this chapter describes the two theoretical models used to guide the design and implementation of the simulation study and training evaluation.

High Fidelity Simulation

High fidelity simulations are used in healthcare in order to assess the learner's clinical competencies and enhance the reality of the clinical environment (Cheng et al., 2015; McGaghie et al., 2011; Issenberg et al., 2002). Simulation allows for building and integration of knowledge into practice, which helps learners to engage in real-life situations in a controlled setting without putting patients at risk (Mundell, Kennedy, Szostek, & Cook, 2013; Perkins, 2006). Simulation provides an opportunity to directly address the learners' needs by allowing them to make mistakes and practice to build their competence (McGaghie et al., 2011).

Simulation offers a systematic approach to education, training and retention of knowledge and clinical skills in a safe environment. Education in simulation puts emphasis on the "conceptual knowledge, basic skills, and an introduction to the actual work", while training using simulation emphasizes "actual tasks and work to be performed" (Gaba, 2004).

Gaba (2004) describes eleven dimensions useful in categorizing simulation in healthcare: 1) aims and purposes of the simulation activity; 2) unit of participation; 3) experience level of participants; 4) health care domain; 5) professional discipline of

participants; 6) type of knowledge; 7) the simulated patient's age; 8) technology applicable or required; 9) site of simulation; 10) extent of direct participation; 11) and method of feedback used.

The current study seeks to apply two different education interventions to adult learners. Playing a role in a life-like clinical situation and actively participating in a scenario allows adult learners to learn cognitively and emotionally through an experiential learning process (Fanning & Gaba, 2007). High fidelity simulation creates an opportunity for such a learning process by offering analysis and reflection on the simulation experience in order to bring change to clinical practice. Debriefing is utilized to enrich the educational simulation experience (Cheng et al., 2014). The debriefing process is described later in this Chapter.

The ultimate goal of high fidelity simulation is to transfer acquired knowledge, clinical skills, and features of professionalism from a simulation laboratory setting to improved patient practices. Simulation can be used in measuring the health care providers' clinical performance, therefore, potentially translating into improved outcomes in hospitalized patients (Zendejas, Brydges, Wang, & Cook, 2013; Barsuk et al., 2009; Wayne et al., 2008). Moreover, adhering to a protocol may improve patient outcomes; however, the best methodology on teaching adherence to the TTM protocol has not been established.

This study will involve the use of high fidelity simulation as an educational intervention of interest in training critical care and ER nurses on the delivery of TTM at 32°C - 34°C for post-CA patients. Description of the high-fidelity intervention using SimMan 3G (Laerdal Medical, Stavanger, Norway) is described later in Chapter 3.

Targeted Temperature Management

Historical Roots of TTM

Although TTM is a novel treatment in the clinical area, it dates back for over a millennium. Interestingly, the use of cold water was mentioned by Hippocrates as the remedy for various types of swelling, sprains, ulcerations and pain (Varon, Marik, & Einav, 2012). Hua Tuo, an ancient Chinese physician (145-208 A.D.) emphasized therapeutic benefits of immersing oneself into cold water. James Currie (1756-1805), a Scottish physician, utilized body cooling techniques and strategies in treating fever, while the Canadian physician, William Osler (1849-1919), cooled patients during the typhoid fever epidemic and was able to decrease the average mortality by 17% at Johns Hopkins hospital (Varon et al., 2012).

During the Russian campaign, Napoleon's Surgeon General, Baron Dominique Jean de Larrey, utilized cooling for its numbing effects during amputation and for preserving the limbs of the wounded soldiers (Remba, Varon, Rivera, & Sternbach, 2010). He also recognized that wounded soldiers who were placed near the fire died faster than those who were placed in a cooler environment. Interestingly, soldiers who were re-warmed very quickly suffered from more severe gangrene and frostbite (Remba et al., 2010).

Cooling was utilized in the late 1930s by the Philadelphia neurosurgeon, Temple Fay, with the purpose of relieving cancer pain (Alzaga, Salazar, & Varon, 2006). In the 1950s, TTM research was picked up by McBirnie and Bigelow who performed research on monkeys and canines and demonstrated that TTM had neuro-protective qualities during cardiac surgery.

Although researchers have established the link between TTM and decreased oxygen demand, the therapy fell out of favor due to a number of associated complications until the 1980s and 1990s (Marion et al., 1996). The researchers began to make distinctions between various types of hypothermia (e.g., mild vs. moderate) and were able to demonstrate in animal experiments that TTM improved neurological morbidity and

survival after CA (Marion et al., 1996). As a result of two human randomized clinical trials conducted in Europe and Australia in the early 2000s, American Heart Association and International Liaison Committee on Resuscitation recommended the use of TTM at 32°C - 34°C in out-of-hospital CA patients (Peberdy et al., 2010; Nolan et al., 2003; Bernard et al., 2002; HACA, 2002).

Post-cardiac Arrest Syndrome and Reperfusion Injury

Post-cardiac arrest syndrome resembles sepsis syndrome, where elevated markers of global inflammation, endothelial dysfunction and microcirculatory hypoperfusion lead to a multi-system response (Oksanen et al., 2014; Adrie et al., 2004; Adrie et al., 2002). Specifically, ischemia-reperfusion injury leads to reactive oxygen species release, inflammatory cascades and mitochondrial dysfunction. In turn, this potentiates vascular dysfunction, where arterial hypotension and cell apoptosis give way to organ dysfunction and cerebral edema. Individuals with post-CA syndrome experience hemodynamic instability within the first 24 hours and cardiac stunning, with depressed myocardial function for a variable period of time even after reperfusion (Adrie et al., 2004; Adrie et al., 2002).

Restoration of blood flow to the ischemic myocardial tissue is in fact more injurious than the ischemia itself. Two sets of mechanisms involved in post-arrest reperfusion injury include hypoxia-associated and reperfusion-associated mechanisms (Alkadri, Peters, Katz, & White, 2013; Lampe & Becker, 2011). Reperfusion injury leads to the release of reactive oxygen species, inflammatory cascades and mitochondrial dysfunction (Polderman, 2009; Polderman & Herold, 2009; Adrie et al., 2004; Ambrosia & Tritto, 1999). Other sources of injury include extracerebral causes and blood composition derangements due to CA blood stasis (Sterz et al., 1993). Temperature plays a key role in this chain of events. Previous studies have demonstrated that fever is linked to adverse

neurologic outcomes, including patients who suffered a CA, where fever is associated with inflammatory cytokine activation and a sepsis-like response (Polderman, 2009; Polderman & Herold, 2009; Adrie et al., 2004).

Oxygen radicals (i.e., chemical species with an unpaired electron) and neutrophils are the culprits of reperfusion injury. Specifically, activated neutrophils can release oxygen radicals in large amounts and, in turn, oxygen radicals have been shown to attack any biologically relevant molecule (Ambrosia & Tritto, 1999). One of the major sites for production of the free radicals is the mitochondria, therefore, it serves as the target for TTM intervention before reperfusion of within intra-arrest timeframe. Cell necrosis and apoptosis take place over hours and days, and the current TTM treatment targets this mechanism (Ambrosia & Tritto, 1999).

Targeted Temperature Management Mechanisms

During TTM therapy, the core body temperature is intentionally lowered between 32°C and 34°C (Peberdy et al., 2010). Primarily, TTM after CA helps to alleviate the reperfusion response by decreasing cellular metabolism, oxygen demand and brain metabolism. However, it also supports adequate adenosine triphosphate (ATP) levels, improves the pH balance and decreases cell death. TTM at 32°C - 34°C lowers the free radical production along with improving ion pump functioning (Polderman, 2009). TTM suppresses injurious effects, such as calcium shifts, release of excitatory amino acids and free radical production associated with reperfusion injury (Polderman, 2009). TTM inhibits lipid peroxidation, slows down the destructive enzymatic processes, decreases cytochrome *c* release, caspase activation, which reduces the ischemic brain regions and cell apoptosis (Zhu et al., 2004; Lei et al., 1994; Clark et al., 1996; Chopp et al., 1989). The metabolic rate during TTM at 32°C - 34°C decreases by approximately 8%/°C due to

the decrease in oxygen consumption and the rate of elimination during treatment (Alkadri et al., 2013; Polderman, 2009; Polderman & Herold, 2009). TTM also reduces the normal electrical activity of the brain in addition to decreasing cerebral oxygen metabolic demand. Specifically, for every 1°C reduction in brain temperature above 28°C, the cerebral metabolic rate of oxygen will decrease by 6% (Polderman & Herold, 2009).

Clinical implementation of TTM at 32°C - 34°C consists of four stages: 1) induction, 2) maintenance; 3) re-warming, and 4) post-rewarming (Noyes & Lundbye, 2013). According to Polderman (2009), the induction phase is the period when the therapeutic goal is to decrease the temperature as quickly as possible below 34°C. The aim of the maintenance phase is to maintain the temperature between 32°C and 34°C without any or with very minor fluctuations. This stage is usually between 12 to 24 hours in duration. The re-warming phase is marked by slow and controlled re-warming with a goal between .2°C and .5°C per hour for cardiac arrest patients (Peberdy et al., 2010). Recently, some of the TTM research literature has focused on the post-rewarming stage, specifically, related to post-rewarming pyrexia and maintenance of normothermia (Bro-Jeppesen et al, 2013, Cocci et al., 2013; Gebhardt et al., 2013; Leary et al., 2013; Winters et al., 2013). The post-rewarming stage will be discussed in more detail in the following section. Clinical implications of TTM at 32°C - 34°C pertinent to the proposed study's teaching scenario will be discussed in a separate section.

Recently, we sought to examine a sample of TTM protocols from US hospitals in order to describe current practice patterns and to identify discrepancies from the AHA-identified parameters of post-arrest resuscitation care. The protocols were obtained from a public website and with a permission of the Center for Resuscitation Science at the University of Pennsylvania. Our analysis of 83 TTM protocols demonstrated varied practice patterns in ways that may be important in achieving desired patient outcomes (Starodub, Abella, Leary, & Riegel, 2014). The TTM protocol guidelines in US hospitals

are not currently standardized, but are similar enough to choose the protocol from one major institution that follows the AHA recommendations on the delivery of TTM after CA (Peberdy et al., 2010). The TTM care occurrence at this specific institution is approximately 3 times per month although this remains highly variable. Therefore, nursing practices on implementing TTM on post-CA patients may differ at individual hospitals and the best nursing training strategies for TTM are unknown.

Literature Supporting TTM Clinical Practices

Search Strategy

Bibliographic databases were searched for relevant articles in PubMed Plus, Medline and Cochrane published before January 15, 2014. The search strategy was based on the following terms: “therapeutic hypothermia” OR “therapeutic hypothermia after cardiac arrest”. The search with “therapeutic hypothermia” yielded 22,925 articles and “therapeutic hypothermia after cardiac arrest” yielded 2,354 articles. The articles were reviewed and then grouped into four main investigational TTM areas relevant to the proposed study: 1) target temperature; 2) duration of treatment; 3) type (i.e., active vs. passive) and rate of rewarming; and 4) post-rewarming pyrexia. These investigational areas were selected because they are relevant to the clinical practice of critical care and ER nurses to be taught how to perform TTM by simulation. The articles were then selected for review if they were: 1) original human research involving TTM after CA (i.e., randomized clinical trials, observational prospective and/or retrospective studies with concurrent and historical controls); 2) included human patients ≥ 18 years old; and 3) written in English. Complete reference lists of the major meta-analyses on the treatment of post-CA patients with TTM were reviewed to ensure inclusion of the pertinent studies on the aforementioned four research sub-topics. Individual patient case studies were not included in the review.

Five randomized clinical trials comparing TTM to no temperature management were identified for review and described in Appendix 2. The Nielsen et al. (2013) Temperature Management Trial will be discussed separately as it is currently the only large multi-center randomized trial comparing two different temperature management strategies, 33°C versus 36°C, in adult post-CA patients. Additionally, 24 observational retrospective and prospective trials with concurrent or historical controls were identified and reviewed on the use of TTM after CA. These observational studies included data on the use of TTM in patients with mixed initial rhythms (i.e., shockable and non-shockable) in out-of-hospital and/or in-hospital CA and the association of TTM treatment with survival and neurological outcomes (Appendix 3). Five original prospective and retrospective research studies were identified and reviewed describing the association of post-TTM pyrexia with survival and neurologic outcomes after CA (Appendix 4).

Target Temperature

The 2010 AHA recommendations supported the use of target temperature between 32°C and 34°C based on multiple animal and two landmark human randomized clinical trials (Peberdy et al., 2010; Bernard et al., 2002; HACA et al., 2002). Following these recommendations, other TTM randomized controlled studies and observational prospective and retrospective studies cooled patients between the target temperatures of 32°C and 34°C (Appendix 2 and 3). The randomized clinical trials comparing TTM treatment to no temperature management demonstrated improvement in neurological outcomes and survival at hospital discharge in the TTM-treated groups (Bernard et al., 2010; Castren et al., 2010; Bernard et al., 2002; HACA, 2002; Hachimi-Idrissi et al., 2001).

A recent large international multicenter randomized clinical trial by Nielsen et al. (2013) compared two target temperatures, 33°C versus 36°C, in patients after an out-of-hospital CA with mainly shockable (i.e., ventricular fibrillation, ventricular tachycardia)

initial rhythms. This trial enrolled 939 patients. Both of the treatment groups in this study focused on fever prevention. Nearly half of all of the patients in each group failed to survive until discharge (235/473 [50%] and 225/466 [48%] in 33°C and 36°C groups, respectively, with 95% CI [.89, 1.28], $p = .51$). The investigators found no benefit in neurological outcomes or survival in the 33°C versus 36°C post-CA groups. Unlike in the two landmark studies, the mean temperature in the Nielsen et al. (2013) trial's comparison group was maintained at 36°C, which can be considered as active temperature management. In addition, compared to the other landmark studies, the first measured body temperature in both groups was quite low, $35.2^{\circ}\text{C} \pm 1.3^{\circ}\text{C}$ and $35.3^{\circ}\text{C} \pm 1.1^{\circ}\text{C}$, in 33°C and 36°C groups, respectively.

It is important to consider the varying degree of the individual's post-arrest injury when titrating temperature. Patients with mild post-arrest injury may have good outcomes regardless of a specific TTM because they had short down-time and little to non-existent anoxic injury. This group of patients may not require any specific type of TTM. In the Nielsen et al. (2013) trial, patients received a high rate of bystander-assisted cardiopulmonary resuscitation, 344/473 (73%) of those in the 33°C group and 338/466 (73%) of those in the 36°C group, which may have favorably influenced outcomes in both comparison groups. On the other hand, patients with severe post-cardiac injury may remain severely neurologically injured after any type of TTM. Finally, patients with moderate post-cardiac arrest injury who may have had longer down-time and did not receive timely and/or appropriate cardiopulmonary resuscitation may require deeper cooling. Nevertheless, clinicians do not know how to identify and group patients according to the mode of anoxic injury and this hypothesis has not been tested in clinical trials.

The immediate post-cardiac arrest period is the prime time for modifying neurologic injury. The TTM trial provides evidence that a more flexible approach is possible for patients intolerant of 33°C due to TH side effects (e.g., marked bradycardia, increased

bleeding, marked QT prolongation, etc.). Therefore, in 2015, the AHA and ILCOR updated the TTM recommendations to accommodate for a wider therapeutic temperature frame (32°C - 36°C).

In this study, nurses were taught to cool patients between 32°C and 34°C as was recommended by the American Heart Association in 2010 and according to the Hospital of the University of Pennsylvania TTM protocol at the time of the study. Both AHA recommendations and Nielsen et al. (2013) TTM trial emphasizes the delivery of comprehensive best practice post-CA care. As the science of TTM continues to evolve, a specific temperature may be identified for a particular group of post-CA patients based on future trials.

Duration of TTM Treatment

In 2010, the AHA recommended the duration of TTM between 12 to 24 hours after the return of spontaneous circulation (Peberdy et al., 2010). Among the randomized clinical controlled studies comparing TTM to no targeted temperature management, the length of TTM varied between 4 and 24 hours (Bernard et al., 2002; HACA, 2002; Bernard et al., 2010; Castren et al., 2010; Hachimi-Idrissi et al., 2001). Only one study cooled patients for 4 hours, however, the investigators' priority in this study was to test the feasibility and speed of a glycerol-containing helmet device delivering TTM and its ability to reach the target temperature as quickly as possible (Hachimi-Idrissi et al., 2001). Nielsen et al. (2013) began rewarming after 28 hours since initiation of TTM therapy although this study compared two different targeted temperatures, 33°C versus 36°C. Similarly, other observational prospective and retrospective studies cooled patients between 12 to 24 hours (Appendix 3).

Time to target temperature among the clinical randomized studies varied from 60 to 480 minutes (Nielsen et al., 2013; Bernard et al., 2010; Castren et al., 2010; Bernard et al., 2002; HACA et al., 2002; Hachimi-Idrissi et al., 2001) (Appendix 2). Two studies cited differences in time to reach target temperature due to various measurement devices and one study utilized pre-hospital and post-admission cooling (Kim et al., 2014; Castren et al., 2010; Hachimi-Idrissi et al., 2001). Kim et al. (2014) compared post-CA patients who have been cooled in the field by paramedics to a group of patients who had TTM initiated in the hospital and did not find any significant difference.

One animal study randomized 10-minute asphyxiated rats to either 33°C or 37°C temperature intervention, maintained for 24 hours or 48 hours immediately, one, four, or eight hours after the return of spontaneous circulation (Che, Li, Kopil, Liu, & Neumar, 2011). There was no difference between the animals' outcomes among those being cooled at 24 hours versus 48 hours and the TTM neurologic outcomes were preserved up to 4 hours of the TTM intervention delay (Che et al., 2011). The neuron counts were better preserved when the animals were cooled for 48 hours. A similar retrospective study was performed in humans with asphyxial arrest. Patients cooled at 32°C for 72 hours did not have more favorable neurologic outcomes over patients cooled at 32°C for 24 hours (Lee et al., 2013). The limitations of this study include the retrospective data, historical controls and only inclusion of asphyxial arrest, while the population of interest for the proposed study is post-CA period.

In this study, the nurses were taught that, according to the 2010 American Heart Association guidelines, the recommended time frame for TTM is between 12 to 24 hours. The nurses were taught to maintain the TTM temperature for 24 hours after the target temperature has been achieved as specified in the Hospital of the University of Pennsylvania TTM protocols. In the future, the randomized clinical trials may pinpoint to a

specific number of hours of required cooling for particular patient population with very similar ischemic injuries.

Rate of Re-warming

In 2010, the AHA recommended rewarming patients slowly at approximately .25°C to .5°C per hour and warned against active re-warming in the first 48 hours after the return of spontaneous circulation in patients who spontaneously develop a mild degree of hypothermia (Class IIIC) (Peberdy et al., 2010). The rewarming techniques among the randomized clinical trials varied from active (i.e., TTM technology-assisted) to passive (i.e., allowing to rewarm without TTM technology assistance) and between .25°C/hour and .50°C/hour (Nielsen et al., 2013; Bernard et al., 2010; Castren et al., 2010; Bernard et al., 2002; HACA, 2002; Hachimi-Idrissi et al., 2001) (Appendix 2). Additionally, in the Nielsen et al. (2013) trial, the fever-control measures after the TTM intervention were maintained until 72 hours after CA at the discretion of the 36 Intensive Care Units at different medical centers in Europe.

Some of the studies on re-warming rates after TTM have been performed on animal models. These studies conclude that favorable neurologic outcomes depend on the slow rate of hypothermia reversal. Recently, Lu et al. (2014) published a prospective randomized controlled animal study that randomized four groups of Sprague-Dawley rats to three different rewarming rates (i.e., .50°C/hour, 1°C/hour, 2°C/hour) and one normothermia group acting as a control. The rats that were more rapidly rewarmed at 2°C/hour lost the neuroprotective effect of TTM intervention compared with the rats that were rewarmed more slowly. Slowly rewarmed rats had improved myocardial function (i.e., cardiac output, ejection fraction), reduced neurologic deficit scores and longer survival. The study authors emphasized the importance of slow and careful rewarming.

There was one human retrospective analysis, which investigated whether active rewarming, the rate of rewarming or development of pyrexia after TTM was correlated with an unfavorable post-CA outcome (Bouwes et al., 2012). From 124 TTM-treated patients, poor outcome was found in 12/21 (71%) of patients rewarmed at a rate of $>.5^{\circ}\text{C}/\text{hour}$ when compared to patients rewarmed at $<.5^{\circ}\text{C}/\text{hour}$ in 54/103 (52%) (95% CI [.88 - 7.73], $p = .08$) (Bouwes et al., 2012). In this study, pyrexia after CA did not have a statistically significant effect on patient outcomes. These results may be due to low sample size and specific institution's treatment protocol. The studies on post-rewarming pyrexia will be discussed in more detail in the following section. Some data support that older age and initial rhythm along with the extent of brain injury can impact the patient's spontaneous re-warming rate (Bisschops, Hoedemaekers, Mollnes, & van der Hoeven, 2012; Bouwes et al., 2012).

In the proposed study, the nurses were taught that in 2010, the American Heart Association recommended rewarming patients between $.25^{\circ}\text{C}/\text{hour}$ to $.50^{\circ}\text{C}/\text{hour}$. According to the University of Pennsylvania TTM protocol, the nurses were taught to rewarm patients at a rate of $.33^{\circ}\text{C}$ using the Meditherm III Gaymar Stryker blue-faced TH cooling machine until the patient reaches 37°C . As the science of TTM continues to evolve, future trials may delineate confounders (e.g., older age, presence of co-morbidities, initial rhythm, extent of hypoxic brain injury) in slow spontaneous vs. active re-warming and identify an individual optimal re-warming rate.

Post-rewarming Pyrexia

Occurrence of fever after CA is not uncommon. The scientific debate about whether fever is a marker for patients with more severe anoxic injury or whether it worsens the injury itself is not settled. The animal data suggests that besides being a marker, fever after CA also contributes to even more ischemic degeneration. Previous animal

experiments demonstrated that the induction of the high body temperature can lead to unfavorable neurological outcomes, where hippocampal and neocortex damage causes immunohistochemical neurodegeneration similar to Alzheimer's disease (Favero-Filho, et al., 2008; Sinigaglia-Coimbra, Cavelheiro, & Coimbra, 2002; Baena, Busto, Dietrich, Globus, & Ginsberg, 1997; Coimbra, Boris-Moller, Drake, & Wieloch, 1996; Wass, Lanier, Hofer, Scheithauer, & Andrews, 1995).

Human clinical studies investigating the development of pyrexia in conditions such as stroke and traumatic brain injury, described an association between pyrexia development in the post-injury period and poor neurological outcomes (Greer, Funk, Reaven, Ouzounelli, & Uman, 2008; Jiang, Gao, Li, Yu, & Zhu, 2002; Stocchetti et al., 2002; C. Hajat, S. Hajat, & Sharma, 2000; Wang, Lim, Levi, Heller, & Fisher, 2000). The contributing mechanisms associated with pyrexia and poor neurological outcomes include: cerebral blood flow increase leading to increased intracranial pressure, oxygen demand increase in ischemic brain areas, increase of free radical production, calcium homeostasis disturbance, neuronal necrosis, increase of blood-brain barrier and vascular permeability (Thornhill & Corbett, 2001; Chatzipanteli, Alonso, Kraydieh, & Dietrich, 2000; Corbett & Thornhill, 2000; Castillo, Davalos, & Noya, 1997).

Five observational prospective and retrospective studies that examined the association of pyrexia development after TTM in CA patients with survival and neurological outcomes were selected for review. The studies used terms "fever", "pyrexia", and "hyperthermia" interchangeably. Each study had a specific definition for hyperthermia after rewarming (Appendix 4). There are currently no randomized clinical trials evaluating the difference in post-rewarming neurological and survival outcomes after controlling pyrexia versus no treatment of fever. The data describing the outcomes of post-rewarming pyrexia were collected mostly from retrospective (Cocchi et al., 2013; Gebhardt et al., 2013; Leary et al., 2013), retrospective observational (Winters et al., 2013) or prospective

observational studies (Bro-Jeppesen et al., 2013). The study samples varied between 141 and 336 patients. Only Cocchi et al. (2013) and Leary et al. (2013) studies defined pyrexia similarly as $T \geq 38^{\circ}\text{C}$ within 24 hours following rewarming after TTM treatment. Other studies defined pyrexia differently either in terms of the temperature and/or the number of hours the fever developed after the initial arrest or rewarming. Studies either included patients who only underwent TTM (Bro-Jeppesen et al., 2013; Leary et al., 2013; Winters et al., 2013) or composed more than half of the studies' samples (Cocchi et al., 2013; Gebhardt et al., 2013). The majority included patients with out-of-hospital CA (79-100%) and shockable initial rhythms (32-86%).

Pyrexia after CA was present in approximately half of the populations studied; however, the pyrexia definition varied according to each study's preference of the description. Gebhardt et al. (2013) found that pyrexia was less common in TTM cohort (79/221, 36%) versus non-TTM cohort (62/115, 54% chi-squared = 9.35, $p = .002$). The study results on the effect of pyrexia on neurological and survival outcomes were mixed. Some studies found a significant negative association between neurologic outcomes, survival outcomes and presence of post-CA pyrexia (Bro-Jeppesen et al., 2013; Winters et al., 2013). Leary et al. (2013) found a significant association between the $T \geq 38.7^{\circ}\text{C}$ and lower proportion of good neurologic outcomes (58% vs. 80%, $p = .04$), but no difference in survival. Other studies did not find significant associations between pyrexia, neurologic outcomes and survival post-CA (Cocchi et al., 2013; Gebhardt et al., 2013). However, Gebhardt et al. (2013) described that subjects with fever in non-TTM cohort were less likely to have good neurologic outcomes (31% versus 69%, $p = .003$).

The AHA recommends identifying and treating the post-rewarming fever (Peberdy et al., 2010). In this study, the nurses were taught to maintain normothermia with the help of the cooling device and acetaminophen administration 48 hours after rewarming as indicated in the Hospital of the University of Pennsylvania TTM protocol. Future studies

may help to pinpoint specific normothermia after rewarming time intervals for patients with particular post-CA injuries.

Clinical Considerations for Targeted Temperature Management

TTM induces multi-system effects – therapeutic as well as side effects. Certain risks and management problems will correspond to a specific TTM stage, especially during induction vs. re-warming. If the temperature reaches below the recommended mild hypothermia frame, there is a higher risk of developing arrhythmias and coagulopathy (Polderman & Herold, 2009). Patients undergoing TTM are at a higher risk for infection with the suppression of immune system, skin breakdown, hyperglycemia, coagulopathies, electrolyte abnormalities and ventricular arrhythmias. By providing good intensive care, it is possible to prevent and circumvent the complications of this advantageous treatment (Polderman & Herold, 2009).

This study focused on the recognition, assessment, management and re-assessment of most commonly identified side effects of TTM, including: 1) shivering during induction; 2) overcooling; 3) bradycardia; 4) hypotension during rewarming; 5) hyperkalemia during rewarming; 6) post-rewarming pyrexia; and 7) neurologic prognostication. A panel of experts with a cumulative experience of over 30 years in resuscitation research and TTM implementation established the following list of these TTM-associated effects.

Shivering. During TTM induction, the body will respond to the rapid decrease in temperature by shivering in order to generate heat. Shivering is an undesired effect in a post-CA patient with a hypoxic event because it increases oxygen consumption by 40 to 100% (Polderman, 2004). It may cause tachycardia, hypertension and vasoconstriction (Nayes & Lundbye, 2013). A recent study reported on the association between shivering during TTM induction and favorable neurologic outcomes (Nair & Lundbye, 2013).

However, the study did not account for the confounding variable of the use of neuromuscular blockade medication, which was different between the two comparison groups and may have influenced the study's results (Nair & Lundbye, 2013; Ramjee & Abella, 2013). Additionally, more research is needed in objectively quantifying shivering.

Shivering is usually controlled with sedatives, analgesics and, in many cases, neuromuscular blocking agents. Low doses of intravenous Meperidine (pethidine) boluses are frequently used to control intermittent episodes of shivering by inhibiting the thermoregulatory response. Alternative agents may be considered if paralytic agents are contraindicated (Alkadri, Peters, Katz, & White, 2013; Naves & Lundbye, 2013). Addition of buspirone to meperidine prior to the TTH induction can help to decrease the shivering threshold by 2°C to 4°C (Mokhtarani, Mahgoub, Morioka, Doufas, & Sessler, 2001). Neuromuscular blocking agents, such as pancuronium and vecuronium, and analgesic and sedative medications, such as fentanyl and midazolam are also commonly used in controlling shivering (Chamorro, Borrallo, Romera, Silva, & Balandin, 2010).

In this study, nurses were taught to consider the cause for shivering. According to the University of Pennsylvania TTM protocol, shivering will not be present in patients who are paralyzed with paralytics. Nurses were taught to administer meperidine 12.5 mg to 25 mg every 4 to 6 hours intravenously. Additionally, shivering can be prevented by adding buspirone and using other non-pharmacologic skin counter-warming measures, such as warming of hands and feet or using an air-circulating blanket (Logan, Sangkachand, & Funk, 2011; Kimberger et al., 2007). Nurses should be aware that elderly patients are cooled more rapidly versus the younger and obese patients (Polderman & Herold, 2009). Differentiation between shivering and seizing often presents a challenge in the clinical area. Seizures are associated with poor neurologic outcomes and should be prevented (Rossetti, Oddo, Liaudet, & Kaplan, 2009). Therefore, it is important to initiate the monitoring of electroencephalography (EEG) early during the TTM treatment, when the

neurologist is available to monitor any changes (Rittenberger, Popescu, Brenner, Guvette, & Callaway, 2012).

Bradycardia and other hemodynamic changes. Increased systemic vascular resistance, increased myocardial contractility and bradycardia are the primary hemodynamic changes during cooling. When TTM is initiated, the heart rate will increase in an attempt to oxygenate the vital organs. The peripheral blood will shift to the core vasculature and cardiac preload will increase. The metabolic demand throughout the body and the diastolic repolarization in sinus node cells is decreased during TTM. As a result, the heart rate will too decrease (Noyes & Lundbye, 2013; Polderman, 2004).

Bradycardia allows for a TTM-induced positive inotropic effect to occur due to increased intracellular calcium concentration in cardiac myocytes (Noyes & Lundbye, 2013). Due to the decreased metabolic demand and ample oxygen delivery, the mixed venous saturation temperature-corrected measurements will increase (Polderman, 2004). Bradycardia during TTM is not usually treated in order to prevent counteracting the beneficial β -blockade and heart muscle work reduction. Walters et al. (2011) recommend the following hemodynamic parameters during TTM: central venous pressure greater than 12 mm Hg, mean arterial pressure greater than 65 mm Hg and mixed venous oxygen saturation of greater than 70%. Hospital practice may vary by location and clinician's preference.

TTM leads to electrocardiogram changes with increase in P wave, QRS and QTc interval (Lebiedz et al., 2012). Arrhythmias due to TTM above 32°C are infrequent, however, electrolyte imbalance may contribute to the arrhythmia development. In a recent meta-analysis, the authors found an increase in TTM-induced arrhythmias, but pointed out that only one of the studies in the meta-analysis significantly contributed to this reported outcome (Xiao et al., 2013).

In this study, the nurses were taught not to treat bradycardia if the mean arterial pressure is above 80 mm Hg in non-acute coronary syndrome patients and above 60 mm Hg in acute coronary syndrome patients as indicated in the Hospital of the University of Pennsylvania TTM protocol. Otherwise, bradycardia should not be treated due to its beneficial inotropic effects.

Overcooling. Overcooling or cooling the body below the recommended target temperature of 32°C may lead to the development of TTM-induced complications. Skulec et al. (2013) reported on retrospective analysis of 56 consecutive CA patients undergoing TTM and the incidence of overcooling and side effects when TTM is induced using ice packs and cold normal saline infusion. The authors reported a high overcooling rate (41%) in patients with asystole and those who initially presented with a lower core body temperature. Overcooled patients tend to have a significantly worse neurologic outcomes, however, the sample size was small and other confounding variables, such as non-shockable initial rhythm, could have influenced the outcome. Nevertheless, this study emphasizes the importance of vigilant temperature monitoring and consideration of other medical issues that may influence the rate of cooling and overcooling occurrence.

In this study, the nurses were taught that in order to prevent overcooling, the patient should have a placed temperature probe that continuously monitors temperature. Core temperature is usually measured using the pulmonary artery, bladder, or esophageal sites (Peberdy et al., 2010; Heindenreich, Giuffre & Doorley, 1992). According to the Hospital of the University of Pennsylvania TTM protocol, if one route becomes unavailable (i.e., bladder), then an alternative route must be considered (i.e., esophageal). The nurse should monitor the location of the probe to assure that it is in the proper position and is not in contact with cooling equipment (e.g., ice packs, cooling pads). The nurse should also be familiar with the specific facility's cooling equipment and management of that equipment during TTM. If the patient is overcooled, administration of warm normal saline

boluses can be administered to increase the temperature above 32°C. Warm 40°C 250 ml intravenous boluses should be administered to reverse hypothermia below 32°C. Other medical conditions should be considered in overcooled patients.

Hypotension during rewarming. Vasodilation of the peripheral vascular beds and a decrease in venous return may lead to hypotension during the rewarming stage (Alkadri et al., 2013). If hypotension develops, it is important for the nurse to consider the patient's fluid status as reflected by the central venous pressure measurement. Hemodynamic goals vary at different facilities. Early goal-directed hemodynamic optimization similar to early sepsis management can be combined together with TTM treatment (Gaieski et al., 2009).

In this study, the nurses were taught to monitor and correlate low venous central pressure to volume depletion and administer intravenous fluid boluses as ordered by the provider or based on the algorithm. The central venous pressure requires hourly monitoring as indicated by the Hospital of the University of Pennsylvania TTM protocol. Urine output requires frequent monitoring as per the Intensive Care Unit's practice algorithm. If the patient is adequately resuscitated and/or there are contraindications to administering more fluid, intravenous continuous vasopressor drips can be considered to support blood pressure.

Hypokalemia during rewarming and other electrolyte disturbances. As cooler blood shifts to the extremities during rewarming and the venous return decreases, the patient will experience decreased blood pressure, decreased cardiac output and decreased central venous pressure (Alkadri et al., 2013; Noyes & Lundbye, 2013). Potassium shifts inside the cell during the hypothermia due to sodium-potassium pump changes and gets released from the cell during rewarming (Alkadri et al., 2013).

In this study, the nurses were taught that all of the potassium-containing fluids should be discontinued prior to the rewarming stage in order to avoid hyperkalemia. The

nurses should draw and follow serial serum potassium values and obtain an electrocardiogram as necessary. Other important electrolyte disturbances include hypophosphatemia and hypomagnesemia and should be monitored and corrected according to hospital protocol on electrolyte replacement during TTM treatment.

Post-rewarming pyrexia. There is no conclusive evidence on the association of a period of controlled normothermia after completion of the TTM intervention and improved survival and neurological outcomes. However, recent observational prospective and retrospective studies, described earlier in this Chapter, demonstrate a link between post-rewarming pyrexia and patient outcomes (Bro-Jeppesen et al., 2013; Cocchi et al., 2013; Gebhardt et al., 2013; Leary et al., 2013; Winters et al., 2013). Temperature management strategies after rewarming vary across the hospitals. Pharmacologic agents, such as acetaminophen, and keeping the cooling equipment after rewarming may be considered to maintain the patient at the desired post-rewarming target temperature.

The AHA recommends monitoring and identification of the post-rewarming fever (Peberdy et al., 2010). In this study, the nurses were taught to maintain normothermia for 48 hours after rewarming using the cooling device and acetaminophen as needed to maintain temperature at 37°C. The nurses were taught to examine and document any skin breakdown after removing the superficial TTM equipment.

Neurologic awakening. Time to awakening after TTH treatment in CA patients varies and for some patients may be longer than 72 after the return of spontaneous circulation. The awakening of patients after the initial insult varies due to the associated brain injury, administration of pharmacologic agents (i.e., paralytics, sedatives and/or analgesics), co-morbid conditions (i.e., end-stage renal disease) and seizures during the post-arrest period. The American Academy of Neurology (AAN) recommended delaying neuroprognostication for 72 hours after CA (Wijdicks et al., 2006). The results of the studies describing the time to awakening after TTH treatment in post-CA patients are not

consistent. The reasons for this challenge are multiple and include a lack of a unified definition for “awakening” and there is no single optimal neuroprognostication tool that is predictive of the patient’s awakening after TTH.

On average, it takes approximately 3 - 5 days for a patient to awaken (Grossestreuer et al., 2013). In this study, the nurses were taught that neuroprognostication does not occur for at least 72 hours after CA or for 72 hours after the rewarming at some institutions. According to the University of Pennsylvania TTM protocol, the neuroprognostication should be performed after 72 hours after rewarming. The patient will not have a papillary or gag reflex while paralyzed. Neurology consult is necessary for patients undergoing TTM after CA.

High Fidelity Simulation in Resuscitation Training

Bibliographic databases were searched for relevant articles in PubMed, Medline and CINAHL prior to January 15, 2014 and then updated after the study completion on August 15, 2015. The search strategy was based on the following terms: “simulation OR simulator” AND “therapeutic hypothermia OR resuscitation training OR advanced cardiac life support OR rapid response OR sepsis OR shock”. Also, complete reference lists for the three major meta-analysis on simulation in resuscitation training were reviewed. This search process identified 872 articles prior to January 15, 2014 and 1295 articles on August 15, 2015. Studies were selected if they were: 1) two–group randomized-controlled experiments; 2) compared traditional training to simulation training; 3) written in English. As a result, nine studies were eligible for full review prior to January 15, 2015. Two more eligible studies were added to this review on August 15, 2015.

Simulation-based healthcare education is a form of translational science that progresses from the results achieved in the simulation laboratory (i.e., T1) to patient practices (i.e., T2) and patient and public health outcomes (i.e., T3) (McGaghie et al.,

2011). Many studies in simulation have measured cross-sectional outcomes (Cook et al., 2013). However, there are select studies that successfully transitioned through all translational science stages with some of them demonstrating improved clinical practice and patient outcomes after employing specific simulation interventions. These select studies focused on procedural skills and have evaluated surgical and/or diagnostic procedures, such as laparoscopic cholecystectomies, episiotomy repairs, central line placements, colonoscopies and endoscopies (McGaghie et al., 2011). Similar to translation effectiveness, the simulation-based education effectiveness can be evaluated based on the Kirkpatrick's (2006) "The Four Levels" model, described later in this chapter. The simulation outcomes pyramid moves from the basic level of self-efficacy (i.e., improvement in learner's self-confidence) and progresses to competence (i.e., skill improvement in simulation setting), operational performance in clinical setting and improved patient outcomes (McGaghie, Issenberg, Petrusa, Gordon, & Scalese, 2006).

A technology-enhanced simulation intervention when compared to no intervention results in large differences in knowledge, skills, and behaviors (Cheng, Lang, Starr, Pusic, & Cook, 2014; Cook et al., 2011). Nevertheless, one may argue that implementing any kind of intervention may lead to favorable difference in knowledge, skills and behaviors when compared to no intervention. One meta-analysis compared the technology-enhanced simulation for training in Emergency Medicine and selected 56 studies comparing simulation to no intervention and 12 studies comparing simulation with another form of instruction (Ilgen, Sherbino, & Cook, 2013). The pooled effect sizes were large (range = 1.13 to 1.48) for knowledge, time and skills outcomes among the studies comparing simulation to no intervention. However, when simulation was compared with another form of instruction, the pooled effect sizes were small ($\leq .33$) for knowledge, time and process skills (all $p > .10$) (Ilgen et al., 2013). There was a high heterogeneity among the studies ($I^2 \geq 50\%$) and more research is needed to compare the benefits of simulation

over other modes of instruction, specifically for knowledge outcomes. After teaching resuscitation scenarios and measuring pre-/post-test scores, Adams et al. (2015) found no difference in knowledge between the control (lecture only), video-based, low-, and high-fidelity groups. Similarly, a different study comparing high-fidelity simulation versus case-based discussion for teaching pediatric emergencies found no difference in knowledge acquisition and retention (Couto, Farhat, Geis, Olsen, & Schwartsman, 2015). Another recent meta-analysis evaluated the effectiveness of high versus low fidelity manikins in advanced life support training and found no significant knowledge benefit for high fidelity manikins (Cheng et al., 2015).

Simulation for resuscitation training has been shown to be effective for specific outcomes, such as skills. One large meta-analysis focused on simulation-based resuscitation training to determine the effectiveness and best practices for instruction design (Mundell et al., 2013). From the 182 studies and 16,636 participants, the authors reported on the post-simulation training outcomes of knowledge (Hedges' g 1.05, 95% CI [.81 - 1.29]), process (i.e., "observed proficiency, economy of movements, or minor errors") (OR 1.13, 95% CI [.99 - 1.27]), product (i.e., "successful task completion or major errors") (OR 1.92, 95% CI [.81 - .29]) and time skill (i.e., "time to complete the task") (OR 1.77, 95% CI [1.13 - 2.42]) as well as patient outcomes (OR .26, 95% CI [.047 - .48]). Although evidence from the 21 studies suggested that simulation-based training was more effective for process skills, the improvement for knowledge was not statistically significant. This meta-analysis had high between-study inconsistency of I^2 values of >50% (Mundell et al., 2013). McGaghie et al. (2011) performed a meta-analytic comparative review of literature comparing the effectiveness of high fidelity simulation education with deliberate practice versus traditional clinical education in terms of clinical skills acquisition. The authors demonstrated that in 14 studies that met the rigorous inclusion criteria, simulation-based education was superior in achieving specific clinical skills acquisition goals (effect

size .71, 95% CI [.65 - .76], $p < .001$). However, resuscitation performance retention decreases significantly over time even after the students are allowed to practice to achieve mastery-level performance. In one study, less than 60% of the study participants retained mastery-level performance in a resuscitation scenario at 6 months (Braun et al., 2015).

Several advanced cardiac life support (ACLS) studies have compared the effectiveness of standardized simulation-based practice over traditional clinical learning in scripted scenarios. All of the studies demonstrated a benefit of simulation-based learning. One study performed a randomized controlled trial of a simulation-based education among 38 second year internal medicine residents with a wait-list control group and a crossover design (Wayne et al., 2005). In this study, performance was based on the AHA guidelines for ACLS and inter-rater and internal consistency reliability estimates were provided. The pre-intervention ACLS performance did not differ and after the first educational intervention, the total ACLS performance in the simulation group was 38% higher than in the control group ($p < .0001$) (Wayne et al., 2005). Similar results were found after completion of the second cross-over educational simulation intervention.

Teaching with simulation has been shown to be successful in trauma and septic shock training. Lee et al. (2003) performed a prospective randomized study on trauma assessment training with a patient simulator. Sixty surgical interns attended a basic trauma course and were then randomized to either trauma assessment sessions with a patient simulator or a moulage patient, an actor with mock injuries. After practicing, the interns were again randomized to an evaluation either on a trauma moulage patient or a clinical simulator. Mean trauma assessment scores for all simulator-trained interns were higher when compared with all moulage-trained interns (71 ± 8 vs. 66 ± 8 , respectively; $p = .02$). Ottestad and colleagues (2007) sought to create a measurement tool for exploration of factors regarding the inadequate resuscitative skills and compared the performance of interns and teams during septic shock management using patient

simulation. A retrospective review of videotapes was performed and ICU conditions were re-created using simulation for individual intern and ICU team septic shock management. Although this study did not compare simulation-based education with traditional clinical education, it provided useful information on objective measurement of both behavioral and knowledge-based skills as well as identified poor and adequate performance.

Currently, there is no published study that compares the effectiveness of knowledge and psychomotor skills outcomes of high fidelity simulation over video lecture in training nurses to deliver therapeutic hypothermia. The design for this study's educational simulation intervention was drawn from simulation studies that focused on evaluating competence during Advanced Cardiac Life Support (ACLS) execution, trauma and sepsis management (McEvoy et al., 2012; Wayne et al., 2008; Ottestad, Boulet, & Lighthall, 2007; Wayne et al., 2005). In order to progress continuously through the simulation-based education effectiveness structure, the designs of these studies focused on the comparative effectiveness of video lecture versus high fidelity simulation in the domains of knowledge, clinical skills acquisition and confidence.

Debriefing

The AHA recommends the use of a debriefing technique after actual resuscitation events with a goal of improving future performance (Cheng, Eppich, Grant, Sherbino, Zendejas, & Cook, 2014; Mullan, Kesler, & Cheng, 2014; Bhanji et al., 2010). Debriefing is the most important part of simulation learning although the research on simulation debriefing is sparse (Fanning & Gaba, 2007; Jeffries, 2005). Debriefing supports a constructivist framework of learning, "where knowledge is individually constructed and thought about as learning occurs" (Dreifuerst, 2009). It offers an opportunity for participants and the facilitator to re-examine the clinical encounter (Dreifuerst, 2009). Lederman (1984) described debriefing as the "cognitive assimilation of experience", which

allows to examine and retain the thought process and cognitive maps that the learners use to view the situation. It is known that subsequent participants' performance improves with debriefing and perceived quality of simulation highly correlates with perceived debriefer skills (Fanning & Gaba, 2007; Rudolph, Simon, Dufresne, & Raemer, 2006).

Debriefing begins with the so-called "pre-debriefing" stage, where the facilitator sets expectations for the simulation session (Zigmont, Kapus, & Sudikoff, 2011). The facilitator and the debriefer can be the same individual if s/he has been trained in debriefing techniques. The role of the facilitator and the debriefer are explained in the pre-debriefing stage (Fanning & Gaba, 2007). The simulation session is described as either educational or an assessment and the level of difficulty is discussed with the participants. The facilitator explains the limitations of the simulator mannequin. The fiction contract is introduced, where the facilitator explains that this is not a real patient but the participants should do their best to "suspend disbelief" and make it as real as possible. Finally, the confidentiality of the participants' performance in the simulation space and case content confidentiality are emphasized (Zigmont et al., 2011).

The primary goal of debriefing is to discuss and reshape frames (Rudolph, Simon, Riyard, Dufresne, & Raemer, 2007; Rudolph et al., 2006). Frames lead to actions, which lead to results. If the patient outcome in the simulation session was unfavorable, then the debriefer needs to trace back to the participants' actions and needs to shape or "frame" the participants' thought process with a goal of getting a more optimal result in the future. The emphasis is on the thinking process rather than the unfavorable outcome and the provided feedback should be generalized for the participants in order to prevent personalizing guilt or blame (Rudolph et al., 2006).

This debriefing process requires a supporting learning environment, where the participants can feel safe to share their thoughts about the simulation case. As the participants in the proposed study were adults with previous critical care and/or

emergency care nursing experience, the debriefer was asked to consider the main purpose of the adult learning theory and be aware of the fact that adults want to be actively involved in the learning process. The debriefer should encourage the participants' self-reflection and talk less than half of the time in the debriefing session. Nevertheless, instructor-led debriefing rather than participants-guided debriefing is preferable at this time (Rudolph et al., 2007; Rudolph et al., 2006).

Each simulation session should accomplish 2 to 3 goals and knowledge gaps with 5 to 6 content points to cover. This study's goals and main simulation content points are described in further detail in Chapter 3 under Specific Aims and Intervention. The content of focus can range from cognitive to technical to behavioral. This study addressed all three of these foci. The recommended time in the debriefing research literature ranges from 20 minutes to an hour and was approximately 25 - 30 minutes in this study. Most other randomized educational trials using simulation conducted the debriefing at the end of the simulation activity and outside of the simulation area (Rudolph et al., 2007; Rudolph et al., 2006).

Rudolph and colleagues (2006) are well known in simulation research for reporting on the 35-year theoretical and empirical research in behavioral sciences and designing the debriefing approach known as "debriefing with good judgment". This approach has a three-fold structure consisting of the reaction phase, the understanding phase and the summary phase. The first element includes the participants' "frames" of knowledge, assumptions and feelings that drive actions. During the reaction phase, the debriefer may spend 3 to 5 minutes eliciting information regarding the feeling about the simulation. By uncovering participants' feelings and assumptions, the debriefer can address those frames to produce more favorable results in the future. In the understanding phase, the debriefer attempts to discover the participants' "frames" through genuine inquiry and focusing on solving the "puzzles" rather than blaming the participants for errors and

mistakes. To accomplish this, the debriefer uses advocacy in a conversational technique to include the subjective participants' judgment and objective observation. This process should uncover the participants' "frames" in terms of their actions as perceived by the debriefer. This process usually lasts between 20 to 25 minutes. Finally, the summary phase spans 1 to 2 minutes, where the debriefer emphasizes "take-away" messages for future clinical practice (Rudolph et al., 2007; Rudolph et al., 2006).

Learning

It was imperative to understand the adult learners' characteristics or premises of adult learning before proceeding on to developing an effective clinical education training for critical care and ER nurses in this study. Adult learners are characterized by their need to be a part of the learning process, desire to learn to improve and build on previous experiences and their motivation and emotions that they bring to the learning environment. In a teaching setting, adult learners desire to be respected and recognized for their knowledge and prior experiences (Friedlander et al., 2011). If the teacher (i.e., simulation facilitator) is able to engage the adult learner in the learning process, this teacher-learner relationship leads to the learner's intellectual growth and is also gratifying for the teacher.

Learning in adults depends on the neuroplasticity of the brain, genetic factors and other modulating processes that can affect the individual's learning process (Mahan & Stein, 2014; Nader & Hardt, 2009). Memories are not static and are always available for alteration. This depends on the emotions, memory context and individuals factors, such as level of attention, stress and any subsequent events that may influence the retention of the learning experience. There is a commonly known dichotomy of how humans think and learn. One type of learning involves a fast emotional processing where new information is associated with existing patterns. The second learning system requires

more deliberate thought processing and is a slower and logical process (Mahan & Stein, 2014).

From a neurobiological stand, learning and memory retention have objective anatomic locations in the brain. Neuronal connections and networks in the temporal and parietal lobes are responsible for the memory retention (Nader & Hardt, 2014). Additionally, there are three structural and physiological learning mechanisms. One of such processes is characterized by the speed of the chemical synaptic transmission, expression of the neuro-receptors and release of the neurotransmitters. The second such process is defined by the production of the new neuronal connections, dependent on the epigenetic processes and the activation of the specific protein synthesis in pertinent brain sites. The third structural process that underlies learning involves the generation of the new neurons, which has been shown to be effective in processing new stimuli, especially in the hippocampal region. According to some research evidence, neurons that are newly formed in adulthood may be better equipped to process new signals and to aid in memory retention (Mahan & Stein, 2014; Nader & Hardt, 2009).

Theoretical Framework

The Simulation Model

The framework that guided the process of design and implementation of simulation in this study was the Simulation Model developed by Pamela R. Jeffries (Jeffries, 2005). This model has five major components: 1) teacher practices; 2) student practices; 3) educational practices; 4) design characteristics/simulation intervention, and 5) outcomes. Based on this model, successful outcomes depended on whether the best education practices were embedded into the design and implementation of the study (Jeffries, 2005).

The best education practice relies on the teacher and student roles with their identified expectations and corresponding interventions. In the Simulation Model, the

teacher acts as a facilitator in the student's learning process. The teacher may require help with design of the simulation, setting up the simulator and simulation equipment. Moreover, when used for learning purposes, the teacher needs to be comfortable with performing a specific simulation. Similarly, the student needs to assume the role of an active learner, which is more likely to occur when the student "knows the ground rules for the activity" and the simulation itself is process-based, or requires selection of presented information over time (Jeffries, 2005; Cioffi, 2001).

The educational practice in the Simulation Model include seven principles: active learning, prompt feedback, student/faculty interaction, collaborative learning, high expectations, allowing diverse styles for learning and time on task (Jeffries, 2005). As part of active learning, providing immediate feedback helps to reinforce the student's learning. Simulation also allows for previously described debriefing after the simulation intervention in order to reflect and build on the participant's knowledge. Therefore, an effective student-faculty interaction during and after high fidelity simulation helps to accomplish complex learning strategies requiring assessment and decision-making. When the students collaborate with each other and learn together, they are able to share the decision-making process as well as bond with faculty. Simulations also accommodate both college students and adult learners with diverse learning styles and different academic backgrounds. Simulation faculty should set high expectations and identify the amount of time it will take the students to complete the task.

According to the Simulation Model, a successful simulation design should address the objectives, fidelity, complexity, cues, and debriefing. The objectives for the simulation must match the students' experiences and knowledge that can be achieved within a specified timeframe. Simulations need to mimic reality and have an established validity. Simulations also vary from simple to complex, where the teacher is able to use timely cuing to direct the simulation and progress to the next step in the scenario. At the end of

the activity, debriefing should be utilized in order to address the process, outcome and application of the scenario.

Kirkpatrick's "The Four Levels" Model

Kirkpatrick's "The Four Levels" model was used as a conceptual framework for measuring outcomes in this study (Kirkpatrick & Kirkpatrick, 2006). The main outcome of interest in the study was the measurement of individual knowledge after training with video lecture versus simulation case study. A sequence of training levels measurements are described in the Kirkpatrick's model. The four levels include: 1) Reaction; 2) Learning; 3) Behavior; and 4) Results (Kirkpatrick & Kirkpatrick, 2006, p. 21). The model posits that no level can be bypassed in order to reach the next level and each level has an impact on the next level. As the levels increase, the complexity to execute a specific evaluation along with associated time and cost increase as well.

Kirkpatrick's Level 1 describes the evaluation of the trainee's reactions (Kirkpatrick & Kirkpatrick, 2006, p. 27). In most cases, this measures the "customer" satisfaction with the training program. Favorable responses are highly desired by the training program organizers and/or instructors because positive reactions are linked to the participants' learning motivation. The participants who positively react to the training program are more inclined to learn. According to Kirkpatrick, "learning can be defined as the extent in which participants change attitudes, improve knowledge, and/or increase skills as a result of attending the program" (Kirkpatrick & Kirkpatrick, 2006, p. 27). This study focused on the resulting increase in post-training knowledge, psychomotor skills, confidence and satisfaction among critical care and ER nurses taught the delivery of TTM with video lecture versus high fidelity simulation. Thus, the focus of evaluation in this study remained on Kirkpatrick's Level 1 and 2 Learning outcome. Level 3 requires behavior evaluation in the working clinical environment, where the nurses take care of post-cardiac arrest

patients undergoing TTM. Finally, Kirkpatrick's Level 4 Results targets the evaluation of the effect of the proposed training on the patient and institutional outcomes (Figure 2.1). The current study focused on the assessment of Level 1 Reaction and Level 2 Learning outcomes due to an infrequent occurrence of TTM in the clinical setting.

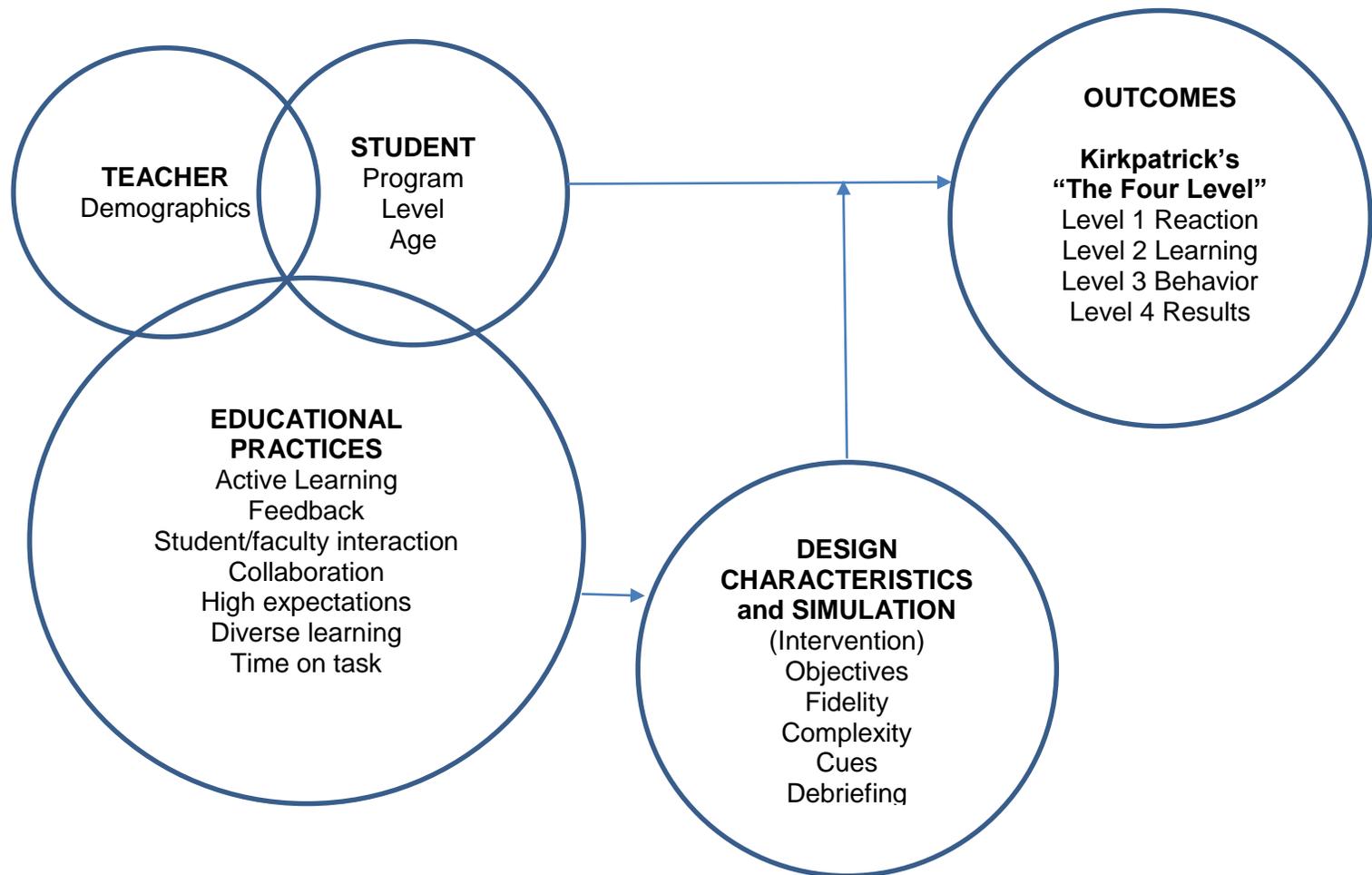


Figure 2.1. Theoretical framework, adapted from Jeffries (2005) and Kirkpatrick (2006)

Gaps in the Literature

The best strategies for improving clinical knowledge and potential clinical performance on the delivery of TTM by the critical care and ER nurses have not been determined. Only one study has evaluated the effectiveness of specific TTM training. Recently, Blewer et al. (2013) described that a focused post-arrest targeted temperature program led to increased TTM implementation and confidence among the conference participants, including nurses. Nevertheless, there is a lack of literature describing the best strategies to train nurses on TTM delivery.

CHAPTER 3: METHODOLOGY

Introduction

This study was designed to test the benefit of simulation as an educational intervention for nurses learning targeted temperature management (TTM). Following a description of the research design and sample, an in-depth explanation of the control and simulation interventions are provided. Procedures for participant recruitment, screening, data collection, management, and analysis are described. Finally, human subject protection is reviewed.

Research Design

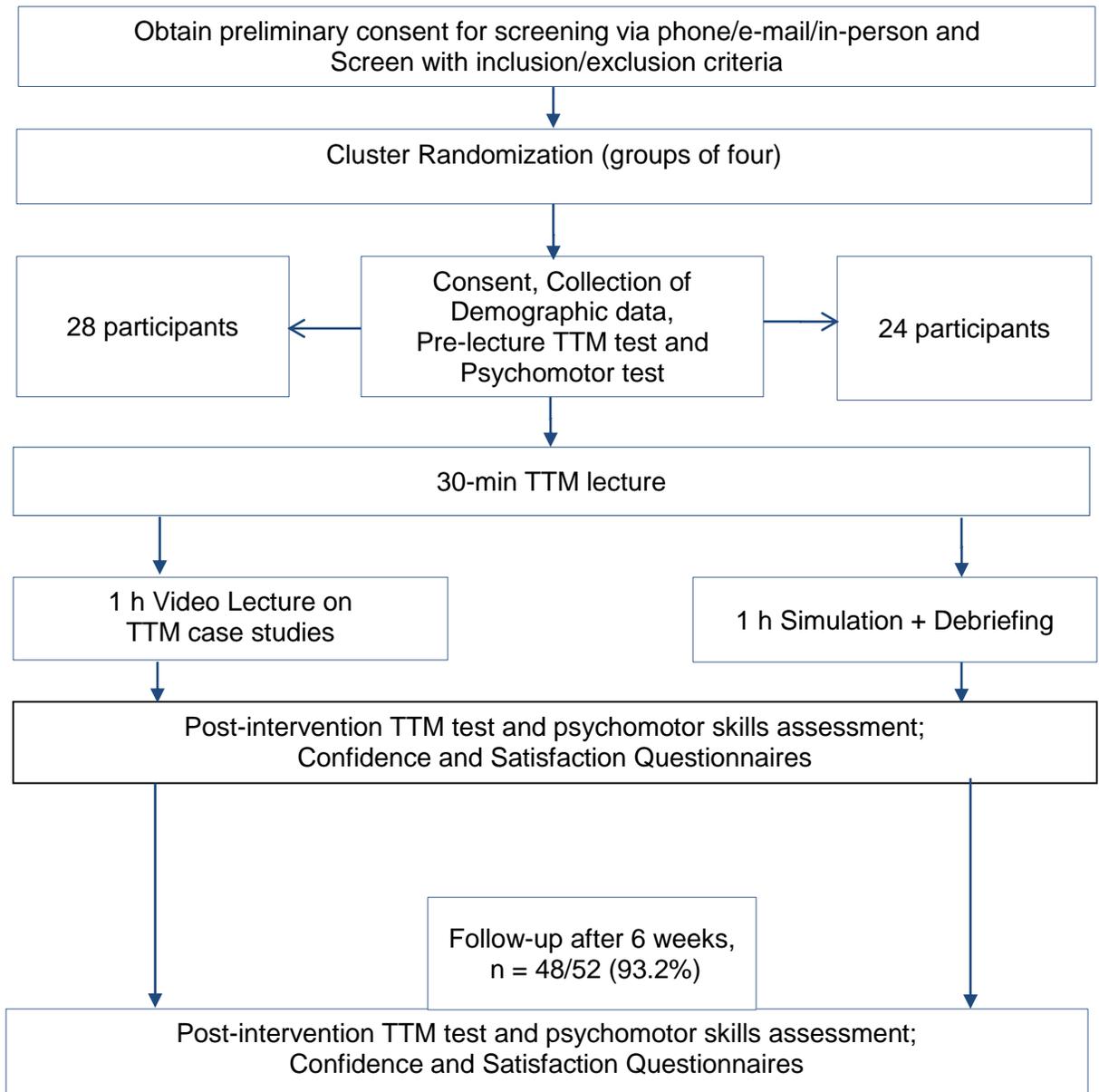
This study was a cluster randomized, educational intervention-controlled, single-center study of the effects of high fidelity simulation of TTM after cardiac arrest on individual knowledge, skills, confidence and satisfaction of critical care and emergency room (ER) nurses. Evaluation of individual knowledge by using a multiple choice post-test was chosen as the primary outcome because the study focused on learning rather than performance. In longitudinal follow-up of six weeks after receiving one of two educational training interventions, the participants' knowledge was evaluated using a pencil-and-paper multiple choice test. Skills were assessed with a psychomotor skills competency checklist. Confidence and satisfaction were assessed using a questionnaire (Appendix 5 and 6).

Sample

The power analysis of two sample t-test was performed using statistical software PASS 12 (NCSS LLC, Kaysville, Utah, 2013) to compute the study's sample size based on previous studies with a similar design (Nguyen et al., 2009; Rodgers, Securro, & Pauley, 2009; Rosenthal et al., 2006; Wayne et al., 2005). A sample of sixty-six

participants was deemed to be sufficient to achieve 80% power to detect a difference of 5.9 points between the null hypothesis that both group means are 79.1 and the alternative hypothesis that the mean of the simulation group is 85.00 with the estimated group deviations of 8.5 and 8.5 (respectively) with a significance level (alpha) of 0.05. The calculated effect size based on the difference of means divided by standard deviation was 0.7, which is a good estimate for informing a larger study (Cohen, 1988). To account for an approximate 10% attrition rate after longitudinal follow-up, the target sample size for this study was 74 participants. A total of 52 participants were enrolled in the study due to difficulty of enrolling critical care nurses and limited resources. Cluster randomization procedure is discussed further below.

Figure 3.1. Schematic Diagram of the Cluster Randomized Trial Design (N = 52)



Inclusion and exclusion criteria. The participants were included in the study if they were: 1) In possession of an unrestricted Registered Nurse (RN) license in any state and were working or had previous RN work experience in an adult intensive care unit (ICU) (i.e., Medical ICU, Coronary Care ICU, Neurosurgical ICU, Surgical ICU) or Emergency Department; 2) Willing to complete all study procedures (i.e., fill out the required demographic data and take the TTM pre-test; dedicate approximately 1 hour to a randomized intervention activity; take the post-test immediately after intervention; and, return in 6 weeks for a post-intervention final evaluation). Nurses were excluded from the study if they had not delivered direct nursing bedside care for more than 2 years. Willing individuals were not excluded if they had previously delivered care to a post-CA patient undergoing TTM, participated in simulation activities, had previous TTM training or assisted a colleague with caring for a post-CA patient undergoing TTM without formal TTM training. The participants were asked to provide more information on these points on the Demographic Data Form (Appendix 7). Throughout the length of the study, the participants were asked to not participate in any other learning modalities on the delivery of therapeutic hypothermia or those involving the use of high fidelity simulation in order to minimize confounding variables.

Recruitment Procedures. This study was exempt by the University of Pennsylvania's Institutional Review Board (IRB) because the study's intervention was not significantly different from approaches used in educational and clinical settings. Recruitment and screening of the participants took place at the University of Pennsylvania School of Nursing. Registered nurses with current or recent (within the past 2 years) critical care and/or emergency nursing experience were recruited as potential participants from all of the graduate nursing programs at the University of Pennsylvania School of Nursing. After obtaining permission from the school's administration, the study advertisement flyers were posted on bulletin boards at different locations at the University of Pennsylvania

School of Nursing and a general e-mail was sent out to all of the School of Nursing graduate students describing the study with an invitation to participate. The study was also advertised in two different weekly electronic newsletters for graduate and doctoral students. Study enrollment was not limited to students. In order to increase recruitment and enrollment numbers, an addendum was submitted to the institutional IRB with a request to advertise the study at all of the University of Pennsylvania Health System's (UPHS) hospitals and increase gift card amount compensation to \$50.00 per individual per visit. After obtaining permission from the IRB and the unit managers, the PI advertised the study via flyers and in-person at all of the critical care and ER units at the three UPHS hospitals (i.e., Hospital of the University of Pennsylvania, Penn Presbyterian Medical Center, Pennsylvania Hospital).

Screening and Assigning Participants to Groups. Willing individuals were contacted by the principal investigator either by phone, e-mail or in-person. After explaining the purpose of the study and getting preliminary consent, willing individuals were screened for the inclusion/exclusion criteria. The participants were randomized as a "cluster" of four participants with an intent of training nurses in groups. This randomization scheme was chosen because health care providers are trained in groups during the Hypothermia and Resuscitation Training Institute at Penn (HART) conference simulations, described later in this Chapter. The participants were clustered according to their entry sequence into the study. As participants accumulated, a cluster of four eligible individuals was randomly assigned to one of two educational interventions (e.g., video). The next cluster of enrolled individuals was assigned to the other educational intervention (e.g., simulation). The randomization sequence was generated using a table of random numbers. Due to scheduling conflicts, we allowed the participants to be trained in pairs or individually, but the randomization scheme remained unchanged. Each individual or pair had the study explained and was provided with a consent form (Appendix 8). After signing

the consent, the participant(s) completed the demographic data form, TTM 20-question pre-test and a cooling equipment psychomotor skills test. Due to the nature of the study, the participants and the investigators were unable to remain blinded to which intervention they were assigned.

Intervention and Operationalization of the Theory

SimMan 3G (Laerdal Medical AS, Stavanger, Norway) was used in this educational high-fidelity simulation intervention. This patient simulator has an active monitor displaying real-time electrocardiographic rhythm, non-invasive blood pressure, temperature, continuous pulse oximetry, and capability for displaying other hemodynamic parameters (e.g., central venous pressure, invasive arterial blood pressure, pulmonary artery pressures, etc.). Other important features of the simulator include: palpable pulses, audible heart and lung sounds, reactive pupils, ability to shiver/seize and a mouth speaker controlled from a remote location. The patient simulator was controlled remotely by one of the simulation facilitators.

The intervention was based on the 2010 American Heart Association's (AHA) recommendations for TTM delivery after CA (Peberdy et al., 2010). A lecture supported with a PowerPoint presentation was prepared by the Principal Investigator and reviewed by a panel of experts via a "walk-through" method to match the information from the case studies taught in the educational high fidelity simulation and video lecture. Initially, the classroom-based traditional lecture format was chosen as a comparison control because this type of training is offered to nurses at the Hospital of the University of Pennsylvania. However, the study investigators decided to present the lectures in a video format in order to deliver consistent information each time. The information presented during the simulation intervention and lecture remained consistent between and throughout the study.

The lecturer in the control video lecture was a hired individual, not the Principal Investigator, and had more than eight years of teaching experience using high-fidelity simulation technology. The lecturer was presented with the PowerPoint presentation material approximately one month in advance. The same lecturer was also a hired simulation instructor who facilitated and debriefed study simulations.

In this study, the “teacher” or rather the hired simulation instructor participated in the simulation study development workshop. This instructor went through the motions of the TTM simulation to experience similar feelings to those of students and familiarize herself with the content of the simulation. The instructor was also trained by a critical care nurse with more than 10 years of experience in TTM delivery and the Principal Investigator to instruct on the use of the Gaymar 7900 (blue-faced) cooling machine. The psychomotor assessment skills checklist was graded by the Principal Investigator each and every time throughout the duration of the study.

While the hired and trained simulation instructor was responsible for facilitating the instructional simulation component and guided debriefing, the second simulation instructor (Principal Investigator) was responsible for managing the physical and hemodynamic responses of the simulator and grading the psychomotor assessment skills checklist. The simulation instructors’ roles remained consistent for the most of the study’s duration. On a few occasions, the Principal Investigator facilitated and debriefed several study simulations due to scheduling conflicts.

All of the participants received a pre-recorded 30-minute introductory lecture on TTM-induced physiologic changes, corresponding patient clinical assessment and common TTM protocol-driven interventions. The lecturer in the first video was the Emergency Room attending physician and researcher with over 10 years of experience in post-cardiac arrest and TTM delivery. At the beginning of a 30-minute introductory lecture, the participants were reminded that the focus of the training was based on the clinical

practices at a single institution. Although the institutional TTM protocol followed the 2010 AHA guidelines, clinical practice may vary at other institutions.

The participant(s) who was/were randomized to the intervention group were provided a 5-minute orientation to the simulator and simulation environment in order to identify the rules and increase the self-learning motivation during the simulation learning. The participant(s) was/were expected to actively engage in the simulation learning process using the process-based method by selecting the necessary information from the case study and intervening over the duration of the simulation.

The simulation case study focused on the recognition, assessment, management and re-assessment of most commonly identified side effects of TTM, including: 1) shivering during induction; 2) overcooling; 3) bradycardia; 4) hypotension during rewarming; 5) hyperkalemia during rewarming; 6) post-rewarming pyrexia; and 7) neurologic prognostication. The focus on the management of these TTM-associated effects was established by a panel of experts with a cumulative experience of over 30 years in resuscitation research and TTM implementation. The control group was instructed on the same case study via a pre-recorded video lecture. The same content addressing the TTM-associated side effects was discussed during the lecture with the control group participants.

In this study, the high-fidelity simulation group differed from the control video lecture group in that with high-fidelity simulation, participants: 1) actively engaged in learning; 2) practiced psychomotor skills using TTM equipment; and 3) received facilitator-guided debriefing based on the performance during the simulation case study. The standards of performance on post-arrest care and the delivery of TTM after CA are described in the 2010 AHA recommendations (Peberdy et al., 2010). The simulation that was used as an intervention in this study included the components from the HART conference simulation case studies offered twice per calendar year by the University of

Pennsylvania Center for Resuscitation Science. High-fidelity simulation technology is used during this conference to provide practical hands-on TTM training. Blewer et al. (2013) described increased TTM implementation and confidence among the conference participants, including nurses, who attended HART conference.

Permission for the use of the content from the conference simulation case studies was obtained from the clinical director and researchers at the University of Pennsylvania Center for Resuscitation Science after guaranteeing that the content of the case studies and the TTM knowledge test would not be featured in any publication that result from this study to respect ownership of the materials. The simulation case studies were developed for the Center for Resuscitation Science by a group of experts with greater than 30 years of cumulative experience in resuscitation research and TTM implementation.

Instruments

The participants from both groups were evaluated using a multiple choice knowledge test given before the intervention, immediately after the intervention and again at 6 weeks. The pre- and post-test used in this study contained the same questions and multiple choice answers utilized for testing during the HART biannual conference. HART pre- and post-test are based on the 2010 AHA recommendations for TTM delivery after CA (Peberdy et al., 2010). The content validity of the knowledge test was determined by a panel of experts. Permission to use the pre- and post-test in this study was obtained from the clinical center director at the University of Pennsylvania Perelman School of Medicine Center for Resuscitation Science.

The TTM psychomotor nursing competency demonstration checklist for use of Gaymar Cooling Units was developed by the clinician educators at the University of Pennsylvania Presbyterian Medical Center. This checklist was used in this study to assess

psychomotor skills in using TTM equipment. The reliability and validity of the checklist has not been previously published, although content validity can be assumed because it is used by the clinician educators at the University of Pennsylvania Presbyterian Medical Center.

In our study, confidence and satisfaction scores at Visit 1 were not compared to the scores at baseline in each group because of the high heterogeneity in prior TTM training and our interest in measuring the participants' confidence and satisfaction specifically only after our study intervention. Self-reported confidence regarding TTM knowledge and equipment was assessed using a 10-point rating scale adapted and expanded from a previously published study comparing traditional versus high-fidelity simulation in retention of the Advanced Cardiac Life Support knowledge (Lo et al., 2011) (Appendix 5). Cronbach's alphas for the seven Visit 1 and Visit 2 confidence questionnaire items were .92 and .91, respectively, indicating high internal consistency. Similarly, the satisfaction with TTM training questionnaire was adapted and expanded to fit the current study's TTM educational intervention (Appendix 6). Cronbach's alphas for the six Visit 1 and Visit 2 satisfaction questionnaire items were .93 and .94, respectively, indicating high internal consistency.

Procedures

Timing of Data Collection. The duration of the individual's participation ranged between 5 and 8 weeks from recruitment to the time when the final evaluation was completed. The study was advertised for a total of 8 months and the randomized study training and follow-up visits took place over a 9 month period in 2014 and 2015.

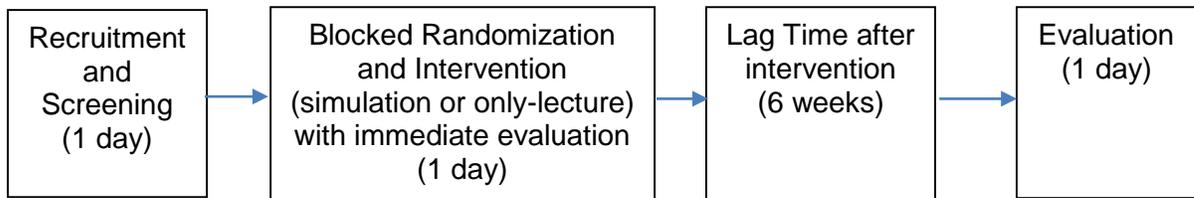


Figure 3.2. Individual progress in the study

Recruitment and screening (1 day): After screening willing individuals by phone, e-mail or in-person, a group of four eligible individuals were scheduled for one of two randomly-assigned educational interventions (i.e., video or simulation). The intervention was scheduled on days that were mutually agreeable.

Intervention (simulation or only-lecture) with immediate evaluation (1 day): After signing the consent (Appendix 8), the participants filled out the demographic data form (Appendix 7) and took a 20-question TTM knowledge pre-test. The percentages of correctly answered test items from 0 – 100% were used in the statistical analysis. Participants from both simulation and video performed a brief psychomotor test using superficial cooling equipment. After completing the randomly assigned intervention, participants from both groups were evaluated using the same 20-question multiple choice knowledge post-test, psychomotor competency checklist, confidence and satisfaction questionnaires. The instructors were asked to keep brief notes after each lecture and simulation regarding the number of students trained and the group dynamics. Participants were given a \$25 gift card at the completion of the intervention, an amount that was increased to \$50 later in the study to stimulate participation.

Post-intervention time: All of the participants were scheduled for the final evaluation of their knowledge, psychomotor skills, confidence and satisfaction 6 weeks, give or take 2 weeks after completing the intervention. They were contacted to arrange testing according to their specified preference using e-mail or phone. The final evaluation was scheduled on days that were mutually agreeable. The specific lag time was chosen based on similar

previously published studies on the use of simulation in management of ACLS and septic shock (Nguyen et al., 2009; Wayne et al., 2005). According to 2010 AHA report on education and implementation of basic and advanced cardiac life support, basic skills deteriorate as quickly as 1 to 6 months or 4 to 24 weeks after training (Bhanji et al., 2010).

Evaluation: During the final evaluation, participants from both groups were evaluated using the same 20-question multiple choice knowledge test, psychomotor competency checklist, confidence and satisfaction questionnaires. The participants were provided with a \$25 gift card at the completion of the final evaluation for a total compensation of \$50 per participant. After the first 20 participants completed the study, the compensation increased to \$50 for a total compensation of \$100 per participant.

Preparation for and Administration of the Study

Individuals who were qualified to participate were scheduled to receive one of the two education interventions. Scheduling of the intervention was attempted on three different occasions via e-mail and/or telephone. If the Principal Investigator or one of the research staff was not able to contact the participant on any of these three occasions and the participant did not return communication in any form in two weeks, the participant was considered to have changed his/her mind about participating. That is, willing participants who failed to attend the initial session where they provided baseline data and received their assigned educational intervention were not be considered as participants, even though they were willing to participate.

After completion of the educational intervention, pre-test and post-test, the participants were scheduled for the final evaluation six weeks after receipt of the intervention. All randomized participants who received any of their assigned intervention were included in the analysis.

Data Monitoring

The collected data was entered into the Research Electronic Data Capture (REDCap) database on the University of Pennsylvania School of Nursing secure web server. REDCap is a secure web application for building and managing databases. Access to specific folders was governed by the study's investigators and permissions were managed by the School's REDCap administrator. Only the study's investigators and the statistician had access to the collected data. No personal identifiers were captured as part of the electronic dataset.

Data Analysis

Statistical Methods. Individual knowledge was the primary outcome. The specific aim and hypotheses were as follows:

Critical care and/or ER nurses who have been trained and de-briefed on the delivery of TTM via high fidelity simulation compared to those trained using a traditional lecture format will:

H1: Achieve higher TTM knowledge immediately after training and after 6 weeks (primary aim);

H2: Achieve higher psychomotor skills of TTM equipment use immediately after training and after 6 weeks;

H3: Report higher confidence immediately after the simulation training program and after 6 weeks;

H4: Report higher satisfaction with training immediately after the simulation training program and after 6 weeks.

From the collected demographic data, continuous variables were described with means plus/minus standard deviations, while categorical variables were described as

numbers out of the total and their corresponding percentages. The composite score for correct and incorrect items was listed as percentage of correct items for each individual. Demographic continuous variables were compared using independent t-tests between the two groups. Categorical variables were compared using chi-squared tests and Fisher's exact tests if the frequency per cell was less than 5.

In the univariate analysis, independent t-tests were used to compare the differences between the groups on different occasions. Two questions were removed from the test at baseline, Visit 1 and Visit 2, respectively, because the information needed to answer these questions was not covered in the PowerPoint slides. Bonferroni correction was used for secondary variables. The correction, set at .03 (alpha = .03), was used to adjust the statistical significance for the differences in the change in psychomotor skills evaluation scores by visit and by group. The same adjustment was used for confidence and satisfaction scores by visit and by group. The difference in change of the scores on different occasions between the groups were computed and also compared using independent t-tests. Non-parametric tests (i.e., Mann-Whitney) were used to verify the results of the parametric tests (i.e., independent t-tests) when comparing outcome variables between the two groups. The significance level was set at .05 (alpha = .05) between the group means on different occasions. Cronbach's alpha, a measure of scale reliability, was computed in order to measure internal consistency or how closely a set of items in the confidence and satisfaction questionnaires (respectively) were related as a group. Cronbach's alphas for the 7 Visit 1 and Visit 2 confidence questionnaire items were .92 and .91, respectively, indicating high internal consistency. Cronbach's alphas for the 6 Visit 1 and Visit 2 satisfaction questionnaire items were .93 and .94, respectively, also indicating high internal consistency. STATA 13 was used as a statistical software package for analysis (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP).

A mixed effects model was used to determine if an intervention effect was evident when the outcome variables of knowledge, skills, confidence and satisfaction were tested over the three different occasions (i.e., baseline, Visit 1 and Visit 2). A mixed effects model was chosen for this analysis because it allowed for inclusion of both fixed and random effects. The mixed effects model allowed us to assess repeated outcome measures while taking into an account multiple sources of variation. Results provide between and within the group differences. Each participant contributed four outcome data points: knowledge, psychomotor skills, confidence and satisfaction. The fixed effect was the treatment level (i.e., video or simulation), while the random effects included the demographic variables found to be significantly different between the two groups. These random effect variables were: 1) the number of nurses who delivered TTM prior to participating in the study; and, 2) the number of nurses who received some type of TTM education without any prior clinical experience in TTM delivery. Repeated measures of the analysis of variance and regression analyses of the difference in change of the scores on different occasions between the groups were computed while controlling for the significant demographic variables to compare with the results from the mixed effects model.

Data were analyzed using an intention to treat approach, where all of the subjects were included in the analysis even if they dropped out at some point in the study. As part of an intention to treat analysis, all-randomized population who received either one of two study educational interventions (i.e., video or simulation) were included in the analysis regardless of missing data. A secondary analysis was performed to evaluate the differences in the outcome variables for the participants who completed the entire study. Participants who did not complete an educational intervention and/or final evaluation were not included in these analyses.

Human Subjects

The study was a low risk randomized clinical trial using an educational intervention. The intervention was not significantly different from approaches used in educational and clinical settings, therefore, it was granted exempt status by the IRB. However, there was some risk of causing psychological discomfort due to being observed during high-fidelity simulation and evaluated during psychomotor assessment. Every effort was taken to minimize any psychological discomfort.

There was also a risk of loss of confidentiality concerning the participants' demographic information, however, only the study investigators and the statistician had access to the collected data. We monitored for the possibility of an unforeseen risk and every effort was taken to minimize the effect of such a risk on a participant. The participants were not audio- or video-recorded. To protect the study data and its confidentiality, all demographic data and evaluation results were stored in the REDCap secure database on a University's secure web server. All of the identifying demographic data are stored separately in the School of Nursing. These data will be destroyed 7 years after the completion of the study.

The participants may have benefited from this research study by gaining knowledge about the delivery of TTM and care of the patient undergoing this treatment. They may be able to apply the learned knowledge and clinical skills in the future when taking care of a patient undergoing TTM. This study also contributes to the growing body of knowledge, benefitting the society.

Ethical Considerations

This study was conducted according to U.S. and international standards of Good Clinical practice (FDA Title 21 part 312 and International Conference on Harmonization guidelines), applicable government regulations and Institutional research policies and procedures.

This protocol and an amendment were submitted to a properly constituted independent IRB at the study facility, in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study was made in writing to the investigator and the study was deemed as exempt. All of the study's participants were provided with a consent form describing this study and providing sufficient information for the participants to make an informed decision about their participation in this study. See Appendix 8 for a copy of the Subject Informed Consent Form. This consent form was submitted with the protocol for review and approval by the IRB. The formal consent of a subject was obtained before that subject underwent any study procedure. The consent was signed by the participant and the Principal Investigator obtaining the consent. Compensation for participation was not considered undue inducement, considering the typical salary of practicing nurses.

CHAPTER 4: RESULTS

Introduction

The purpose of this study was to compare post-training knowledge, psychomotor skills, confidence and satisfaction between critical care and emergency room (ER) nurses taught the delivery of TTM with a pre-recorded video lecture versus high fidelity simulation. This chapter presents the results of the analysis for the four stated hypotheses. The presentation of the findings is arranged by the four research hypotheses.

Descriptive Statistics

A sample of nurses who care for a population at high risk of cardiopulmonary resuscitation was enrolled. Although we planned to enroll 72 participants, we enrolled 52 nurse-participants due to difficulty in enrollment and limited resources. The demographic characteristics of the sample are shown and compared by group in Table 4.1. The TTM knowledge and psychomotor skill test scores collected before (i.e., baseline), immediately after (i.e., Visit 1) and at 6 weeks (+/- 2 weeks) after the initial randomized training (i.e., Visit 2) are shown in Table 4.2 and 4.3, respectively. The confidence and satisfaction questionnaire scores collected at the same intervals are shown in Table 4.4 and 4.5, respectively.

All 52 (100%) critical care and emergency room nurse-participants completed the baseline and Visit 1 assessment and 48/52 (93.2%) completed the Visit 2 assessment. Most (38/52, 73.1%) were female, most were Caucasian (35/52, 67.3%), and the mean age was 33.6 (\pm 9.5) years.

The groups differed in only two demographic characteristics. Thirty-one out of 52 (59.6%) of the nurses in the study sample had delivered TTM after a cardiac arrest at their work setting prior to the study; significantly more nurses in the video group had delivered TTM (21/28, 75.0%) versus in the simulation group (10/24, 41.7%). Nine out of 52 (17.3%)

nurses without prior TTM care experience had previous TTM education; 1/28 (3.6%) in the video group and 8/24 (33.3%) in the simulation group. These two group differences were included and adjusted for in the mixed effects model.

Table 4.1

Demographics of Study Sample

Variable	<u>All study sample, n=52</u>			<u>Video lecture, n=28</u>			<u>High-fidelity Simulation, n=24</u>		
	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>
Age	52 (100)	33.6	9.5	28 (100)	35.2	8.9	24 (100)	31.6	10
<u>Gender</u>									
Female	38 (73.1)			21 (75)			17 (70.8)		
<u>Race</u>									
Asian	9 (17.3)			8 (28.6)			1 (4.2)		
Black or African American	4 (7.7)			2 (7.1)			2 (8.3)		
White	35 (67.3)			16 (57.1)			19 (79.2)		
More than one race	3 (5.8)			1 (3.6)			2 (8.3)		
Unknown	1 (1.9)			1 (3.6)			0 (0)		
<u>Ethnicity</u>									
Hispanic or Latino	4 (7.7)			2 (7.1)			2 (8.3)		
Not Hispanic or Latino	38 (73.1)			19 (67.9)			19 (79.2)		
Unknown or Not reported	10 (19.2)			7 (25)			3 (12.5)		

Note. N = number; SD = standard deviation.

Table 4.1

Demographics of Study Sample

Variable	<u>All study sample, n=52</u>			<u>Video lecture, n=28</u>			<u>High-fidelity Simulation, n=24</u>		
	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>
<u>Nursing Experience</u>									
Total years	52 (100)	7.4	7.4	28 (100)	7.6	6.1	24 (100)	7.2	8.7
Critical Care	42 (80.8)	5.6	6.3	24 (85.7)	5.4	5.8	18 (75)	5.8	7.1
ER	10 (19.2)	4.1	3.2	4 (14.3)	3.9	1.2	6 (25.0)	4.3	4.1
<u>Simulation Experience</u>									
Yes	43 (82.7)			22 (78.6)			21 (87.5)		
Number of times participated		9.4	15.2		10.6	10.7		12.1	20.5
No	9 (17.3)			6 (21.4)			3 (12.5)		
<u>Graduate Program</u>									
Yes	32 (61.5)			18 (64.3)			14 (58.3)		
Master's specialty	27 (51.9)			16 (57.1)			11 (45.8)		
PhD	4 (7.7)			1 (3.6)			3 (12.5)		
DNP	1 (1.9)			1 (3.6)			0 (0)		
N/A	20 (38.5)			10 (35.7)			10 (41.7)		

Note. DNP = Doctor of Nursing Practice; ER = Emergency Room; N = number; N/A = not applicable; PhD = Doctor of Philosophy; SD = standard deviation.

Table 4.1

Demographics of Study Sample

Variable	<u>All study sample, n=52</u>			<u>Video lecture, n=28</u>			<u>High-fidelity Simulation, n=24</u>		
	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>	<i>N (%)</i>	<i>Mean</i>	<i>SD</i>
<u>TTM nursing care</u>									
Yes*	31 (59.6)			21 (75.0)			10 (41.7)		
Number of times		7.1	9.7		7.5	10.8		6.1	7.4
TH education	21 (40.4)			15 (53.6)			6 (25.0)		
TH training									
simulations	10 (19.2)			6 (21.4)			4 (16.7)		
<u>No TTM care</u>									
experience									
TH education*	9 (17.3)			1 (3.6)			8 (33.3)		
<u>Learn best by</u>									
Reading	22 (42.3)			11 (39.3)			11 (45.8)		
Practicing	49 (94.2)			26 (92.9)			23 (95.8)		
Talking	22 (42.3)			13 (46.4)			9 (37.5)		
Watching	31 (59.6)			20 (71.4)			11 (45.8)		
Listening	12 (23.1)			8 (28.6)			4 (16.7)		
Mixed	44 (84.6)			23 (82.1)			21 (87.5)		

Note. N = number; SD = standard deviation; TTM = targeted temperature management. * Statistically significant difference between the groups at $p < .05$.

Testing the Research Hypotheses

TTM knowledge. The first study hypothesis was as follows:

Critical care and/or ER nurses who have been trained and de-briefed on the delivery of TTM via high fidelity simulation compared to those trained using a pre-recorded video format will achieve higher TTM knowledge immediately after training and after 6 weeks.

The descriptive summary statistics for the TTM knowledge test scores by study group and visit are presented in Table 4.2.

Table 4.2

Targeted Temperature Management (TTM) Knowledge Test Scores (%), adjusted¹ (out of 18)

Variable	<u>All study sample, n=52</u>		<u>Video lecture, n=28</u>		<u>High-fidelity Simulation, n=24</u>		<u>p-value</u>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Baseline	68.3	18.1	68.6	19.7	67.8	16.4	.87
Visit 1	80.2	12.0	79.0	14.2	81.7	8.9	.42
Visit 2	82.6	13.3	79.1	15.6	86.5	9.1	.05

Note. Knowledge test scores (%) by visit and by group. Baseline = prior to any training; SD = standard deviation; Visit 1 = immediately after the training; Visit 2 = 6 weeks after the training.¹ adjusted = two questions removed from the test at baseline, Visit 1 and Visit 2, respectively.

The means and standard deviations of the knowledge test scores (%) by visit and by group are presented in the Table 4.2. The results of the non-parametric tests were consistent with those of the independent t-tests. There was no significant difference in knowledge between the video and simulation groups at baseline, $t(50) = .16, p = .87$. At Visit 1, there was no significant difference between the video and simulation groups scores, $t(50) = -.82, p = .42$. At Visit 2, there was a statistical trend for a difference between the video and simulation groups in knowledge test scores, $t(46) = -1.97, p = .05$, with the simulation group demonstrating higher knowledge.

A box plot of the knowledge test scores (%) by visit and by group is presented in the Figure 4.1. There was no significant difference in the amount of change in scores from baseline to Visit 1 between the video and simulation groups, $t(50) = -1.01, p = .32$. There was a trend towards better improvement in the amount of change in knowledge scores from baseline to Visit 2 scores between the video and the simulation groups, $t(46) = -1.96, p = .06$.

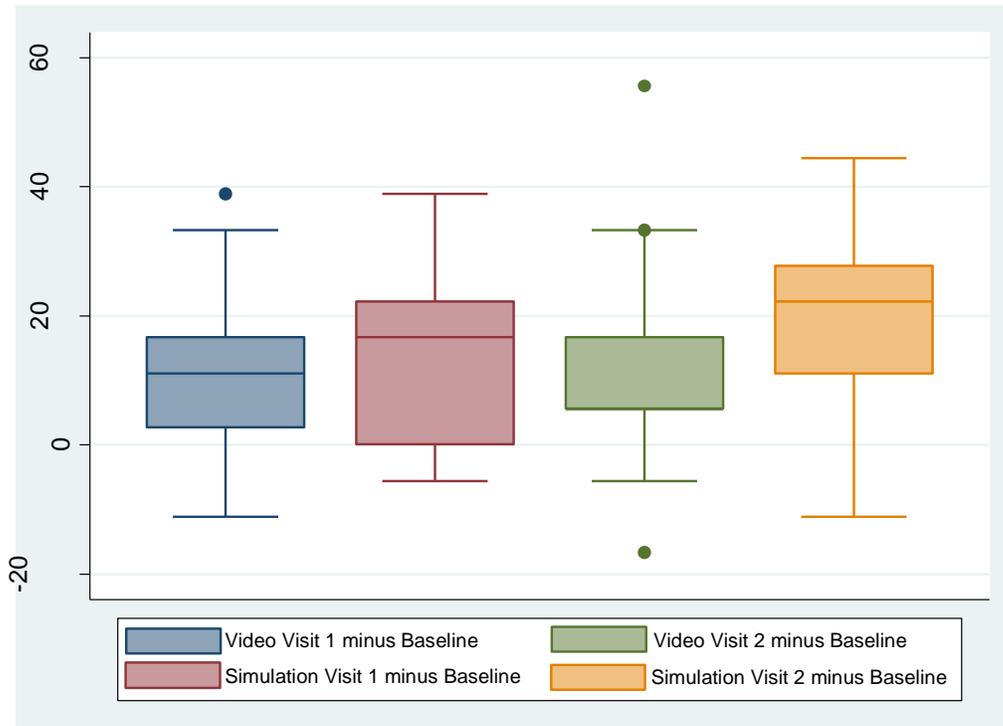


Figure 4.1. Box plot of the differences in the change in knowledge test scores (%) by visit and by group. There was no significant difference in the amount of change in scores from baseline to Visit 1 between the video and simulation groups, $t(50) = -1.01$, $p = .32$. There was a trend towards better improvement in the amount of change in knowledge scores from baseline to visit 2 scores between the video and the simulation groups, $t(46) = -1.96$, $p = .06$. Baseline = prior to any training; Visit 1 = immediately after the training; Visit 2 = 6 weeks after the training.

A graph of mean knowledge scores (%) by visit and by group is presented in Figure 4.2. In the mixed effects model with unstructured covariance, the interaction term of group (i.e., video or simulation) and time between baseline and Visit 2 remained significant when two covariates of prior TTM clinical experience and TTM education without clinical experience were included in the model (beta = 7.93, SE = 3.88, p = .04). The interaction term of group and time between baseline and Visit 1 remained non-significant in the model (beta = 3.80, SE = 3.47, p = .27). The results from the mixed effects model, repeated measures analysis of variance and simple regressions were all consistent. A graph of the adjusted linear predictions of group and time interaction term with 95% confidence intervals on knowledge test scores is presented in Figure 4.3.

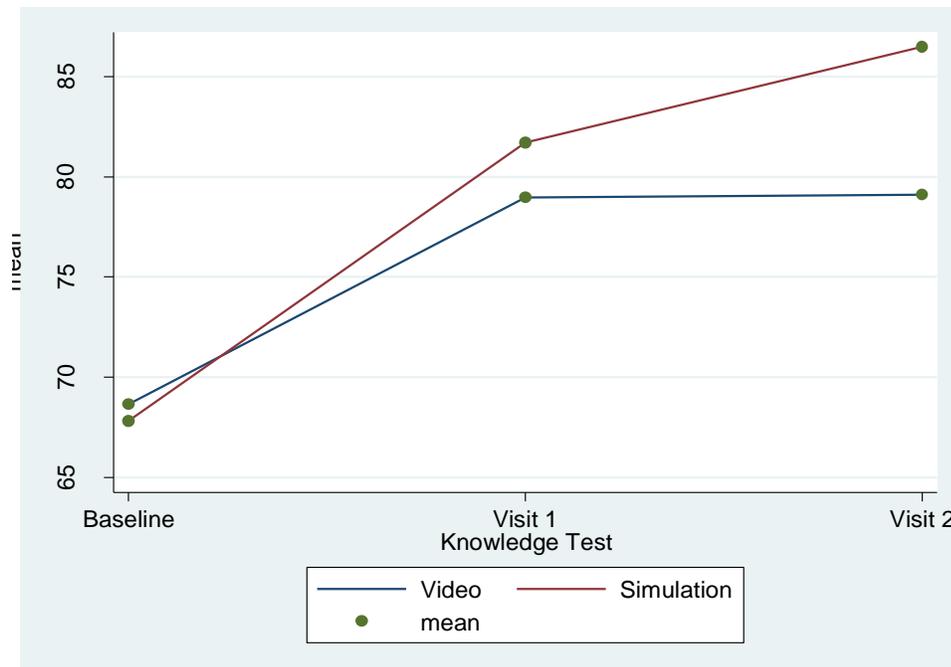


Figure 4.2. A graph of mean knowledge test scores (%) by visit and by group. Visit 1 = immediately after the intervention; Visit 2 = 6 weeks after the intervention.

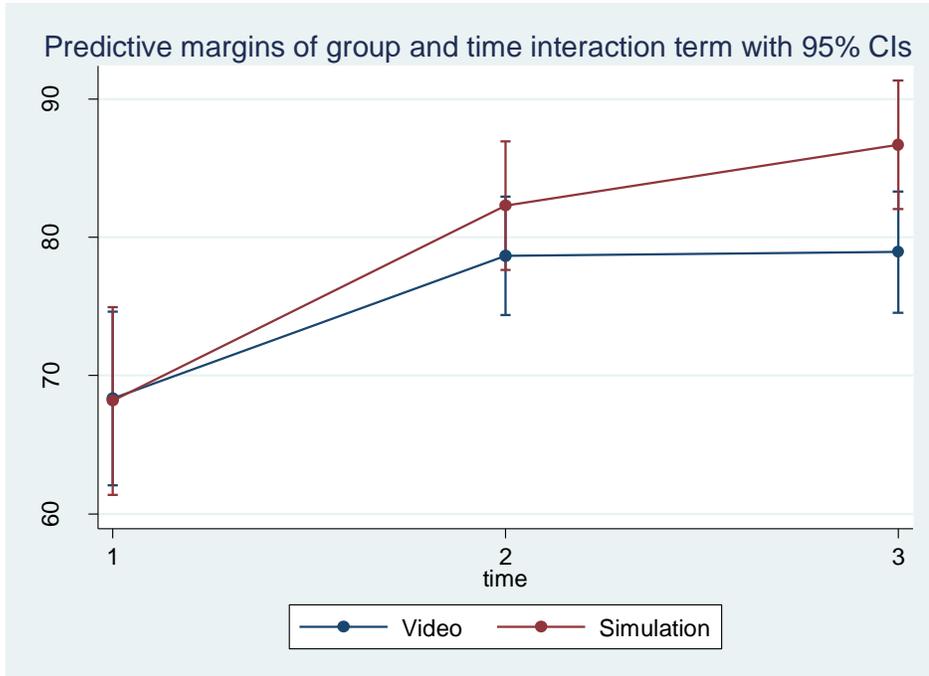


Figure 4.3. A graph of the adjusted linear predictions of group and time interaction term with 95% confidence intervals on knowledge test scores. In the mixed effects model with unstructured covariance, the interaction term of group (i.e., video or simulation) and time between baseline and Visit 2 remained significant when two co-variables of prior TTM clinical experience and TTM education without clinical experience were included in the model (beta = 7.93, SE = 3.88, p = .04). The interaction term of group and time between baseline and Visit 1 remained non-significant in the model (beta = 3.80, SE = 3.47, p = .27).

Psychomotor skills. The second study hypothesis was as follows:

Critical care and/or ER nurses who have been trained and de-briefed on the delivery of TTM via high fidelity simulation compared to those trained using a pre-recorded video format will achieve higher psychomotor skills of TTM equipment use immediately after training and after 6 weeks.

The descriptive summary statistics for the cooling equipment psychomotor skills evaluation scores (%) by study group and visit are presented in Table 4.3. The results of the non-parametric tests were consistent with those of the unpaired t-tests. Using a Bonferroni correction of $p = .03$, at baseline, there was no significant difference in the skills evaluation scores between the video and simulation groups, $t(50) = -1.06$, $p = .29$. At visit 1, the simulation group was significantly higher in psychomotor skills than the video group, $t(50) = -5.74$, $p = .00001$. At Visit 2, there was a significant trend between the video and simulation groups in psychomotor skills, $t(46) = -2.00$, $p = .05$.

A box plot of the differences in psychomotor skill scores (%) by visit and by group is presented in the Figure 4.4. Bonferroni correction for this analysis was set at $p < .03$. The change in psychomotor skills from baseline to visit 1 was significant between the video and the simulation groups, $t(50) = -2.86$, $p = .01$. There was no significant change from baseline to visit 2 scores between the video and the simulation groups, $t(46) = -.70$, $p = .49$.

Table 4.3

Psychomotor Skills Evaluation Scores (%)

Variable	<u>All study sample, n=52</u>		<u>Video lecture, n=28</u>		<u>High-fidelity Simulation, n=24</u>		<u>p-value</u>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Baseline	54	15.9	51.8	17.6	56.5	13.6	.29
Visit 1*	87	13.2	79.4	12.7	95.8	6.4	.00001
Visit 2	67	15.4	62.9	15.1	71.5	14.3	.05

Note. Psychomotor skills scores (%) by visit and by group. Baseline = prior to any training; SD = standard deviation; Visit 1 = immediately after the intervention; Visit 2 = 6 weeks after the intervention. * Statistically significant difference with Bonferroni's correction between the groups at $p < .03$.

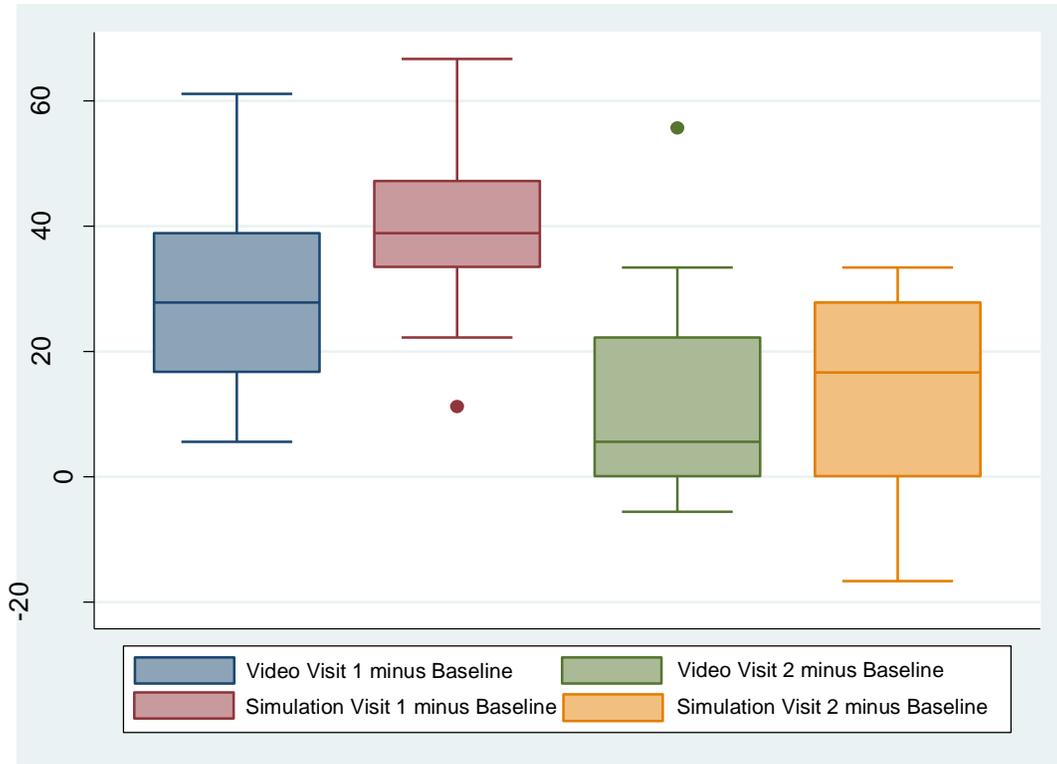


Figure 4.4. Box plot of the differences in the change in psychomotor skills evaluation scores (%) by visit and by group with Bonferroni's correction for statistical significance. The change in psychomotor skills from baseline to visit 1 was significant between the video and the simulation groups, $t(50) = -2.86$, $p = .01$. There was no significant change from baseline to visit 2 scores between the video and the simulation groups, $t(46) = -.70$, $p = .49$. Visit 1 = immediately after the intervention; Visit 2 = 6 weeks after the intervention.

A graph of mean psychomotor scores (%) by visit and by group is presented in Figure 4.5. In the mixed effects model with unstructured covariance, the interaction term of group (i.e., video or simulation) and time between baseline and Visit 1 remained significant when two covariates of prior TTM clinical experience and TTM education without clinical experience were included in the model ($\beta = 11.77$, $SE = 4.12$, $p = .004$). The interaction term of group and time between baseline and Visit 2 remained nonsignificant in the model ($\beta = 3.88$, $SE = 4.48$, $p = .39$). The results from the mixed effects model, repeated measures analysis of variance and simple regressions were all consistent. A graph of the adjusted linear predictions of group and time interaction term with 95% confidence intervals on psychomotor skills scores is presented in Figure 4.6.

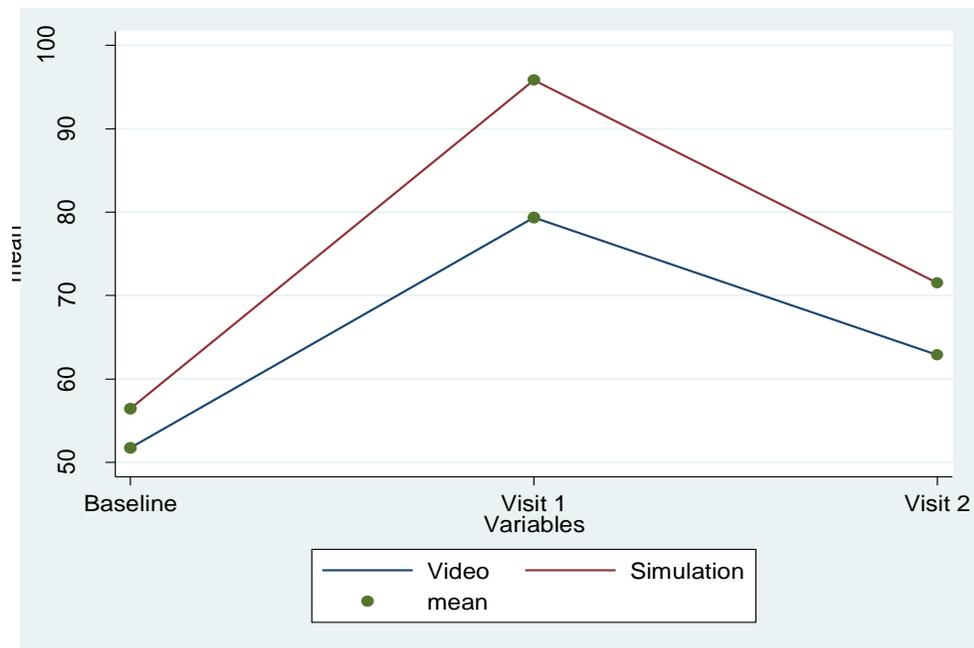


Figure 4.5. Mean psychomotor skills scores (%) by visit and group. Visit 1 = immediately after the intervention; Visit 2 = 6 weeks after the intervention.

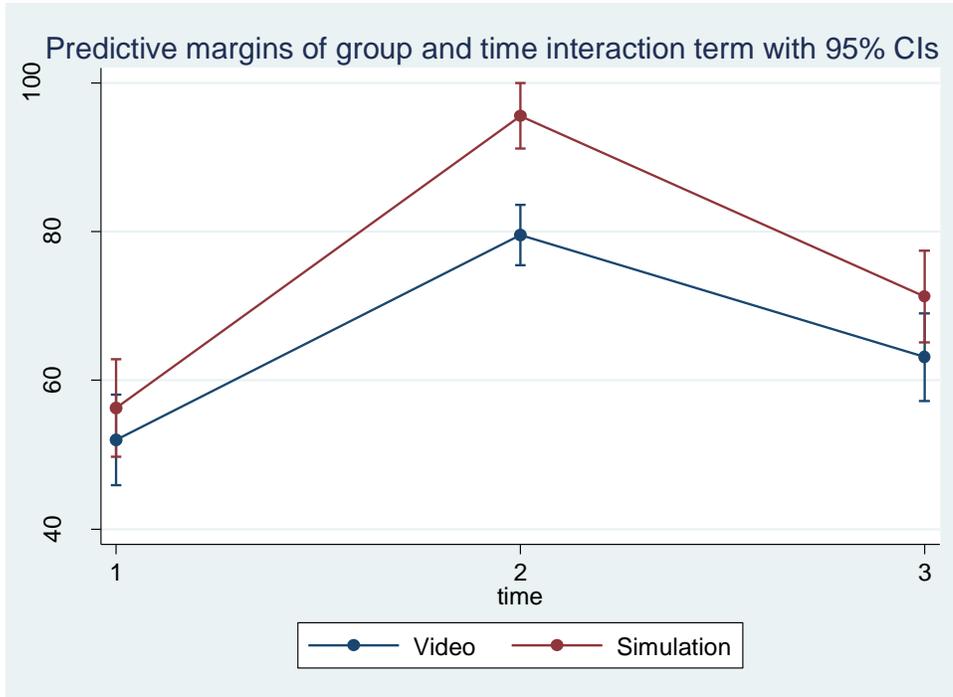


Figure 4.6. A graph of the adjusted linear predictions of group and time interaction term with 95% confidence intervals on psychomotor skills scores. In the mixed effects model with unstructured covariance, the interaction term of group (i.e., video or simulation) and time between baseline and Visit 1 remained significant when two covariates of prior TTM clinical experience and TTM education without clinical experience were included in the model (beta = 11.77, SE = 4.12, p = .004). The interaction term of group and time between baseline and Visit 2 remained not significant in the model (beta = 3.88, SE = 4.48, p = .39).

Confidence scores. The third study hypothesis was as follows:

Critical care and/or ER nurses who have been trained and de-briefed on the delivery of TTM via high fidelity simulation compared to those trained using a pre-recorded video format will report higher confidence immediately after the simulation training program and after 6 weeks.

A descriptive summary of the self-reported confidence in TTM knowledge and cooling equipment skills is presented in the Table 4.4. A box plot of mean confidence scores (out of 10) by visit and group with Bonferroni's correction at a significance level of $p < .03$ is presented in the Figure 4.7. The results of the non-parametric tests were consistent with those of the independent t-tests. At Visit 1, there was no significant difference in confidence between the video and simulation groups, $t(50) = -.92$, $p = .36$. At Visit 2, there also was no significant difference between the video and simulation groups, $t(46) = -.17$, $p = .87$.

Table 4.4

Comparison of the self-reported confidence of targeted temperature management (TTM) knowledge and cooling equipment skills (1=not at all confident to 10=extremely confident)

Variable	<u>All study sample, n=52</u>		<u>Video lecture, n=28</u>		<u>High-fidelity Simulation, n=24</u>		<u>p-value</u>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Summary score							
Visit 1	7.7	1.0	7.6	1.1	7.8	1.0	.36
Visit 2	7.3	1.3	7.2	1.4	7.3	1.2	.87

Note. Mean confidence scores by visit and by group with Bonferroni correction for statistical significance set at $p < .03$. SD = standard deviation; Visit 1 = immediately after the training; Visit 2 = 6 weeks after the training.



Figure 4.7. Box plot of mean confidence scores (out of 10) by visit and group with Bonferroni's correction for statistical significance. There was no significant difference between video and simulation groups at Visit 1, $t(50) = -.92$, $p = .36$. There was no significant difference between video and simulation groups at Visit 2, $t(46) = -.17$, $p = .87$. Visit 1 = immediately after the intervention; Visit 2 = 6 weeks after the intervention.

Satisfaction scores. The following was the fourth study hypothesis:

Critical care and/or ER nurses who have been trained and de-briefed on the delivery of TTM via high fidelity simulation compared to those trained using a pre-recorded video format will report higher satisfaction with training immediately after the simulation training program and after 6 weeks.

A descriptive summary of the self-reported satisfaction with TTM training is presented in the Table 4.5. A box plot of mean satisfaction scores (out of 10) by visit and group with Bonferroni's correction at a significance level at $p < .03$ is presented in the Figure 4.8. The results of the non-parametric tests were consistent with those of the independent t-tests. At Visit 1, there was a significant difference in the training satisfaction scores between video and simulation groups, $t(50) = -3.21, p = .002$. At Visit 2, there was a significant difference in the training satisfaction scores between video and simulation groups, $t(46) = -4.08, p = .0002$, with the simulation group more satisfied than the video group.

Table 4.5

Comparison of the self-reported satisfaction of targeted temperature management (TTM) training (1=not at all satisfied to 10=extremely satisfied), n=52

Variable	<u>All study sample, n=52</u>		<u>Video lecture, n=28</u>		<u>High-fidelity Simulation, n=24</u>		<u>p-value</u>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Summary score							
Visit 1 *	8.6	1.2	8.1	1.4	9.2	0.9	.002
Visit 2 *	8.6	1.3	8.0	1.4	9.3	0.8	.0002

Note. Mean satisfaction scores by visit and by group. At Visit 1, there was a significant change in the training satisfaction scores between video and simulation groups, $t(50) = -3.21, p = .002$. At Visit 2, there was a significant change in the training satisfaction scores between video and simulation groups, $t(46) = -4.08, p = .0002$. SD = standard deviation; Visit 1 = immediately after the training; Visit 2 = 6 weeks after the training. * Statistically significant difference with Bonferroni's correction between the groups at $p < .03$.

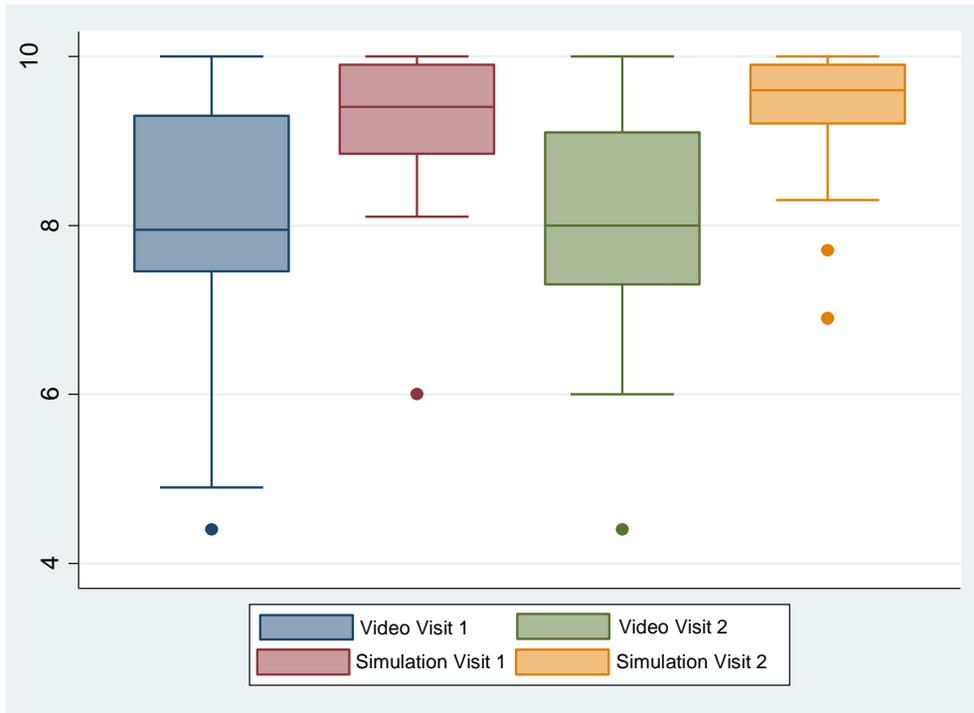


Figure 4.8. Box plot of mean satisfaction scores (out of 10) by visit and group with statistical significance adjusted using Bonferroni's correction. At Visit 1, there was a significant difference in the training satisfaction scores between video and simulation groups, $t(50) = -3.21$, $p = .002$. At Visit 2, there was a significant difference in the training satisfaction scores between video and simulation groups, $t(46) = -4.08$, $p = .0002$. Visit 1 = immediately after the intervention; Visit 2 = 6 weeks after the intervention.

Summary

In this chapter, the results of statistical analyses were described. In the mixed effects model with unstructured covariance, the interaction term of group (i.e., video or simulation) and time between baseline and Visit 2 knowledge test scores remained significant when two co-variables of prior TTM clinical experience and TTM education without clinical experience were included in the model. However, the interaction term of group and time between baseline and Visit 1 knowledge test scores remained non-significant in the model. In the mixed effects model with unstructured covariance, the interaction term of group (i.e., video or simulation) and time between baseline and Visit 1 psychomotor skills scores remained significant when two covariates of prior TTM clinical experience and TTM education without clinical experience were included in the model. However, the interaction term of group and time between baseline and Visit 2 psychomotor skills scores remained not significant in the model. There was no significant difference in confidence scores between the groups at either visit 1 or visit 2. Satisfaction with training was significantly higher in the simulation group at Visit 1 and Visit 2. These results will be discussed in the next chapter.

CHAPTER 5: DISCUSSION

Summary of the Study

Chapter 5 includes a summary of the study, discussion of the findings, implications for practice, recommendations for further research, and conclusions. This chapter begins with a summary of the study purpose, followed by the major findings. Conclusions from the findings are discussed in relation to the adapted Jeffries Simulation and Kirkpatrick's theory of "Four Levels" and the existing literature. Finally, implications for practice and recommendations for further research are discussed.

Discussion of the Findings

The purpose of this study was to compare the level of post-training knowledge, psychomotor skills, confidence and satisfaction among nurses taught the delivery of targeted temperature management (TTM) with a pre-recorded video lecture versus high fidelity simulation. In the primary analysis, we found that knowledge test scores did not differ between the groups immediately after the training, but 6 weeks later, there was a strong trend, with the simulation group appearing to have higher knowledge test scores. Skills were significantly better in the simulation group immediately after the training; however, 6 weeks later, there was no significant difference between the groups. No difference in confidence was found between the groups at either post-test point. Satisfaction with training was significantly higher in the simulation group at both post-testing points. Together these results suggest that nurses can benefit from the use of high-fidelity simulation when training on the delivery of TTM by retaining knowledge longer after the training, demonstrating better psychomotor skills immediately after the training and being more satisfied with the training approach.

Primary Outcome. An adaptation of Kirkpatrick’s “The Four Levels” model was used to frame the assessment of outcomes in this study (Kirkpatrick & Kirkpatrick, 2006). The primary study outcome was individual knowledge, which corresponds to Kirkpatrick’s second level of training evaluation, i.e., “Learning”. When measured immediately after the intervention, the non-significant change in knowledge scores between the two groups (i.e., video and high-fidelity simulation) was consistent with several previous studies with similar research designs (Adams et al., 2015; Couto et al., 2015; Mundell et al., 2013). A recent meta-analysis evaluated the effectiveness of high versus low fidelity simulation in the context of advanced life support training and also demonstrated no significant benefit in knowledge scores in the high fidelity simulation groups (Cheng et al., 2015). At the 6 weeks follow-up, the significant trend of better knowledge scores in the simulation group in our study differed from the studies with varied longitudinal follow-up periods (Couto et al., 2015; Mundell et al., 2013). Many of the older studies collected data on knowledge after longer follow-up periods, i.e., 3 months, 6 months and up to 1 year after the original training and have demonstrated a decline in the retention of knowledge and skills over time.

We engaged adult learners with simulation in order to elicit an active learner. It is known that adults learn best when fully engaged, motivated, find the topic important and pertinent to their field and are able to elicit an emotional connection while learning. Learning is a dynamic process, which involves multiple domains, where the thinking (i.e., cognitive) process can be separated from the physical (i.e., psychomotor) and emotional learning (Mahan & Stein, 2014).

One of the reasons for the trend toward a significant difference in knowledge scores immediately after training and at 6 weeks in the simulation group could be attributed to the neurobiology of learning. Initially, short-term memory is stored in the hippocampal

regions prior to being transferred to other brain regions (Nader & Hardt, 2009). This short-term transient working memory has a limited capacity and time frame. Time away from the problem-solving session may be needed in order to formulate new neuronal connections and make the memory accessible in the temporal and parietal lobes, which may explain why there was no change in knowledge scores between the two groups immediately after the intervention.

Another reason for higher knowledge scores in the simulation group at 6 weeks could be due to a stronger emotional connection that participants develop while being involved in the hands-on simulation training. Studies have shown that experiential learning, such as simulation training, evokes an emotional connection to the learning experience that may help to increase the memory of those who participate (Mahan & Stein, 2014; Perkins & Salmon, 1992). This emotional or affective type of learning may help learners to retain the material.

Another element of simulation that may have promoted learning is visualization, which is known to activate select neural circuitry, corresponding to the brain's sensory, motor and decision-making pathways. Since simulation training allows for direct visualization and interaction with the environment, a better neuronal process formation may occur, resulting in longer retention of the explicit memory (i.e., storage of facts and experiences) (Friedlander et al., 2011).

Yet another reason for higher scores in the simulation group at 6 weeks can be attributed to the range of learning that is used during simulation. Neurobiologists demonstrated that a more long-lasting learning results from a process that involves multiple domains, i.e., cognitive, psychomotor and affective (emotional) (Friedlander et al., 2011). In our simulation intervention, the nurse participants were able to involve multiple domains by learning the TTM delivery content while being guided by the facilitator, practice

psychomotor skills by applying equipment during the simulation scenario, and emotionally connect to a life-like scenario similar to that which they experience at work in the hospital.

There are certain memory modulators, such as personal experiences, levels of attention, stress level and motivation factors, which were not measured in our study, but could have influenced the formation of long-lasting memories and recall and led to higher knowledge scores at 6 weeks (Mahan & Stein, 2014). These modulators may have helped to reinforce the quality and quantity of neuronal connections and led to a stronger retention of the learning experience. For instance, participants in the simulation group could have been more motivated to actively engage in learning because they were randomized to the simulation group; they may have been more attentive, which would lead to better neuronal efficiency and overall better long-term retention of the learning experience. Therefore, they would have performed better on the knowledge test at 6 weeks after the training as compared to the control video group. Although all of the participants were asked to not participate in any educational sessions on TTM delivery during the 6-week lag period, some of the participants in the simulation group may have had a greater opportunity to practice the delivery of TTM at bedside. Reviewing and revisiting learned information helps to strengthen acquired neuronal networks and may help with information recall. Simulation participants were aware that simulation was the intervention of interest in our study and may have been more motivated to review the TTM overview study guide, their units' TTM protocols or use another mode of self-education before their 6-week study follow-up appointment, which ultimately would have led to a better performance on the TTM knowledge test. Finally, only the simulation group had an opportunity to be debriefed after their simulation training exercise, which may have resulted in deeper understanding and better retention of the material.

Secondary Outcomes. Measurement of the participants' psychomotor skills also corresponds to Kirkpatrick's second level of training evaluation, i.e., "Learning". Immediately after the training, psychomotor skills scores were significantly better in the simulation group compared to the video group. However, after 6 weeks, there was no significant difference between the groups. These findings were consistent with the results of previous studies with a similar design. In one meta-analysis that included studies comparing simulation with another form of instruction, small statistically significant effects were seen in process skill after the training, favoring simulation (Mundell et al., 2013). Another meta-analysis included 8 research studies comparing simulation with other forms of instruction and showed improved, but not statistically significant, outcomes for product skills in the simulation group (Ilgen, Sherbino, & Cook, 2013). The authors attributed the reason for non-significant results due to high heterogeneity of the studies ($I^2 \geq 50\%$). In yet another recent meta-analysis, the use of high fidelity when compared to low-fidelity manikins for advanced life support training was associated with moderate benefits for improving skills performance at course conclusion (Cheng et al., 2015). On the other hand, studies that measured skill performance at one year found no significant difference in skills performance (Cheng et al., 2015).

One of the reasons for the difference in psychomotor skill scores between the two groups immediately after the intervention, but not at 6 weeks, could be related to the neurobiology of psychomotor skill learning. In fact, the domains of thinking or cognitive learning processes are different from the physical or psychomotor learning (Krathwohl, 2001). Motor learning, or establishing of the ability to execute a skill, belongs to the implicit or unconscious type of learning, while storing of the concepts and establishing memories of the event belong to the explicit or conscious type of learning (Mahan & Stein, 2014). Therefore, it may require less effort, time and energy to learn a new psychomotor skill,

such as application and operation of the cooling machine, compared to cognitive problem-solving, such as multi-organ system management during the delivery of TTM. Additionally, unlike the participants in the video group, simulation group participants were able to practice the application of the cooling equipment during the simulation session. Repetition in learning psychomotor skills can result in better retention and efficiency in the execution of certain skills. As the occurrence of TTM in the hospital is not frequent, study participants in both groups may not have had the opportunity to practice their TTM delivery skills at the patient bedside. The lack of significance in psychomotor skills scores between the groups at 6 weeks suggests a different neuronal learning mechanism for acquiring psychomotor skills versus cognitive problem-solving.

The participants' self-reported confidence scores correspond to Kirkpatrick's first level of training evaluation, i.e., "Reaction". No difference in confidence was found between the groups at either post-test point. Previous research studies are inconsistent on the direction of change on self-reported confidence surveys when comparing simulation with other forms of instruction. Select studies comparing low- and high-fidelity simulation reported increased confidence scores in the high-fidelity simulation group (Curran et al., 2015).

The occurrence of TTM after CA in the hospital setting is infrequent. Therefore, after completing their first study visit, the nurses may not have had the opportunity to practice their skills on the delivery of TTM after CA due to low frequency of this therapy in the hospital and may still have considered themselves to be novices. Another explanation for the lack of difference in the groups' confidence scores could be due to our clear and organized video presentation on TTM delivery in the control group. It was the intention of the investigators to present consistent information in both groups (i.e., video and

simulation) and to limit any bias that would result in better scores in one group over the other.

In the adapted theoretical framework, Kirkpatrick's Level 1 describes the evaluation of the trainee's reactions, such as self-reported satisfaction with the training. Positive reactions are linked to the participants' learning motivation and are sought after by the instructors. Satisfaction with training was significantly higher in the simulation group at both post-testing points. These results are consistent with the other studies' findings. In one meta-analysis, 21 out of 182 studies compared simulation to non-simulation instruction and found that learners' satisfaction was higher in the simulation group (Mundell et al., 2013). In one recent study with a similar design, the investigators compared high fidelity simulation with case-based discussion for teaching medical students about pediatric emergencies and found that simulation was highly significant in terms of student satisfaction (Couto et al., 2015).

After the nurses complete their official training, continuing education is often unstructured. Throughout their careers, simulation is applicable to support their adult learning. In fact, adult professionals are more satisfied when trained by practicing and/or refreshing the skills that they feel are pertinent to their job obligations (Mahan & Stein, 2014). They bring their pre-existing knowledge on the subject and are accountable for what they choose to learn or not learn, which depends on how pertinent they consider the material to be to their job duties. We enrolled nurses who take care of patients after resuscitation with a likelihood of receiving TTM therapy and used simulation to resemble their work environment. Therefore, the simulation group participants may have found this type of learning environment to be directly applicable to their job duties and provided higher training satisfaction scores. Adult learners prefer to learn and apply new concepts immediately and learning via simulation allows these adult learners to practice newly

learned concepts and skills in real time, thereby increasing their level of satisfaction with the simulation training (Mahan & Stein, 2014). Although there is evidence to support that students who learn with simulation experience higher self-reported satisfaction, the relationship between increased knowledge and high training satisfaction has not been confirmed in the clinical setting.

Implications for Practice

A recent report by the Institute of Medicine (2015) on strategies to improve cardiac arrest survival stressed the importance of prioritizing “research related to identifying, evaluating and adopting best practices and new implementation strategies for treatments” (p. 3). The Institute of Medicine (2015) report also made recommendations for adaptation of the continuous quality improvement programs in order to translate national guidelines into clinical practice. Although the use of TTM after cardiac arrest has been recommended by the AHA and ILCOR for over a decade, the practice of TTM remains relatively new, infrequent with variable practice patterns. The frequency of the TTM at the specific University-affiliated urban hospital is approximately 3 patients per calendar month. Implementing institutional training programs, based on the national recommendations, should be a priority when translating science into clinical patient practice. The findings of our study have implications for putting into effect an institutional training program on the delivery of TTM after cardiac arrest.

In order to optimize simulation training and to maintain cooling equipment institutional clinical competency, nurse educators may consider employing “booster” skills practice at more frequent intervals, such as every 4 weeks (Oermann, Kardong-Edgren, & Odom-Maryon, 2011). Select studies have shown that “booster” practice leads to higher

process skill outcomes when compared to courses without such practice (Mundell et al., 2013).

Hospital educators should be aware that the use of high fidelity simulation in training nurses on the delivery of TTM after CA may help to maintain procedural knowledge for a longer time period after the initial training. In order to optimize the high fidelity simulation training, nurses may require frequent cooling equipment “refreshers” or “booster” practice in order to maintain competency on the application and maintenance of the cooling equipment. Nurses who learn via simulation also feel more satisfied with this type of training compared to simply watching an instructional video, which may affect their willingness to learn and ability to retain information.

Recommendations for Further Research

The ultimate goal of the proposed research was to discover the best way to educate nurses in executing evidence-based practice, i.e., TTM delivery after CA. The next steps in building the science of simulation education will be to evaluate: 1) the effect of simulation training on knowledge and skills in experienced versus novice nurses; 2) the effect of simulation training on TTM delivery in clinical practice; and, 3) patient outcomes (i.e., neurologic survival) after training nurses with one of two educational interventions. The measurement of these outcomes corresponds to the Kirckpatrick’s theoretical framework’s evaluation levels of “Behavior” and “Results”. The use of high fidelity simulation for training requires resources, such as the availability of the simulation space, equipment, scenario programming/set-up, and trained simulation instructors with experience in facilitating and debriefing those simulation sessions. Hence, future research should also concentrate on the cost-benefit analysis of the TTM training via high fidelity simulation in the clinical setting.

Additionally, clinical educators should recognize that the foundation of instructional design is rooted in the human neurobiology of learning. New instructional methods require a scientific rationale that links neurocognitive learning to a specific design in order to emphasize its value. Future research should concentrate on classifying and quantifying the neurocognitive processes to specific instructional approaches, such as the use of simulation.

Limitations

One of the limitations of this study is that after receiving training, the participants were evaluated on individual knowledge, psychomotor skills, satisfaction, and self-reported confidence delivering TTM therapy using paper and pencil tests. However, the participants' behavior change in the clinical setting and patient outcomes were not evaluated in this study due to infrequent occurrence of TTM in the clinical setting. This limits the translation of the study's findings as the degree of behavioral change in the clinical setting and the resulting patient outcomes remain unknown and warrant further investigation. Transfer of this learning to the patient bedside is essential to moving beyond learning in the simulation environment. This limits our understanding of how frequent such learning transfer occurs, regardless of whether the learned behavior is applied in the same context (i.e., TTM delivery after cardiac arrest) or a new context (e.g., targeted temperature management after traumatic brain injury, acute ischemic stroke, hepatic encephalopathy, etc.).

Another limitation of this study is that it was underpowered due to recruitment/enrollment difficulties and limited resources. As we did not reach the target sample size, statistical significance of the outcome variables may have been more heavily influenced by the outliers and potentially resulted in the Type I error. Also, on several

occasions, the Principal Investigator facilitated the study simulation when the simulation instructor was not available due to scheduling conflicts. The Principal Investigator was the only rater of the participants' psychomotor skills at all evaluation time points. This may have inadvertently biased the findings because the Principal Investigator had prior knowledge of the study design/evaluation tools and was also not blinded to the intervention.

A significant number of nurses had some exposure to the TTM therapy, which may have influenced the findings. All of the study participants needed to watch a 30-minute introductory lecture on the effects of the TTM, regardless of their assigned intervention group. This video was based on the institutional TTM protocol and may have by itself provided sufficient information on the nursing care of the post-cardiac patient undergoing this therapy. Also, it is important to consider that there were significantly more nurses with previous TTM education without TTM care experience in the simulation group versus in the video group. Although we controlled for this variable in the mixed effects model, the knowledge score difference between the two groups was in favor of simulation training by 7.4 points.

In addition, some participants in the simulation group may have had difficulty suspending disbelief, possibly interfering with the learning process. Several nurses participated in the study immediately after finishing their work shifts, which may influenced their learning process and outcomes due to fatigue.

Conclusions

In our study, we sought to compare the level of post-training knowledge, psychomotor skills, confidence and satisfaction among nurses taught the delivery of TTM with a pre-recorded video lecture versus high fidelity simulation. We found that knowledge

test scores did not differ between the groups immediately after the training, but there was a strong trend 6 weeks after the training with the simulation group appearing to have higher knowledge test scores. In the simulation group, skills were significantly better immediately after the training, however, there was no significant difference between the groups 6 weeks later. No difference in confidence was found between the groups at either post-test point. Satisfaction with training was significantly higher in the simulation group at both post-testing points. These results suggest that critical care and ER nurses who take care of post-cardiac arrest patients and are trained with high fidelity simulation may benefit from such training by maintaining their TTM knowledge for longer periods of time. Hospital educators should be aware that nurses may require frequent “booster” sessions to maintain their competency on the use of TTM cooling equipment. Further research should focus on the assessment of the effect of TTM delivery via simulation training on the transfer of the nurses’ knowledge and skills to bedside patient care and the effect on patient outcomes.

Appendix 1: Cerebral Performance Category (CPC) Scale

CPC 1	Good cerebral performance: Conscious, alert, able to work
CPC 2	Moderate cerebral disability: Conscious, sufficient cerebral function for independent activities for daily life
CPC 3	Severe cerebral disability: Conscious, dependent on other for daily support
CPC 4	Coma or vegetative state: Any degree of coma without the presence of all brain death criteria
CPC 5	Brain death: apnea, areflexia, EEG silence, etc.

Note: CPC - Cerebral Performance Category scale; EEG – electroencephalography.

Appendix 2. TTM for Out-of-Hospital CA Randomized Controlled Studies

Author (Reference)	Hachimi-Idrissi et al., 2001	Bernard et al., 2002	HACA, 2002	Bernard et al., 2010	Castren et al., 2010	Nielsen, et al., 2013	Kim et al., 2014
Sample (n)	30	77	275	234	200	939	1359
Country	Belgium	Australia	Austria	Australia	Sweden	Europe	USA
Control group	Normothermia	Normothermia	Normothermia	In-hospital TH	In-hospital TH	36°C	In-hospital TH
Initial Rhythm	PEA/Asystole	VF/VT	VF/VT	VF/VT	VF/VT, PEA/Asystole	VF/VT, PEA/Asystole	VF/VT, PEA/Asystole
Location of TTM Initiation	In-hospital	In-hospital	In-hospital	OOH and in-hospital	OOH and in-hospital	In-hospital	OOH and in-hospital
Methods of Temperature Measurement	Bladder	Tympanic or bladder before pulmonary-artery catheter	Tympanic, bladder	Bladder	Initial tympanic; then, rectal, bladder or intravascular	Bladder, intravascular or esophageal	Esophageal or tympanic
Time to Target Temperature (min)	180 ^a and 60 ^b	120	480	>60	102 vs. 282 ^b 155 ^a vs. 284 ^a	~240	60 min reduction in OOH group
Target Temperature (°C)	34	33	32-34	33	34	33 vs. 36	<34
Hypothermia Duration (h)	4 from initiation or when 34°C reached	12 after hospital arrival	24 from the start of cooling	24 from target temperature	ND	28 from the start of cooling	24
Cooling Method	Glycerol-containing cooling helmet	Ice packs	External cooling device; ice packs	Cold fluids, ice packs, surface cooling	RhinoChill nasal cooling device	Cold fluids, surface, intravascular	Cold fluids, surface, intravascular

Rewarming	Passive	Active with heated blanket over 6 h and passive rewarming	Passive	0.25°C/h	ND	0.5°C/h to 37°C	ND
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^aCore temperature (bladder); ^bCentral temperature (tympanic); ^cPre-hospital and post-admission cooling, respectively; CA – cardiac arrest; ND – not described; OOH – out-of-hospital; RR – Risk Ratio or Hazard Ratio; TTM – targeted temperature management.

Appendix 3. Characteristics of observational prospective and retrospective studies on TTM after CA

Study	Holzer et al., 2006	Oddo et al., 2006	Arrich, ERC-HACA, 2007	Heer et al., 2007	Sunde et al., 2007
Sample (n)	1038	109	587	76	119
Study Design	Retrospective, single institution	Retrospective, single institution	Prospective, multi-center (19)	Retrospective, single institution	Prospective; single institution
Country	Austria	Switzerland	Europe (7)	Germany	Norway
Control Group	Concurrent; standard care	Historical; standard care	Concurrent; normothermia	Historical; standard care	Historical; standard care
Poor Outcome Definition	CPC 3-5	CPC 3-5	CPC 3-5	NA	CPC 3-5
TTM Inclusion (n)	28	55	462	18	40
OHCA	(67%)	(100%)	83%	Mixed	100%
Location of TH Initiation	In-hospital	In-hospital	In-hospital	In-hospital	In-hospital
Target Temperature (°C)	32-34°C	32-34°C	32-34°C	33°C	33°C
Hypothermia Duration (h)	24 h from start of cooling	24 h at the target temperature	24 h at the target temperature	24 h at the target temperature	24 h at the target temperature
Cooling Method	Endovascular with or without cold fluid	Surface	Mixed	Endovascular	Cold fluid, surface or endovascular
Rewarming	0.5°C/h to 36C	Passive	Over 8 h	0.5°C/h to 36C	0.5°C/h

CA – cardiac arrest; CPC – Cerebral Performance Category scale; ND – not described; OHCA – out-of-hospital cardiac arrest; OOH – out-of-hospital; TTM – targeted temperature management.

Appendix 3 (continued). Characteristics of observational prospective and retrospective studies on TTM after CA

Study	Rittenberger et al., 2008	Storm et al., 2008	Bro-Jeppesen et al., 2009	Derwall et al., 2009	Don et al., 2009
Sample (n)	241	126	61	68	491
Study Design	Retrospective; single institution	Prospective; single institution	Prospective; EMS & single institution	Prospective; EMS & multi-center (5)	Retrospective; single institution
Country	USA	Germany	Denmark	Germany	USA
Control Group	Concurrent; normothermia	Historical; standard care	Historical; standard care	Concurrent; normothermia	Historical; standard care
Poor Outcome Definition	Discharged to a nursing home	CPC 3-5	CPC 3-5	CPC 3-5	Discharge
TTM Inclusion (n)	69	52	79	33	204
OHCA	56%	100%	100	100%	100%
Location of TTM Initiation	In-hospital	In-hospital	Pre/In-hospital	Pre/In-hospital	In-hospital
Target Temperature (°C)	32-34°C	33°C	32.5-33.5°C	33°C	32-34°C
Hypothermia Duration (h)	24 h from ROSC	24 h at the target temperature	24 h at the target temperature	24 h at the target temperature	24 h at the target temperature
Cooling Method	Cold fluid and surface	Cold fluid and surface	Cold fluid and surface	Cold fluid and surface	Surface
Rewarming	<1°C/h	0.25°C/h	Active at 0.5°C/h to 37°C	<1°C/h	Passive

CA – cardiac arrest; CPC – Cerebral Performance Category scale; ND – not described; OHCA – out-of-hospital cardiac arrest; OOH – out-of-hospital; ROSC - return of spontaneous circulation; TTM – targeted temperature management.

Appendix 3 (continued). Characteristics of observational prospective and retrospective studies on TTM after CA

Study	Gaieski et al., 2009	Whitfield et al., 2009	Dumas et al., 2011	Pfeifer et al., 2011	Testori et al., 2011
Sample (n)	38	123	1145	210	374
Study Design	Prospective; single institution	Retrospective; EMS & single institution	Prospective; single institution	Retrospective; single institution	Retrospective cohort; single institution
Country	USA	Australia	France	Germany	Austria
Control Group	Historical; standard care	Historical; standard care	Historical; standard care	Historical; normothermia	Historical; standard care
Poor Outcome Definition	CPC 3-5	Discharged to nursing home	CPC 3-5	CPC 4-5	CPC 3-5
TTM Inclusion (n)	20		718	143	135
OHCA	100%	100%	100%	58%	100%
Location of TTM Initiation	In-hospital	Pre/In-hospital	In-hospital	In-hospital	In-hospital
Target Temperature (°C)	32-34°C	32.5-33.5°C	32-34°C	32.5-33.5°C	32-34°C
Hypothermia Duration (h)	24 h from start of cooling	24 h from hospital presentation	24 h from ICU admission	24 h from target temperature	24 h from target temperature
Cooling Method	Cold fluid and surface	Cold fluid and surface	External cooling by forced air	Crushed ice or surface cooling or intravascular cooling	Surface, invasive, or combined cooling techniques
Rewarming	Active at 0.25°C/h	Over 12 h	Passive at 0.3°C/h	Active at 0.3°C/h with intravascular cooling	ND

CA – cardiac arrest; CPC – Cerebral Performance Category scale; ICU – Intensive Care Unit; ND – not described; OHCA – out-of-hospital cardiac arrest; OOH – out-of-hospital; ROSC - return of spontaneous circulation; TTM – targeted temperature management.

Appendix 3 (continued). Characteristics of observational prospective and retrospective studies on TTM after CA

Study	Horburger et al., 2012	Kory et al., 2012	Lundbye et al., 2012	Maclean et al., 2012	Soga et al., 2012
Sample (n)	828	33	100	29	372
Study Design	Retrospective;	Retrospective; single institution	Retrospective; single institution	Retrospective; single institution	Retrospective; Multi-center (14)
Country	Austria	USA	USA	Canada	Japan
Control Group	Historical; spontaneous normothermia and hyperthermia groups	Historical; standard care	Historical; standard care	Historical; standard care	None
Poor Outcome Definition	CPC 1-2	CPC 3-5	CPC 3-5	CPC 3-5	CPC 3-5
TTM Inclusion (n)	467	17	52	20	372
OHCA	100	None; all in-hospital	52%	100%	100%
Location of TTM initiation	In-hospital	In-hospital	In-hospital	In-hospital	In-hospital
Target Temperature (°C)	32-34°C	32-34°C	32-34°C	32-34°C	32-34°C
Hypothermia Duration (h)	24 h from target temperature	24 h from target temperature	18 h from target temperature	24 h from target temperature	12-72 h from target temperature
Cooling Method	"Various methods"	Cold saline, evaporative cooling by fanning wetted patient, and iced water gastric lavage	Cold fluid and ice packs, followed by intravascular cooling	Ice packs and/or cooling blanket and/or cold NSS	Infusion of cold saline, surface or intravascular cooling
Rewarming	12 h	Passive	0.35 °C/h	Passive	"Gradual" for 24-72 h

CA – cardiac arrest; Cerebral Performance Category scale; ND – not described; NSS – Normal saline; OHCA – out-of-hospital cardiac arrest; OOH – out-of-hospital; TTM – targeted temperature management.

Appendix 3 (continued). Characteristics of observational prospective and retrospective studies on TTM after CA

Study	Storm et al., 2012	Nichol et al., 2013	Vaahersalo et al., 2013	Bosson et al., 2014
Sample (n)	175	8316	504	927
Study Design	Prospective observational	Retrospective; multi-hospital (454)	Prospective observational; 21 ICUs	Retrospective; County EMS Agency
Country	Germany	USA	Finland	USA
Control Group	Historical	None	None	Historical
Poor Outcome Definition	CPC 3-5	CPC 3-5	CPC 3-5	CPC 3-5
TTM Inclusion (n)	201	214	311	387
OHCA	73%	None; all in-hospital	100%	100%
Location of TTM initiation	In-hospital	In-hospital	In-hospital	In-hospital
Target Temperature (°C)	33°C	≤34°C	ND	32-34°C
Hypothermia Duration (h)	24 h from target temperature	First 24 h post event	ND	Minimum of 20 h
Cooling Method	Cold saline and circulating water blankets	ND	“Majority used endovascular cooling”	ND
Rewarming	Controlled at 0.25 °C/h	ND	ND	ND

CA – cardiac arrest; CPC – Cerebral Performance Category scale; EMS – Emergency Medical Services; ND – not described; OHCA – out-of-hospital cardiac arrest; OOH – out-of-hospital; TTM – targeted temperature management.

Appendix 4. Review of post-TTM pyrexia studies

Study	Bro-Jeppesen et al., 2013	Cocchi et al., 2013	Gebhardt et al., 2013	Leary et al., 2013	Winters et al., 2013
Sample (n)	270	149	336	236	141
Study Design	Prospective observational data from one tertiary care centers, 2004-2010	Retrospective data from two tertiary care centers, 12/07-04/10	Retrospective review from a tertiary care facility, 1/1/05 – 6/30/10	Retrospective multicenter US clinical registry, 11 hospitals, 5/05-10/11	Retrospective observational data, 4 hospitals, 01/07-01/11
Pyrexia Definition	Median peak $T \geq 38.5^{\circ}\text{C}$ within the 36h after rewarming	$T > 38^{\circ}\text{C}$ within 24h following rewarming	$T \geq 38^{\circ}\text{C}$ within the first 48h of initial arrest	$T \geq 38^{\circ}\text{C}$ within 24h following rewarming	$T \geq 38.5^{\circ}\text{C}$ within 24h of cessation of TH
TTM Inclusion	270/270 (100%)	82/149 (55%); 54/54 (100%)	221/336 (66%)	236/236 (100%)	141/141 (100%)
Shockable rhythm	233/270 (86%)	31/54 (57%)	133/336 (40%)	76/236 (32%)	97/141 (68.8%)
OHCA	270/270 (100%)	149/149 (100%)	212/336 (63%)	187/236 (79%)	141/141 (100%)
Presence of pyrexia	136/270 (50%)	28/54 (52%), where 54/14 (36%) survived for >24h after rewarming	141/336 (40%); Pyrexia less common in TTM cohort (79/221, 36%) vs. non-TTM cohort (62/115, 54%, chi-squared 9.35, $p=0.002$)	69/167 (41%), where 167/236 (71%) survived at least 24h after TTM	42/141 (29.8%)

Neurological Outcomes	Association exists good (CPCs 1-2) vs. unfavorable outcomes (CPCs 3-5) at hospital D/C found in pyrexia vs non-pyrexia group (61% vs. 39% compared to 75% vs. 25%, respectively; p=0.02)	No association of pyrexia and poor outcomes (CPCs 3-5) in the pyrexia group (16/28, 57%) or non-fever group and good (CPCs 1-2) outcomes (15/26, 58%, p=0.62)	No association of pyrexia and good (CPCs 1-2) outcomes in whole cohort (OR 0.83, CI 0.49-1.40), TH cohort (OR 1.09, CI 0.56-2.13) or non-TTM cohort (OR 0.34, CI 0.11-1.06)	No difference in patients with vs. without pyrexia and good (CPCs 1-2) outcomes (26/37, 70% vs. 42/51, 82%, p=0.21). T \geq 38.7°C associated with lower proportion of good outcomes (58% vs. 80%, p=0.04)	Pyrexia is associated with increased neurological morbidity (i.e. Rankin score) (p=0.011)
Survival Outcomes	Pyrexia associated with 30-days mortality rate in pyrexia and non-pyrexia group, respectively (36% vs. 22%, p _{log-rank} =0.02; adjusted hazards ratio 1.8, 95% CI 1.1-2.7, p=0.02)	No difference in mortality in patients with vs. without pyrexia (15/28, 52% vs. 14/26, 54%; p=0.62)	Pyrexia not associated with survival within whole cohort (OR 0.32, CI 0.15-0.68) or TTM cohort (OR 1.21, CI 0.64-2.14), but fever associated with survival in non-TTM cohort (OR 0.47, CI 0.20-1.10). Subjects with fever in non-TTM cohort less likely to survive (31% vs 69%, p=0.003)	No difference in patients with vs. without pyrexia and survival (37/69, 54% v. 51/98, 52%; p=0.88). T \geq 38.7°C not associated with survival (40% vs. 56%, p=0.16)	Pyrexia associated with increased mortality in pyrexia and non-pyrexia group, respectively (64.3% vs 40.4%, OR 2.66, 95% CI 1.26-5.61; p=0.001)

CA – cardiac arrest; CI – confidence interval; CPC – Cerebral Performance Category scale; ND – not described; OHCA – out-of-hospital cardiac arrest; OOH – out-of-hospital; OR – odds ratio; TH – targeted temperature management.

Appendix 5: Self-reported confidence of therapeutic hypothermia (TH) knowledge

ID #:

Date completed:

Visit #:

Self-reported confidence of therapeutic hypothermia (TH) knowledge to be tested at baseline and after 6 weeks. Questions are based out of a 10-point scale (1=not at all confident to 10=extremely confident).

How would you rate your confidence in:

1. your TH knowledge?
2. using surface cooling equipment for TH?
3. identifying TH side effects?
4. managing TH side effects?
5. trouble-shooting TH equipment?
6. taking care of a post-cardiac arrest patient receiving TH?

Appendix 6: Self-reported satisfaction of therapeutic hypothermia (TH) training

ID #:

Date completed:

Visit #:

Self-reported satisfaction of therapeutic hypothermia (TH) training to be tested at baseline and after 6 weeks. Questions are based out of a 10-point scale (1=not at all satisfied to 10=extremely satisfied).

1. How would you rate your satisfaction with the specific method of TH training you received?
2. How would you rate this training for meeting your needs or expectations?
3. How would you rate the clarity of the information presented?
4. How would you rate the presentation skills of the lecturer in the first video?
 - 4a. How would you rate presentation skills of the lecturer in the second video (if applicable)?
 - 4b. How would you rate simulation facilitation skills of your simulation instructor (if applicable)?
5. How would you rate your overall satisfaction with this training?
6. How would you rate the likelihood of recommending this training to your friends or colleagues?
7. Please share with us any suggestions for improving this training:

Appendix 7: Demographic Data Form

Date completed:

Demographic Data Form

Each participant in this study is asked to complete the Demographic Data form. All information will be kept confidential. The information provided on this form will be used for the purpose of this study only.

1. Name:

2. E-mail Address:

3. Cell phone number:

4. Home phone number:

5. Work phone number:

6. What is your preferred method of contact?

7. Age:

8. Gender:
 Female
 Male

9. Race ("X" those with which you identify):
 American Indian or Alaska Native
 Asian
 Black or African-American
 Native Hawaiian or Other Pacific Islander
 White
 More than one race
 Unknown or not reported

10. Ethnicity ("X" ONLY one with which you MOST CLOSELY identify):
 Hispanic or Latino
 Not Hispanic or Latino
 Unknown or not reported

11. Please list the number of years of your previous nursing work experience:

12. Please list the number of years of your previous critical care (i.e., Intensive Care Unit only) nursing work experience:

13. Please list the number of years of your previous Emergency Room nursing work experience:

14. Most Recent Prior Area of Nursing Experience:

- Critical Care, please specify _____
- Cardiac
- Interventional Radiology
- Neurology
- Neurosurgery
- Oncology
- Orthopedics
- Pediatrics
- Primary Care
- Pulmonary
- Renal
- Surgery
- Transplant
- Women's Health
- Other, please specify _____

15. Have you ever previously participated in clinical simulation scenarios?
Yes ___ No ___

If yes, where?

- College/university education
- Work training
- Professional Conference
- Other, specify _____

16. How many **times** have you participated in simulation activities?

17. If you are currently enrolled in a graduate nursing program, please tell us which one.

___ Master's
Specialty: _____

___ Post-master's certificate
Specialty: _____

___ DNP

___ PhD
Research focus: _____

18. Have you previously delivered primary direct bedside nursing care to a post-cardiac arrest patient undergoing therapeutic hypothermia?

Yes ___ No ___

a. If "Yes", how many times?

b. If "Yes", have you participated in any educational activities on the delivery of therapeutic hypothermia after cardiac arrest? If so, please describe the activity.

c. If "Yes", how long ago was the educational activity?

d. If "Yes", did you take part in any therapeutic hypothermia nursing care training simulations?

e. If you did not participate in any therapeutic hypothermia educational activities prior to taking care of the patient receiving this treatment, would it have been helpful to have a prior training course?

Yes ___ No ___

19. Have you helped a colleague at work provide direct nursing care to a patient receiving therapeutic hypothermia?

Yes ___ No ___

a. If "Yes", how many times?

20. If you have not delivered any primary direct bedside nursing care to a patient receiving therapeutic hypothermia, have you participated in any educational activities on the delivery of therapeutic hypothermia?

Yes ___ No ___

a. If "Yes", please describe the educational activity?

b. If "Yes", how long ago was the educational activity?

c. If "Yes", did you take part in any therapeutic hypothermia nursing care training simulations?

21. How do you learn best? *Circle all that apply.*

___ Reading ___ Practicing ___ Talking ___ Watching ___ Listening
___ Other _____

Consent Form

Helene Fuld Pavillion for Innovative Learning and Simulation
University of Pennsylvania School of Nursing, Philadelphia, PA
Consent to Take Part in a Research Study

Participant

Name: _____

**The Role of High Fidelity Simulation in Training Nurses on the Delivery of
Therapeutic Hypothermia after Cardiac Arrest**

Principal Investigator's Name: Roksolana Starodub, MSN, CRNP-BC

Co-Investigator: Barbara Riegel, DNSc, RN, FAAN, FAHA

Consenting to the Research Study: Upon signing this document, you are authorizing the University and its researchers to perform a research study involving you as a subject. You should take your time and read the document carefully. You can also take a copy of this consent form to discuss it with your family member or anyone else you would like before signing the document.

Purpose of Research: You are being asked to participate in a research study. The primary goal of the current study is to compare two different forms of training of critical care and emergency nurses in delivering therapeutic hypothermia (TH) to patients after cardiac arrest. Currently, the best strategy for such training has not been identified.

Volunteer subjects are being asked to participate in this project in order to determine the best strategy for improving individual knowledge, skills, satisfaction and confidence in the delivery of TH by critical care and Emergency Room nurses.

Volunteers with current and/or previous nursing work experience in the Intensive Care Units and/or Emergency Room are eligible to participate. Volunteers who have been previously trained in TH, provided bedside care to a patient undergoing TH or have previously assisted a colleague in the care of a patient undergoing TH

may participate Volunteers who have not provided direct bedside nursing care for 2 or more years will be excluded.

This research study is being completed in partial fulfillment to obtain a Doctoral degree.

Procedures and Duration:

- After consent has been obtained and signed by you, you will be asked to complete a Demographic Data form.
- You will then be asked to take a 20-question pre-test.
- You will be asked to perform a brief psychomotor test using superficial cooling equipment.
- You will then be presented with your randomized training assignment.
- You and other participants will receive a 30-minute lecture on TH background information.
- You will then proceed to your previously randomized training assignment, which will be either a classroom-based or simulation-based instruction on the delivery of TH held at the University of Pennsylvania School of Nursing Simulation Center. Each lecture and simulation-based instruction will last approximately 1 hour to 1.5 hours. If you are randomized to the simulation instruction, you may be working individually or with another nurse. A group facilitator will guide your activities. If you are randomized to the lecture instruction, you will be listening to the lecture without group involvement.
- You will complete a post-test evaluating your TH knowledge and skills immediately after participating in the instruction. You will also complete brief questionnaires on confidence and training satisfaction. The evaluation will last approximately 30-40 minutes.
- Approximately 6 weeks later, you will be scheduled, at a time convenient for you, to participate in an evaluation of your knowledge and psychomotor skills on the delivery of TH after cardiac arrest. You will also complete the brief questionnaires on confidence and training satisfaction. Your test will be evaluated individually. All your responses will be kept confidential; neither your work supervisor or your academic faculty (if you are a student) will be

given access to your responses. The evaluation will last approximately 30-40 minutes.

Risks and Discomforts/Constraints: You will be asked to complete a demographic data form. The recognized risk to you is that identifying data could be divulged. But, every effort will be taken to protect you from having any of your information released to anyone other than those who are directly involved in the conduction of this study. All demographic data and evaluation results will be stored in the REDCap secure database. All of the demographic data and evaluation results will be destroyed 7 year after the completion of the study.

Unforeseen Risks: In addition to anticipated risks, we will monitor for unforeseen risks and minimize their effects on you.

Benefits: Your participation in this research study will provide you with TH training either via traditional lecture or simulation training. You may be able to apply the learned knowledge and skills in the future when taking care of a patient undergoing TH after cardiac arrest. However, no personal benefit can be promised based on your participation in this study. Subjects may not benefit from participating in this research. The results of the study will be published, though, and may improve the training given to nurses learning how to perform rare interventions such as TH.

Alternative Procedures: The alternative is not to participate in this study.

You may be required to stop before the end of the study for any of the following reasons:

- If all or part of the study is discontinued for any reason by the investigator or university authorities.
- If you are a student and participation in the study is adversely affecting your academic performance.
- If you fail to adhere to requirements for participation established by the researcher.
- If a mutually convenient time for you to participate in the intervention training session or post-intervention intervention is not obtainable.

- Voluntary Participation: Participation in this study is voluntary, and you can refuse to be in the study or stop at any time. There will be no negative consequences if you decide not to participate or to stop.

Payment: If you complete the entire study, you will receive a \$50.00 gift card. This amount will be broken down into two payments. You will be given \$25.00 gift card after completing the training and you will receive \$25.00 upon the completion of the final evaluation of your performance 6 weeks after the initial training.

Responsibility for Costs: You will be responsible for the cost of parking and transportation to the University's School of Nursing.

Confidentiality: Your identity will be kept confidential in any presentation or publication of research results, but there is a possibility that records that identify you may be inspected by authorized individuals, such as institutional review board (IRB) authorities. Your individual study results will not be accessible to faculty (if you are a student) or hospital authorities (if you are a staff nurse). By signing this document, you consent to such inspections and to the copying of excerpts of your records, if required by any of these representatives.

Every effort will be taken to protect you from having any of this information divulged to anyone other than those who are directly involved in the conduction of this study. All demographic data and evaluation data will be destroyed 7 years after completion of the study.

Other Considerations: If you wish further information regarding your rights as research subject or if you have problems with a research-related injury, please contact the Institution's Office of Research Compliance.

Consent:

I have been informed of the reasons for this study.

I have had the study explained to me and all of my questions answered.

I have carefully read this consent form, initialed every page and have received a signed copy.

Subject Name

Date

Subject Signature

Date

Witness to Signature

Date

Appendix 9. Therapeutic Hypothermia (TH) Overview Lecture Guide

Delivering Nursing Care to Patients Undergoing Therapeutic Hypothermia after Cardiac Arrest

Presented by Benjamin Abella, MD, MPhil
University of Pennsylvania

Cardiac Arrest (US data)

- In 2013, 359,400 individuals suffered out-of-hospital cardiac arrest (CA) with 9.5% survivor rate
- In 2013, 209,000 patients suffered in-hospital CA with 23.9% survivor rate
- Over the past decade, survival & neurologic outcomes improved at some settings due to the use of TH and aggressive critical care management

Definition of Post-Cardiac Arrest

- Post-cardiac arrest: Absence of pulses requiring chest compressions, regardless of location or presenting rhythm followed by return of spontaneous circulation (ROSC)

2010 AHA Recommendations

- Adult patients with ROSC after **out-of-hospital VF** cardiac arrest should be cooled between 32°C and 34°C (89.6°F to 93.2°F) for 12 to 24 hours (Class I, LOE B)
- May be considered for comatose adult patients with ROSC after **in-hospital cardiac arrest of any initial rhythm** or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electric activity or asystole (Class IIb, LOE B)

2010 AHA Recommendations

- Active rewarming should be avoided in comatose patients who spontaneously develop a mild degree of hypothermia (>32°C [89.6°F]) after resuscitation from cardiac arrest during the first 48 hours after ROSC. (Class III, LOE C)

Cardiac Arrest Background

- During cardiac arrest:
 - blood flow to the brain ceases → neuronal injury begins → loss of consciousness
- After restoration of effective circulation:
 - ongoing injury during reperfusion injury → release of free radicals and excessive neurotransmitters

Cardiac Arrest Background

- During the first 24 hours after ROSC – significant effect of brain temperature on neurological recovery and survival

Post-arrest injury mechanisms

- Post-arrest reperfusion injury
 - a. hypoxia-associated mechanisms
 - b. reperfusion-associated mechanisms
 - c. release of free radicals and excessive excitatory neurotransmitters

TH Background

- Primary TH mechanisms:
 - suppress injurious effects, such as calcium shifts, release of excitatory amino acids and free radical production
 - shift oxyhemoglobin curve to the left → decrease in oxygen delivery **BUT**
 - decrease in oxygen metabolic demand, consumption and the rate of elimination
 - metabolic rate during TH decreases by approximately 8%/°C
 - reduction of normal electrical activity of the brain

TH-associated changes

- Hemodynamic effects:
 - initially, tachycardia → then, bradycardia
 - decreased HR and increased BP due to increased systemic vascular resistance
 - decreased CO/CI - decreased SV

TH-associated changes

- Hemodynamic effects:
 - decreased ScVO₂, decreased coronary blood perfusion, decreased oxygen supply, **BUT**
 - decreased oxygen demand → decreased PaO₂ and PaCO₂
- Cardiovascular/EP effects:
 - increased PR, QRS, QTc
 - arrhythmias are rare if T>30°C

TH-associated changes

- Musculoskeletal Effects:
 - shivering → increases oxygen demand (by 40-100%), increases respiratory rate and work of breathing; increases HR
 - prevent shivering by neuromuscular paralysis prior to induction
 - elderly cool more quickly than younger and obese patients

TH-associated changes

- Renal/Electrolytes:
 - volume depletion due to cold diuresis
 - due to the polyuria → decreased secretion of potassium, magnesium, phosphorus (electrolytes move inside the cell)
 - close monitoring of potassium, magnesium, phosphorus as will rebound to higher value during re-warming
 - aggressive fluid repletion

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TH-associated changes

- Endocrine Effects:
 - hyperglycemia results from decreased insulin sensitivity/secretion
- Immune System Effects:
 - increased the risk for pneumonia if hypothermia lasts more than 24 hours
 - increased risk of wound infections due to decreased WBC function and skin vasoconstriction

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TH-associated changes

- Hematologic Effects:
 - decreased platelet function at 35°C
 - decrease in the function of plasma proteins at less than 34°C → effect on drug pharmacodynamics/ pharmacokinetics
 - increased risk for bleeding with procedures due to reduced platelet function
 - in-vivo coagulopathy → not detectable by lab testing due to blood being warmed during testing

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TH Stages

Mild hypothermia (32-34°C) stages:

- Pre-cooling
- Induction
- Maintenance
- Rewarming
- Post-rewarming

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Eligibility Criteria

1. Post-cardiac arrest
2. Full code or DNR-A
3. Comatose at enrollment with a Glasgow Coma Motor Scale <6 pre-sedation (i.e., does not follow commands – two thumbs up, squeeze and release)
4. Patient's pre-arrest cognitive status is not severely impaired (i.e., GCS of 15 or performed ADLs independently)

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Eligibility Criteria

5. No other obvious reasons for coma (e.g., mass lesions, seizures, metabolic coma, etc.)
6. No uncontrolled bleeding
7. No evidence of uncontrollable dysrhythmias
8. Absence of multi-organ dysfunction syndrome, severe sepsis, or a comorbidity associated with minimal chance of meaningful survival

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Eligibility Criteria

9. Less than 12 h since ROSC
10. Pregnancy – consult Maternal Fetal Medicine
11. Start ASAP !!!

Pre-cooling Stage

- Head CT – as deemed necessary to rule out intracranial hemorrhage, or other causes of coma

Induction: Equipment

- Two 1L bags of cold (4°C) normal saline
- Central venous catheter and tubing set-up
- Arterial catheter and tubing set-up
- Gaymar III external cooling system: 1 torso and 2 thigh cooling pads, 2 sets of hoses
- Neuromuscular blockade equipment (i.e., TOF)

Induction: Equipment

- Temperature probe foley cath with adapter for cooling device or esophageal probe
- BIS monitor equipment
- Know location of the fluid warmer if needed

Induction Stage

- Obtain baseline labs:
- CBC/BMP (Chem7)/Mg/Phos, PT/PTT/INR/Fibrinogen, ABG, iCa+, lactate, CPK-MB/CK/Troponin, cortisol level if indicated, urinalysis/urine culture, blood cultures, sputum cultures, amylase/lipase, toxicology screen if appropriate, beta HCG on all women of child-bearing age, ScvO2 (central co-oximetry); 12-lead ECG/check blood sugar

Induction Stage

- Neurology consult for:
 - continuous EEG monitoring beginning ASAP while paralyzed
 - seizure monitoring indication
 - EEG must be initiated within 6-12 hours of starting TH

Induction Stage

- Cardiology consult for:
 - indeterminate ECG, suspected non-STEMI, arrhythmia, or hemodynamic instability;
 - early echocardiogram consideration;
 - early re-vascularization

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Induction Stage

- Ensure that arterial line is placed before or simultaneously with initiation of cooling
- Place temp probes (bladder; if contraindicated, esophageal)
- Assess/document neurological eval – Glasgow Coma Scale
- Assess/document skin assessment

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Induction Stage

- Sedate first → then, paralyze
- BIS monitor for sedation monitoring
- TOF for neuromuscular blockade monitoring
- If no evidence of pulmonary edema, infuse 2L cold NSS over 30 minutes

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Induction Stage

- Connect and fill wraps before placing them on the patient
- Set temperature on surface cooling device to 33°C
- Titrate sedatives to bispectral index (BIS) goal of 40-60
- Use peripheral nerve stimulator for adequate paralysis
- Goal: Reach target temp of 33°C over 4 h

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Maintenance Stage

- Maintain temperature between 32-34°C for 24 hours after reaching target temp
 - check Temp every hour

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Maintenance Stage

- Obtain serial labs per protocol
- check ABG every 6 hours and prn, glucose and potassium every 6 hours until re-warming process, lactate every 6 hours x 2 days, CBC/BMP (Chem7), iCa/Mg/Phos every 6 hours; PT/PTT/INR, repeat CPK-MB/CK/Troponin every 6 hours; check blood sugar per insulin drip protocol
- SvO2 cath cont. or central venous blood samples every 1-2 hours for first 6 hours; then every 6 hours and prn

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TH Maintenance

- Hemodynamic goals
- MAP 80-100mmHg (unless acute coronary syndrome); CVP >8 cmH2O; ScVO2 >=65%; urine output >30 ml/hr
- Assess for and treat for shivering
- Assess skin for breakdown every 4 hours
 - re-adjust cooling pads every 4 hours

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TH Maintenance

- Eye care every 4 hours
 - ophthalmic lubricant 3.5 gm; dose 1 app both eyes every 2 hours
- Check urine output every 2 hours
- If temp <31°C → infuse 250ml bolus of warm 40°C
 - IV NSS or LR until Temp >32°C
 - monitor closely for arrhythmias when Temp < 32°C

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Rewarming Stage

- Hold all potassium-containing fluids if potassium is >3.5 immediately before and during rewarming
- Rewarm appropriately to 37°C
- Stop neuromuscular blockade after core temp reaches 36°C
 - if TOF 4/4, then D/C BIS monitoring

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Rewarming Stage

- Blue-faced Gaymar III, set 37°C Moderate mode
 - automatically increases 0.33°C/hr (~12 hrs); don't change Automatic to Manual

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Rewarming Stage

- Check CVP every 1h until 37°C
- Check potassium levels every 6h
 - increased risk of hyperkalemia
- Check blood sugar every 1 h if on insulin drip
 - increased risk of hypoglycemia

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Rewarming Stage

- Check ABGs – adjust vent settings
- Follow CVP, ScVO2, urine output
 - anticipate decrease in cardiac output and BP with decreased CVP
 - aggressive IV fluids to maintain adequate volume status and perfusion
- Maintain paralysis until T>36°C, then stop if TOF 4/4, then D/C BIS monitoring

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Post-rewarming Stage

- Maintain normothermia for 48 hours after rewarming using acetaminophen, cooling device if needed
- Remove wraps and fully assess skin
- Document any skin breakdown –obtain wound care consult
- Do NOT neuro-prognosticate before 72 hours after rewarming!

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Documentation

- VS/hemodynamics, VS with CVP every 1 hour during induction and re-warming; every 4 hours during maintenance
- Baseline and ongoing neuro exam every 2 hours;
- Baseline pain assessment
- Administration of analgesia – pain management
- Administration of sedation – use of BIS monitoring
- Administration of NMB agents – use of peripheral nerve stimulator
- Cooling blanket settings in °C with each change – record temp in °C
- Eye care every 2 hours
- Skin care and repositioning

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REFERENCES

1. Adams, A. J., Wasson, E. A., Admire, J. R., Gomez, P., Babayeuski, R. A., Sako, E. Y., & Willis, R. E. (2015). A comparison of teaching modalities and fidelity of simulation levels in teaching resuscitation scenarios. *Journal of Surgical Education, 27* (5), 778-785.
2. Adrie, C., Laurent, I., Monchi, M., Cariou, A., Dhainaou, J. F., & Spaulding, C. (2004). Post-resuscitation disease after cardiac arrest: A sepsis-like syndrome? *Current Opinion in Critical Care, 10* (3), 208-212.
3. Adrie, C., Adib-Conquy, M., Laurent, I., Monchi, M., Vinsonneau, C., Fitting, C, . . . Cavaillon, J. M. (2002). Successful cardiopulmonary resuscitation after cardiac arrest as a "sepsis-like" syndrome. *Circulation, 106* (5), 562-568.
4. Alkadri, M. E., Peters, M. N., Katz, M. J., & White, C. J. (2013). State-of-the-art paper: Therapeutic hypothermia in out of hospital cardiac arrest survivors. *Catheterization and Cardiovascular Interventions, 82* (4), E482-E490.
5. Alzaga, A. G., Salazaar, G. A., & Varon, J. (2006). Resuscitation great. Breaking the thermal barrier: Dr. Temple Fay. *Resuscitation, 69* (3), 359 - 364.
6. Ambrosia, G., & Tritto, I. (1999). Reperfusion injury: Experimental evidence and clinical implications. *American Heart Journal, 138* (2), S69-S75.
7. Arafeh, J. M. R., Hansen, S. S., & Nichols, A. (2010). Debriefing in simulated based learning: Facilitating a reflective discussion. *The Journal of Perinatal and Neonatal Nursing, 24* (4), 302-309.
8. Arrich, J. & European Resuscitation Council Hypothermia After Cardiac Arrest Registry Study Group. (2007). Clinical application of mild therapeutic hypothermia after cardiac arrest. *Critical Care Medicine, 35* (4), 1041-1047.

9. Baena, R. C., Busto, R., Dietrich, W. D., Globus, M. Y., & Ginsberg, M. D. (1997). Hyperthermia delayed by 24h aggravates neuronal damage in rat hippocampus following global ischemia. *Neurology*, *48* (3), 768-773.
10. Barsuk, J. H., McGaghie, W. C., Cohen, E. R., O'Leary, K. J., & Wayne, D. B. (2009). Simulation-based mastery learning reduces complications during central venous catheter insertion in a medical intensive care unit. *Critical Care Medicine*, *37* (10), 2697-2701.
11. Bernard, S. A., Gray, T. W., Buist, M. D., Jones, B. M., Silvester, W., Gutteridge, G., & Smith, K. (2002). Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *New England Journal of Medicine*, *346* (8), 557-563.
12. Bernard, S. A., Smith, K., Cameron, P., Masci, K., Taylor, D. M., Cooper, D. J., . . . Silvester, W.; Rapid Infusion of Cold Hartmanns (RICH) Investigators. (2010). Induction of therapeutic hypothermia by paramedics after resuscitation from out-of-hospital ventricular fibrillation cardiac arrest: a randomized controlled trial. *Circulation*, *122* (7), 737-742.
13. Bhanji, F., Mancini, M. E., Sinz, E., Rodgers, D. L., McNeil, M. A., Hoadley, T. A., . . . Hazinski, M. F. (2010). Part 16: Education, implementation, and teams: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*, *122* (18 Suppl 3), S920-933.
14. Bisschops, L. A., Hoedemaekers, C. W. E., Mollnes, T., & van der Hoeven, J. (2012). Rewarming after hypothermia after cardiac arrest shifts the inflammatory balance. *Critical Care Medicine*, *40* (4), 1136-1142.

15. Blewer, A. L., Delfin, G., Leary, M., Gaieski, D. F., & Abella, B. S. (2013). A structured educational intervention to improve targeted temperature management utilization after cardiac arrest. *Journal of Critical Care, 28* (3), 259-264.
16. Bosson, N., Kaji, A. H., Niemann, J. T., Eckstein, M., Rashi, P., Tadeo, R., . . . Koenig, W. (2014). Survival and neurologic outcome after out-of-hospital cardiac arrest: Results one year after regionalization of post-cardiac arrest care in a large metropolitan area. *Prehospital Emergency Care, 18* (2), 217-223.
17. Bro-Jeppesen, J., Kjaergaard, J., Horsted, T. I., Wanscher, M. C., Nielsen, S. L., Rasmussen, L. S., & Hassager, C. (2009). The impact of therapeutic hypothermia on neurological function and quality of life after cardiac arrest. *Resuscitation, 80* (2), 171-176.
18. Bouwes, A., Binnekade, J. M., Kuiper, M. A., Bosch, F. H., Zandstra, D. F., Toornvriet, . . . Horn, J. (2012). Prognosis of coma after therapeutic hypothermia: A prospective cohort study. *Annals of Neurology, 71* (2), 206-212.
19. Braun, L., Sawyer, T., Smith, K., Hsu, A., Behrens, M., Chan, D., . . . Lopreiato, L. (2015). Retention of pediatric resuscitation performance after a simulation-based mastery learning session: A multicenter randomized trial. *Pediatric Critical Care Medicine, 16* (2), 131-138.
20. Bro-Jeppesen, J., Hassager, C., Wanscher, M., Soholm, H., Thomsen, J. H., Lippert, F. K., . . . Kjaergaard, J. (2013). Post-hypothermia fever is associated with increased mortality after out-of-hospital cardiac arrest. *Resuscitation, 84* (12), 1734-1740.
21. Callaway, C. W., Donnino, M. W., Fink, E. L., Geocadin, R. G., Golan, E., Kern, K. B. . . . Zimmerman, J. L. (2015). Part 8: Post-cardiac arrest care: 2015 American

- Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*, 132 (suppl 2), S465-S482.
22. Castillo, J., Davalos, A., & Noya, M. (1997). Progression of ischaemic stroke and excitotoxic aminoacids. *Lancet*, 349 (9045), 79-83.
23. Castrén, M., Nordberg, P., Svensson, L., Taccone, F., Vincent, J. L., Desruelles, D., . . . Barbut, D. (2010) Intra-arrest transnasal evaporative cooling: a randomized, prehospital, multicenter study (PRINCE: Pre-ROSC IntraNasal Cooling Effectiveness). *Circulation*, 122 (7), 729-36.
24. Cavanaugh, S. (1997). Computerized simulation technology for clinical teaching and testing. *Academic Emergency Medicine*, 4 (10), 939-943.
25. Chatzipanteli, K., Alonso, O. F., Kraydieh, S., & Dietrich, W. D. (2000). Importance of posttraumatic hypothermia and hyperthermia on the inflammatory response after fluid percussion brain injury: Biochemical and immunocytochemical studies. *Journal of Cerebral Blood Flow*, 20 (3), 531-542.
26. Chamorro, C., Borrallo, J. M., Romera, M. A., Silva, J. A., & Balandin, B. (2010). Anesthesia and analgesia protocol during therapeutic hypothermia: A systematic review. *Anesthesia and Analgesia*, 110 (5), 1328-1335.
27. Chang, E. (2013). The role of simulation training in obstetrics: A healthcare training strategy dedicated to performance improvement. *Current Opinion in Obstetrics and Gynecology*, 25 (6), 482-486.
28. Che, D., Li, L., Kopil, C. M., Liu, Z., Guo, W., & Neumar, R. W. (2011) Impact of therapeutic hypothermia onset and duration on survival, neurologic function, and neurodegeneration after cardiac arrest. *Critical Care Medicine*, 39 (6), 1423-30.

29. Cheng, A., Leng, T., Starr, S., Pusic, M., & Cook, D. (2014). Technology-enhanced simulation and pediatric education: A meta-analysis. *Pediatrics*, 133 (5), e1313-1323.
30. Cheng, A., Lockey, A., Bhanji, F., Lin, Y., Hunt, E. A., & Lang, E. (2015). The use of high-fidelity manikins for advanced life support training – A systematic review and meta-analysis. *Resuscitation*, 93 (ahead of print), 142-149.
31. Cheng, A., Eppich, W., Grant, V., Sherbino, J., Zendejas, B., & Cook, D. A. (2014). Debriefing for technology-enhanced simulation: A systematic review and meta-analysis. *Medical Education*, 48 (7), 657-666.
32. Chopp, M., Knight, R., Tidwell, C. D., Helpers, J. A., Brown, E., & Welch, K.M. (1989). The metabolic effects of mild hypothermia on global cerebral ischemia and recirculation in the cat: comparison to normothermia and hyperthermia. *Journal of Cerebral Blood Flow and Metabolism*, 9 (2), 141-8
33. Cioffi, J. (2001). Clinical simulations: development and validation. *Nurse Education Today*, 21 (6), 477-86.
34. Clark, R. S., Kochanek, P. M., Marion, D. W., Schiding, J. K., White, M., Palmer, A. M., & DeKosky, S.T. (1996). Mild posttraumatic hypothermia reduces mortality after severe controlled cortical impact in rats. *Journal of Cerebral Blood Flow and Metabolism*, 16 (2), 253-61.
35. Cocchi, M. N., Boone, M. D., Giberson, B., Giberson, T., Farrell, E., Saliccioli, J. D., . . . Donnino, M. W. (2013). Fever after rewarming: Incidence of pyrexia in post-cardiac arrest patients who have undergone mild therapeutic hypothermia. *Journal of Intensive Care Medicine*, 84 (8), 1056-1061.
36. Cohen, J. (1988). *Statistical power analysis of the behavioral sciences* (2nd ed.). Hillsdale, NJ: Lawrence Earlbaum Associates.

37. Coimbra, C., Boris-Möller, F., Drake, M., & Wieloch, T. (1996). Diminished neuronal damage in the rat brain by late treatment with the antipyretic drug dipyrene or cooling following cerebral ischemia. *Acta Neuropathologica*, 92 (5), 447-453.
38. Cook, D. A., Hamstra, S. J., Brydges, R., Zendejas, B., Szostek, J. H., Wang, A. T., . . . Hatala, R. (2013). Comparative effectiveness of instructional design features in simulation-based education: Systematic review and meta-analysis. *Medical Teacher*, 35 (1), e867-898.
39. Cook, D. A., Hatala, R., Brydges, R., Zendejas, B., Szostek, J. H., Wang, A. T., . . . Hamstra, S. J. (2011). Technology-enhanced simulation for health professions education: A systematic review and meta-analysis. *Journal of American Medical Association*, 306 (9), 978-988.
40. Corbett, D. & Thornhill, J. (2000). Temperature modulation (hypothermic and hyperthermic conditions) and its influence on histological and behavioral outcomes following cerebral ischemia. *Brain Pathology*, 10 (1), 145-152.
41. Couto, T. B., Farhat, S. C., Geis, G. L., Olsen, O., & Schwartsman, C. (2015). High-fidelity simulation versus case-based discussion for teaching medical students in Brazil about pediatric emergencies. *Clinics*, 70 (6), 393-399.
42. Cronberg, T. & Nielsen, N. (2013). Fever after therapeutic hypothermia – does rebound pyrexia matter? *Resuscitation*, 84 (8), 1011-1012.
43. Curran, V., Fleet, L., White, S., Bessell, C., Deshpandev, A., Drover, A., . . . Vacour, J. (2015). A randomized controlled study of manikin simulator fidelity on neonatal resuscitation program learning outcomes. *Advances in Health Sciences Education Theory and Practice*, 20 (1), 205-218.

44. Derwall, M., Stoppe, C., Brücken, D., Rossaint, R., & Fries, M. (2009). Changes in S-100 protein serum levels in survivors of out-of-hospital cardiac arrest treated with mild therapeutic hypothermia: a prospective, observational study. *Critical Care*, 13 (2): R58.
45. Don, C. W., Longstreth, W. T. Jr, Maynard, C., Olsufka, M., Nichol, G., Ray T., & Kim F. (2009). Active surface cooling protocol to induce mild therapeutic hypothermia after out-of-hospital cardiac arrest: A retrospective before-and-after comparison in a single hospital. *Critical Care Medicine*, 37 (12), 3062-3069.
46. Donnino, M. W., Andersen, L. W., Berg, K. M., Reynolds, J. C., Nolan, J. P., Morley, P. T. . . . ILCOR ALS Task Force (2015). Temperature management after cardiac arrest: An advisory statement by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. *Resuscitation*, ahead of print. doi: 10.1016/j.resuscitation.2015.09.396
47. Dreifuerst, K. T. (2009). The essentials of debriefing in simulation learning: A concept analysis. *Nursing Education Perspectives*, 30 (2), 109-114.
48. Dumas, F., Grimaldi, D., Zuber, B., Fichet, J., Charpentier, J., Pene, F., . . . Cariou, A. (2011). Is hypothermia after cardiac arrest effective in both shockable and nonshockable patients? Insights from a large registry. *Circulation*, 123 (8), 877-886. Elliott, V. J., Rodgers, D. L., & Brett, S. J. (2011). Systematic review of quality of life and other patient-centred outcomes after cardiac arrest survival. *Resuscitation*, 82 (3), 247-56.
49. Fanning, R. M. & Gaba, D. M. (2007). The role of debriefing in simulation-based learning. *Simulation in Healthcare*, 2 (2), 115-125.

50. Favero-Filho, L. A., Borges, A. A., Grassl, C., Lopes, A. C., Sinigaglia-Coimbra, R., & Coimbra, C. G. (2002). Postischemic hyperthermia induces Alzheimer-like pathology in the rat brain. *Acta Neuropathologica*, 103 (5), 444-452.
51. Friedlander, M. J., Andrews, L., Armstrong, E. G., Aschenbrenner, C., Kass, J. S., Ogden, P., . . . Viggiano, T. R. (2011). What can medical education learn from the neurobiology of learning? *Academic Medicine*, 86, 415-420.
52. Gaba, D. M. (2004). The future vision of simulation in health care. *Quality and Safety in healthcare*, 13 (Suppl 1), i2-i10.
53. Gaieski, D. F., Band, R. A., Abella, B. S., Neumar, R. W., Fuchs, B. D., Kolansky, D. M., . . . Goyal, M. (2009). Early goal-directed hemodynamic optimization combined with therapeutic hypothermia in comatose survivors of out-of-hospital cardiac arrest. *Resuscitation*, 80 (4), 418-424.
54. Gebhardt, K., Guyette, F. X., Doshi, A. A., Callaway, C. W., & Rittenberger, J. C. (2013). Prevalence and effect of fever on outcome following resuscitation from cardiac arrest. *Resuscitation*, 84 (8), 1062-1067.
55. Greer, D. M., Fink, S. E., Reaven, N. L., Ouzounelli, M., & Uman, G. C. (2008). Impact of fever on outcomes in patients with stroke and neurologic injury: A comprehensive meta-analysis. *Stroke*, 39 (11), 3029-3035.
56. Grossestreuer, A. V., Abella, B. S., Leary, M., Perman, S. M., Fuchs, B. D., Kolansky, D. M., . . . Gaieski, D. F. (2013). Time to awakening and neurologic outcome in therapeutic hypothermia-treated cardiac arrest patients. *Resuscitation*, 84 (12), 1741-1746.
57. Heidenreich, T., Giuffre, M., & Doorley J. (1992). Temperature and temperature measurement after induced hypothermia. *Nursing Research*, 41 (5), 296-300.

58. Hachimi-Idrissi, S. Corne, L., Ebinger, G., Michotte, Y. & Huyghens, L. (2001). Mild hypothermia induced by a helmet device: A clinical feasibility study. *Resuscitation*, *51*, 275-281.
59. Hajat, C., Hajat, S., & Sharma, P. (2000). Effects of post-stroke pyrexia on stroke outcomes: A meta-analysis of studies in patients. *Stroke*, *31* (2), 410-414.
60. Heer, C. (2007). Hypothermia after cardiac arrest – experiences in routine use on a medical intensive care unit. *Intensivmedizin und Notfallmedizin*, *44*, 303-307.
61. Herlitz, J., Bang, A., Aune, S., Lundstrom, G., & Holmberg, S. Characteristics and outcome among patients suffering in hospital cardiac arrest in monitored and non-monitored areas. *Resuscitation*, *48*, 125-135.
62. Holzer, M., Müllner, M., Sterz, F., Robak, O., Kliegel, A., Losert, H., & Laggner, A. N. (2006). Efficacy and safety of endovascular cooling after cardiac arrest: cohort study and Bayesian approach. *Stroke*, *37* (7), 1792-1797.
63. Hörburger, D., Testori, C., Sterz, F., Herkner, H., Krizanac, D., Uray, T., . . . Holzer M. (2012). Mild therapeutic hypothermia improves outcomes compared with normothermia in cardiac-arrest patients: A retrospective chart review. *Critical Care Medicine*, *40* (8), 2315-2319.
64. Hypothermia after Cardiac Arrest Study Group. (2002). Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. *New England Journal of Medicine*, *346* (22), 549-556.
65. Ilgen, J. S., Sherbino, J., & Cook, D. A. (2013). Technology-enhanced simulation in emergency medicine: A systematic review and meta-analysis. *Academic Emergency Medicine*, *20* (2), 115-125.
66. Issenberg, S. B., McGaghie, W. C., Gordon, D. L., Symes, S., Petrusa, E. R., Hart, I. R., & Harden, R. M. (2002). Effectiveness of a cardiology review course for

internal medicine residents using simulation technology and deliberate practice.

Teaching and Learning in Medicine: An International Journal, 14 (4), 223-228.

67. Jeffries, P. R. (2005). A framework for designing, implementing, and evaluating simulations used as teaching strategies in nursing. *Nursing Education Perspectives*, 26 (2), 96-103.
68. Jiang, J. Y., Gao, G. Y., Li, W. P., Yu, M. K., & Zhu, C. (2002). Early indicators of prognosis in 46 cases of severe traumatic brain injury. *Journal of Neurotrauma*, 19 (17), 869-874.
69. Kennedy, C. C., Cannon, E. K., Warner, D. O., & Cook, D. A. (2014). Advanced airway management simulation training in medical education: A systematic review and meta-analysis. *Critical Care Medicine*, 42 (1), 169-178.
70. Kim, F., Nichol, G., Maynard, C., Hallstrom, A., Kudenchuk, P. J., Rea, T., . . . Cobb, L. A. (2014). Effect of prehospital induction of mild hypothermia on survival and neurological status among adults with cardiac arrest: a randomized clinical trial. *Journal of American Medical Association*, 311 (1), 45-52.
71. Kimberger, O., Ali, S. Z., Markstaller, M., Zmoos, S., Lauber, R., Hunkeler, C., & Kurz, A. (2007). Meperidine and skin surface warming additively reduce the shivering threshold: A volunteer study. *Critical Care*, 11 (1), R29.
72. Kirkpatrick, D. L. & Kirkpatrick, J. D. (2006). Evaluating training programs: The four levels (3rd ed.). San Francisco, CA: Berrett-Koehler Publishers, Inc.
73. Ko, P. Y., Scott, J. M., Mihai, A., & Grant, W. D. (2011). Comparison of a modified longitudinal simulation-based advanced cardiovascular life support to a traditional advanced cardiovascular life support curriculum in third-year medical students. *Teaching and Learning in Medicine*, 23 (4), 324-330.

74. Kory, P., Fukunaga, M., Mathew, J. P., Singh, B., Szainwald, L., Mosak, J., . . . Mayo, P. H. (2012). Outcomes of mild therapeutic hypothermia after in-hospital cardiac arrest. *Neurocritical Care*, *16*, 406-412.
75. Krathwohl, D. R. (2001). A revision of Bloom's taxonomy: An overview. *Theory Practice*, *41*, 212-218.
76. Lampe, S. W. & Becker, L. B. State of the art in therapeutic hypothermia. (2011). *Annual Review of Medicine*, *62*, 79-93.
77. Leary, M., Grossestreuer, A. V., Iannacone, S., Gonzalez, M., Shofer, F. S., Povey, C. ... Abella, B. S. (2013). Pyrexia and neurologic outcomes after therapeutic hypothermia for cardiac arrest. *Resuscitation*, *84* (8), 1056-1061.
78. Lederman, L. C. (1984). Debriefing: A critical reexamination of the post-experience analytic process with implications for its effective use. *Simulation & Gaming*, *15* (4), 415-431.
79. Lee, B. K, Lee, S. J., Jeung, K. W., Lee, H. Y., Heo, T., & Min, Y. I. (2014). Outcome and adverse events with 72-hour cooling at 32°C as compared to 24-hour cooling at 33°C in comatose asphyxial arrest survivors. *American Journal Emergency Medicine*, *32* (4), 297-301.
80. Lee, S. K., Pardo, M., Gaba, D., Sowb, Y., Dicker, R., Straus, E. M., . . . Knudson, M. M. (2003). Trauma assessment training with a patient simulator: A prospective, randomized study. *The Journal of Trauma*, *55* (4), 651-657.
81. Lei, B., Tan, X., Cai, H., Xu, Q., & Guo, Q. (1994). Effect of moderate hypothermia on lipid peroxidation in canine brain tissue after cardiac arrest and resuscitation. *Stroke*, *25* (1), 147-52.

82. Lebedz, P., Meiners, J., Samol, A., Wasmer, K., Reinecke, H., Waltenberger, J., & Eckardt, L. (2012). Electrocardiographic changes during therapeutic hypothermia. *Resuscitation*, *83*, 602-606.
83. Lo, B. M., Devine, A. S., Evans, D. P., Byars, D. V., Lamm, O. Y., Lee, R. J., . . . Walker, L. L. (2011). Comparison of traditional versus high-fidelity simulation in the retention of ACLS knowledge. *Resuscitation*, *82* (11), 1440-1443.
84. Logan, A., Sangkachand, P., & Funk, M. (2011). Optimal management of shivering during therapeutic hypothermia after cardiac arrest. *Critical Care Nurse*, *31* (6), e18-30.
85. Lu, X., Ma, L., Sun, S., Xu, J., Zhu, C., & Tang, W. (2014). The effects of the rate of postresuscitation rewarming following hypothermia on outcomes of cardiopulmonary resuscitation in a rat model. *Critical Care Medicine*, *42* (2), 106-113.
86. Lundbye, J. B., Rai, M., Ramu, B., Hosseini-Khalili, A., Li, D., Slim, H. B., Bhavnani, S. P., . . . Kluger, J. (2012). Therapeutic hypothermia is associated with improved neurologic outcome and survival in cardiac arrest survivors of non-shockable rhythms. *Resuscitation*, *83* (2), 202-207.
87. Maclean, D. A., Stevenson, R. S., Bata, I., & Green, R. S. (2012). Therapeutic hypothermia for out-of-hospital cardiac arrest: An analysis comparing cooled and not cooled groups at a Canadian center. *Journal of Emergencies, Trauma, and Shock*, *5* (4), 328-32.
88. Mahan, J. D., & Stein, D. S. (2014). Teaching adults – best practices that leverage the emerging understanding of the neurobiology of learning. *Current Problems in Pediatric and Adolescent Health Care*, *44*, 141-149.

89. Marion, D. W., Leonov, Y., Ginsberg, M., Katz, L. M., Kochanek, P. M., Lechleuthner, A., . . . Zar, H. (1996). Resuscitative hypothermia. *Critical Care Medicine*, 24 (2 Suppl), S81-S89.
90. McEvoy, M. D., Smalley, J. C., Nietert, P. J., Field, L. C., Furse, C. M. , Blenko, J. W., . . . Schaefer, J. J. (2012). Validation of a detailed scoring checklist for use during advanced cardiac life support certification. *Journal of the society for Simulation in Healthcare*, 7 (4), 222-235.
91. McGaghie, W. C., Draycott, T. J., Dunn, W. F., Lopez, C., & Stefanidis, D. (2011). Evaluating the impact of simulation of translational patient outcomes. *Journal for the Society in Simulation in Healthcare*, 6 (7), S42-S47.
92. McGaghie, W. C., Issenberg, S. B., Cohen, E. R., Barsuk, J. H., & Wayne, D. B. (2011). Does simulation-based medical education with deliberate practice yield better results than traditional clinical education? A meta-analytic comparative review of the evidence. *Academic Medicine: Journal of the Association of American Medical Colleges*, 86 (6), 706-11.
93. Mokhtarani, M., Mahgoub, A. N., Morioka, N. Doufas, A. G., & Sessler, D. I. (2001). Buspirone and meperidine synergistically reduce the shivering threshold. *Anesthesiology and Analgesia*, 93 (5), 1233-1239.
94. Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., . . .Turner, M. B. (2015). Heart disease and stroke statistics - 2015 update: A report from the American Heart Association. *Circulation*, 131, 00-00. DOI: 10.1161/CIR.0000000000000152
95. Mullan, P., Kessler, D., & Cheng, A. (2014). Educational opportunities with postevent debriefing. *The Journal of the American Medical Association*, 312 (22), 2333-2334.

96. Mundell, W. C., Kennedy, C. C., Szostek, J. H., & Cook, D. A. (2013). Simulation technology for resuscitation training: A systematic review and meta-analysis. *Resuscitation, 84* (9), 1174-1183.
97. Nader, K. & Hardt, O. (2009). A single standard for memory: The case for reconsolidation. *Nature Reviews Neuroscience, 10* (3), 224-234.
98. Nair, S. U., & Lundbye, J. B. (2013). The occurrence of shivering in cardiac arrest survivors undergoing therapeutic hypothermia is associated with a good neurologic outcome. *Resuscitation, 84*, 626-629.
99. Nguyen, H. B., Daniel-Underwood, L., Van Ginkel, C., Wong, M., Lee, D., San Lucas, A., . . . Clem, K. (2009). An educational course including medical simulation for early goal-directed therapy and the severe sepsis resuscitation bundle: An evaluation for medical student training. *Resuscitation, 80* (6), 674-679.
100. Nichol, G., Huszti, E., Kim, F., Fly, D., Parnia, S., Donnino, M., . . . Callaway, C. W. (2013). American Heart Association Get With the Guideline-Resuscitation Investigators. Does induction of hypothermia improve outcomes after in-hospital cardiac arrest? *Resuscitation. 84* (5), 620-5.
101. Nielsen, N., Wettersley, J., Cronberg, T., Erlinge, D., Gasche, Y., Hassager, C., . . . Friberg, H. (2013). Targeted temperature management at 33°C versus 36°C after cardiac arrest. *New England Journal of Medicine, 369* (23), 2197-2206.
102. Nolan, J. P., Morley, P. T., Vanden Hoek, T. L., Hickey, R. W., Kloeck, W. G., Billi, J., . . . Atkins D; International Liaison Committee on Resuscitation. (2003). Therapeutic hypothermia after cardiac arrest: an advisory statement by the advanced life support task force of the International Liaison Committee on Resuscitation. *Circulation, 108* (1), 118-121.

103. Noyes, A. M. & Lundbye, J. B. (2013). Managing the Complications of Mild Therapeutic Hypothermia in the Cardiac Arrest Patient. *Journal of Intensive Care Medicine*, 30 (5), 259-269.
104. Oermann, M. H., Kardong-Edgren, S. E., & Odom-Maryon, T. (2011). Effects of monthly practice on nursing students' CPR psychomotor skill performance. *Resuscitation*, 82, 447-453.
105. Oksanen, T., Skrifvars, M., Wilman, E., Tierala, I., Pettila, V., & Varpula, T. (2014). Postresuscitation hemodynamics during therapeutic hypothermia after out-of-hospital cardiac arrest with ventricular fibrillation: A retrospective study. *Resuscitation*, 85 (8), 1018-1024.
106. Oddo, M., Schaller, M. D., Feihl, F., Ribordy, V., & Liaudet, L. (2006). From evidence to clinical practice: effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest. *Critical Care Medicine*, 34 (7), 1865-73.
107. Orledge, J., Phillips, W. J., Murray, W. B., & Lerant, A. (2012). The use of simulation in healthcare: from systems issues, to team building, to task training, to education and high stakes examinations. *Current Opinion in Critical Care*, 18 (4), 326-332.
108. Ottestad, E., Boulet, J. R., & Lighthall, G. K. (2007). Evaluating the management of septic shock using patient simulation. *Critical Care Medicine*, 35 (3), 769-775.
109. Peberdy, M. A., Callaway, C. W., Neumar, R. W., Geocadin, R. G., Zimmerman, J. L., Donnino, M., . . . Kronick, S. L. (2010). Part 9: Post-Cardiac Arrest Care: 2010 American Heart Association guidelines for cardiopulmonary

- resuscitation and emergency cardiovascular care. *Circulation*, 122 (18 suppl 3), S786-S786.
110. Peberdy, M. A., Kaye, W., Ornato, J. P., Larkin, G. L., Nadkarni, V., Mancini, M. E., . . . Lane-Trullt T. (2003). Cardiopulmonary resuscitation of adults in the hospital: a report of 14720 cardiac arrests from the National Registry of Cardiopulmonary Resuscitation. *Resuscitation*, 58 (3), 297-308.
111. Perkins, G. D. (2007). Simulation in resuscitation training. *Resuscitation*, 73 (2), 202-211.
112. Pfeifer, R., Jung, C., Purle, S., Lauten, A., Yilmaz, A., Surber, R., . . . Figulla, H. R. (2011). Survival does not improve when therapeutic hypothermia is added to post-cardiac arrest care. *Resuscitation*, 82 (9), 1168-1173
113. Polderman, K. H. (2004). Application of therapeutic hypothermia in the intensive care unit. *Intensive Care Medicine*, 30 (5), 757-769.
114. Polderman, K. H. (2009). Mechanisms of action, physiological effects, and complications of hypothermia. *Critical Care Medicine*, 37 (7) Suppl., 186-202.
115. Polderman, K. H. & Herold, I. (2009). Therapeutic hypothermia and controlled normothermia in the intensive care unit: Practical considerations, side effects, and cooling methods. *Critical Care Medicine*, 37 (3), 1102-1120.
116. Ramjee, V. & Abella, B. S. (2013). The neuroprognostic challenge of post-arrest care. *Resuscitation*, 84, 537-538.
117. Remba, S. J., Varon, J., Rivera, A. & Sternbach, G. L. (2010). Dominique-Jean Larrey: The effects of therapeutic hypothermia and the first ambulance. *Resuscitation* 81 (3), 268-271.

118. Rittenberger, J. C. & Callaway, C. W. (2013). Temperature management and modern post-cardiac arrest care. *New England Journal of Medicine*, 369 (23), 2262-2263.
119. Rittenberger, J. C., Guyette, F. X., Tisherman, S. A., DeVita, M. A., Alvarez, R. J., & Callaway, C. W. (2008). Outcomes of a hospital-wide plan to improve care of comatose survivors of cardiac arrest. *Resuscitation*, 79 (2), 198-204.
120. Rittenberger, J. C., Popescu, A., Brenner, R. P., Guyette, F. X., & Callaway, C. W. (2012). Frequency and timing of nonconvulsive status epilepticus in comatose post-cardiac arrest subjects treated with hypothermia. *Neurocritical Care*, 16 (1), 114-122.
121. Rosenthal, M. E., Adachi, M., Ribaud, V., Mueck, J. T., Schneider, R. F., & Mayo, P. H. (2006). Achieving housestaff competence in emergency airway management using scenario based simulation training: Comparison of attending vs housestaff trainers. *Chest*, 129 (6), 1453-1458.
122. Rossetti, A. O., Oddo, M., Liaudet, L., & Kaplan, P. W. (2009). Predictors of awakening from postanoxic status epilepticus after therapeutic hypothermia. *Neurology*, 72 (8), 744-749.
123. Rudolph, J. W., Simon, R., Dufresne, R. L., & Raemer, D. B. (2006). There's no such thing as a "nonjudgemental" debriefing: A theory and method for debriefing with good judgement. *Simulation in Healthcare*, 1 (1), 49-55.
124. Rudolph, J. W., Simon, R., Riyard, P., Dufresne, R. L., & Raemer, D. B. (2007). Debriefing with good judgment: Combining rigorous feedback with genuine inquiry. *Anesthesiology Clinics*, 25 (2), 361-376.

125. Sinigaglia-Coimbra, R., Cavalheiro, E. A., & Coimbra, C. G. (2002). Postischemic hyperthermia induces Alzheimer-like pathology in the rat brain. *Acta Neuropathologica*, 103 (5), 444-452.
126. Skulec, R., Kovárník, T., Bělohávek, J., Dostálová, G., Kolár, J., Linhart, A., . . . Seblová, J. (2008). Overcooling during mild hypothermia in cardiac arrest survivors--phenomenon we should keep in mind. *Vnitřní Lekarství*, 54 (6), 609-614.
127. Soga, T., Nagao, K., Sawano, H., Yokoyama, H., Tahara, Y., Hase, M., . . . Nonogi, H.; J-PULSE-Hypo Investigators. (2012). Neurological benefit of therapeutic hypothermia following return of spontaneous circulation for out-of-hospital non-shockable cardiac arrest. *Circulation Journal*, 76 (11), 2579-2585.
128. Starodub, R., Abella, B. S., Leary, M., & Riegel, B. (2014, May). Identifying current practice patterns in U.S. hospitals' therapeutic hypothermia protocols. Poster *to be presented* at the annual American Association of Critical-Care Nurses (AACN) National Teaching Institute & Critical Care Exposition. Research Poster Presentation, Denver, U.S.
129. Sterz, F., Safar, P., Diven, W., Leonov, Y., Radovsky, A., & Oku, K. (1993). Detoxification with hemabsorption after cardiac arrest does not improve neurologic recovery. Review and outcome study in dogs. *Resuscitation*, 25 (2), 137-60.
130. Stocchetti, N., Rossi, S., Zanier, E. R., Colombo, A., Beretta, L., & Citerio, G. (2002). Pyrexia in head-injured patients admitted to intensive care. *Intensive Care Medicine*, 28 (11), 1555-1562.
131. Storm, C., Nee, J., Roser, M., Jorres, A., & Hasper, D. (2012). Mild hypothermia treatment in patients resuscitated from non-shockable cardiac arrest. *Journal of Emergency Medicine*, 29, 100-103.

132. Storm, C., Steffen, I., Schefold, J. C., Krueger, A., Oppert, M., Jorres, A., & Hasper, D. (2008). Mild therapeutic hypothermia shortens intensive care unit stay of survivors after out-of-hospital cardiac arrest compared to historical controls. *Critical Care*, 12 (3), R78.
133. Sunde, K., Pytte, M., Jacobsen, D., Mangschau, A., Jensen, L. P., Smedsrud, C., . . . Steen, P. A. (2007). Implementation of a standardized treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation*, 73 (1), 29-39.
134. Testory, C., Sterz, F., Behringer, W., Haugk, M., Uray, T., Zainer, A., . . . Losert, H. (2011). Mild therapeutic hypothermia is associated with favourable outcome in patients after cardiac arrest with non-shockable rhythms. *Resuscitation*, 82, 1162 – 1167.
135. Thornhill, J. & Corbett, D. (2001). Therapeutic implications of hypothermic and hyperthermic temperature conditions in stroke patients. *Canadian Journal of Physiology and Pharmacology*, 79 (3), 254-261.
136. Vaahersalo, J., Hiltunen, P., Tiainen, M., Oksanen, T., Kaukonen, K. M., Kurola, J., . . . Pettilä, V.; FINNRESUSCI Study Group. (2013). Therapeutic hypothermia after out-of-hospital cardiac arrest in Finnish intensive care units: the FINNRESUSCI study. *Intensive Care Medicine*, 39 (5), 826-837.
137. Varon, J. Marik, P. E., & Einav, S. (2012). Therapeutic hypothermia: A state-of-the-art emergency medicine perspective. *American Journal of Emergency Medicine*, 30, 800-810.
138. Wang, Y., Lim, L. L., Levi, C., Heller, R. F., & Fisher, J. (2000). Influence of admission body temperature on stroke mortality. *Stroke*, 31 (2), 404-409.

139. Wass, C. T., Lanier, W. L., Hofer, R. E., Scheithauer, B. W., & Andrews, A. G. (1995). Temperature changes of $\geq 1^{\circ}\text{C}$ after functional neurologic outcome and histopathology in a canine model of complete cerebral ischemia. *Anesthesiology*, *83* (2), 325-335.
140. Wayne, D. B., Butter, J., Siddall, V. J., Fudala, M. J., Linqvist, L. A., Feinglass, J., . . . McGaghie, W. C. (2005). Simulation-based training of internal medicine residents in advanced cardiac life support protocols: A randomized trial. *Teaching and Learning in Medicine*, *17* (3), 202-206.
141. Wayne, D. B., Didwania, A., Feinglass, J., Fudala, M. J., Barsuk, J. H., & McGaghie, W. C. (2008). Simulation-based education improves quality of care during cardiac arrest team responses at an academic teaching hospital: a case-control study. *Chest*, *133* (1), 56-61.
142. Whitfield, A. M., Coote, S., & Ernest, D. (2009). Induced hypothermia after out-of-hospital cardiac arrest: one hospital's experience. *Critical Care and Resuscitation*, *11* (2), 97-100.
143. Wijdicks, E. F., Hijdra, A., Young, G. B., Bassetti, C. L., & Wiebe, S.; Quality Standards Subcommittee of the American Academy of Neurology. (2006). Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*, *67* (2), 203-210.
144. Winters, S. A., Wolf, K. H., Kettinger, S. A., Seif, E. K., Jones, J. S., & Bacon-Baguley, T. (2013). Assessment of risk factors for post-rewarming "rebound hypothermia" in cardiac arrest patients undergoing therapeutic hypothermia. *Resuscitation*, *84* (9), 1245-1249.

145. Xiao, G., Guo, Q., Shu, M., Xie, X., Deng, J., Zhu, Y., & Wan, C. (2013). Safety profile and outcomes of mild therapeutic hypothermia in patients following cardiac arrest: Systematic review and meta-analysis. *Emergency Medicine Journal, 30*, 91-100.
146. Zendejas, B., Brydges, R., Wang, A. T., & Cook, D. A. (2013). Patient outcomes in simulation-based medical education: A systematic review. *Journal of general Internal Medicine, 28* (8), 1078-1089.
147. Zhu, C., Wang, X., Cheng, X., Qiu, L., Xu, F., Simbruner, G., & Blomgren, K. (2004). Post-ischemic hypothermia-induced tissue protection and diminished apoptosis after neonatal cerebral hypoxia-ischemia. *Brain Research, 996* (1), 67-75.
148. Zigmont, J. J., Kappus, L. J., & Sudikoff, S. N. (2011). The 3D model of debriefing: Defusing, discovering, and deepening. *Seminars in Perinatology, 35* (2), 52-58.