Effect of Pre-hospital Therapeutic Hypothermia on Neurologic Outcome Following Sudden Cardiac Arrest

Principal Investigator:

Michael R. Sayre, MD,
Associate Professor
Department of Emergency Medicine
The Ohio State University Medical Center
4510 Cramblett Hall
456 W. 10th Avenue
Columbus, Ohio 43210

Table of Contents

Executive Summary

Sudden cardiac arrest (SCA) is a leading cause of death in the United States and Canada.[1-3] While estimates of the annual number of deaths due to out-of-hospital SCA vary widely, it is estimated that in the United States approximately 330,000 people die annually in the out-of-hospital and emergency department settings from coronary heart disease. [1-5] About 250 000 of these deaths occur in the out-of-hospital setting and the annual incidence of SCA in North America is 55 per 100,000 population.[4]

In Columbus, Ohio, each year approximately 450 cardiac arrest resuscitations are attempted by EMS, and about 30 percent of these survive to be admitted to the hospital. Overall survival to hospital discharge has shown general improvement since 2004 when the survival rate was 4.3 percent. As overall survival increases, ensuring that survivors retain intact neurologic faculties becomes even more important. Providing hypothermia therapy at the earliest possible point in the chain-of-survival is believed to significantly improve neurologically intact survival while also serving to remind hospital emergency department personnel to continue the therapy.

This project evaluated the effect of a new pre-hospital hypothermia protocol which was initiated by EMS on July 1, 2008. By protocol, hypothermia therapy was to be provided by paramedics in the field, following the restoration of spontaneous circulation (ROSC) for comatose SCA victims whose initial rhythm is ventricular fibrillation. Prior to the implementation of pre-hospital hypothermia, all hospitals receiving out-of-hospital cardiac arrest patients had in-hospital therapeutic hypothermia (TH) protocols in place.

In this paper, we describe SCA survival rates and neurologic status for the year preceding and the year following the institution of the pre-hospital therapeutic hypothermia protocol.

Information/Qualifications of principal and co-investigators

The principal investigator, Michael Sayre, MD is an associate professor in Emergency Medicine at The Ohio State University in Columbus, OH. Dr. Sayre has experience in conducting pre-hospital cardiac arrest research and has published extensively in the field.

Review of the literature related to project

Recent advances in resuscitation science have focused on providing improved care for victims of sudden cardiac arrest (SCA) both in and outside of the hospital.[6,7] Implementation of these advances are believed to have the power to enhance the quality of care; and ultimately, improve survival rates for out-of-hospital SCA from the dismal overall survival baseline of 5% nationwide, to over 20%.8 For a disease that claims the lives of over 250,000 individuals each year, this incremental improvement could save help to save many more lives each year in the US.[9]

In years past, the majority of patients who were resuscitated from out-of-hospital cardiac arrest and delivered to the emergency department did not survive to be discharged from the hospital. Most patients died from massive brain injury, secondary to the effects of brain hypoxia followed by reperfusion. With the renewed emphasis on providing high quality cardiopulmonary resuscitation (CPR) early defibrillation and the relatively new introduction of hypothermia therapy, many SCA victims can benefit from this improved post resuscitation care and survive to hospital discharge.[10,11] Both the International Liaison Committee on Resuscitation, (ILCOR) and the American Heart Association (AHA) recommend that post resuscitation care include the provision of mild therapeutic hypothermia for comatose out-of-hospital sudden cardiac arrest victims who attain restoration of spontaneous circulation (ROSC). [6.7]

Improvements in survival and neurologic outcome reported for SCA victims who have received mild therapeutic hypothermia during the post resuscitation period are impressive. A systematic review of therapeutic hypothermia used to treat cardiac arrest patients cites the number-need-to-treat to save one life as seven, and the number-needed-to-treat to improve neurologic outcome as five.[12] Implementing mild therapeutic hypothermia during the post resuscitation period across the US would save an estimated 2,298 to

5,171 additional lives per year.[13] In Columbus Ohio, where the city EMS service reports approximately 425 SCA victims each year, the lives saved could include 60 additional individuals each year over and above those who are currently survivors. For patients who achieve restoration of spontaneous circulation during resuscitation, hypothermia therapy has the greatest potential to improving both survival and neurologic outcome of any single therapy in the arsenal against SCA.

Historical perspectives on topic

Anecdotal observations from as early as the 1800s are believed to provide the basis for the initial experimentation with hypothermia as a means to extend the window of survivability. Successful resuscitations of children pulled from frozen lakes and rivers after prolonged time periods of up to an hour inspired several individuals to experiment with hypothermia as a therapy. However, it wasn't until 2002 that the randomized clinical trials reported success and gained the attention of resuscitation scientists worldwide. Following publication several articles in the early 2000s, the repertoire of treatments for post resuscitation care for SCA victims improved dramatically. Post resuscitation use of mild therapeutic hypothermia with surface cooling was adopted over the next decade, and has been followed by a variety of more technical methods for inducing cooling, including endovascular cooling, whole body submersion, use of extracorporeal membrane oxygenation and other various combination therapies.

Several EMS systems in the nation have published manuscripts that demonstrate that pre-hospital cooling is feasible and that core temperature can be quickly, safely and easily lowered by infusing 2 liters of ice cold saline into a peripheral vein or even by intraosseou infusion.[14] This has been shown to considerably shorten the time it takes for the patient to reach the target temperature once therapy is continued in the destination hospital, and serves as a reminder to busy emergency department personnel to continue the hypothermia therapy.[15]

Review of current status of topic in Ohio and surrounding states and nationally

By 2009, several EMS agencies in Ohio have successfully implemented the pre-hospital use of therapeutic hypothermia. In Columbus, The Columbus Division of Fire has had a pre-hospital therapeutic hypothermia protocol since July 2008, and all receiving hospitals in Central Ohio have the protocols in place to ensure that the therapy can be continued upon hospital admission.

Future trends, regionally and nationally

Trends in hypothermia regionally include the continued provision of the therapy, and perhaps may involve research into providing the therapy during the intra-arrest period prior to achievement of ROSC. Other potential research in the pre-hospital application of therapeutic hypothermia could include intra-nasal cooling in the future. Nationally, pre-hospital therapeutic hypothermia continues to be adopted by EMS services around the country.

Financial issues and considerations

Providing pre-hospital therapeutic hypothermia is extremely cost effective. The cost of infusing 2 liters of cold saline is insignificant. Low tech beverage coolers and ice can be used in the medic vehicles to keep saline cold, and saline is readily available in all EMS systems.

Education and training issues and considerations

As the infusion of saline is currently well within the scope of duties of the paramedic, there is little education required, but for a review of the inclusion criteria for the therapy. The most common barrier to be overcome could be simply remembering to start the infusion at the scene of the resuscitation.

Legislative and regulatory issues and considerations

Currently, there are no known legal or regulatory issues related to the provision of this therapy.

The researchers findings

Comparison of 2008-2009 SCA statistics with the previous 12 month period.

During the two years under study, the number of resuscitations attempted and the cases of cardiac etiology were similar. The bystander CPR rate rose from 15.4% during 2007-2008 to 22.8 % during 2008-2009. Overall survival decreased slightly during 2008-2009 from 13% during the baseline year to 10.9% during the year in which pre-hospital hypothermia was initiated. (Table 1.)

Table 1. General SCA Statistics For Baseline Year Treatment Year.

SCA Statistics	Prior to Institution of Pre-hospital Cooling (7-1-07 to 6-30-08)	During First Year of Pre-hospital Cooling (7-1-08 to 6-30-09)
Resuscitations Attempted	422	461
Cardiac Etiology	361	368
Overall Survival Rate, Cardiac Etiology	13.0%	10.9%
Survival to Hospital Discharge	47	40
Bystander CPR Rate	15.4%	22.8%
Cases of pre-hospital hypothermia	0	53

Snapshot of Neurologic Outcome for Baseline and Treatment Year

Neurologic outcome for SCA survivors did not differ significantly over the two year study period. During the year prior to instituting the pre-hospital cooling protocol, 77% of survivors were discharged with good or moderate neurologic function, and 23% with severe neurologic deficits. (Table 2) During the 12 months after institution of the pre-hospital cooling protocol, 80% were discharged with good to moderate neurologic function and 20% with severe deficits.

Table 2. Neurologic Outcome for All Survivors Baseline and Treatment Years.

	2007-2008 Prior to Cooling Protocol	2008-009 During 1st Year of Pre-hospital Cooling
CPC 1 or 2	**36/47 (77%)**	**11/40 (80%)**
CPC 3 or 4	**32/47 (23%)**	**8/40 (20%)**

Among patients with ventricular fibrillation (VF) as the presenting rhythm, the neurologic outcomes at survival were also not significantly different. The VF survival rate in the baseline year was 36.4% and during the treatment year, VF survival rate was 28.3%. (Table 3)

Table 3. Neurologic Outcome for Survivors with VF as the Initial Rhythm

	VF Survival Rate	CPC 1 or 2	CPC 3 or 4
2007-2008	36.4% (32/88)	26 (81.3%)	6 (18.8%)
2008-2009	28.3% (26/92)	23 (88.5%)	3 (11.5%)

Survival and neurologic outcome for pre-hospital hypothermia recipients.

During the first 12 months after the institution of the pre-hospital protocol, 53 sudden cardiac arrest victims received hypothermia in the field. The median age of the pre-hospital hypothermia recipients was 66 years; 27 were men, and 26 were women.

The survival rate among those who received the treatment was 22.6% (24 of 53), and the median age of the survivors was 55 years. As was expected, the majority of these patients presented in ventricular fibrillation.

From among the 53 who received hypothermia in the field, 17 died in the ED and 24 died in the hospital, 12 were discharged alive (Table 4). , and the median age of those who survived was 55 years, and survivors were composed of 10 men and 2 women.

Table 4. Disposition of SCA Victims who received PH TH

Admitted to Emergency Department	Admitted to Hospital	Survived to hospital Discharge
53	36 (67.9%)	12 (22.6%)

Neurologic status of the survivors was measured using Cerebral Performance Categories (CPC) determined at hospital discharge. A CPC of 1 or 2 is correlated with good to moderate neurologic function; CPC of 3 or 4 represent severe brain injury making the survivor dependent on others.

Cerebral Performance Category Scale

CPC 1. Good cerebral performance: conscious, alert, able to work, might have mild neurologic of psychologic deficit.

CPC 2. Moderate cerebral disability: conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.

CPC 3. Severe cerebral disability: conscious, dependent on others for daily support due to impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.

CPC 4. Coma or vegetative state: any degree of coma without the presence of all brain death criteria. Cerebral unresponsiveness

CPC 5. Brain death.

Safar P: Resuscitation after Brain Ischemia, in: Grenvik A. and Safar P, Eds: Brain Failure and Resuscitation, Churchill Livingstone, New York, 1981; 155-184.

Of the 12 survivors who received pre-hospital hypothermia, seven were discharged from the hospital with good to moderate neurologic status (CPC 1 or 2). Five survivors (41.7%) were discharged with a severe neurologic deficit (CPC 3 or 4).

Eight of the 12 survivors who received pre-hospital hypothermia had initial cardiac rhythms of ventricular fibrillation. Of these eight, seven were discharged to home with good neurologic status (CPC 1 or 2), and one was discharged to a skilled nursing home with a severe neurologic deficit (CPC # or 4). (Table 5)

Table 5. Neurologic Outcome for Subset of Patients Receiving Pre-hospital Hypothermia during year 2008-2009

	Number Treated with PH PH Survival Rate)	CPC 1 or 2	CPC 3 or 4
Subset of patients who received pre-hospital hypothermia (PH)	12/53 (22.6%)	7/12 (58.3%)	5/12 (41.6%)

Recommendations

During the two year period observed, there was no significant difference noted in survival or neurologic outcome which could be attributed to the institution of a pre-hospital cooling protocol for sudden cardiac arrest victims. It should be noted however, that while no significant improvement was seen, neither was there a negative effect on neurologic outcome during the year in which the pre-hospital hypothermia protocol was initiated.

Recommendations based on this information would include:

- EMS systems should continuously collect detailed, accurate and complete cardiac arrest data including neurologic outcome statistics which enable analysis of new practices and improvements in survival.

- EMS professionals must maintain both skills and knowledge related to advances in resuscitation science, particularly because these patients are not encountered on a regular basis.

- Improving the quality of pre-hospital care is of ultimate importance in the chain-of-survival for victims of sudden cardiac arrest. Implementation of true continuous quality improvement (CQI) is imperative. To be effective, CQI cannot be episodic or target only outliers or poor outcomes. Improved survival for SCA victims reflects the quality and dedication to detail of the EMS system caring for these patients.

References

(1) Chugh SS, Jui J, Gunson K, et al. Current burden of sudden cardiac death: multiple source surveillance versus retrospective death certificate-based review in a large U.S. community. J Am Coll Cardiol 2004;44:1268-75.

(2) Vaillancourt C, Stiell IG. Cardiac arrest care and emergency medical services in Canada. Can J Cardiol 2004;20:1081-90.

(3) Zheng ZJ, Croft JB, Giles WH, Mensah GA. Sudden cardiac death in the United States, 1989 to 1998. Circulation 2001;104:2158-63.

(4) Rea TD, Pearce RM, Raghunathan TE, et al. Incidence of out-of-hospital cardiac arrest. Am J Cardiol 2004;93:1455-60.

(5) Cobb LA, Fahrenbruch CE, Olsufka M, Copass MK. Changing incidence of out-of-hospital ventricular fibrillation, 1980-2000. JAMA 2002;288:3008-13.

(6) 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2005;112:IV-1- IV-206.

(7) 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Post Reusucitation Support. Circulation 2005;000:IV-1-84-IV-88.

(8) Rea TD, Eisenberg MS. Long-term survival after resuscitation from cardiac arrest: cause for optimism and continued efforts. Am Heart J 2003;145:749-50.

(9) Rea TD, Eisenberg MS, Sinibaldi G, White RD. Incidence of EMS-treated out-of-hospital cardiac arrest in the United States. Resuscitation 2004;63:17-24.

(10) Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med 2002;346:549-56.

(11) Bernard SA, Gray TW, Buist MD, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med 2002;346:557-63.

(12) Cheung KW, Green RS, Magee KD. Systematic review of randomized controlled trials of therapeutic hypothermia as a neuroprotectant in post cardiac arrest patients. CJEM 2006;8:329-37.

(13) Majersik JJ, Silbergleit R, Meurer WJ, Brown DL, Lisabeth LD, Morgenstern LB. Public health impact of full implementation of therapeutic hypothermia after cardiac arrest. Resuscitation 2008.

(14) Kim F, Olsufka M, Longstreth WT, Jr., et al. Pilot randomized clinical trial of pre-hospital induction of mild hypothermia in out-of-hospital cardiac arrest patients with a rapid infusion of 4 degrees C normal saline. Circulation 2007;115:3064-70.

(15) Covaciu L, Allers M, Lunderquist A et al: Intranasal cooling with or without intravenous cold fluids during and after cardiac arrest in pigs. Acta Anaesthesiol Scand. 2009 Nov 12.