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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

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Abstract

Objective—This study evaluated whether implementation of a therapeutic hypothermia (TH) protocol upon arrival in a community hospital improved survival and neurologic outcomes in patients initially found to have ventricular fibrillation (VF), pulseless electrical activity (PEA), or asystole and then successfully resuscitated from out-of-hospital cardiac arrest

Design and Setting—This is a retrospective study of patients who presented after implementation of a TH-protocol compared to those who presented before the protocol was implemented at Harborview Medical Center, Seattle, Washington.

Patients—We evaluated 491 consecutive adults with out-of-hospital, non-traumatic cardiac arrest who presented between January 1, 2000 and December 31, 2004.

Interventions—An active cooling TH-protocol using ice packs, cooling blankets, or cooling pads to achieve a temperature of 32–34 °C was initiated on November 18, 2002 for unconscious patients resuscitated from cardiac arrest.

Measurements—Demographics and outcomes were obtained from medical records and an emergency medical database. The primary outcomes were survival and favorable neurologic outcome at discharge associated with the TH-protocol. An adjusted analysis was performed using a multivariate regression.

Main results—During the TH-period, 204 patients were brought to emergency department; of these, 132 (65%) ultimately achieved temperatures of less than 34 °C. Of the 72 patients who did not achieve goal temperatures: 40 (20%) died in the emergency department or shortly after being admitted to the hospital, 15 (7%) regained consciousness, 4 (2%) had contraindications 13 (6%) had temperature increase or did not have documented use of the TH protocol. In the prior period, none of the 287 patients received active cooling. Patients admitted in the TH-period had a mean esophageal temperature of 34.1°C during the first 12 hours compared to 35.2°C in the pre-TH period ($p < 0.01$). Survival to hospital discharge improved in TH period in patients with an initial rhythm of VF (OR 1.88, 95% confidence interval (CI) 1.03–3.45), however not in patients with

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non-VF (OR 1.17, 95% CI 0.66–2.05). In adjusted analysis, VF patients during the TH period trended toward improved survival (OR 1.71, 95% CI 0.85–3.46) and had favorable neurologic outcome (OR 2.62, 95% CI 1.1–6.27) compared to the earlier period. This benefit was not observed in patients whose initial rhythm was PEA or asystole.

Conclusions—The therapeutic hypothermia period was associated with a significant improvement in neurologic outcomes in patients whose initial rhythm was VF, but not in patients with other rhythms.

Keywords

Hypothermia; Cardiac arrest; Sudden cardiac death; Ventricular fibrillation; Asystole; Pulseless electrical activity (PEA); Resuscitation; Cardiopulmonary resuscitation (CPR)

INTRODUCTION

Several emergency departments and intensive care units have implemented therapeutic hypothermia (TH) protocols for patients with out-of-hospital cardiac arrest, with the aim of improving neurologic outcomes and potentially survival.(1–5) The American Heart Association (AHA) and the International Liaison Committee on Resuscitation (ILCOR) recommends cooling to 32°C to 34°C for 12–24 hours in unconscious patients who present after having been resuscitated from out-of-hospital cardiac arrest when the presenting rhythm was ventricular fibrillation.(6, 7) In the 2005 AHA guidelines for post-resuscitation support, the committee gave TH a Class 2A recommendation (It is reasonable to perform treatment) for the use in out-of-hospital and in-hospital VF, and Class 2B (Treatment may be considered) for non-VF.(8)

The clinical justification for these recommendations stems primarily from two randomized trials in patients hospitalized following resuscitation from out-of-hospital ventricular fibrillation.(9, 10) These studies demonstrated reduced neurologic disability among those receiving TH, and one study also showed reduced mortality at 6-months in the TH group.(9) Utilization of TH in clinical practice has been incorporated slowly for a variety of reasons. (2) Some of the reasons cited for the under-utilization of TH in practice surveys include lack of clinical data, lack of knowledge in the method of achieving TH, and difficulty in implementation.(11, 12) Whether the beneficial effects demonstrated in these randomized trials can be translated into clinical practice remains to be seen, and little has been published regarding practical non-investigational experience with TH. Furthermore, the applicability of TH for patients with presenting rhythms other than ventricular fibrillation remains to be demonstrated.

In November 2002, Harborview Medical Center (Seattle, Washington) implemented a TH protocol that used ice packs, cooling blankets, or cooling pads for all patients presenting to the emergency department following resuscitated out-of-hospital cardiac arrest. This provided a unique opportunity to explore the benefit of TH, by comparing outcomes of patients with a historical control period 2 years prior to the implementation of this protocol in the same hospital. We evaluated survival and neurologic outcomes among patients presenting in periods before and after adoption of the TH protocol. Importantly, we also evaluated the impact of the TH protocol on outcomes for patients whose initial rhythms had been ventricular fibrillation (VF) or ventricular tachycardia in contrast to those with pulseless electrical activity (PEA) or asystole as the initial presenting cardiac rhythms during resuscitation, given that there is little data to support the use of TH in the latter.

METHODS

The implementation of a TH policy at an urban teaching hospital provided an opportunity to conduct a non-randomized observational study of clinical outcomes of all resuscitated out-of-hospital cardiac arrest patients treated before and after implementation. This study was performed on consecutive patients presenting to Harborview Medical Center after out-of-hospital cardiac arrest between January 1, 2000 and December 23, 2004 (Figure 1). During the 23 month period January 1, 2000 to November 30, 2001, no attempts were made to cool patients. (In an 11.5 months observation period December 1, 2001 to November 17, 2002, esophageal temperature and clinical data were collected prospectively, but no active measures used to cool the patients.) On November 18, 2002, a TH protocol was initiated using active cooling with ice packs, cooling blankets, or cooling pads. The protocol was intended for all unconscious patients who were brought to the emergency department after an out-of-hospital cardiac arrest who did not have a contraindication. Outcomes were compared in patients presenting in the periods before and after initiation of this TH protocol.

Therapeutic hypothermia protocol

Unconscious patients whom paramedics resuscitated from non-traumatic out-of-hospital cardiac arrest and brought to the emergency department were eligible for the TH protocol; however, the ultimate decision for implementation was at the discretion of the treating physicians. Patients were excluded from the TH protocol if there was evidence for significant active bleeding, severe infection (sepsis or pneumonia), recent burn or if skin was not intact, or if the patient was in a pre-existing persistent vegetative state. Patients were actively cooled using ice packs, cooling blankets, cooling pads (Arctic Sun[®] Temperature Management System, Medivance Inc., Louisville, CO) or some combination of these means. The goal was to achieve a temperature of 32 to 34 °C as soon as possible and maintain it for 24 hours. Cooling blankets, using circulating cold water or air, were adjusted manually in order to keep temperatures close to the goal of 33 °C. This task was demanding, and the goal difficult to achieve. In late 2003, cooling pads were introduced at the hospital, and by mid 2004, most patients were being treated with cooling pads, sometimes after initial treatment with ice packs, cooling blankets, or both.

All unconscious patients were mechanically ventilated via endotracheal tubes. As described previously,(13) the TH protocol also used intravenous vecuronium and diazepam to enhance the efforts at cooling and to control shivering. If the temperature was greater than 34.5 °C in the emergency department or upon arrival to the critical care unit, vecuronium was given as a loading dose of 0.1 mg/kg) and was maintained using an infusion of 1 to 4 mg/h. If shivering was noted, additional vecuronium was given. *Neuromuscular blockade was tested using a train of four.* The infusion was discontinued when goal temperature was reached.

The TH protocol was initiated as soon as possible after arrival at hospital. Efforts to cool the patient were temporarily suspended if the temperature dropped below 32 °C, or if the patient was transported out of the emergency department or intensive care unit for procedures. The protocol was discontinued if the patient regained consciousness. *Otherwise, the protocol was continued and no attempts were made to wean sedatives and paralytics unless clinically indicated.* After 24 hours of cooling, the patient was allowed to rewarm passively and no patient was actively re-warmed.

Patient data

All patient data were abstracted from medical records and a linked first-responder database. Information abstracted included location of arrest; times from call to dispatch, arrival at scene and arrival at hospital; presenting cardiac rhythm; whether the arrest was witnessed;

and whether bystander cardiopulmonary resuscitation was performed. Starting December 1, 2001 temperatures were measured by esophageal probes. In most of the admitted out-of-hospital cardiac arrest patients, information on esophageal temperatures was abstracted from hospital records for the first 12 hours following presentation. Medical records of patients presenting after November 18, 2002 were reviewed concerning use of ice packs, cooling blankets, or cooling pads. If one or more of these methods were mentioned, the patient was considered as having been actively cooled. Survival and neurologic function were assessed for all patients at hospital discharge based on review of medical records. Patients were categorized at discharge as having favorable neurologic outcomes if there were no evidence of impairments, or as having unfavorable neurologic outcomes if they had mild impairments, were conscious with severe cognitive or motor impairments, or were in a coma. Follow-up beyond hospital discharge was not available.

Because of concerns about the accuracy of temperature measurements by standard means in these patients, comparisons of temperatures in the two periods were limited to esophageal temperatures. Esophageal temperatures in patients admitted in the pre-TH period were only acquired in the observation period from December 1, 2001 through November 18, 2002. Comparisons beyond 12 hours could not be made since patients from the pre-TH period had esophageal temperatures measured only for the first 12 hours.

Patient Exclusions

Between January 1, 2000 and December 31, 2004, 538 patients were brought to Harborview Medical Center after out-of-hospital cardiac arrest. These patients represent about one-half of all such patients brought to hospitals in Seattle over this period. Patients treated for cardiac arrest but not regaining spontaneous circulation were not transported. Excluded from these analyses were one patient with a missing data form, 13 patients transferred to other hospitals from the emergency department, 11 patients less than 18 years of age, and 22 patients who were included in a pilot study of hypothermia induced with a rapid infusion of 4 °C normal saline.⁽¹³⁾ Thus 491 patients were eligible for our analyses: 287 who presented before initiation of the TH protocol on November 18, 2002 and 204 who presented during the TH intervention period (Figure 1).

The primary outcome was based on an intention-to-treat analysis including all patients presenting to the emergency department, where the cooling protocol was started immediately on arrival. Occasionally patients required prolonged stabilization in the emergency department if beds are not available for patient admission. Since patients who died early in the emergency room would not likely have benefited from TH, even if it were started immediately, we also conducted a secondary analysis directed to those patients who were admitted to an inpatient service; however we recognize the potential selection bias of restricting our analysis to these patients.

The University of Washington Human Subjects Division Institutional Review Board reviewed and approved this study.

Statistical Analyses

Bivariate analyses were performed with chi-square tests or Student's t-test, as appropriate, to compare characteristics of patients from the pre-TH and TH periods. To determine independent predictors of survival and favorable neurologic outcome, we performed multivariate logistic regression. A common set of predictor variables was used for all analyses and included age < 65 years, witnessed cardiac arrest, initial rhythm, cardiopulmonary resuscitation by bystanders, and time from dispatch to first responder arrival. Since early arrival of paramedic personnel would be the most likely to confer a

positive benefit on patient outcomes(14, 15) arrival to scene by paramedics was considered as a continuous variable in 1 minute increments. After all these variables entered the model, the TH period variable was forced in to determine its association with outcome. Based on our prior pre-hospital hypothermia study (16) we anticipated differences in outcomes according to initial rhythms: ventricular fibrillation or tachycardia (VF) versus PEA or asystole (non-VF). Time to cooling was not included as a variable in our multivariate model because this information would have only been available for patients in the TH-period. Patients with ventricular tachycardia as the presenting rhythm were uncommon. Given the similarity of ventricular tachycardia with VF in terms of resuscitation procedures and shared etiology, they were grouped with VF patients. Thus outcome results were presented stratified by initial rhythms. Analyses were performed using Intercooled STATA Version 9.2 for Windows (StataCorp, College Station, Texas) or SPSS version 16.0 (SPSS Inc, Chicago, Illinois).

The authors had full access to the data and take responsibility for its integrity. All authors have agreed to the manuscript as written.

RESULTS

Baseline age, gender, ethnicity, presenting arrhythmia type, and use of revascularization were similar between the patients from the two periods, before and after initiation of the TH protocol (Table 1). Witnessed arrests were more common in the TH compared to the pre-TH period. During the TH-period, 204 patients were brought to emergency department, of whom, 132 (65%) ultimately achieved temperatures of less than 34 °C. Of the 72 patients who did not achieve goal temperatures: 40 patients (20%) died in the emergency department or shortly after being admitted to the hospital (less than 6 h), 15 patients (7%) regained consciousness, 4 patients (2%) had contraindications (GI bleeding or possible infection), 7 patients (6%) had temperature increases despite cooling and in 6 patients, it was unclear why patients did not receive cooling (staff overlooked or contraindications not documented). In the prior period, none of the 287 patients received active cooling (Figure 1). During both periods, patients with EKG criteria for an acute myocardial infarction (i.e. new ST-elevations or left-bundle branch block on EKG) were routinely taken to the cardiac catheterization laboratory for angiography and revascularization if clinically indicated. These patients comprised a very small number of patients in this study. The rates of revascularization were equivalent in the two periods.

Esophageal Temperature

Average esophageal temperatures at arrival to the emergency department were similar between the observational period and the TH period, but were significantly lower during the TH period by the second hour and throughout the first 12 hours (Figure 2). On average, temperatures within the first 12 hours among patients from the observational period (pre-TH) increased by 1.54 ± 0.26 °C, while among patients from the TH period it decreased by 0.77 ± 0.17 °C ($p < 0.001$). A significantly greater proportion of these patients from the TH period reached a goal temperature less than 34 °C compared to those in the observation period (Table 2). These findings were similar for subgroups of VF and non-VF patients. In the VF subgroup, patients in the TH-period had an average decrease in esophageal temperature of -1.03 °C and an average temperature over the first 12 hours of 34.3°C, which was slightly above the recommended temperature goal of less than 34°C.

Survival and Neurologic Outcomes

When stratifying patients by presenting rhythm, the overall survival rate to discharge from the hospital was greater in the TH period than in the pre-TH period in those with VF (pre-

TH (36/93, 38.7%) vs. TH (44/81, 54.3%) $p=0.04$). Similarly, favorable neurologic outcomes (pre-TH (14/93, 15%) vs. TH (28/81, 34.6%) $p<0.01$) were evident in the TH period compared to the pre-TH period. A similar benefit was lacking among those with non-VF (survival: pre-TH (37/191, 19.4%) vs. (26/122, 21.3%) $p=0.65$) and favorable neurologic outcomes: pre-TH (17/191, 8.9%) vs. TH (14/122, 11.5% $p=0.44$)) (Figure 3).

The univariate and multivariate predictors of survival to discharge and favorable neurologic outcome are shown in Table 3. Patients with an initial rhythm of VF during the TH-period had significantly improved rates of favorable neurologic outcome, adjusted for patient age, witnessed arrest, bystander CPR, and EMS arrival times (Table 3) when compared to the pre-TH period. Although witnessed arrest and EMS response time as a continuous variable were not significant in the adjusted analysis they were left in the model for estimation of OR for the other variables given their a priori importance. Among patients with non-VF, significant associations by TH-period were not found (Table 3).

When restricting the analysis to those patients who survived to inpatient admission, 44 (62.9%) of patients with VF survived during the TH period compared to 36 (50.7%) in the pre-TH period ($p=0.145$). During the TH-period such patients had a higher proportion discharged with favorable neurologic outcome 40% v. 19.7% ($p=0.008$). There was no improvement in mortality or neurologic outcome during the TH period among patients presenting with non-VF rhythms.

A sensitivity analyses was performed to evaluate whether patients with very long transport times (with transport times from the scene to the hospital more than two standard deviations longer than the mean) or who arrested after the arrival of EMS personnel confounded our findings. The OR for the primary findings was not substantively changed by excluding these patients. In order to assess the impact of witnessed arrest on the benefit of TH-period, we performed an adjusted analysis including an interaction term between witnessed arrest and TH-period. For the survival outcome, the OR for the interaction term was not significant among patients with VF arrest (0.19, 95% CI 0.03–1.14) nor those patients with non-VF arrest (4.19, 95% CI 0.98–17.74). The interaction term for the neurologic outcome was not significant for patients with non-VF arrest and could not be generated for VF patients given that there were no patients with favorable neurologic outcomes among those with unwitnessed arrests in the pre-TH group.

DISCUSSION

The implementation of a hospital TH protocol improved neurologic outcomes in patients with out-of-hospital VF, but had no benefit on patients whose presenting rhythm was asystole or pulseless-electrical activity. Previous studies using a similar before-and-after design reported considerably smaller patient samples and evaluated primarily VF patients, although the results for VF patients were similar to our findings.(17–19)

In this retrospective, observational, before-and-after comparison, we describe both temperature and outcomes during a TH period, when active surface cooling procedures were used, compared to a pre-TH period. While the initial post-arrest temperatures were similar in the two periods, the pre-TH period temperatures increased over time with return of spontaneous circulation, compared to the TH-period in which hypothermia was maintained. As expected, mean esophageal temperatures were significantly lower during the TH period. Patients with an initial rhythm of VF who were brought to the ED during the TH period, had significantly improved survival and neurologic outcomes compared to VF patients in the pre-TH period. After adjusting for potentially confounding factors, the TH period continued

to be associated with significant favorable neurologic outcomes and a non-significant trend for improved survival in the adjusted analysis.

Temperature of less than 34 °C was achieved in 132/204 (65%) patients with the use of ice packs, cooling blankets, and cooling pads. Recovery of consciousness and early death in the emergency department (55/72) explained the failure to achieve the goal temperature in a majority of the cases. The TH period also includes the early phases of implementation of TH protocol, and TH was sometimes not implemented due to lack of familiarity with the protocol, lack of available cooling devices, or if the physician or nursing staff simply overlooked the protocol. Only 4 patients out of 170 had evidence for GI bleeding or possible infection and TH was stopped or not initiated by the attending physician, suggesting that a small minority of patients had a contraindication to active TH. So as to avoid bias, we considered all eligible patients during both periods, including those in the TH period who were not cooled.

As noted by other investigators, the use of ice packs and cooling blankets sometimes resulted in slow cooling or overcooling.(20) The main advantage of the cooling pad device was the more precise temperature control, and by the end of the TH period, the majority of patients were managed with the cooling pad device.

We demonstrated a significant average difference in esophageal temperature between the later TH and early pre-TH periods. The TH period was associated with a mean temperature of 34.1°C in the first 12 hours, which was slightly outside our target range of 32 to 34°C. We would expect that the actual temperature difference would be closer to the target if a greater proportion of the patients had received TH, since untreated patients would not be expected to spontaneously cool. It is difficult to correct for these differences in our analysis, since patients who are spontaneously hypothermic may be so because they are in severe shock or dying, while patients who did not achieve temperatures less than 34°C may have been re-warmed due to the prompt restoration of circulation and organ function. In addition, 7 patients were noted to actually increase their esophageal temperature despite active TH. It is unclear whether these patients had evidence for infection that manifested as a febrile response since these data were not collected. Nevertheless, these data demonstrate that an effective TH protocol involving active surface cooling can be implemented successfully as a routine in a non-investigational setting.

One possible implication with these data is that a target of 34 °C may be sufficient for resuscitated VF patients and outcomes can be improved even if the temperatures are not in the currently recommended 32–34°C range. Animal studies of cardiac arrest (21, 22) and small studies of traumatic brain injury in humans(23) have suggested that 34°C may be an effective temperature, while benefits may diminish as lower temperatures are used. Determining the optimal temperature for improving neurologic outcomes in patients with cardiac arrest needs further prospective study.

Among VF patients admitted to the inpatient services there was a non-significant improvement in survival, while the improvement in favorable neurologic outcomes at discharge remained significant. Evaluating only such admitted patients is problematic because it is difficult to control for selection bias affecting admission criteria, such as bed availability or time spent stabilizing the patient in the emergency department. Nevertheless, the favorable neurologic outcome remained significant and the relative survival improvement associated with the TH period was similar to the intention-to-treat analysis, although not statistically significant.

We found that patients presenting with asystole or PEA did not benefit from TH, a finding suggested by previous studies,(24) but contradicted by others(25). This difference in

outcome was not related to differences in the effectiveness of TH since both VF and non-VF groups had a similar proportion of patients with measured temperature of less than 34 °C. Prehospital variables such as witnessed arrest, bystander CPR, or time from dispatch to EMS arrival were also not significantly different between the two periods.

The time to restoration of circulation after cardiac arrest is of critical importance to neurologic outcome and one of the potential differences between VF and non-VF (PEA or asystole) is the increased time from cardiac arrest to the restoration of circulation when compared to a rapidly resuscitated patient in VF. Before the restoration of circulation there is limited brain perfusion/oxygenation and after a certain point, the application of TH may no longer be beneficial. The lack of efficacy of TH in non-VF due to a delay in restoration of circulation is supported by recent work from Oddo and et al. Time from collapse to restoration of circulation was an independent predictor of survival for patients receiving TH(26). Secondly, animal studies have demonstrated that intra-arrest TH or TH within 15 minutes after return of spontaneous circulation offers the best brain protection after cardiac arrest(27, 28). These animal studies also suggest that time may be an important factor in whether TH is beneficial. While our data show that TH does not improve survival or neurologic outcomes in patients with non-VF rhythms, further prospective, controlled studies are necessary to definitively address this issue.

LIMITATIONS

The retrospective nature of this (29) study leaves it open to several biases. Comparing patients in the TH period to historical controls raises the possibility that the differences in outcome were the result of temporal trends in improved emergency medical services and critical care management of cardiac arrest patients. Temperature measurement and outcome assessment were performed in a similar fashion in the two periods, so differences in ascertainment would not explain our findings. By an intention to treat analysis, we chose to include all patients presenting to the emergency department since cooling was started immediately upon arrival and some patients may have had longer times to admission due to administrative delays. While the proportion of patients with comorbidities such as COPD, diabetes, prior stroke, renal failure, and cancer for the pre-TH and TH periods were roughly similar, detailed adjustment for patient comorbidities was limited by missing data. Additionally, patients who were treated under the TH protocol may have been observed for a longer period of time awaiting an anticipated neurologic recovery than those who did not receive active cooling, such a prolonged observation could have allowed more time for patients to awaken, while families of patients not treated under the TH protocol might have chosen withdrawal of support earlier. Nevertheless, the similar rates of admission during the pre-TH and TH periods suggest that this was not the case as far as observation and triage in the emergency department.

CONCLUSIONS

A hospital-wide hypothermia protocol using ice packs, cooling blankets, or cooling pads for patients with resuscitated out-of-hospital cardiac arrest led to the attainment of esophageal temperatures of less than 34 °C in 65% of all patients during the TH period. In this retrospective study within a single hospital, the implementation of a TH protocol was associated with a significant improvement in neurologic outcome in patients whose initial rhythm was VF; however, patients with non-VF brought to the ED during the TH period had similar outcomes to those in the pre-TH period. Further studies are needed to better define the optimal degree of hypothermia and its role in patients whose initial rhythm is not VF.

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Figure 1. Study dates and patient treatments

The study has two distinct periods: the pre-TH period and the TH period, which started November 18, 2002. The pre-TH period includes an observation period in which esophageal temperatures were measured, but active therapeutic hypothermia was not attempted. During the TH period, active cooling with ice packs, cooling blankets, and cooling pads were used and esophageal temperatures were measured. The TH protocol was stopped prior to achieving a temperature $\leq 34^{\circ}\text{C}$ due to patients waking up, withdrawal of care, severe coagulopathy, or death.

Number of patients with temperatures available at each time point

Time (H)	Admit	1	2	3	4	5	6	7	8	9	10	11	12
Pre-TH period	68	33	36	36	35	32	29	29	30	24	25	27	26
TH Period	155	101	112	109	110	107	108	107	101	90	96	92	97

Figure 2. Mean esophageal temperatures following admission to the emergency department comparing patients during the pre-TH period to those during the TH-period
 Bars represent $\pm$ S.E. from the mean. $P < 0.01$, at each time point after hour 2, comparing the average temperature between the two groups. Not all patients had temperatures measured at every time point.

A.

B.

Figure 3. Survival and neurologic outcomes by rhythm type between the pre-TH and TH period
A. Survival outcomes in patients with initial rhythm of VF during pre-TH (36/93) vs. TH (44/81) and favorable neurologic outcome pre-TH (14/93) vs. TH (28/81). **B.** Survival outcomes in patients with PEA or asystole during pre-TH (37/191) vs. (26/122) and favorable neurologic outcomes pre-TH (17/191) vs. TH (14/122).

TABLE 1

Baseline characteristics of eligible patients resuscitated from out-of-hospital cardiac arrest and transported to hospital in the pre-TH period and the period after the TH protocol was implemented

ALL PATIENTS	Pre-TH period (287)	% or SD (17.3)	TH Period (204)	% or SD (16.8)	All (491)	% or SD (17.1)	Significance (P-value)
Mean Age (SD)	56.5	(17.3)	57.2	(16.8)	56.8	(17.1)	0.67
Gender (male)	209	73%	142	69%	349	71%	0.65
Race							0.29
Caucasian	203	71%	141	69%	342	70%	
African American	50	17%	38	19%	88	18%	
Asian	23	8%	15	7%	38	8%	
Other	12	4%	11	5%	24	5%	
Presenting Arrhythmia/Status							0.12
Ventricular Fibrillation	90	31%	75	36%	164	33%	
Ventricular Tachycardia	3	1%	7	3%	10	2%	
Asystole	73	25%	49	24%	122	25%	
PEA	118	41%	73	36%	191	39%	
Mechanism of Arrest							0.27
Primary Cardiac	238	83%	181	89%	419	85%	
Overdose	28	10%	15	7%	43	9%	
Drowning	7	2%	4	2%	11	2%	
Strangulation	4	1%	4	2%	8	2%	
Burns	3	1%	0	0%	3	1%	
Other/Unknown	7	3%	0	0%	7	1%	
Presentation							
Witnessed Arrest	156	57%	130	66%	286	61%	0.04
Bystander CPR	93	38%	72	36%	165	37%	0.57
Dispatch to arrival <5 min	249	88%	180	91%	429	89%	0.39
Hospital Procedure							
Admission to hospital	229	79.8%	169	82.8%	398	81.1%	0.40
Coronary catheterization	31	25%	50	26%	81	26%	0.45
Percutaneous coronary intervention	9	7%	15	8%	24	8%	0.45
Coronary artery bypass grafting surgery	3	2%	6	3%	9	3%	0.43

ALL PATIENTS		Pre-TH period (287)		% or SD		TH Period (204)		% or SD		All (491)		% or SD		Significance (P-value)	
Pre-hospital EMS time (min)		Time (min)		SD		Time (min)		SD		Time (min)		SD			
Dispatch to arrival* (first unit)		3:03		1.9		2:47		1.9		2:57		1.9		0.13	

* Times (minutes from dispatch to arrival of first EMS unit) include response times of zero minutes, which include cardiac arrest occurring after arrival by Seattle Fire Department or arrest discovered at a site not requiring a vehicular response. During the pre-TH period there were 39 cases of zero time and in the TH period 41 cases of zero time.

TABLE 2

Comparison of average esophageal temperatures (centigrade) during the first 12 hours after admission between patients during the pre-TH and TH periods

All Patients	Observation period (69)	SD	TH Period (170)	SD	Significance (p-value)
Admit Temp (°C)	34.3	1.91	34.9	1.76	0.04
Average Temp	35.2	1.80	34.1	1.38	<0.01
Average Minimum Temp	33.9	1.78	32.8	1.65	<0.01
ΔTemperature from Admission	+1.54	2.16	-0.77	2.14	<0.01
Measured Temp <34°C* (%)	10/49 (20.4%)		105/138 (76.1%)		<0.01
Ventricular Fibrillation	(16)		(71)		
Admit Temp (°C)	33.9	1.79	35.1	1.19	<0.01
Average Temp	35.0	1.94	34.3	1.09	0.01
Average Minimum Temp	33.6	1.65	33.3	1.53	0.44
ΔTemperature from Admission	+1.78	1.94	-1.03	1.67	<0.01
Measured Temp <34°C* (%)	0/12 (0.0%)		42/57 (73.7%)		<0.01
Asystole or PEA	(53)		(99)		
Admit Temp (°C)	34.4	1.94	34.6	2.07	0.52
Average Temp	35.3	1.77	34.1	1.55	<0.01
Average Minimum Temp	34.0	1.82	32.7	1.69	<0.01
ΔTemperature from Admission	+1.46	2.23	-0.58	2.43	<0.01
Measured Temp <34°C* (%)	10/37 (27.0%)		63/81 (77.8%)		<0.01

Temperature achieved between the hours 3–12 after admission. The denominator from hour 3–12 differs from the total due to patients with missing values and patients who died.

TABLE 3

The unadjusted and adjusted odds ratios of survival to discharge and discharge with favorable neurologic recovery

UNADJUSTED	OR Survival to Discharge	95% CI	OR Favorable Neurologic Recovery	95% CI
All Patients				
Age < 65	1.77	1.15–2.72	1.49	0.86–2.57
TH Period	1.55	1.05–2.30	2.08	1.26–3.44
Initial rhythm				
Asystole	----		----	
VF/VT	9.53	4.67–16.41	13.22	3.99–43.80
PEA	4.19	2.04–8.62	6.69	1.98–22.59
Witnessed Arrest	2.34	1.51–3.64	3.50	1.86–6.60
Bystander CPR	1.63	1.08–2.07	1.36	0.80–2.29
Time from dispatch to first in (minutes)	0.92	0.83–1.03	0.86	0.75–0.99
Ventricular Fibrillation				
Age < 65	2.54	1.36–4.75	2.27	1.07–4.83
TH Period	1.88	1.03–3.45	2.85	1.37–5.92
Witnessed Arrest	1.82	0.85–3.87	2.63	0.95–7.28
Bystander CPR	1.60	0.86–2.97	1.47	0.71–3.03
Time from dispatch to first in (minutes)	0.78	0.63–0.95	0.68	0.53–0.86
PEA/Asystole				
Age < 65	1.80	0.94–3.44	1.14	0.50–2.58
TH Period	1.17	0.66–2.05	1.39	0.65–2.95
PEA	4.19	2.04–8.62	6.69	1.98–22.59
Witnessed Arrest	1.73	0.96–3.12	3.21	1.32–7.80
Bystander CPR	0.97	0.51–1.86	0.69	0.27–1.78
Time from dispatch to first in (minutes)	0.99	0.86–1.14	0.98	0.81–1.19
Adjusted multivariate				
	OR Survival to Discharge	95% CI	OR Favorable Neurologic Recovery	95% CI
Ventricular Fibrillation		(n=154)		(n=149)
Age < 65	2.41	1.19–4.90	2.23	0.94–5.25
Witnessed Arrest	1.74	0.77–4.00	2.56	0.86–7.34
Bystander CPR	2.16	1.08–4.35	2.45	1.04–5.78
Time from dispatch to arrival on scene (minutes)	0.72	0.57–0.92	0.65	0.48–0.89
TH Period	1.71	0.85–3.46	2.62	1.10–6.27
PEA/Asystole		(n=260)		(n=256)
Age < 65	2.70	1.28–5.68	1.62	0.64–4.11
Witnessed Arrest	1.73	0.86–3.47	2.94	1.09–7.92
Bystander CPR	1.12	0.56–2.27	0.75	0.27–2.03
Time from dispatch to arrival on scene (minutes)	0.97	0.81–1.17	1.03	0.81–1.30
PEA	4.49	2.06–9.77	5.76	1.61–20.5
TH Period	0.82	0.41–1.60	0.92	0.37–2.32

CI confidence interval OR odds ratio PEA pulseless electrical activity TH therapeutic hypothermia VF/VF ventricular fibrillation ventricular tachycardia