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Clinical paper

Prevalence and effect of fever on outcome following resuscitation from cardiac arrest

Kory Gebhardt[a], Francis X. Guyette[b], Ankur A. Doshi[b], Clifton W. Callaway[b], Jon C. Rittenberger[b,*], The Post Cardiac Arrest Service[bc]

[a] Northwestern University, Department of Emergency Medicine, United States
[b] University of Pittsburgh, Department of Emergency Medicine, United States

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ABSTRACT

Objective: Evaluate the prevalence of fever in the first 48 h after cardiac arrest and its effect on outcomes.
Methods: Review of patients treated between 1/1/2005 and 6/30/2010. Fever was defined as $T \geq 38.0\,^{\circ}C$. We classified categories of post-cardiac arrest illness severity as (I) awake, (II) coma + mild cardiopulmonary dysfunction (SOFA cardiac + respiratory score <4), (III) coma + moderate-severe cardiopulmonary dysfunction, and (IV) deep coma. Associations between fever and survival or good neurologic outcome were examined between hypothermia (TH) and non-TH groups.
Results: In 336 patients, mean age was 60 years (SD 16), 63% experienced out-of-hospital cardiac arrest and 65% received TH. A shockable rhythm was present in 40%. Post arrest illness severity was category II in 38%, category III in 20%, and category IV in 42%. Fever was present in 42% of subjects, with a post-arrest median onset of 15 h in the non-TH cohort and 36 h in TH cohort. Fever was not associated with survival within the whole cohort (OR 0.32, CI 0.15, 0.68) or TH cohort (OR 1.21, CI 0.69, 2.14), but was associated with survival in non-TH cohort (OR 0.47, CI 0.20, 1.10). Fever was not associated with good outcomes in the whole cohort (OR 0.83, CI 0.49, 1.40), TH cohort (OR 1.09, CI 0.56, 2.12) or non-TH cohort (OR 0.34, CI 0.11, 1.06).
Conclusions: The development of fever within the first 48 h after ROSC is common. Fever is associated with death in non-TH patients. TH treatment appears to mitigate this effect, perhaps by delaying fever onset.

1. Introduction

In the United States, sudden cardiac arrests claim approximately 300,000 lives per year.[1] Over the past decade, induced therapeutic hypothermia (TH) has been adopted to attenuate neurological injury after the return of spontaneous circulation (ROSC) after cardiac arrest.[2,3] TH has become an integral component of the American Heart Association's recommendations in post-arrest care.[4]

Conversely, hyperthermia exacerbates acute neurological injury and contributes to poor outcomes.[5–11] As little as 1 °C increase in brain temperature adversely affects histologic and functional outcome after cerebral ischemia in rats and dogs.[12–14] Clinical studies also find that post-arrest hyperthermia is associated with poor neurological outcomes.[7,9–11] However, these studies involved small sample sizes and were completed prior to the widespread use of TH. This study examines a larger and more diverse patient population to evaluate the consequences of fever in post-arrest patients with and without TH. The advances made in understanding the post-cardiac arrest syndrome[15] and applying increasingly protocol-driven care,[16] coupled with TH use, merit further evaluation of the association and predictive value between temperature and outcomes.

The aim of this study is to determine the association between the presence, degree, and duration of fever and outcomes after cardiac arrest, after adjustment for other factors associated with outcome. Secondary aims of the study were to determine the prevalence and timing of fever after cardiac arrest.

2. Methods

2.1. Setting

Data were collected as part of a prospective quality improvement database. The University of Pittsburgh Institutional Review

* Corresponding author at: University of Pittsburgh, Department of Emergency Medicine, 3600 Forbes Avenue, Suite 400A, Pittsburgh, PA 15261, United States.
E-mail address: rittjc@upmc.edu (J.C. Rittenberger).
[c] For the group of The Post Cardiac Arrest Service researchers, see Appendix A.

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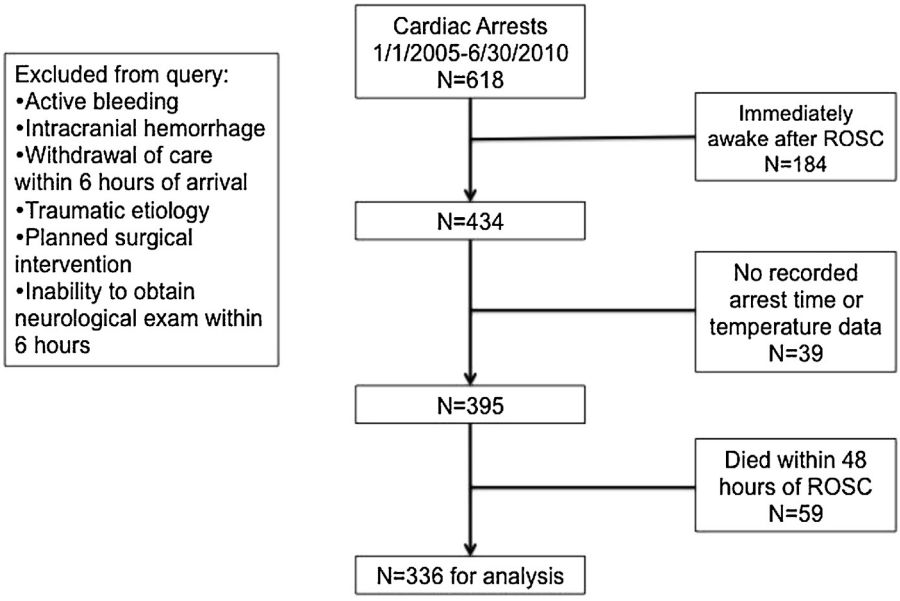

Fig. 1. Selection of patients for review.

Board deemed review and analysis of these quality improvement data as exempt.

2.2. Study population

A total of 618 patient records from a tertiary care facility were reviewed between 1/1/2005 and 6/30/2010. Subjects were adults (>18 years) admitted to the hospital after in-hospital cardiac arrest (IHCA) or out-of-hospital cardiac arrest (OHCA) with ROSC. We defined cardiac arrest as receiving chest compressions or rescue shock by a professional healthcare provider. Cardiac arrests in the emergency department were classified as IHCA. In 2007, our facility implemented a multi-disciplinary post-cardiac arrest care plan, including TH, for this patient population.[16] Patients were included regardless of whether they were treated with TH. Patients were excluded if they were awake immediately following ROSC, died within 48 h of initial arrest, did not have any recorded temperature data, or did not have a specific arrest time recorded. In 2008, our facility transitioned to an electronic medical record system, and 35 subjects were excluded because records of detailed physiological data were lost during this transition (Fig. 1).

2.3. Treatment protocol

TH was rapidly induced with intravenous infusion of 20–30 cc kg^{-1} of 4 °C saline solution and the use of cooling blankets. These measures could be supplemented by the administration of 4 °C saline solution via nasogastric lavage. Endovascular cooling was rarely used in our facility. The target was to reach and maintain a core temperature between 32 °C and 34 °C until 24 h after ROSC. The preference of temperature monitoring sites was: pulmonary artery catheter, esophagus, bladder and rectum. Most patients were monitored with esophageal temperature probes. Rewarming was carried out at a goal rate of 0.25 °C h^{-1}. Sedation with propofol or benzodiazepines was recommended to prevent shivering. Paralytics were frequently employed during induction of TH, but continuous infusions once at goal temperature were rare.

Fluid infusion and use of vasopressors and inotropes were recommended to achieve a mean arterial pressure of ≥80 mm Hg and a urine output of ≥0.5 mL kg^{-1} h^{-1}. Given its association with good outcomes, cardiac catheterization was performed immediately if the patient had anginal symptoms prior to the arrest or current evidence of an acute coronary syndrome.[17] Beginning in August 2009, our facility provided continuous electroencephalography monitoring for all comatose post-arrest patients given the risk of nonconvulsive status epilepticus.[18] Neuroprognostication in our facility includes categorization of initial illness severity, CT imaging of the brain, continuous electroencephalography, somatosensory evoked potentials, magnetic resonance imaging and serial examinations. The presence of fever is not considered an indication to limit or withdraw support.

2.4. Study design

We abstracted the following demographics: age, gender, location of arrest (OHCA or IHCA), initial rhythm, initial neurologic examination off sedation or paralysis using the Glasgow coma score (GCS) and full outline of unresponsiveness (FOUR) score,[19] initial sequential organ failure assessment (SOFA),[20] TH, survival to discharge, discharge disposition (home, acute rehabilitation facility, skilled nursing facility, long-term acute care facility, hospice or death), and hospital length of stay (LOS). Cerebral performance category (CPC) at discharge and modified Rankin score (mRS) at discharge were estimated from the medical record using standard instruments.

We defined four categories of illness severity using components of the FOUR score and SOFA: (I) awake, (II) coma (not following commands but intact brainstem responses) + mild cardiopulmonary dysfunction (SOFA cardiac + respiratory score <4), (III) coma + moderate-severe cardiopulmonary dysfunction (SOFA cardiac + respiratory score ≥4), and (IV) coma without brainstem reflexes.[21] Good outcome was defined as discharge disposition to home or acute rehabilitation facility.

We collected all available temperature data points in the medical record during the 48 h after cardiac arrest. The temperature data varied in method of measurement (axillary, rectal, esophageal, bladder) and frequency of measurement. Axillary temperatures were not used for analysis. Presence of fever was defined as any temperature data point ≥38 °C recorded within 48 h of the reported arrest time. We recorded the time of onset of fever in those patients that developed one. The peak temperature achieved (Tmax) within

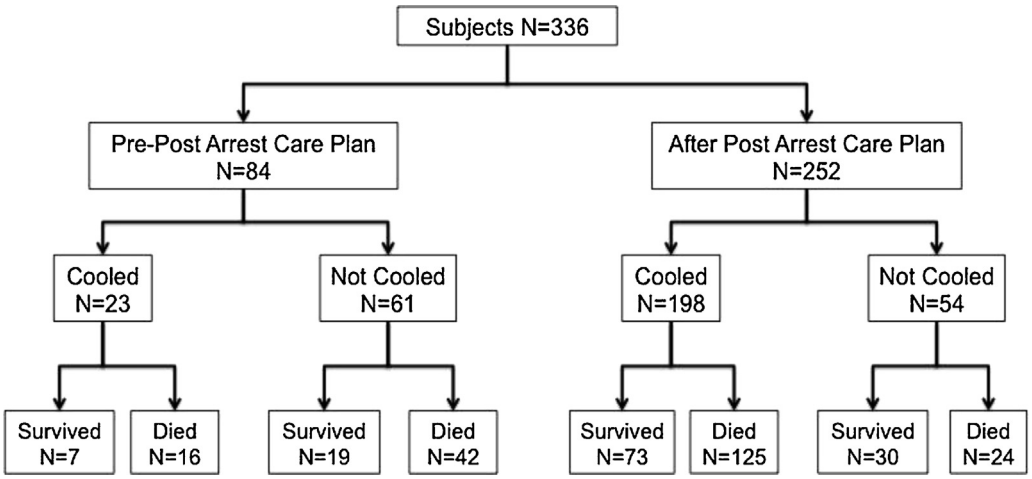

Fig. 2. Treatment with therapeutic hypothermia and survival by pre- and post-arrest care plan time epoch.

this 48-h time period was also recorded. We sought to quantify patients' total *fever burden* over this 48-h window by measuring the cumulative number of hours they maintained a temperature ≥38 °C. To help account for gaps in charted temperatures, we recorded both a *low estimated fever burden* and *high estimated fever burden*. Any single fever-range temperature recorded was assumed to represent an hour of fever burden unless another non-fever temperature was recorded within that hour. *Low estimated fever burden* included the time between consecutive fever-range temperatures and an assumed 1-h burden for a fever point followed by a non-fever point. *High estimated fever burden* included time from the initial fever to the next non-fever temperature recorded.

The statistical mean ± standard deviation (SD) was calculated for normally distributed demographic characteristics and the median and interquartile range (IQR) were reported for non-normally distributed variables. Percentages were reported for dichotomous variables. The study population was analyzed as the whole cohort and also stratified into a TH cohort and a non-TH cohort. The Wilcoxon rank sum test was used for comparisons of non-normally distributed data. Chi squared testing was used as appropriate. Univariable logistic regression analysis was performed for each cohort to determine variables associated with either good outcome or survival to hospital discharge. Candidate variables included age, gender, location of arrest, TH, primary rhythm of arrest, category of post arrest illness severity, presence of fever, low estimated fever burden, and high estimated fever burden. Fever burden was not normally distributed and was log-transformed for the regression analyses. Variables with $p < 0.1$ in the univariable analysis were included in the multivariable analysis. As the intention of the analysis was to determine the effect of fever and fever burden on survival to discharge and good neurologic outcome on discharge, these variables were forced into the models. This yielded 3 models: fever in first 48 h, low fever burden, and high fever burden. Interaction terms were explored as appropriate, but none were significant. Each regression model was assessed for goodness of fit with the Hosmer–Lemeshow test, and a reasonable fit was assumed if $p > 0.05$.[22] Regression results were reported using odds ratios (ORs) and the corresponding 95% confidence intervals (CI). Data were analyzed using STATA v. 11.0 (College Station, TX).

3. Results

A total of 336 patients were included in the analysis. Most were treated after development of a standardized post-cardiac arrest protocol (Fig. 2). Table 1 lists their demographic, cardiac arrest, and post-resuscitation characteristics. Overall, 141 patients (42%) developed fever within the 48 h after their arrest, and fever was less common in the TH cohort (79/221, 36%) than in the non-TH cohort (62/115, 54%) (Chi-square = 9.35; $p = 0.002$). The median low estimate of fever burden was 4 h (IQR 1, 11) and high estimate was 6 h (IQR 3, 14). Median time of fever onset for all subjects was 28 h after arrest (IQR 10, 39). Fever onset was significantly delayed in the TH cohort at 36 h (IQR 27, 41) compared to 15 h (IQR 8, 22) in the non-TH cohort ($p < 0.001$).

Subjects with fever, compared to subjects with no fever, were less likely to survive in the non-TH cohort (31% vs. 69%; $p = 0.003$). Subjects with fever, compared to subjects with no fever, demonstrated similar survival in the TH cohort (39% vs. 35%; $p = 0.483$) and in the whole cohort (35% vs. 41%; $p = 0.305$). Subjects in the TH cohort demonstrated a shorter fever duration than subjects in the non-TH cohort, using either the low or high estimated fever burden ($p < 0.001$).

In the multivariable analysis, an initial rhythm of ventricular fibrillation or ventricular tachycardia (VF/VT) was associated with survival to discharge within the whole cohort (OR 2.21, CI 1.02, 4.80). Category IV illness severity was negatively associated with survival in the whole cohort (OR 0.21, CI 0.08, 0.57) and TH cohort (OR 0.22, CI 0.09, 0.55) (Table 2). Fever during the first 48 h following resuscitation was not associated with survival.

Age was associated with good outcome in the whole cohort (OR 0.97, CI 0.95, 0.99) and in the non-TH cohort (OR 0.96, CI 0.93, 0.99). Male gender was associated with good outcome in the whole cohort (OR 1.96, CI 1.05, 3.64) and in the non-TH cohort (OR 3.91, CI 1.13, 13.58). An initial rhythm of VF/VT was associated with good outcome in the whole cohort (OR 3.51, CI 1.74, 7.10) and TH cohort (OR 2.47, CI 1.07, 5.73). Category IV illness severity was negatively associated with good outcome in the whole cohort (OR 0.21, CI 0.08, 0.52) and TH cohort (OR 0.28, CI 0.09, 0.87). A primary rhythm of PEA was negatively associated with good outcome in the TH cohort (OR 0.17, CI 0.03, 0.83) (Table 3). Presence of fever during the first 48 h following resuscitation was not associated with good outcome. The Hosmer–Lemeshow p-value was >0.05 for all models.

In the low fever burden multivariable analysis, only category IV initial illness severity was associated with survival in the TH cohort (OR 0.15, CI 0.03, 0.90). No variable was associated with survival in the high fever burden multivariable analysis (Supplementary Tables).

In the whole cohort analysis, age was associated with good neurologic outcome in both the low fever burden model (OR 0.94, CI 0.91, 0.97) and high fever burden model (OR 0.94, CI 0.91, 0.97). A primary rhythm of VF/VT was also associated with good neurologic outcome in the low fever burden model (OR 7.77, CI 2.24,

Table 1
Demographic, cardiac arrest, and post-resuscitation data of included patients.

	N = 336	Therapeutic hypothermia(*N* = 221)	No therapeutic hypothermia(*N* = 115)
Age, in years (SD)	60 (16)	58 (16)	64 (16)
Male	181 (54%)	121 (55%)	61 (53%)
OHCA	212 (63%)	172 (78%)	40 (35%)
Therapeutic hypothermia	221 (65%)	221 (100%)	–
Survival to discharge	129 (38%)	80 (36%)	49 (43%)
Good outcome	75 (22%)	48 (22%)	27 (23%)
48 h Tmax (SD)	37.8 °C (1.06 °C)	37.6 °C (1.02 °C)	38.2 °C (1.02 °C)
Fever in first 48 h	141 (42%)	79 (36%)	62 (54%)
Fever onset, hour after ROSC (IQR)	28 (10, 39)	36 (27, 41)	15 (8, 22)
Fever burden-low estimate, h (IQR)	4 (1, 11)	2 (1, 6)	11 (3, 18)
Fever burden-high estimate, h (IQR)	6 (3, 14)	4 (2, 7)	13 (6, 18)
Hospital LOS, days (IQR)	7 (4, 15)	6 (4, 12)	10 (6, 18)
Survivors (IQR)	14 (9, 21)	14 (9, 21)	14 (9, 21)
Died in hospital (IQR)	5 (3, 8)	4 (3, 6)	7 (3, 15)
GCS motor on arrival (IQR)	3 (1, 4)	2 (1, 4)	3 (1, 4)
Initial rhythm			
VF/VT	133 (40%)	94 (43%)	38 (34%)
PEA	96 (28%)	56 (25%)	39 (35%)
Asystole	63 (19%)	43 (19%)	20 (18%)
Unknown	44 (13%)	28 (13%)	16 (14%)
Initial illness severity category			
II	119 (38%)	90 (42%)	29 (30%)
III	62 (20%)	30 (13%)	32 (33%)
IV	133 (42%)	97 (45%)	36 (37%)
CPC on discharge			
1	14 (4%)	7 (3%)	7 (6%)
2	2 (1%)	1 (1%)	1 (1%)
3	98 (29%)	60 (27%)	38 (33%)
4	14 (4%)	11 (5%)	3 (3%)
5	208 (62%)	142 (64%)	64 (57%)
mRS on discharge			
0	7 (2%)	2 (1%)	5 (4%)
1	7 (2%)	5 (2%)	2 (2%)
2	2 (1%)	1 (0.5%)	1 (1%)
3	1 (1%)	1 (0.5%)	0 (0%)
4	90 (26%)	55 (35%)	35 (31%)
5	21 (6%)	15 (7%)	6 (5%)
6	208 (62%)	142 (54%)	64 (57%)

OHCA – out-of-hospital cardiac arrest; Tmax – maximum temperature; LOS – length of stay; GCS – Glasgow Coma Score; VF/VT – ventricular fibrillation/ventricular tachycardia; PEA – pulseless electrical activity; CPC – cerebral performance category; mRS – modified Rankin score.

27.0) and high fever burden model (OR 7.78, CI 2.23, 27.1). Both low and high fever burden were associated with good outcome in the TH cohort (low fever burden model: OR 10.1, CI 1.56, 65.6; high fever burden model: OR 13.3, CI 1.63, 108.3). No variables were associated with good neurologic outcome in the non-TH cohort. The Hosmer–Lemeshow *p*-value was >0.05 in all of these models. Time of fever onset was not different between subjects with good outcomes (31.6 h) and subjects without good outcomes (31.9 h; $p = 0.92$) (Supplementary Tables).

4. Discussion

Development of fever after cardiac arrest is a common occurrence (42%) but is less common in those treated with TH (36%) than in those not treated with TH (55%). Consistent with previous studies, fever is associated with lower survival in non-TH patients.[7,9–11] In our study, much of this non-TH cohort is from an earlier time period. As time progressed, staff education and system changes led to increased utilization of TH at our institution.[16] Our finding that,

Table 2a
Univariable regression for predictors of survival by cohort. Data presented as odds ratio and 95% confidence interval.

	Whole cohort	TH cohort	Non-TH cohort
Age	1.00 (0.99, 1.02)	1.00 (0.99, 1.03)	0.99 (0.96, 1.01)
Gender	1.15 (0.74, 1.79)	0.94 (0.54, 1.63)	1.68 (0.79, 3.55)
OHCA	1.09 (0.69, 1.72)	1.30 (0.67, 2.52)	1.36 (0.63, 2.94)
TH	0.74 (0.47, 1.18)	–	–
Rhythm			
VF/VT	3.02 (1.91, 4.78)	3.63 (2.04, 6.44)	2.35 (1.07, 5.17)
PEA	0.46 (0.27, 0.78)	0.38 (0.19, 0.78)	0.52 (0.23, 1.16)
Asystole	0.53 (0.29, 0.97)	0.48 (0.22, 1.03)	0.68 (0.25, 1.85)
Unknown	0.81 (0.41, 1.57)	0.68 (0.29, 1.63)	1.06 (0.36, 3.06)
Initial illness severity category			
II	4.05 (2.52, 6.51)	5.62 (3.10, 10.20)	2.90 (1.21, 6.92)
III	1.80 (1.03, 3.13)	1.23 (0.56, 2.69)	2.35 (1.03, 5.36)
IV	0.13 (0.07, 0.23)	0.12 (0.60, 0.24)	0.17 (0.06, 0.45)
Fever in 48 h	0.79 (0.51, 1.24)	1.21 (0.69, 2.14)	0.32 (0.15, 0.68)
Low estimated fever burden (log-transformed)	0.62 (0.30, 1.27)	1.38 (0.45, 4.20)	0.95 (0.89, 1.02)
High estimated fever burden (log-transformed)	0.60 (0.28, 1.29)	1.05 (0.46, 4.92)	0.95 (0.89, 1.02)

Table 2b
Multivariable regression for predictors of survival in the whole cohort. Data presented as odds ratio and 95% confidence interval.

	Odds ratio	95% CI
Fever in 48 h	0.95	0.57, 1.59
VF/VT	2.21	1.02, 4.80
PEA	0.81	0.35, 1.89
Asystole	1.04	0.42, 2.61
Category II	1.72	0.65, 4.53
Category III	1.21	0.44, 3.35
Category IV	0.21	0.08, 0.57

Hosmer–Lemeshow value 0.18.

Table 2c
Multivariable regression for predictors of survival in the TH cohort. Data presented as odds ratio and 95% CI.

	Odds ratio	95% CI
Fever in 48 h	1.38	0.70, 2.69
VF/VT	2.02	0.95, 4.26
PEA	0.56	0.22, 1.42
Category II	1.97	0.87, 4.46
Category IV	0.22	0.09, 0.55

Hosmer–Lemeshow value 0.92.

Table 2d
Multivariable regression for predictors of survival in the non-TH cohort. Data presented as odds ratio and 95% CI.

	Odds ratio	95% CI
Fever in 48 h	0.47	0.20, 1.10
VF/VT	2.28	0.95, 5.47
Category II	2.43	0.67, 8.87
Category III	2.01	0.57, 7.17
Category IV	0.40	0.10, 1.56

Hosmer–Lemeshow value 0.97.

Table 3b
Multivariable regression for predictors of good outcome in the whole cohort. Data presented as odds ratio and 95% confidence interval.

	Odds ratio	95% CI
Fever in 48 h	0.95	0.52, 1.75
Age	0.97	0.95, 0.99
Gender	1.96	1.05, 3.64
OHCA	1.93	0.93, 3.99
VF/VT	3.51	1.74, 7.10
Asystole	1.22	0.45, 3.29
Category II	1.47	0.71, 3.04
Category IV	0.21	0.08, 0.52

Hosmer–Lemeshow value 0.30.

Table 3c
Multivariable regression for predictors of good outcome in the TH cohort. Data presented as odds ratio and 95% confidence interval.

	Odds ratio	95% CI
Fever in 48 h	1.25	0.58, 2.68
VF/VT	2.47	1.07, 5.73
PEA	0.17	0.03, 0.83
Category II	1.65	0.65, 4.16
Category IV	0.28	0.09, 0.87

Hosmer–Lemeshow value 0.86.

Table 3d
Multivariable regression for predictors of good outcome in the non-TH cohort. Data presented as odds ratio and 95% confidence interval.

	Odds ratio	95% CI
Fever in 48 h	0.34	0.11, 1.06
Age	0.96	0.93, 0.99
Gender	3.91	1.13, 13.58
OHCA	3.06	0.90, 10.41
VF/VT	1.55	0.52, 4.63
Category II	1.85	0.57, 6.04
Category IV	0.25	0.05, 1.25

Hosmer–Lemeshow value 0.17.

within the TH cohort, neither functional outcome nor survival is associated with development of a fever is novel.

In the TH population, fever remains common (36%), however it does not appear to carry the same detrimental consequences as it does in those not receiving TH. These data differ from others[7,9–11] and may be due to several factors. First, time of fever onset in the TH cohort (36 h, IQR 27, 41) was delayed compared to the non-TH cohort (15 h, IQR 8, 22). It is likely the earlier after an insult that hyperthermia occurs, the greater its consequences. Preclinical studies demonstrate hyperthermia 24 h after arrest, but not at 48 h, will worsen brain injury.[6,23] These data suggest a time dependence of neuronal vulnerability to hyperthermia. The total fever burden was also higher in the non-TH cohort. This is a possible reason for the worsened outcome seen in the febrile non-TH cohort. The positive association between fever burden and good neurologic outcome in the TH cohort bears additional discussion. While an early fever is associated with poor outcome, the ability to thermoregulate and generate a fever may indicate a neurologically intact subject. We have previously demonstrated that initial core temperature was lower in subjects with more severe illness severity.[21] Recent data have demonstrated a positive correlation between heat generation during TH and survival.[24]

Second, our study included substantially more IHCA patients (37%) than other studies. These patients typically have greater

Table 3a
Univariable regression for predictors of good outcome by cohort. Data presented as odds ratio and 95% confidence interval.

	Whole cohort	TH cohort	Non-TH cohort
Age	0.98 (0.96, 0.99)	0.98 (0.96, 1.00)	0.96 (0.93, 0.99)
Gender	1.92 (1.12, 3.30)	1.35 (0.70, 2.58)	4.01 (1.48, 10.89)
OHCA	2.37 (1.31, 4.29)	3.07 (1.14, 8.21)	3.15 (1.29, 7.67)
TH	0.88 (0.52, 1.51)	–	–
Rhythm			
VF/VT	4.64 (2.67, 8.05)	5.89 (2.86, 12.17)	3.33 (1.37, 8.14)
PEA	0.23 (0.11, 0.51)	0.09 (0.02, 0.40)	0.45 (0.17, 1.23)
Asystole	0.45 (0.20, 0.99)	0.53 (0.21, 1.35)	0.31 (0.07, 1.44)
Unknown	0.75 (0.33, 1.68)	0.57 (0.19, 1.74)	1.10 (0.32, 3.75)
Initial illness severity category			
II	3.52 (2.07, 5.99)	4.03 (2.05, 7.94)	3.34 (1.32, 8.43)
III	1.27 (0.67, 2.40)	1.39 (0.58, 3.36)	1.06 (0.41, 2.74)
IV	0.17 (0.08, 0.35)	0.16 (0.07, 0.38)	0.21 (0.06, 0.75)
Fever in 48 h	0.83 (0.49, 1.40)	1.09 (0.56, 2.12)	0.48 (0.20, 1.14)
Low estimated fever burden	1.07 (0.46, 2.49)	3.52 (0.95, 13.1)	0.94 (0.85, 1.03)
High estimated fever burden	1.24 (0.50, 3.10)	5.41 (1.17, 25.0)	0.92 (0.84, 1.01)

organ system dysfunction and have been reported to be more likely than OHCA patients to die from multisystem organ failure than anoxic encephalopathy.[25] Thus, it is possible that baseline comorbidities are more predictive of a poor outcome than fever. This possibility is supported by prior work in this population.[21] Alternatively, fever may be a representation of severe organ failure (i.e. sepsis). Finally, many of the patients in this study were admitted after implementation of a hospital-wide care plan[16] for post-cardiac arrest patients. Thus, it is possible that in the setting of aggressive post-arrest care with TH, fever following resuscitation may be less deleterious. The emphasis on protocol-driven and goal-directed care creates a distinctive setting compared to that evaluated by previous studies.

Our findings associating Category IV illness severity with lower survival rates and worse outcomes are similar to prior work.[21] Initial VF/VT rhythm has also been previously shown to be associated with improved survival and better outcomes. Similarly, a primary rhythm of PEA has been associated with poor outcomes in prior work. Interestingly, male gender was associated with improved outcomes in the whole cohort and non-TH cohort. This may be due to historically differential treatment delivered.[17] This association was not seen in the TH cohort, suggesting that the implementation of a regimented post-arrest care plan may help ensure equal treatment to all post-arrest patients.

There are several limitations of this study. First, temperature data are clinical and recorded at various intervals. Variation in temperature within interval gaps may influence outcome and cannot be accounted for in this study. Second, this data set is limited to the first 48 h of temperature data. Prior work evaluated temperature for a total of 24 h following rewarming.[26] However, the rate of fever in our cohort is similar. Our finding of earlier fever and increased fever burden in subjects not treated with TH may represent an additional benefit of regimented post-cardiac arrest care. While the site of temperature measurement was not standardized, the majority of patients treated with TH received esophageal monitoring. Data were obtained before and after implementation of a comprehensive care plan, including TH. Thus, we lack the rigor of a controlled trial. Additionally, some patients were transferred to our facility from outside hospitals. These patients lacked initial post-arrest temperature measurements in the medical record. We believe that post-arrest hyperthermia shortly after ROSC is unlikely, but remains possible.

5. Conclusions

The development of fever within the first 48 h after ROSC from cardiac arrest is common in both TH and non-TH patients. Previous studies and our observations support the association between development of fever and death in non-TH patients. However, treatment with TH appears to mitigate this effect, perhaps by delaying fever onset.

Conflict of interest statement

The authors have no conflicts of interest to report.

Appendix A.

The Post Cardiac Arrest Service researchers are:
Jon C. Rittenberger, MD, MS
Clifton W. Callaway, MD, PhD
Francis X. Guyette, MD, MPH
Ankur A. Doshi, MD
Cameron Dezfulian, MD
Josh C. Reynolds, MD
Adam Frisch, MD

Appendix B. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.resuscitation.2013.03.038.

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