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Effects of variation in temperature management on cerebral performance category scores in patients who received therapeutic hypothermia post cardiac arrest☆

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ABSTRACT

Aim: To assess differences in cerebral performance category (CPC) in patients who received therapeutic hypothermia post cardiac arrest by time to initiation, time to target temperature, and duration of therapeutic hypothermia (TH).
Methods: A secondary data analysis was conducted using hospital-specific data from the international cardiac arrest registry (INTCAR) database. The analytic sample included 172 adult patients who experienced an out-of-hospital cardiac arrest and were treated in one Midwestern hospital. Measures included time from arrest to ROSC, arrest to TH, arrest to target temperature, and length of time target temperature was maintained. CPC was assessed at three points: transfer from ICU, discharge from hospital, and post discharge follow-up.
Results: Average age was 63.6 years and 74.4% of subjects were male. Subjects had TH initiation a mean of 94.4 min (*SD* 81.6) after cardiac arrest and reached target temperature after 309.0 min (*SD* 151.0). In adjusted models, the odds of a poor neurological outcome increased with each 5 min delay in initiating TH at transfer from ICU (OR = 1.06, 95% C.I. 1.02–1.10). Similar results were seen for neurological outcomes at hospital discharge (OR = 1.06, 95% C.I. 1.02–1.11) and post-discharge follow-up (OR = 1.08, 95% C.I. 1.03–1.13). Additionally the odds of a poor neurological outcome increased for every 30 min delay in time to target temperature at post-discharge follow-up (OR = 1.17, 95% C.I. 1.01–1.36).
Conclusion: In adults undergoing TH post cardiac arrest, delay in initiation of TH and reaching target temperature differentiated poor versus good neurologic outcomes. Randomized trials assessing the range of current recommended guidelines for TH should be conducted to establish optimal treatment protocols.

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1. Introduction

Every year in the United States, there are 295,000 out-of-hospital cardiac arrests (OHCA) and an estimated 200,000 in-hospital cardiac arrests.[1–3] Mortality rates for out-of-hospital cardiac arrest are dismal with estimates of survival between 2% and 13%[4–8] and between 17% and 18% for in-hospital cardiac arrest[9,10] with neurological injury being an important cause of mortality and morbidity post cardiac arrest.[11] With the advent of therapeutic hypothermia, post cardiac arrest survival rates with good neurological recovery have ranged from 44% to 55%.[11–13] Among those discharged from the hospital, 6–12-month survival rates were 91% with good neurological recovery.[12] In a systematic review of randomized controlled trials, it was demonstrated that the numbers needed to treat were 7 patients to save 1 life, and 5 patients to improve neurologic outcome.[14] TH has now become a standard of care for patients experiencing a cardiac arrest.[14]

Both the International Liaison committee of Resuscitation (ILCOR)[15] and the American Heart Association[16] (Class I, Level of Evidence B) have recommended TH post cardiac arrest in their guidelines on resuscitation. However, the science is still evolving regarding best practices in temperature management.[17] TH researchers have noted the need for more studies on specific components of temperature management including: time to cooling and rewarming,[18–21] optimal target temperature,[18] duration of cooling,[12,18,21,22] optimal methodology for cooling patients[21]

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and core temperature measurement site.[23] This knowledge gap is demonstrated by the variability of current practice in target temperature (32–34 °C) and duration of TH (12–48 h).

Neurological function post cardiac arrest is frequently measured by the cerebral performance category (CPC) scores (see Appendix A). Originally created as an assessment after severe brain damage[24] it was adapted by the Brain Resuscitation Clinical Trial Study Group to measure cerebral performance capabilities.[25] Collecting CPC scores is also a part of the recommended uniform reporting for out-of-hospital arrests established by the Utstein Consensus Conference.[26] CPC scores range from 1 to 5 with CPC 1 as the best possible outcome to CPC 5 as the worst outcome, death. Most studies collapse CPC 1[27] and CPC 2[27] when comparing neurological outcomes in patients undergoing TH post cardiac arrest to normothermic patients post cardiac arrest.[11,13] However, the differentiation between CPC 1 and CPC 2 is significant when planning for patient discharge. Patients with a CPC score of 2 includes those who may work in a sheltered environment, whereas patients with a CPC score of 1 are able to return to work without supervision. CPC scores only indicate gross functional status and do not discriminate well at the high end of neurological function.[28]

The initiation of therapeutic hypothermia (TH) post-cardiac arrest has dramatically improved survival rates of patients after cardiac arrest. Among survivors, however, anoxic neurologic injury remains an important cause of subsequent mortality and morbidity. The aim of this study was to identify salient predictors of neurological outcomes in patients who received therapeutic hypothermia post cardiac arrest. In contrast to most published studies examining neurological function, we did not collapse CPC scores 1 and 2 into one category. Neurological function was defined as good (CPC 1); moderate (CPC 2); or poor (CPC 3–5). Our primary interest was to determine if there were differential rates of neurologic outcomes by time to initiation and duration of TH and time to ROSC.

2. Methods

2.1. Study population and setting

A secondary data analysis was conducted using Minneapolis Heart Institute data entered into and uploaded from the International Cardiac Arrest Registry (INTCAR) database (http://www.hypothermianetwork.com/INTCAR.htm). INTCAR is a secure, web-based registry of cardiac arrest survivors employing standardized data definitions, and used by over 80 sites worldwide to evaluate all aspects of post-resuscitation care.[29]

From February 2006 to July 2010, 172 OHCA patients were treated with mild therapeutic hypothermia (32 °C) at one urban tertiary care hospital. The study population includes all patients who met the TH criteria in the specified period of time: (1) non-traumatic cardiac arrest; (2) ROSC within 60 min of collapse; (3) unconscious (does not follow commands); (4) an out-of-hospital cardiac arrest. Exclusion criteria were: (1) persistent hypotension despite administration of vasopressors (i.e., unable to maintain adequate BP with the use of two or more vasopressor); (2) active bleeding; (3) DNR/DNI code status; and/or (4) chronic comatose or vegetative state prior to arrest (by asking the family, healthcare personnel, and/or from healthcare record).

Abbott Northwestern Hospital (ANW) is a tertiary care hospital located in Minneapolis that developed a standardized protocol for cardiac arrest that includes timely initiation of TH and implemented of the program in 2006.[30] ANW collaborates with a network of 33 hospitals within a 210-mile radius to provide training, education, protocols and tool kits to participating hospitals, emergency medical services (EMS) agencies, and emergency transport providers to provide state-of-the-art cardiac services.[30] Program details have been published previously.[30] Since the program's inception, over 270 patients have undergone TH post cardiac arrest.

The study protocol was approved by the Allina Hospitals & Clinics Institutional Review Board.

2.2. Data collection

We conducted a retrospective, non-experimental observational study to identify key predictors of neurological outcome in patients who received therapeutic hypothermia post cardiac arrest. All data were originally documented in EMS and healthcare records in the course of standard clinical care. Clinical documentation for TH patients was done using standardized INTCAR definitions for patient characteristics, care processes, and outcomes. Pre-arrest CPC scores were assigned according to history given by healthcare personnel, relatives, witnesses or previous medical records. All data were abstracted locally by a Certified Clinical Nurse Research Coordinator (http://www.acrpnet.org/) with expertise in emergency and critical care nursing and 10 years of research experience in cardiology. Abstracted data were entered into a password protected on-line INTCAR database. Quality controls included, (1) standardized education and protocol training for the network of 33-referral hospital emergency healthcare personnel and at the helicopter and ground bases of 45 independent EMS providers,[30] and (2) adjudication of every tenth chart by a physician with expertise in the care of patients receiving TH post cardiac arrest.

2.3. Measures

Our primary outcome of interest was neurological function, measured by the 5-category CPC score. CPC categories were collapsed into a trichotomous variable distinguishing good (CPC = 1), moderate (CPC = 2), and poor (CPC $\geq$ 3) outcomes. The outcome was examined at transfer from ICU, at hospital discharge, and at least 1 month post-discharge follow-up (telephone call or abstracted from the chart from the clinic visit). If a patient died while in the ICU (CPC = 5), a '5' was also assigned for the CPC score at hospital discharge and at follow-up.

The predictors of interest were a set of temperature management variables related to the application of TH. Time to initiation of TH was evaluated using estimated minutes from arrest to initiation of TH and minutes to target temperature (Appendix B). If the arrest was unwitnessed, the time from the emergency call to initiation of TH was documented. The initiation of TH was defined as the time point when the first attempt to reduce body temperature was made (pre-hospital or in-hospital). Duration of TH was defined from the target temperature until the onset of rewarming ($T > 34$ °C). For analysis, number of minutes to TH initiation was aggregated to reflect 5 min increments in delay of starting treatment. Time to target temperature was aggregated to reflect 30 min increments in time from arrest to reaching target temperature. These intervals were chosen to increase both interpretability and clinical application of the findings.

Additional potential confounding factors that were available for examination included: gender, age, pre-arrest health conditions, time to ROSC, initial rhythm, length of stay in ICU, and length of hospital stay. If the patient did not have days recorded for length of stay in the hospital (i.e. patient deceased in ICU), the number of days of ICU stay was used for the missing hospital day values (Table 1).

2.4. Statistical analysis

Summary characteristics, including frequency and percentage for categorical variables and, mean, standard deviation, interquartile range values for continuous variables, were calculated for the

Table 1
Spearman correlation of covariates and outcome of interest.

	CPC ICU	CPC hospital	CPC follow-up
Arrest to target temperature	0.12	0.17*	0.17
Arrest to hypothermia treatment	0.23*	0.22*	0.22*
Target temperature maintained	−0.06	−0.11	−0.09
Age (years)	0.31*	0.31*	0.34*
Gender	−0.04	−0.08	−0.11
Current smoking	−0.16	−0.17*	−0.14
Rhythm at arrival	0.09	0.07	0.01
Days from arrest to hospital discharge	−0.52*	−0.63*	−0.66*

* Significant correlation $p < 0.05$.

variables of interest. Cross tabulations were used to describe the movement across CPC categories from ICU to hospital discharge and to follow-up appointment. Given the ordered nature of CPC scores, ordinal logistic regression was first assessed. One assumption that must be met for ordinal logistic regression is that the regression between levels must be parallel. The Brant test[31] was used to test this assumption; however, the regression lines between levels were not parallel. Therefore, multinomial logistic regression was required. Multinomial logistic regression models were used to estimate the odds of having a poor compared to good neurological outcome at three time points. The three category dependent variable, with a good outcome being the referent category, was used for both unadjusted and adjusted models. We tested goodness of fit using a LR chi-square test of the nested unadjusted and adjusted models. For each model, the use of the fully adjusted model compared to the unadjusted model resulted in a statistically significant improvement of model fit at $p < 0.001$. The association between delay in initiating therapeutic hypothermia and pre-arrest health status, obesity, pre-arrest hypertension, COPD, coronary disease or Type II diabetes and smoking status was analyzed. Only smoking status was associated with delays and thus was added as a covariate in adjusted models. Final models were adjusted for gender, age, current smoking status, initial rhythm, and days of stay in the ICU or in the hospital. Time to ROSC was assessed for impact on the outcomes in the final model. All analyses were conducted using Stata statistical software (SE version 11.1).[32]

Table 2
Characteristics of patients receiving therapeutic hypothermia post cardiac arrest, February 2006 to July 2010.

Variable	*N*	Mean	Std. Dev.	Percentile	
				25th	75th
Patient characteristics					
Age (years)	172	63.6	±13.4	54.5	74
Male	128	74.4%			
Rhythm at arrival					
VT/VF	125	72.7%			
PEA	22	12.8%			
Asystole	19	11.1%			
Unknown	6	3.5%			

Time intervals	*N*	Mean	STD		
Arrest to ROSC (min)	172	23.9	14.6	12.5	32.5
Arrest to hypothermia treatment (min)	172	94.4	81.6	45	112.5
Arrest to target temperature (min)	172	309.0	151.0	205	375
Target temperature maintained (h)	172	23.1	5.4	24	24.5
Days from arrest to hospital discharge[a]	172	9.9	9.0	3	13
Length of stay in ICU (days)	172	7.1	7.3	3	9
Length of post-ICU hospital stay (days)[b]	95	5.0	3.6	3	6
Follow-up contact (months)[c]	88	7.5	5.3	0	11

Neurological outcomes	*N*	%
CPC at ICU transfer		
Good (1)	49	28.5
Moderate (2)	23	13.4
Poor (3–5)	100	58.1
CPC at hospital discharge		
Good (1)	62	36.0
Moderate (2)	18	10.5
Poor (3–5)	92	53.5
CPC at post-discharge follow-up		
Good (1)	73	42.4
Moderate (2)	9	5.2
Poor (3–5)	89	51.7
No F/U data available	1	0.6

[a] Includes patients who did not have a post-ICU hospital stay due to death ($n = 77$).
[b] 77 deaths occurred in the ICU.
[c] 84 total deaths occurred prior to hospital discharge.

3. Results

3.1. Subject characteristics

Data were available for 193 patients who received TH post cardiac arrest. Of those, 21 were excluded as their arrest occurred in-hospital, resulting in an analytic sample of 172 patients. Table 2 shows the characteristics of the sample. The mean age was 63.6 years and the majority of patients were male (74.4%). Mean time from arrest to ROSC was 23.9 min. The mean time interval from arrest to the initiation of therapeutic hypothermia treatment was 94.4 min, while the mean time interval from arrest to target temperature was over 5 h. The target temperature (33 °C) was maintained for 23.1 h, on average.

Length of stay in the ICU, on average, was 7 days, but ranged from 0 days to 2 months. Three stays appeared to be outliers, with stays over 35 days. Sensitivity analysis was conducted with and without these individuals with no substantive changes noted so the full sample was used. Seventy-seven patients died in the ICU. At transfer from the ICU, 28.5% of the patients were in the CPC 1 (good category), 13.4% were in the CPC 2 (moderate category), and 58.1% were in CPC 3–5 (poor or deceased category). The average number of days until discharge from the hospital was 5 days, excluding days in ICU. By discharge from the hospital, 36% had CPC scores classified as good, 10.5% were moderate and 53.5% were poor or deceased. By the follow-up appointment, 42.4% were CPC 1, 5.2% were CPC 2 and 51.7% were CPC 3 or greater.

CPC scores changed from ICU, to hospital discharge, and to post-discharge follow-up. Ten patients who were categorized as CPC 2 at ICU discharge improved to CPC 1 by hospital discharge. Of those who were categorized as CPC 3 at ICU discharge, five patients improved to CPC 2 and three patients improved to CPC 1. By follow-up an additional 11 patients improved to CPC 1 and one patient died, so was classified in the CPC 3 or greater category.

Results from the multinomial logistic regression models are shown in Tables 3–5. Table 3 presents the estimates of the odds of a less than good neurological outcome at transfer from the ICU. Only one temperature management variable was significantly associated with poor versus good outcomes among patients at time of ICU discharge. For every 5 min delay in initiating therapeutic hypothermia, there was a 6% greater odds of the patient having a poor versus good outcome (OR = 1.06, 95% C.I. 1.02–1.10) after adjusting for age, gender, initial cardiac rhythm, and length of ICU stay. No difference was detected in the odds of a moderate outcome compared with good outcome by time to initiation of TH, time to target temperature, or duration target temperature was maintained. When adding the time from arrest to ROSC into the model, the odds decreased by one percent. For example, the OR changed from 1.06 to 1.05 for every 5 min delay in the initiation of TH treatment and there was no change in statistical significance.

Table 3
Multinomial logistic regression estimates of the odds of neurological outcome (CPC score) at ICU transfer in cardiac arrest patients post therapeutic hypothermia.

	Unadjusted				Adjusted[a]			
	OR	SE	95% CI		OR	SE	95% CI	
Time from arrest to TH (5 min increments)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.02	0.02	0.98	1.06	1.03	0.02	0.99	1.08
CPC 3–5: Poor	1.03	0.14	1.01	1.06	1.06	0.02	1.02	1.10
Time to target temperature (30 min increments)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.00	0.05	0.90	1.11	1.00	0.06	0.88	1.14
CPC 3–5: Poor	1.03	0.04	0.96	1.11	1.09	0.06	0.99	1.21
Duration target temperature maintained (h)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.15	0.11	0.94	1.39	1.12	0.12	0.91	1.37
CPC 3–5: Poor	0.96	0.04	0.89	1.03	0.97	0.04	0.89	1.06

[a] Adjusted for age, gender, initial rhythm, current smoking status, ICU length of stay.

Table 4
Multinomial logistic regression estimates of the odds of neurological outcome (CPC score) at hospital discharge in cardiac arrest patients post therapeutic hypothermia.

	Unadjusted				Adjusted[a]			
	OR	SE	95% CI		OR	SE	95% CI	
Time from arrest to TH (5 min increments)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.02	0.02	0.99	1.06	1.04	0.02	0.99	1.08
CPC 3–5: Poor	1.03	0.13	1.01	1.06	1.06	0.02	1.02	1.11
Time to target temperature (30 min increments)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.05	0.06	0.95	1.16	1.06	0.07	0.92	1.21
CPC 3–5: Poor	1.04	0.04	0.97	1.12	1.11	0.07	0.97	1.27
Duration target temperature maintained (h)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.08	0.1	0.89	1.30	1.07	0.12	0.86	1.32
CPC 3–5: Poor	0.93	0.04	0.87	1.01	0.98	0.07	0.89	1.15

[a] Adjusted for age, gender, initial rhythm, current smoking status, hospital length of stay.

Table 4 presents estimates of the odds of a less than good neurological outcome at discharge from the hospital. For, for every 5 min delay in initiating TH treatment, there was a 6% greater odds of poor versus good outcome after adjusting for age, gender, initial rhythm and hospital length of stay (OR = 1.06, 95% C.I. 1.02–1.11).

Table 5 presents estimates of the odds of a less than good neurological outcome at post-discharge follow-up. In adjusted models, for every 5 min delay in initiating hypothermia treatment, there was an 8% greater odds of a poor compared to a good outcome and 5% greater odds of moderate compared to good outcome. For every 30 min delay in reaching target temperature, there was a 17% greater odds of poor versus good outcome (OR = 1.17, 95% C.I. 1.01–1.36) at post-discharge follow-up.

4. Discussion

Our primary interest was whether neurologic outcomes differed significantly by time to initiation of TH, time to reach

Table 5
Multinomial logistic regression estimates of the odds of neurological outcome (CPC score) at post-discharge follow-up in cardiac arrest patients post therapeutic hypothermia.

	Unadjusted				Adjusted[a]			
	OR	SE	95% CI		OR	SE	95% CI	
Time from arrest to TH (5 min increments)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.03	0.02	0.99	1.07	1.05	0.03	1.00	1.10
CPC 3–5: Poor	1.04	0.01	1.01	1.06	1.08	0.02	1.03	1.13
Time to target temperature (30 min increments)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	0.99	0.08	0.85	1.15	1.01	0.10	0.84	1.22
CPC 3–5: Poor	1.04	0.03	0.98	1.11	1.17	0.09	1.01	1.36
Duration target temperature maintained (h)								
CPC 1: Good	1.00				1.00			
CPC 2: Moderate	1.13	0.2	0.94	1.75	1.34	0.29	0.88	2.04
CPC 3–5: Poor	0.92	0.04	0.85	0.99	0.98	0.07	0.85	1.13

[a] Adjusted for age, gender, initial rhythm, current smoking status, hospital length of stay.

target temperature, and duration of target temperature. This study demonstrated that delay in initiation of TH and 30 min delay in reaching target temperature, were consistently associated with a CPC 3–5 (poor or deceased) versus CPC 1 (good) neurological outcome. Although recommendations for rapid initiation of TH in an effort to mitigate poor neurological outcomes appear in the literature, there are limited animal,[33,34] and human studies that support earlier initiation of hypothermic target temperature associated with improved neurological outcome.[35] Previous studies found that neurologically intact survival to discharge was significantly higher in patients cooled intra-arrest in whom CPR was initiated within 10 min of collapse.[35]

In contrast, other studies found no association between neurologic outcomes and earlier cooling.[12,19,36,37] Bernard et al. recognized differences in patient temperature between treatment and control groups were modest (0.8 °C), of relatively short duration, and surmised that the brief difference in core temperature was insufficient to have a measurable difference on patient outcomes.[19] Nielsen et al.[12] measured time from cardiac arrest to initiation of TH as opposed to Vanston et al.[36] who used time from ROSC to initiation of TH. However, neither found any association between time intervals and neurologic outcomes. A recent systematic review recommended that very early cooling needed to be further investigated.[21]

Once cooling was initiated our data demonstrated that a 30-min delay in reaching goal temperature was associated with worse outcomes. Similarly, Wolff et al.,[37] revealed less time to coldest temperature (goal temperature 33 °C) was an independent predictor of good neurological outcome and questioned if more aggressive cooling strategies should be advocated. In sharp contrast, Vanston et al.[36] demonstrated the longer it took to reach the goal temperature, the better the neurological outcome and suggested that it may have been a result of a more preserved hypothalamic thermoregulatory function in those patients. Nielson et al.[12] examined time to goal temperature and found no associations. Further research needs to examine temperature variables including time to goal temperature.

In our study, average duration of therapeutic hypothermia was 23 h, which deviates from the standard protocol of 24 h of TH post cardiac arrest. This was explained by the fact that some patients either died within the first 24 h of initiating TH or family made the decision to withdraw therapy. However, once TH was initiated, these patients were included in the TH registry and in our analysis.

Standard clinical parameters used to assess neurological function, such as the motor score, pupillary reflex or corneal reflex have been unreliable in predicting poor outcomes in patients treated with TH post cardiac arrest.[38] Our data demonstrate favorable neurologic function following discharge from the hospital and suggest a need for further research to more accurately predict long-term outcomes. This is consistent with Holzer et al. who found inducing mild TH in patients could improve favorable neurologic outcome up to 6 months after the event.[39]

4.1. Strengths and limitations

The study findings should be considered in light of limitations. This was a retrospective observational study rather than an experimental design. Therefore, it is not possible to infer that specific values of the temperature management variables related to therapeutic hypothermia were the cause of differences in patient CPC scores. It is possible that those with greater delays in time to initiation of TH or time to target temperature were systematically different than those with shorter time intervals in ways that could influence neurological outcome. Second, there is likely some imprecision in the estimated time to initiation of TH. In many cases, initiation of therapeutic hypothermia occurred in the prehospital setting (e.g. ice packs). However, paramedics in the field sometimes did not document initiation of treatment until they arrived at the hospital. Third, although depth of target temperature was a variable of interest, all patients were documented as having the same target temperature of 33 °C. Future study would benefit from additional data on repeated measures of core temperature over the duration of TH treatment to assess the depth and actual duration of TH temperature. Fourth, the sample is largely comprised of men, so generalization of the same association for women should be cautioned. Finally, although every 10 chart was adjudicated we do not have data to assess interrater reliability for the measuring of the CPC scores and there may have been different interpretations.

5. Conclusion

Our analysis demonstrated that both delay in initiation of TH and delay in reaching target temperature significantly increased the odds of a poor (CPC 3–5) compared to good (CPC 1) neurological outcome. Future prospective, randomized trials that explicitly examine the range of time to initiation, time to target temperature, depth of temperature, and duration of target temperature should be conducted to establish optimal management of all temperature variables and treatment protocols.

Disclaimer

None.

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None.

Appendix A.

CPC scores and definitions.[a]

CPC	Category	Definition
1	Good cerebral performance	Conscious, alert, able to work, might have mild neurologic or psychologic deficit
2	Moderate cerebral disability	Conscious, sufficient cerebral function for independent activities of daily life. Able to work in sheltered environment.
3	Severe cerebral disability	Conscious, dependent on others for daily support because of impaired brain function. Ranges from ambulatory state to severe dementia or paralysis.
4	Coma or vegetative state	Any degree of coma without the presence of all brain death criteria. Unawareness, even if appears awake (vegetative state) without interaction with environment; may have spontaneous eye opening and sleep-awake cycles. Cerebral unresponsiveness.
5	Brain death	Apnea, areflexia, EEG silence, etc.

[a] Safar P. 1981. Resuscitation after brain ischemia. Brain Failure and Resuscitation.[40]

Appendix B. INTCAR definitions

Variable	Definition[a]
Arrest to ROSC (in min)	The time from collapse to either the return of palpable pulses or a systolic blood pressure of >60 mm Hg without ongoing chest compressions. If unwitnessed, then the time from first EMS contact to ROSC.
Arrest to hypothermia treatment (min)	Best estimation. If unwitnessed arrest specify time from emergency call to The time from collapse or (If unwitnessed) first EMS contact to the initiation of treatment. Initiation of treatment is the first attempt to lower body temperature, irrespective of location.
Arrest to target temperature (min)	The time from collapse or (If unwitnessed) first EMS contact to body temperature of <34 °C.
Target temperature maintained (h)	The duration of time in which the patient's core body temperature was maintained between 32 and 34 °C

[a] All definitions are from the INTCAR database (http://www.hypothermianetwork.com/INTCAR.htm)

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