Effectiveness of each target body temperature during therapeutic hypothermia after cardiac arrest

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Introduction

- 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care: unconscious adult patients with ROSC after out-of-hospital cardiac arrest should be cooled to 32°C to 34°C for 12 to 24 hours
- Which target temperature is more efficacious?

METHODS

Study population

- A 1300-bed urban tertiary hospital with an annual ICU census of 900
- A standardized prospective study of patients with ROSC (>24 hours) after an out-of-hospital cardiac arrest and received therapeutic hypothermia between March 2007 and December 2008

Exclusion criteria

- Age<18 years, pregnant, SBP<90 mm Hg under inotropic agents, severe metabolic acidemic pH<7.1, preexisting coagulopathy, informed consent did not obtained.

Therapeutic hypothermia

- After admission to the ICU, hypothermia initiated and maintained for 24 hours, using endovascular cooling system or a surface cooling system ice pack with neuromuscular blocking and sedative agents to prevent shivering.
- After 24 hours, rewarming was started (approximately 0.3°C/h)
- Core temperature was monitored by rectal probe

Clinical evaluation and outcomes

- Mortality and neurologic outcomes(cerebral performance category [CPC])
- Early complications developed during therapeutic hypothermia (inducing, maintaining, and rewarming), and late complications developed after therapeutic hypothermia.

Statistical analysis

- The data were analyzed using SPSS software, version 11.5 (SPSS, Inc, Chicago, Ill).
- Statistical significance was defined as a P value less than 0.05.

RESULTS

Basal characteristics of patients

Table 1 Characteristics of patients (n = 62)

Factors	Clinical characteristics
Sex (male/female)	44 (70.97):18 (29.03)
Age (y)	54.61 ± 15.767
Arrest-CPR time (min)	13.92 ± 9.099
Arrest-ROSC time (min)	34.32 ± 16.441
Initial rhythm	
Ventricular fibrillation	24 (38.7)
Pulseless electrical activity	11 (17.7)
Asystole	27 (43.6)
Cause of arrest	
Cardiac	29 (46.8)
Noncardiac	23 (37.1)
Unknown	10 (16.1)
Epinephrine (mg)	5.6 ± 0.602
Arrest-TH start time (min)	256.90 ± 188.251
TH start-TH reach time (min)	254.07 ± 153.873
Arrest-TH reach time (min)	512.03 ± 258.736
ROSC-TH reach time (min)	477.22 ± 259.046
Rewarming time (min)	703.07 ± 262.538

Basal characteristics of patients

Table 1 Characteristics of patients (n = 62)

Factors	Clinical characteristics
Outcome	
Survivors	38 (61.39)
Nonsurvivors	24 (38.7)
Neurologic outcome	
Good (CPC 1, 2)	14 (22.6)
Poor (CPC 3-5)	48 (77.4)

Outcomes

Table 2 Characteristics by outcome (n = 62)

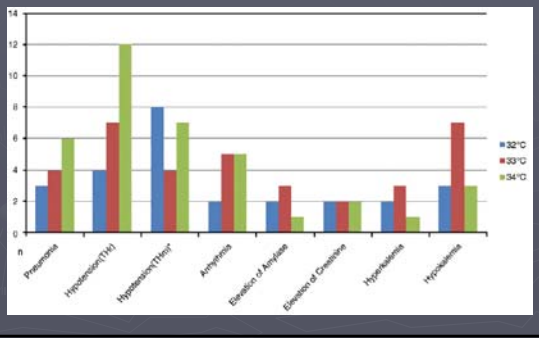
Factors	Survivors (n = 38)	Nonsurvivors (n = 24)	*P*	Good (CPC 1, 2) (n = 14)	Poor (CPC 3-5) (n = 48)	*P*
Sex (male/female)	26:12	18:6	.578	13:1	31:17	.040*
Age (y)	52.89 ± 2.851	57.33 ± 2.499	.284	46 ± 3.529	57.13 ± 2.263	.019*
Arrest-CPR time (min)	12.68 ± 1.425	15.88 ± 1.425	.183	11.43 ± 2.067	14.65 ± 1.358	.206
Arrest-ROSC time (min)	31.89 ± 2.860	38.17 ± 3.209	.075	34.93 ± 4.860	34.15 ± 2.442	.846
Initial rhythm						
Ventricular fibrillation	16	8		10	14	
PEA	6	5	.759	0	11	.010*
Asystole	16	11		4	23	
Cause of arrest						
Cardiac	16	13		11	18	
Noncardiac	16	7	.569	2	21	.025*
Unknown	6	4		1	9	
Epinephrine (mg)	5.03 ± 0.793	6.50 ± 0.905	.086	6.07 ± 1.102	5.46 ± 0.712	.426
APACHE II	21.13 ± 1.120	25.08 ± 1.752	.076	19.36 ± 2.080	23.63 ± 1.095	.100
Arrest-TH start time (min)	279.74 ± 36.772	216.27 ± 19.612	.406	255.57 ± 41.548	256.74 ± 29.658	.906
TH start-TH reach time (min)	264.37 ± 22.697	236.27 ± 37.844	.197	293.50 ± 40.135	242.07 ± 22.793	.274
Target temperature						
32°C (n = 13)	10	3		1	12	
33°C (n = 21)	10	11	.212	4	17	.196
34°C (n = 28)	18	10		9	19	

Basal characteristics of patients following to each target temperature

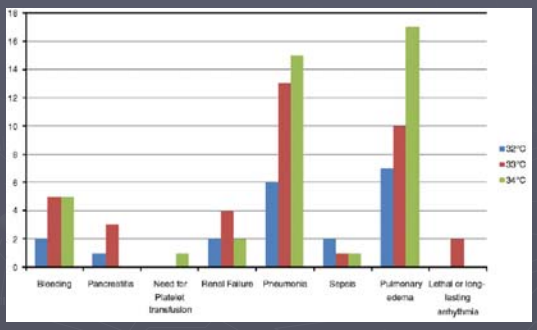
Table 3 Characteristics of patients following each target temperature (n = 62)

Factors	Clinical characteristics			
	32°C (n = 13)	33°C (n = 21)	34°C (n = 28)	*P*
Sex (male/female)	9 (14.5%):4 (6.5%)	13 (20.9%):8 (12.9%)	22 (35.4%):6 (9.6%)	.482
Age (y)	63.31 ± 9.995	52.14 ± 16.587	52.43 ± 16.351	.080
Arrest-CPR time (min)	13.92 ± 9.887	15.05 ± 9.058	13.07 ± 9.006	.754
Arrest-ROSC time (min)	31.92 ± 20.373	38.10 ± 19.002	32.61 ± 13.745	.451
Initial rhythm				
Ventricular fibrillation	4 (6.5%)	10 (16.1%)	10 (16.1%)	
Pulseless electrical activity	4 (6.5%)	2 (3.2%)	5 (8.0%)	.594
Asystole	5 (8.0%)	9 (14.5%)	13 (20.9%)	
Cause of arrest				
Cardiac	5 (8.0%)	11 (17.7%)	13 (20.9%)	
Noncardiac	7 (11.2%)	6 (9.6)	10 (16.1%)	.656
Unknown	1 (1.6%)	4 (6.5%)	5 (8.0%)	
Epinephrine (mg)	5.0 ± 5.050	6.44 ± 6.044	5.25 ± 3.384	.666
Arrest-TH start time (min)	298.92 ± 122.318	255.57 ± 129.407	260.89 ± 243.680	.094
TH start-TH reach time (min)	237.85 ± 165.712	267.90 ± 162.995	251.63 ± 146.132	.757
Arrest-TH reach time (min)	536.77 ± 214.110	501.50 ± 237.966	507.93 ± 298.267	.743
ROSC-TH reach time (min)	498.92 ± 223.770	457.50 ± 236.152	481.37 ± 296.412	.818
Rewarming time (min)	767.92 ± 182.650	766.11 ± 279.693	627.08 ± 268.975	.016

Early complications by target temperature



Late complications by target temperature



Multiple logistic regression analyses

Table 4 Multiple logistic regression analyses for hypotension during maintenance of target temperature (A), mortality (B), and neurologic outcome (C)

Factors	*P*	Odds ratio	95% CI
(A)			
32°C	.016	6.800	1.428-32.373
34°C	.622	1.417	0.355-5.659
(B)			
APACHE II	.023	1.139	1.018-1.275
(C)			
Sex	.031	20.067	1.325-304.027
Noncardiac	.024	16.357	1.435-186.442
Age	.019	1.100	1.016-1.192

APACHE indicates Acute Physiology and Chronic Health Evaluation.

DISCUSSION

- Postcardiac arrest syndrome:
  - Whole body ischemia, global tissue and organ injury
  - Reperfusion
- Post cardiac arrest brain injury
  - Impaired cerebrovascular autoregulation,
  - Cerebral edema,
  - Postischemic neurodegeneration

- Rationale for use of hypothermia
  - Generation of free radicals and other mediators during reperfusion
- Mild degree of therapeutic hypothermia(32-35) should be performed in patients who are hemodynamically stable
  - Coagulopathy, arrhythmias, overdrop of temperature, hypotension, and infection

- Mild hypothermia(32-35)
  - Patient is in an excitation (responsive) stage
  - Attempt to adjust physiologically and retain and generate heat
  - Cardiac output and blood pressure may be markedly depressed(negative inotropic and chronotropic)->hypovolemia
  - Risk for dysrhythmia at body temperatures less than 30˚C;

- 1950s, Moderate hypothermia (28-32˚C) was applied to patients with ROSC
  - Trend to improve outcome
  - Results were inconclusive and therapy was stopped because of the adverse effects

- Hutchison et al: hypothermia therapy after traumatic brain injury in children
  - Target temperature to 32.5˚C for 24 hours
  - Trend toward increased mortality in the hypothermia group
  - No evidence of a benefit to secondary
  - Outcomes(functional and neuropsychologic outcomes,length of stay in the ICU or hospital, and adverse events.)

- External methods are slowed by the body's selfregulating mechanisms, and the target temperature is difficult to control within a narrow range of tolerability
- An endovascular cooling system can maintain a target temperature within a narrow range

- Target temperature at 32˚C, the risk of hypotension was increased over 6-fold compared with the other target temperatures (33˚C and 34˚C).
- Mortality and neurologic outcomes were not significantly different

- If hypotension develops during postresuscitation care, the patient should receive treatment with inotropics and fluids.
- The effects of this on the heart or brain need additional study

- Multiple logistic regression models: neurologic outcome, sex, cause of arrest, and age were related
  - Male, cardiac cause of arrest, and young in age ->good CPC
  - Tendency for a good CPC in male patients was 20-fold greater than female patients

- Limitations
  - small study population
  - Only in one institution
  - Rectal probe to monitor the patient's core temperature(impacted stool or other causes)

CONCLUSIONS

- Risk of hypotension during therapeutic hypothermia maintenance was increased at 32°C.
- Therapeutic hypothermia in patients with ROSC after an out-of-hospital cardiac arrest, the target temperature would be set at 33°C or 34°C
- Further prospective randomized controlled multicenter studies are needed in the future