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

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報告者:PGY何子明

指導老師:王瑞芳醫師

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Introduction

- Therapeutic hypothermia as a neuroprotectant in post cardiac arrest patient
- International Liaison committee of Resuscitation and the American Heart Association
  - TH post cardiac arrest in their guidelines on resuscitation
- Best practices in temperature management ?

- This knowledge gap for variability of current practice
  - target temperature (32–34 °C)
  - duration of TH (12–48 h)
- Neurological function post cardiac arrest
  - measured by the cerebral performance category (CPC) scores

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]

- The aim of this study
  - identify predictors of neurological outcomes
  - patients who received therapeutic hypothermia post cardiac arrest
- determine differential rates of neurologic outcomes
  - time to initiation and duration of TH and time to ROSC.

Method

- A secondary data analysis
  - Minneapolis Heart Institute data
  - entered and uploaded from the International Cardiac Arrest Registry (INTCAR) database
  - web-based registry of cardiac arrest survivors
    - standardized data definitions
    - evaluate all aspects of post-resuscitation care

- Feb 2006 to July 2010
- 172 OHCA patients treated with mild therapeutic hypothermia (32 °C)
- Inclusion criteria
  - nontraumatic cardiac arrest
  - ROSC within 60 min of collapse
  - unconscious (does not follow commands)
  - an out-of-hospital cardiac arrest

- Exclusion criteria
  - persistent hypotension despite administration of vasopressors
  - active bleeding
  - DNR/DNI code status
  - chronic comatose or vegetative state prior to arrest

Data collection

- retrospective, non-experimental observational study
- Clinical documentation for TH patients
  - using standardized 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

- All data were abstracted locally by a Certified Clinical Nurse Research Coordinator (http://www.acrpnet.org/)
- Abstracted data were entered into a password protected on-line INTCAR database

Measure

- neurological function:
  - good (CPC = 1),moderate (CPC = 2), and poor (CPC ≥ 3) outcomes
- The outcome was examined
  - at transfer from ICU
  - at hospital discharge
  - at least 1 month post-discharge follow-up

- Time to initiation of TH
  - estimated minutes from arrest to initiation of TH and minutes to target temperature
- minutes to TH initiation
  - 5 min increments in delay of starting treatment
- Time to target temperature
  - 30 min increments in time from arrest to reaching target temperature

Statistical analysis

- Given the ordered nature of CPC scores
  - ordinal logistic regression was first assessed
- Assumption :
  - ordinal logistic regression: regression between levels must be parallel.
- The Brant test was used to test this assumption
- Regression lines between levels were not parallel

- Multinomial logistic regression models
  - estimate the odds of poor compared to good neurological outcome
- The three category dependent variable
  - with a good outcome being the referent category
  - used for both unadjusted and adjusted models

- Fully adjusted model compared to the unadjusted model
  - statistically significant improvement of model fit at $p < 0.001$
- Final models adjusted
  - gender, age, current smoking status, initial rhythm, and days of stay in the ICU or in the hospital

Result

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

at ICU Transfer

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.

- For every 5 min delay
  - 6% greater odds having a poor versus good outcome
  - after adjusting for age, gender, initial cardiac rhythm, and length of ICU stay

at Hospital Discharge

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.

- For every 5 min delay
  - 6% greater odds of poor versus good outcome
  - after adjusting for age, gender, initial rhythm and hospital length of stay

at Post-discharge Follow-up

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.

- every 5 min delay
  - 8% greater odds of a poor compared to a good outcome, 5% greater odds of moderate compared to good outcome
- every 30 min delay
  - 17% greater odds of poor versus good outcome

Discussion

- neurologically intact survival to discharge
  - higher in patients cooled intra-arrest in whom CPR was initiated within 10 min of collapse
- other studies: no association between neurologic outcomes and earlier cooling
- very early cooling needed to be further investigated

- 30-min delay reaching goal temperature
  - associated with worse outcomes
- Wolff: less time to coldest temperature
  - an independent predictor of good neurological outcome
- Vanston:
  - the longer to reach the goal temperature
  - the better the neurological outcome

Conclusion

- 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

Factors complicating interpretation of capnography during advanced life support in cardiac arrest—A clinical retrospective study in 575 patients

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Introduction

- partial pressure of end tidal carbon dioxide: ETCO2
  - alveolar CO2 tension
  - production, transport to, and elimination from the lungs
  - reflects cardiac output
- Described during anaesthesia in the 1950s
  - in order to verify correct tube placement

- Monitoring of ETCO2 during CPR
  - efficacy
  - return of spontaneous circulation
- Interpretation of ETCO2 during resuscitation
  - the cause of the arrest: higher in asphyxial arrests
  - bystander CPR
  - variation over time

Objective

- Capnography: valuable feedback to the ALS providers
- limit and complicate its interpretation
  - initial heart rhythm
  - cause of the arrest
  - presence of bystander CPR
  - time dependency

Result

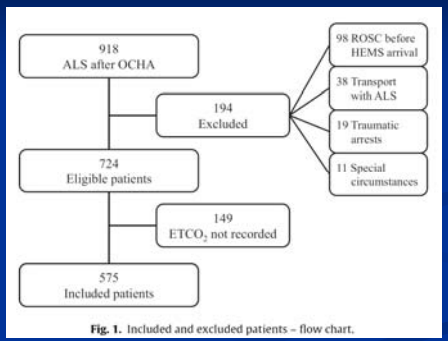


Fig. 1. Included and excluded patients – flow chart.

Baseline characteristics in study population ($n = 575$).

Variable	Mean ± SD
Age (year)	60.7 ± 17.8
Female/male	145/430
Witnessed	414 (72%)
Bystander CPR	438 (76%)
Arrest-CPR (min)	8.6 ± 15.4
Arrest-ACLS (min)	14.7 ± 16.9
Arrest-CO_2 recording (min)	22.5 ± 17.5
Admitted hospital with ROSC	232 (40%)
Any ROSC (%)	286 (50%)
Termination of resuscitation (min)[a]	43.3 ± 22.3
Cause of the arrest	
Cardiac	336 (58%)
Respiratory	117 (20%)
Pulmonary embolism	12 (2%)
Unknown/other	110 (19%)
Initial rhythm	
Ventricular fibrillation	195 (34%)
Ventricular tachycardia	3 (1%)
Asystole	266 (46%)
Pulseless electrical activity	111 (19%)

CPR, cardio pulmonary resuscitation; ACLS, advanced cardiac life support.
[a] Time between arrest and termination of resuscitation.

ETCO2 and different causes

Table 2
Average $ETCO_2$ (kPa) during CPR in patients with or without ROSC, regarding the cause of the arrest.

Cause	Overall $ETCO_2$, mean ± SD	ROSC, mean ± SD	No-ROSC, mean ± SD	*p*-Value[a]
Cardiac	2.8 ± 1.3	3.4 ± 1.2	2.4 ± 1.2	<0.001
Respiratory	3.5 ± 2.2	4.5 ± 2.2	2.3 ± 1.5	<0.001
Pulmonary embolism	1.7 ± 1.1	2.2 ± 1.0	0.9 ± 0.5	0.023
Unknown/Other	2.0 ± 1.2	2.7 ± 1.0	1.3 ± 1.1	<0.001

[a] Contrast between ROSC and no-ROSC using independent samples *t*-test.

Table 3
$ETCO_2$ (kPa) in patients presenting asystole with respiratory and cardiac causes to the arrest.

$ETCO_2$	Cardiac cause, mean ± SD	Respiratory cause, mean ± SD	*p*-Value[a]
Average	2.3 ± 1.4	3.5 ± 2.3	<0.001
Min.	1.5 ± 1.0	2.4 ± 2.0	<0.001
Max.	3.4 ± 2.3	5.1 ± 3.5	<0.001

[a] Contrast between cardiac and respiratory causes using independent samples *t*-test.

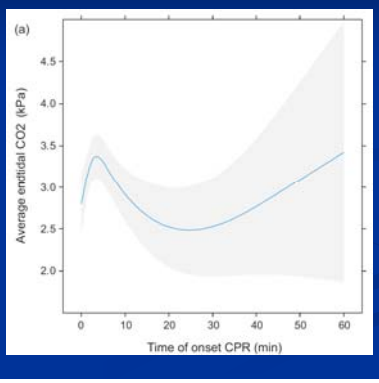
ETCO2 and different initial rhythms

Table 4
Average $ETCO_2$ (kPa) during CPR in patients with or without ROSC, regarding the initial heart rhythm.

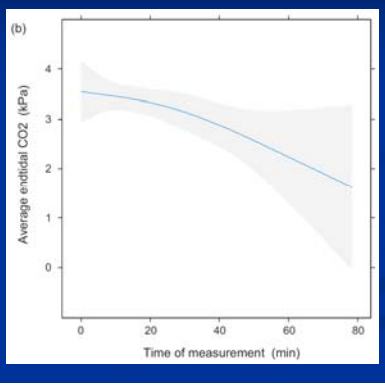
Initial heart rhythm	$ETCO_2$	ROSC, mean ± SD	No-ROSC, mean ± SD	*p*-Value[a]
VF/VT (*n* = 198)	Average	3.4 ± 1.1	2.8 ± 1.2	<0.001
	Min.	2.6 ± 1.0	1.8 ± 0.9	<0.001
	Max.	5.1 ± 2.2	4.3 ± 1.9	0.009
AS (*n* = 266)	Average	4.1 ± 2.1	2.0 ± 1.3	<0.001
	Min.	2.9 ± 1.8	1.4 ± 1.0	<0.001
	Max.	5.9 ± 3.3	3.0 ± 2.1	<0.001
PEA (*n* = 111)	Average	3.1 ± 1.5	2.2 ± 1.3	0.001
	Min.	2.2 ± 1.4	1.3 ± 1.0	<0.001
	Max.	4.4 ± 2.5	3.1 ± 1.9	0.003

[a] Contrast between ROSC and No-ROSC using independent samples *t*-test.

ETCO2 and bystander CPR



ETCO2 and time of measurement



Conclusion

- Confounding factors including
  - cause of arrest
  - initial rhythm
  - bystander CPR
  - time from cardiac arrest
- complicating and limiting prognostic interpretation of capnography during ALS

- Thank you for your attention!