Survival does not improve when therapeutic hypothermia is added to post-cardiac arrest care

Rudiger Pfeifer *, Christian Jung, Sandra Purle, Alexander Lauten, Atilla Yilmaz, Ralf Surber, Markus Ferrari, Hans R. Figulla

報告者:PGY 倪旻白
指導者: VS 王瑞芳
1000910

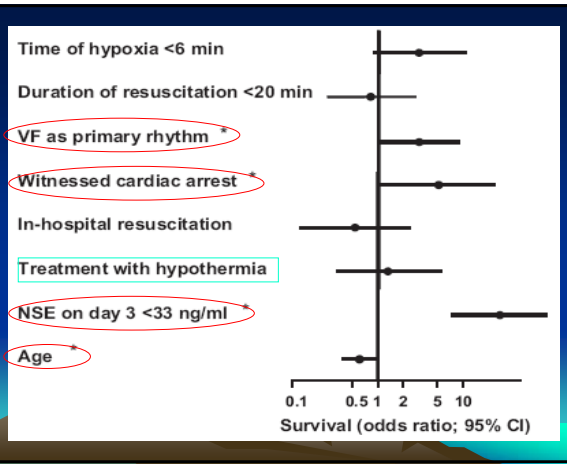
Materials and methods

- Inclusion criteria were defined as:
  - (1) restoration of spontaneous circulation (ROSC) ≤ 60 min,
  - (2) non-traumatic cardiac arrest independent of primary rhythm,
  - (3) persistent unconsciousness
  - (4) estimated time of hypoxia including non-witnessed CA ≤15 min.
- Patients were excluded if:
  - (1) they awoke within a 1-h period without sedation following ROSC
  - (2) the time delay between ROSC and the possible start of hypothermia exceeded 6 h,
  - (3) a hemodynamic stabilisation was not possible, in spite of vasopressor therapy.

Table 1
Baseline, resuscitation, treatment and outcome characteristics of both patient groups.

	Normothermia group (*n* = 67)	Hypothermia group (*n* = 143)	*p*-Value
Mean age (y)	68.5 ± 14.0	62.5 ± 14.1*	0.005
Male (*n*)	40 (60.0%)	111 (77.6%)	–
SAPS II	63.1 ± 15.0	58.2 ± 17.7*	0.003
Factors at resuscitation (*n*)			
Ventricular fibrillation	28 (42.0%)	72 (50.3%)	0.234
Witnessed CA	43 (64.2%)	107 (74.8%)	0.143
Mean duration of CPR	20.5 ± 18.5	22.8 ± 14.2	0.369
Length of anoxia (min)	5.1 ± 4.3	6.1 ± 4.7	0.22
In-hospital CA	41 (61.2%)	47 (33.0%)*	<0.001
Causes of CA (*n*)			
Myocardial infarction	19 (28.3%)	62 (43.4%)	0.079
Cardiovascular diseases	21 (31.3%)	42 (29.4%)	–
Other diseases	27 (40.4%)	39 (27.2%)	–
Number of co-morbidity (*n*) ≤2	42 (62.7%)	64 (44.7%)	0.531
Number of co-morbidity (*n*) ≥3	25 (37.3%)	79 (55.3%)	–
Investigation and treatment			
Serum NSE at 72 h after CA (ng ml^{-1})	67.9 ± 87.5	77.8 ± 112.3	0.553
Length of sedation (*d*)	3.5 ± 5.4	4.1 ± 3.6*	<0.001
Vasopressor therapy (*n*)	55 (82.1%)	136 (95.1%)*	<0.001
Coronary angiography and PCI (*n*)	15 (22.4%)	40 (28.0%)	0.501
IABP (*n*)	12 (18.0%)	41 (28.7%)	0.125
Mortality at 1 month after CA (*n*)			
All patients (*n* = 67/143)	30 (44.8%)	69 (48.2%)	0.659
First ECG VF (*n* = 28/72)	8 (28.6%)	19 (26.4%)	0.807
First ECG asystole/PEA (*n* = 39/71)	22 (56.4%)	50 (70.4%)	0.149

SAPS II, simplified acute physiology score II; CA, cardiac arrest; CPR, cardiopulmonary resuscitation; NSE, neuron-specific enolase; PCI, percutaneous coronary intervention; IABP, intra-aortic balloon pump.
* Significant differences between normothermia and hypothermia patients.



3-1) Results of the hypothermia group

Table 2
Baseline and cooling characteristics of patients undergoing therapeutic hypothermia subdivided accordingly to neurological outcome.

significant	CPC (4&5) (*n* = 93)	CPC (1–3) (*n* = 50)	*p*-Value
Mean age	64.6 ± 12.7	58.6 ± 15.7*	0.014
Ventricular fibrillation (*n*)	32 (34.4%)	40 (80%)*	<0.001
SAPS II	61 ± 18.1	53.3 ± 16.1*	0.004
Witnessed CA (*n*)	62 (66.7%)	45 (90.0%)*	0.001
Time of anoxia (min)	6.9 ± 5.2	5.0 ± 3.6	0.137
Duration of CPR (min)	25.8 ± 14.6	17.5 ± 12.0*	<0.001
Mean serum NSE on day 3 (ng ml^{-1})	112.8 ± 128.7	17.1 ± 7.2*	<0.001
Time from ROSC to achieving goal temp. (min)	260.4 ± 250.2	279.6 ± 226.2	0.667
Duration of TH (h)	23.6 ± 5.4	24.7 ± 3.9	0.192
Maintenance of goal temp. (h)	15.8 ± 8.6	19.2 ± 8.1*	0.008
Time from finishing TH to achieving 36 °C (h)	9.8 ± 5.6	8.6 ± 2.9	0.25
Intravascular cooling (*n*)	64 (68.8%)	32 (64.0%)	0.580

no difference

CPC, cerebral performance category scale; SAPS II, simplified acute physiology score II; CA, cardiac arrest; CPR, cardiopulmonary resuscitation; NSE, neuron-specific enolase; ROSC, restoration of spontaneous circulation; TH, therapeutic hypothermia.
* Significant differences between patients with unfavourable outcome (CPC 4 & 5) and with moderate to good neurological recovery (CPC 3–1).

4) Discussion

- Not a randomised trial
  - selection bias
- To date, in randomised trials, a beneficial effect of hypothermia is only shown for witnessed OHCA in patients with ventricular fibrillation.
  - Our patient population consisted of a wide spectrum of CA survivors.
  - Such a wide and heterogeneous spectrum of CA survivors has not yet been investigated in a randomised controlled trial.

- our investigation to patients who survived at least 48 h not significantly influenced our result
  - a better neurological outcome in comatose survivors after CA most probably is not the sole result of hypothermia, but rather of better post-resuscitation care in general.
- average 8.6 h in our study before the target temperature (32.5–33.5 ◦C) was reached
  - The only cooling parameter that was different between patients with good neurological outcome and patients for whom the outcome was either death or persistent coma was the duration for which the target temperature of 33 ◦C was maintained.

- Improved survival after CA most probably is not solely the result of hypothermia.
- Walter et al.
  - currently investigating a post-cardiac arrest care bundle, consisting of hypothermia and early hemodynamic optimisation.
  - They found better survival in those patients who received all elements of the care bundle.

5) Conclusion

- There was no improvement in survival rates when hypothermia was added to standard therapy in this case series, as compared to standard therapy alone.
- The time at target temperature may be of relevance.
- We need better evidence in order to expand the recommendations for hypothermia after CA.