Sapporo Medical University

Cooling parameters and laboratory value on admission

	Fast group (n = 107)	Moderate group (n = 184)	Slow group (n = 117)	p value
Maximam BP after ROSC	133± 42	131± 43	137± 39	0.58
Target tempeature	34± 0.4	34 ± 0.5	34± 0.4	0.07
Initiation cooling to target temperature (min)	269 ± 271	235± 216	250± 203	0.47
Cooling duration (hour)	28± 12	32 ± 12	35 ± 15	<0.01
Arterial blood pH	7.11± 0.20	7.15± 0.18	7.14± 0.19	0.37
Base excess (mmol/l)	-13.3± 6.6	-12.1 ± 6.1	-12.3 ± 6.6	0.40
Blood sugar(mg/dl)	276± 101	271 ± 92	262± 92	0.53
Potassium(mEq/l)	4.0± 1.0	4.0± 0.9	4.1± 0.8	0.46
Hemoglobin(g/dl)	13± 2	13 ± 2	14 ± 2	0.10
Incidence of complication	33(31%)	61 (33%)	23 (20%)	0.03

Data are presented as mean value ± SD or number (%) of patients.

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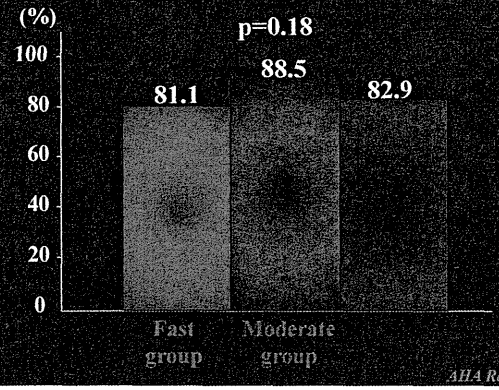
Survival rate at 30 days



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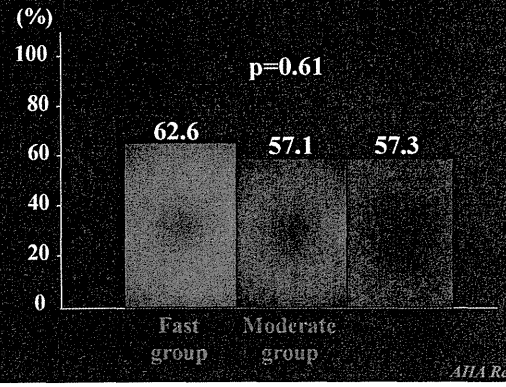
CPC score 1 or 2 rate at 30 days



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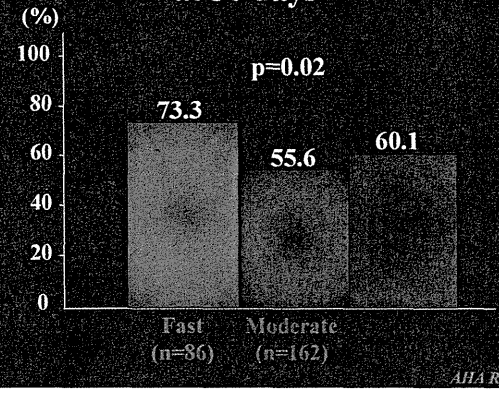
CPC score 1 rate of 345 surviving patients at 30 days



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Summary

In baseline characteristics, there were no significant inter-group differences in gender, age, the presence of witteness, rate of bystander CPR, rate of return of spontaneous circulation (ROSC) before admission and mean laboratory value, but slow group had a lower frequency of ventricular fibrillation in initial ECG, longer cooling duration and a lower incidence of complication during hypothermia compared with the other 2 groups.

Survival rate and CPC 1 or 2 rate at 30 days were comparable among 3 groups.

Of surviving patients at 30 days, CPC 1 rate in fast group was significantly higher than that of the other 2 groups.

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Conclusions

This result may suggest that rewarming speed ≥ 2.0 degrees C/day would be appropriate in therapeutic hypothermia for patients with out-of-hospital cardiac arrest.

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Title: Efficacy of Therapeutic Hypothermia for Out-of-hospital Cardiac Arrest in Patients with Non-ventricular Fibrillation: J-PULSE-Hypo Registry

Yoshio Tahara, Noriyuki Suzuki, Kazuo Kimura, Ken Nagao, Naohiro Yonemoto, Hiroyuki Yokoyama, Hiroshi Nonogi and the J-PULSE-Hypo Investigators

Background: Therapeutic hypothermia is effective for patients who remain comatose after resuscitation from out-of-hospital cardiac arrest due to ventricular fibrillation (VF). However, whether therapeutic hypothermia is effective for cardiac arrest without VF remains unclear.

Methods: We conducted a multicenter retrospective study (J-PULSE-Hypo registry) at 14 institutions to evaluate the effect of therapeutic hypothermia on out-of-hospital cardiac arrest between January 2005 and December 2009. Enrolled patients were divided into the VF group, pulseless electrical activity (PEA) group, and asystole group according to the initial rhythm. Neurologic outcomes at discharge from the hospital were compared with those of patients in the SOS-KANTO study who received standard advanced cardiovascular life support with no therapeutic hypothermia. The SOS-KANTO study was performed from 2002 through 2003 and registered 9,592 patients with out-of-hospital cardiac arrest, including 556 patients who were aged 18-74 years, comatose (Glasgow Coma Scale $\leq$6) on admission, and received no therapeutic hypothermia. A favorable outcome was defined as a Cerebral Performance Category (CPC) of 1-2.

Results: A total of 452 patients were enrolled in the J-PULSE-Hypo registry. The mean age was 59±13 years. Men accounted for 83% of all patients. The patients in the J-PULSE-Hypo registry and the SOS-KANTO study were divided into the VF group (n=353, n=215), the PEA group (n=63, n=97), and the asystole group (n=36, n=244) according to the initial rhythm. The rates of favorable outcomes in the VF group (63% vs. 25%, $p<0.01$), the PEA group (32% vs. 8%, $p<0.01$), and the asystole group (19% vs. 5%, $p<0.01$) were significantly higher in the J-PULSE-Hypo registry than in the SOS-KANTO study.

Conclusions: Although the times of the studies and background characteristics of the subjects differed, our results suggest that therapeutic hypothermia is effective not only for out-of-hospital cardiac arrest due to VF, but also for cardiac arrest due to causes other VF.

Efficacy of Therapeutic Hypothermia for Out-of-Hospital Cardiac Arrest in Patients with Non-Ventricular Fibrillation: J-PULSE-Hypo Registry

Yoshio Tahara*1, Noriyuki Suzuki*1, Kazuo Kimura*1, Ken Nagao*2, Naohiro Yonemoto*3, Hiroyuki Yokoyama*4, Hiroshi Nonogi*4, and the J-PULSE-Hypo Investigators

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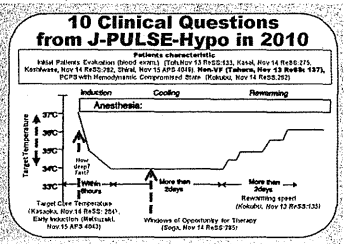
10 Clinical Questions from J-PULSE-Hypo in 2010



INTRODUCTION

- Therapeutic hypothermia is effective for patients who remain comatose after resuscitation from out-of-hospital cardiac arrest due to ventricular fibrillation (VF) [1,2,3].
- However, whether therapeutic hypothermia is effective for cardiac arrest without VF remains unclear [4,5].

OBJECTIVE

- To compare favorable outcome according to the initial rhythm between the patients who received therapeutic hypothermia and the patients who received standard advanced life support with no therapeutic hypothermia.

METHODS

- We conducted a multicenter retrospective study (J-PULSE-Hypo registry) at 14 institutions to evaluate the effect of therapeutic hypothermia on out-of-hospital cardiac arrest between January 2005 and December 2009 (**Table 1, Figure 1**).
- Enrolled patients were divided into the VF group, pulseless electrical activity (PEA) group, and asystole group according to the initial rhythm.
- Neurologic outcomes at discharge from the hospital were compared with those of patients in the SOS-KANTO study who received standard advanced cardiovascular life support with no therapeutic hypothermia.
- The SOS-KANTO study was performed from 2002 through 2003 and registered 9,592 patients with out-of-hospital cardiac arrest, including 556 patients who were aged 18-74 years, comatose (Glasgow Coma Scale ≤6) on admission, and received no therapeutic hypothermia (**Figure 2**).
- A favorable outcome was defined as a Cerebral Performance Category (CPC) of 1-2.

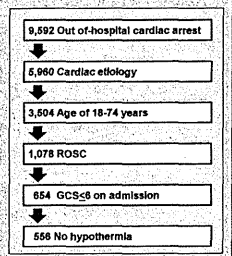


Figure 2. SOS-KANTO study data

Study population:	Patients with therapeutic hypothermia after cardiac arrest from 2005 to 2009 in 14 hospitals.
Inclusion criteria:	Adult (*more than 18 years old*) patients who remained unconscious after resuscitation from out-of-hospital cardiac arrest and presented the stable hemodynamics with drug treatments or mechanical supporting system including IABP or PCPS.
Exclusion criteria:	Patients with pregnancy, acute aortic dissection, pulmonary thromboembolism, drug poisoning or poor daily activity

Table 1. J-PULSE-Hypo registry

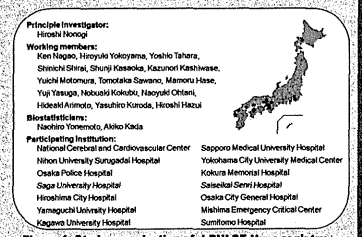


Figure 1. Study organization of J-PULSE-Hypo registry

RESULTS

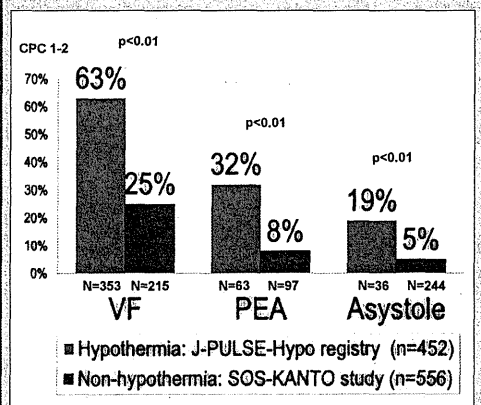


Figure 3. Favorable neurologic recovery rate

	Hypothermia Group (J-PULSE-Hypo registry)	Non-hypothermia Group (SOS-KANTO study)	p-Value
Number of patients	452	556	
Age (years)	58.6±13.5	59.8±11.6	0.137
Male sex (%)	83	74	0.002
Witnessed cardiac arrest (%)	87	73	<0.001
Performed bystander CPR (%)	51	33	<0.001
ROSC before ER (%)	59	19	<0.001
<Initial arrest rhythm>			
VF(%)	78	39	<0.001
PEA(%)	14	17	0.130
Asystole(%)	8	44	<0.001

Table 2. Baseline characteristics

Factor	Odds ratio	(95% CI)	p-Value
Sex (male vs. female)	0.971	(0.566-1.668)	0.916
Witnessed cardiac arrest (yes vs. no)	1.168	(0.664-2.054)	0.590
Performed bystander CPR (yes vs. no)	1.667	(1.125-2.471)	0.011
ROSC before ER (yes vs. no)	5.823	(3.925-8.639)	<0.001
Therapeutic hypothermia (yes vs. no)	3.166	(2.084-4.809)	<0.001

Table 3-1. VF group

Factor	Odds ratio	(95% CI)	p-Value
Sex (male vs. female)	0.493	(0.159-1.528)	0.220
Witnessed cardiac arrest (yes vs. no)	1.331	(0.339-5.228)	0.682
Performed bystander CPR (yes vs. no)	1.755	(0.628-4.907)	0.283
ROSC before ER (yes vs. no)	11.180	(3.981-31.397)	<0.001
Therapeutic hypothermia (yes vs. no)	3.548	(1.259-10.004)	0.017

Table 3-2. PEA group

Factor	Odds ratio	(95% CI)	p-Value
Sex (male vs. female)	0.604	(0.192-1.897)	0.388
Witnessed cardiac arrest (yes vs. no)	12.433	(1.508-102.477)	0.019
Performed bystander CPR (yes vs. no)	1.142	(0.387-3.367)	0.810
ROSC before ER (yes vs. no)	6.521	(2.221-19.141)	0.001
Therapeutic hypothermia (yes vs. no)	4.142	(1.267-13.536)	0.019

Table 3-2. Asystole group

Table 3. Multivariate predictors of favorable outcome

	Favorable Group [N=27]	Non favorable Group [N=72]	p-Value
Age (year)	60.1±14.2	62.0±12.3	0.517
Male sex (%)	78	82	0.643
Witnessed cardiac arrest (%)	93	76	0.069
Performed bystander CPR (%)	67	49	0.111
Initial arrest rhythm: PEA (%)	74	60	0.199
ROSC before ER (%)	74	26	<0.001
The time from collapse to ROSC (min)	21.7±13.1	43.9±22.5	<0.001

Table 4. Factors for favorable outcome in non-VF (PEA, Asystole) J-PULSE-Hypo registry

SUMMARY

- A total of 452 patients were enrolled in the J-PULSE-Hypo registry.
- The mean age was 59±13 years.
- Men accounted for 83% of all patients.
- The patients in the J-PULSE-Hypo registry and the SOS-KANTO study were divided into the VF group (n=353, n=215), the PEA group (n=63, n=97), and the asystole group (n=36, n=244) according to the initial rhythm.
- The rates of favorable outcomes in the VF group (63% vs. 25%, p<0.01), the PEA group (32% vs. 8%, p<0.01), and the asystole group (19% vs. 5%, p<0.01) were significantly higher in the J-PULSE-Hypo registry than in the SOS-KANTO study (**Figure 3**).

LIMITATIONS

- This study was not a prospective randomized trial.
- Since the Hypothermia group in J-PULSE-Hypo registry and the Non-hypothermia group in SOS-KANTO study were investigated at different time points, the historical background in the treatment for out-of-hospital cardiac arrest differed between the groups. This may have affected the favorable neurologic recovery rate in the two groups.
- The criteria to induction of therapeutic hypothermia differed among institutions.

DISCUSSIONS

- Although there are some differences between Hypothermia Group (J-PULSE-Hypo registry) and Non-hypothermia Group (SOS-KANTO study) (**Table 2**), our results suggested that therapeutic hypothermia contribute to favorable outcome in any initial rhythm (**Table 3**).
- In non-VF group of the J-PULSE-Hypo registry, the interval from collapse to return of spontaneous circulation (22+13 vs. 44+23 min, p<0.01) and the rate of return of spontaneous circulation before arrival at the hospital (74% vs. 26%, p<0.01) differed significantly between patients who had favorable outcome (N=27) and those who did not (N=72) (**Table 4**).

CONCLUSION

- Although the times of the studies and background characteristics of the subjects differed, our results suggest that therapeutic hypothermia is effective not only for out-of-hospital cardiac arrest due to VF, but also for cardiac arrest due to causes other VF, particularly in patients with short interval from collapse to return of spontaneous circulation.

REFERENCES

1. Circulation. 2005;112:IV-84-88.
2. N Engl J Med. 2002;346:549-56.
3. N Engl J Med. 2002;346:557-63.
4. Resuscitation. 2001;51:275-81.
5. Crit Care Med. 2005;33:414-8.

ROSC: return of spontaneous circulation, GCS: Glasgow coma scale, IABP: intra-aortic balloon pumping, PCPS: percutaneous cardiopulmonary support, ER: emergency room, CPR: cardiopulmonary resuscitation

Title: Relation between Initial Arterial Blood pH Levels and Neurological Outcomes in Patients Treated with Hypothermia after Out-of-hospital Cardiac Arrest: J-PULSE-Hypo Registry

Background: Therapeutic hypothermia has been shown to improve neurologic recovery in comatose patients after cardiac arrest. However, the indications for therapeutic hypothermia remain controversial. We aimed to determine whether arterial blood gas data evaluated on emergency department (ED) arrival is useful for predicting neurologic outcomes in patients treated with hypothermia.

Methods: We analyzed data from the J-PULSE-Hypo registry, a retrospective, multicenter, observational study using Utstein templates in patients treated with hypothermia from January 2005 through December 2009. We included 210 patients with witnessed arrest and arterial blood sampling within 30 minutes after ED arrival and within 60 minutes after collapse. Clinical outcomes were assessed on the basis of cerebral performance categories (CPC).

Results: The 210 eligible patients (164 men, median age 61 years) were divided into the good recovery (GR) group (N=121) with CPC 1-2 and the non-good recovery (non-GR) group (N=89) with CPC 3-5 according to the neurologic outcomes at discharge from the hospital. As compared with the non-GR group, the GR group had a significantly younger age; higher rates of ventricular fibrillation as initial rhythm and return of spontaneous circulation (ROSC) at ED arrival; a shorter time from collapse to ROSC; higher levels of hemoglobin, HCO_3, base excess (BE), and pH; and lower levels of glucose and $PaCO_2$ ($p<0.01$). A multiple logistic-regression model using significant variables on bivariate analysis showed that neurologic outcomes were significantly ($p<0.05$) related to pH level with an odds ratio of 1.564 (degrees of freedom, 0.1) (95% CI, 1.241-1.971), age with an odds ratio of 0.970 (95% CI, 0.943-0.998) and the rate of ROSC at hospital arrival with an odds ratio of 2.276 (95% CI, 1.100-4.710). Receiver operating characteristic (ROC) curve showed the pH level cutoff value of 7.095 with a sensitivity of 72.7% and a specificity of 74.2% (AUC=0.771, $p<0.01$) for identification of a favorable neurological outcome.

Conclusions: The pH level can be a useful predictor of neurological outcomes in patients with therapeutic hypothermia after out-of-hospital cardiac arrest.

Relation Between Initial Arterial Blood pH Levels and Neurological Outcomes In Patients Treated With Hypothermia after Out-of-hospital Cardiac Arrest
J-PULSE HYPO Registry

Masafumi Toh*1, Shunsuke Takaki*1, Masataka Taguri*1, Yoshio Tahara*1, Kazuo Kimura*1, Ken Nagao*2, Naohiro Yonemoto*3, Hiroyuki Yokoyama*4, Hiroshi Nonogi*4, and J-PULSE-Hypo Investigators

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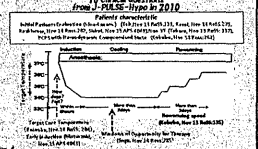
Introduction

- Therapeutic hypothermia has been shown to improve neurological recovery in comatose patients after cardiac arrest. However, the indications for therapeutic hypothermia remain controversial.
- We aimed to determine whether arterial blood gas data evaluated on emergency department (ED) arrival is useful for predicting neurological outcomes in patients treated with hypothermia.

J-PULSE-Hypo Registry

Study population:	Patients with therapeutic hypothermia after cardiac arrest from 2005 to 2009 in each hospitals.
Inclusion criteria:	Adult (more than 18 years old) patients who remained unconscious after resuscitation from out-of-hospital or inhospital cardiac arrest and presented the stable hemodynamics with drug treatments or mechanical supporting system including IABP or PCPS.
Exclusion criteria:	Patients with pregnancy, acute aortic dissection, pulmonary thromboembolism, drug poisoning or poor daily activity



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Hiroshima City Hospital
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Kagawa University Hospital
Sapporo Medical University Hospital
Yokohama City University Medical Center
Kokura Memorial Hospital
Sakaikai Senri Hospital
Osaka City General Hospital
Mishima Emergency Critical Care
Sumitomo Hospital

Methods

- Retrospective study from the J-PULSE-Hypo registry, multicenter database using Utstein templates in patients treated with hypothermia from January 2005 through December 2009.
- The following criteria were used for enrollment: (1) witnessed arrest; (2) arterial blood sampling was obtained within 30 minutes after ED arrival and within 60 minutes after collapse.
- Patients were followed until in-hospital death or discharge from the hospital. At the time of discharge, the neurological recovery was assessed according to the cerebral performance categories (CPC). The patients divided into good recovery (GR) group with CPC 1-2 and non good recovery (non-GR) group with CPC 3-5.
- Univariate analyses on baseline characteristics and blood sampling data on admission were performed and p-values <0.05 were considered to be significant. A multiple logistic regression analysis including significant prognostic factors in univariate analyses was used for identification the independent predictors of neurological recovery.

Results

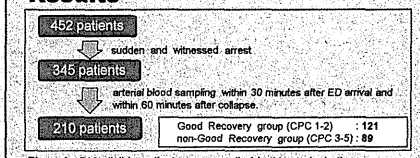


Figure1 : 210 eligible patients were enrolled in this study. In these patients, 121 patients showed good recovery and 89 patients showed unfavorable recovery.

	pH	$PaCO_2$	BE
pH		r=-0.749 p<0.001	r=0.793 p<0.001
$PaCO_2$	r=-0.749 p<0.001		r=-0.281 p<0.001
BE	r=0.793 p<0.001	r=-0.281 p<0.001	

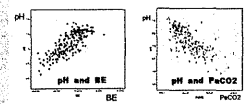


Table3 and Figure2
Pearson's correlation analyses between $PaCO_2$, BE and pH.
It is found strong correlation between pH and $PaCO_2$, pH and BE.

	All data (N=210)	GR group (N=121)	Non-GR group (N=89)	p-value
Age (year)	59.2±13.2	56.8±14.1	62.5±11.3	.002
Male gender	164/210 (78%)	93/121 (77%)	73/89 (80%)	.614
Time from collapse to CPR (min)	4.6±5.8	4.8±6.7	4.5±4.4	.745
Time from collapse to ROSC (min)	29.1±18.4	23.3±13.6	37.0±21.0	<0.001
Time from collapse to ED (min)	29.4±11.7	29.5±10.8	29.3±12.8	.208
By-stander CPR (min)	122/210 (58%)	72/121 (60%)	50/89 (56%)	.629
VF/pulseless VT as initial rhythm	163/210 (78%)	104/121 (86%)	59/89 (66%)	.001
Time from collapse to TH start (min)	119±118	111±71	130±161	.249
Duration of TH (hr)	30±13	31±12	28±13	.172
Complication of TH	65/210 (31%)	33/121 (27%)	32/89 (36%)	.179
Percutaneous Coronary Intervention	92/210 (44%)	50/121 (41%)	42/89 (47%)	.397
IABP use	74/210 (35%)	33/121 (27%)	41/89 (46%)	.005
PCPS use	50/210 (24%)	19/121 (16%)	31/89 (35%)	.002

Table1: Significant differences between two groups at ED arrival were observed in age, time from collapse to ROSC, the ratio of VF or pulseless VT at initial rhythm , IABP use and PCPS use.

	All data (N=210)	GR group (N=121)	Non-GR group (N=89)	p-value
Time from collapse to blood sampling (min)	36.8±11.5	37.4±10.4	37.1±11.9	.411
Time from arrival to blood sampling (min)	7.5±6.8	8.1±7.3	6.8±6.2	.172
WBC (/ul)	12.7±9.0	12.7±10.4	12.7±6.6	.974
Hb (g/dl)	13.6±2.2	14.0±2.1	12.9±2.3	<0.001
K (mEq/L)	4.0±0.9	3.9±0.8	4.2±1.0	.039
BUN (mg/dl)	19.4±13.1	17.8±10.1	21.9±15.9	.200
Cre (mg/dl)	1.46±1.79	1.34±1.80	1.63±1.80	.251
BS (mg/dl)	273±96	256±81	295±111	.005
pH	7.10±0.18	7.18±0.15	7.00±0.18	<0.001
PaO_2 (mmHg)	240±170	284±172	209±163	.200
$PaCO_2$ (mmHg)	55.2±26.7	48.2±22.2	64.8±29.6	<0.001
HCO_3 (mEq/L)	15.4±4.4	16.2±4.5	14.3± 4.0	.002
BE (mEq/L)	-13.8±5.8	-11.8±5.5	-16.6±5.0	<0.001

Table2 : univariate analyses of blood sampling data at ED arrival. K, BS and $PaCO_2$ were significantly lower in GR groups. Hb, pH, BE and HCO_3 were higher in GR groups.

	p-value	Odds Ratio	95% CI for OR
Age	0.009	0.961	0.933 - 0.990
Time from collapse to ROSC	0.001	0.960	0.936 - 0.984
VF/pulseless VT as initial rhythm	0.212	1.758	0.725 - 4.265
Hb	0.059	1.179	0.993 - 1.398
BS	0.35	0.998	0.995 - 1.002
HCO_3	0.288	1.045	0.963 - 1.134
pH (degree of freedom; 0.1)	0.001	1.489	1.184 - 1.134

Table4 : A multiple logistic regression model using significant variables on univariate analyses showed that neurological outcomes were significantly ($p<0.05$) related to age, the time from collapse to ROSC and pH level.

ROC curves of pH on admission

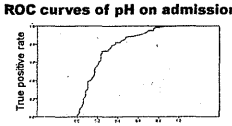


Figure3 : Receiver operating characteristic (ROC) curve showed the pH level cutoff value of 7.095 with a sensitivity of 72.7% and a specificity of 74.2% (AUC=0.768, p<0.01) for identification of a favorable neurological outcome.

Discussion

- The previous study showed that the time to ROSC over 25 minutes was strong predictive factor of poor survival and neurological outcome, none of patients in whom time to ROSC was over 25minutes had good neurological outcome.#1 In our study, the time to ROSC is similar to their study (median 25, IQR 17-38), but it was hard to define a clinical significant cut-off time to determine whether the patient would have severe neurological impairment or not because of considerable false positive rate.
- This could be affected by therapeutic hypothermia, IABP or PCPS.#1-3
- pH, time to CPR and initial VF might become additional predictive indicator of poor outcome in therapeutic hypothermia patients.
- The pH level can be a useful predictor of neurological outcomes in patients with therapeutic hypothermia. It might be the reason of this prediction that pH level can reflect systemic tissue and organ ischemia and hypoxia to ROSC. But it was difficult to estimate correctly each patient prognosis by only pH level due to a lack of reflect additional damages during and after reperfusion.
- Previous study showed significant correlation between CPR duration and pH in 87 out-of-hospital CA patients, but pH was not significant predictor of survival.#4 That study differs from our study in that TH treatment rate and time from collapse to blood sampling are not shown.

Limitation

- The data collection before therapeutic hypothermia start in this study is based on standard medical records, which are occasionally inaccurate.
- A number of pre-arrest factors have been unanalyzed; pre-arrest performance status, conditions such as diabetes, respiratory failure or renal failure could affect patients blood sampling data and outcome.
- The CPR care were relatively heterogeneous in terms clinical details; ventilator settings, perfusion and intravenous drug injection during CPR, these differences might affect blood sampling data.

Conclusion

- In this study, we could demonstrate that age, initial blood gas pH and time from collapse to ROSC associated with favorable neurological outcome in patients with therapeutic hypothermia after out-of-hospital cardiac arrest.
- pH values on admission should taken in consideration for clinical prognosis prediction about comatose patients with therapeutic hypothermia.

Reference

#1: Mauro Oddo, et al. Early predictors of outcome in comatose survivors of ventricular fibrillation and non-ventricular fibrillation cardiac arrest treated with hypothermia: a prospective study. *Crit Care Med* 2008;36:2296-2301.
#2: Kjetil Sunde, et al: Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. *Resuscitation* 2007;73:29-39.
#3: Christophe Adrie, et al: Predicting survival with good neurological recovery at hospital admission after successful resuscitation of out-of-hospital cardiac arrest: the OHCA score. *European heart journal* 2006; 27: 2840-2845.
#4: Akira Takasu, *et al: Arterial base excess after CPR*: the relationship to CPR duration and the characteristics related to outcome. *Resuscitation* 2007;73:394-399.

ROSC: return of spontaneous circulation IABP: intra aortic balloon pumping PCPS: percutaneous cardiopulmonary support AUC: Area Under the Curve

2011 AHA abstract No.13937 M. Matsuzaki

Monday Nov 15, 2010 9:00 AM - 5:00 PM

Poster Board Number: 4043

Session Type:	Abstract Poster Session		
Session Number:	APS.410.02	Session Title:	Clinical and Experimental Cardiac Arrest Horizons
Session Date:	Monday, November 15, 2010, 9:00 am - 5:00 pm	Location:	Hall A2, Core 4

Efficacy of Early Induction of Therapeutic Hypothermia for Patients with Return of Spontaneous Circulation after Out-of-Hospital Cardiac Arrest (J-PLUSE-Hypo Study)

Background: Preclinical and clinical evidence strongly supports mild therapeutic hypothermia as an effective therapy for the post-cardiac arrest syndrome. Animal data has demonstrated that the sooner cooling is initiated after return of spontaneous circulation (ROSC) from cardiac arrest, the better the outcome, although an impressive therapeutic benefit was seen in clinical studies when cooling was delayed for several hours. It is not known whether the neurologically intact survival rate will increase if the cooling is initiated on arrival at the emergency room.

Methods: We did a multicenter observational study of therapeutic hypothermia for unconscious adult patients with return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest. The J-PLUSE-Hypo committee entrusted each hospital with the timing of cooling, cooling methods, target temperature, duration, and rewarming rate. The primary endpoint was favorable neurological outcome at hospital discharge.

Results: Of the 452 unconscious adult patients who were treated with therapeutic hypothermia, 304 who were cooled to 34℃ after ROSC from out-of-hospital cardiac arrest due to ventricular fibrillation were included; 159 received hypothermia using rapid intravenous (IV) infusion of ice-cold saline or Ringer's lactate. Hypothermia was maintained using external devices or extracorporeal devices (IV group). 145 received

hypothermia without IV cold fluid. Hypothermia was maintained using external devices or extracorporeal devices (Non-IV group). The time interval from collapse to initiation of the cooling was shorter in the IV group than in the Non-IV group (a median; 53 minutes vs . 165 minutes, $p<0.001$). The IV group had higher frequency of favorable neurological outcome than the Non-IV group (69.8% vs. 55.9%, $p=0.012$). A multiple logistic-regression analysis showed that the adjusted odds ratio for favorable neurological outcome after the IV group was 1.83 (95% CI, 1.14-2.93, $p=0.012$)

Conclusion: Early initiation of cooling using rapid intravenous infusion with ice-cold fluid had neurological benefits for patients with ROSC after out-of-hospital cardiac arrest due to ventricular fibrillation.

Efficacy of Early Induction of Therapeutic Hypothermia for Patients with Return of Spontaneous Circulation after Out-of-Hospital Cardiac Arrest (J-PULSE-Hypo Study)

Masakazu Matsuzaki, Ken Nagao, Taketomo Soga, Hiroshi Nonogi, Hiroyuki Yokoyama, Naohiro Yonemoto and J-PULSE-Hypo investigators/ J-PULSE-Hypo Study Group

J-PULSE hypothermia registry

Background

- Early induction of hypothermia can be instituted easily and inexpensively with intravenous ice-cold fluids (2000mL or 30mL/kg), but ice-cold fluids alone cannot be used to maintain hypothermia.
- Several clinical studies have demonstrated that early infusion of ice-cold fluids had a neurological benefit for patients with ROSC after out-of-hospital cardiac arrest.

J-PULSE hypothermia registry

Purpose

- We investigated the efficacy of early induction of hypothermia using intravenous ice-cold fluids.

Methods

Multicenter Registry Study With Therapeutic Hypothermia After Cardiac Arrest in Japan (J-PULSE-HYPO)

J-PULSE-Hypo (Japanese Population-based Utstein-style study with defibrillation and basic / advanced Life Support Education and implementation-Hypothermia)

Study Population

Patients with therapeutic hypothermia after cardiac arrest from 2005 to 2009 in each hospitals

Criteria

Inclusion Criteria:

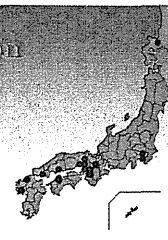
- Adult patients who remained unconscious after resuscitation from out-of-hospital or inhospital cardiac arrest
- Presented the stable hemodynamics with drug treatments or mechanical supporting system including IABP or PCPS

Exclusion Criteria:

- Patients with,
  - pregnancy
  - acute aortic dissection
  - pulmonary thromboembolism
  - drug poisoning
  - poor daily activity

J-PULSE hypothermia registry

Study Organization



Principle Investigator:
Hiroshi Nonogi

Working members:
Ken Nagao, Hiroyuki Yokoyama, Yoshio Tahara, Shinichi Shirai, Shunji Kasaoka, Kazunori Kashiwase, Yuichi Motomura, Tomotaka Sawano, Mamoru Hase, Yuji Yasuga, Nobuaki Kokubu, Naoyuki Ohtani Hideaki Arimoto, Yasuhiro Kuroda, Hiroshi Hazui

Biostatisticians:
Naohiro Yonemoto, Akiko Kada

Participating institution:

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Nihon University Surugadai Hospital
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Saga University Hospital
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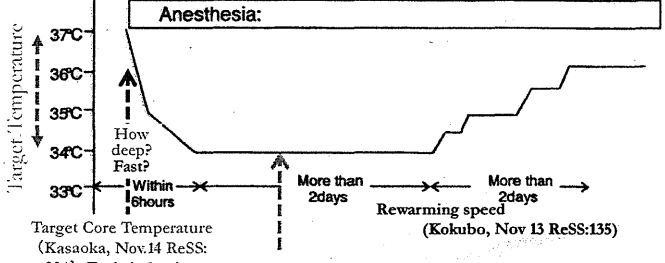
Kagawa University Hospital
Sapporo Medical University Hospital
Yokohama City University Medical Center
Kokura Memorial Hospital
Saiseikai Senri Hospital
Osaka City General Hospital
Mishima Emergency critical Center
Sumitomo Hospital

J-PULSE hypothermia registry

10 Clinical Questions from J-PULSE-Hypo in 2010

Patients characteristic

Initial Patients Evaluation (blood exam.) (Toh,Nov 13 ReSS:133, Kasai, Nov 14 ReSS:275, Kashiwase, Nov 14 Ress:282, Shirai, Nov 15 APS 4048),Non-VF (Tahara, Nov 13 ReSS: 137), PCPS with Hemodynamic Compromised State (Kokubu, Nov 14 Ress:262)



Target Core Temperature (Kasaoka, Nov.14 ReSS: 284), Early induction (Matsuzaki, Nov.15 APS 4043)

Windows of Opportunity for Therapy (Soga, Nov 14 Ress:285)

J-PULSE hypothermia registry

Protocol of Hypothermia

- The anesthetic agent and the muscle relaxant were chosen freely.
- The methods of initiation or maintenance of hypothermia was attempted by one of the following four devices of two methods;
  1) Surface cooling (a: Cooling Blanket (Blanketrol II, CSZ medical, Cincinnati, OH, USA, b: Cooling device with self-adhesive, hydrogel-coated pads (Arctic Sun, Medivance, Louisville, KY, USA).
  2) Direct blood cooling (c: Extracorporeal direct blood cooling (KTEK-III, Kawasumi, Tokyo, Japan, d: Endovascular cooling device (CoolGard 3000, Alsius, Irvine, CA, USA).
- Mild hypothermia (32-34℃) was maintained for 12-72hours.
- Re-warming was conducted slowly and gradually and took at least 12-72 hours.

☆ The protocol of hypothermia was established by each institution.

J-PULSE hypothermia registry

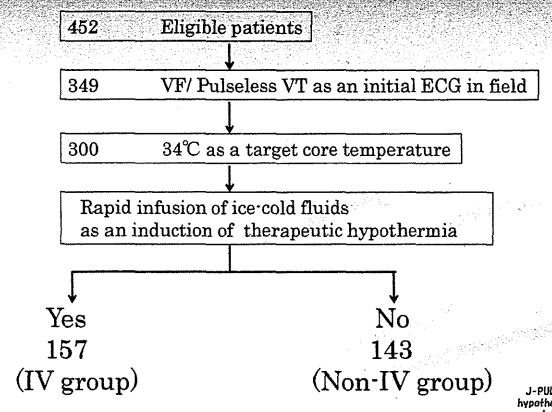
Study Endpoints

The primary endpoint of this study was a favorable neurological outcome at 30 days, defined according to the Glasgow-Pittsburgh cerebral performance category of 1 (good performance) or 2 (moderate disability) on a 5-category scale; the other categories were 3 (severe disability), 4 (vegetative state), and 5 (death).

The secondary endpoint was survival to hospital discharge (Glasgow-Pittsburgh cerebral performance category of 1, 2, 3, or 4) or death at 24 hours, 7 days, 30 days.

J-PULSE hypothermia registry

Patients



J-PULSE hypothermia registry

Background

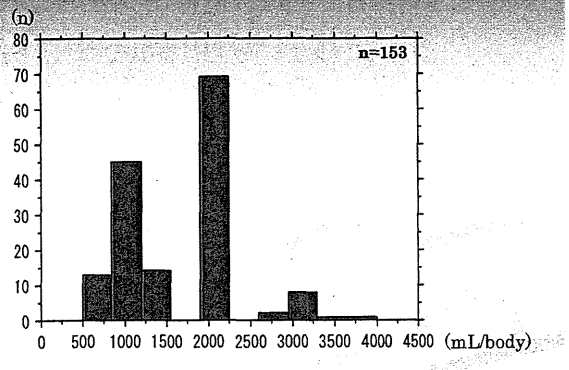
	IV Group (n=157)	Non-IV Group (n=143)	p value
Age (median, IQR; years)	60 (52-68)	62 (53-69)	0.37
Men	131 (83%)	119 (83%)	0.96
Bystander CPR	77 (49%)	78 (55%)	0.34
From collapse to ROSC (median, IQR; min)	18 (12-30)	18 (10-35)	0.84
Core temperature on hospital arrival (℃)	35.8±0.9 (n=125)	35.8±0.9 (n=123)	0.99
Causes of cardiac arrest			0.49
Acute coronary syndrome	105 (67%)	92 (64%)	
Arrhythmia	15 (9%)	18 (13%)	
Cardiomyopathy	14 (9%)	8 (6%)	
Unknown	23 (15%)	25 (17%)	

J-PULSE hypothermia registry

	IV Group (n=157)	Non-IV Group (n=143)	p value
Time interval from collapse to induction of hypothermia (median, IQR; min)	53 (32-80)	165 (67-230)	<0.001
Time interval from collapse attainment to 34℃ (median, IQR; min)	250 (143-410)	352 (210-518)	0.01
Introduction of IABP (*n*)	60 (38%)	62 (43%)	0.82
Introduction of PCPS (*n*)	30 (19%)	41 (28%)	0.52
Techniques of cooling maintenance (n)			0.03
Direct blood cooling	93 (59%)	61 (43%)	
Surface cooling	61 (39%)	79 (55%)	
Combined cooling	1 (1%)	2 (1%)	
Unknown	2 (1%)	1 (1%)	
Cooling duration of 34℃ (n)			0.90
<24 hours	76 (48%)	68 (47%)	
24-48 hours	59 (38%)	58 (41%)	
48-72 hours	17 (11%)	14 (10%)	
Unknown	5 (3%)	3 (2%)	
Rewarming duration (n)			0.13
<24 hours	32 (20%)	35 (25%)	
24-48 hours	41 (26%)	47 (33%)	
48-72 hours	43 (28%)	40 (28%)	
72≦ hours	28 (18%)	14 (10%)	
Unknown	13 (8%)	6 (4%)	

J-PULSE hypothermia registry

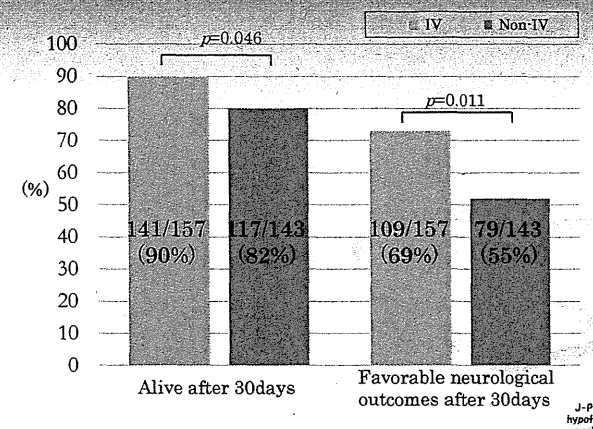
Volume of infusion of ice-cold fluid in IV group



The minimum: 500 mL/body
The maximum: 4000 mL/body
The mean: 1621±689 mL/body
The median: 2000 mL/body

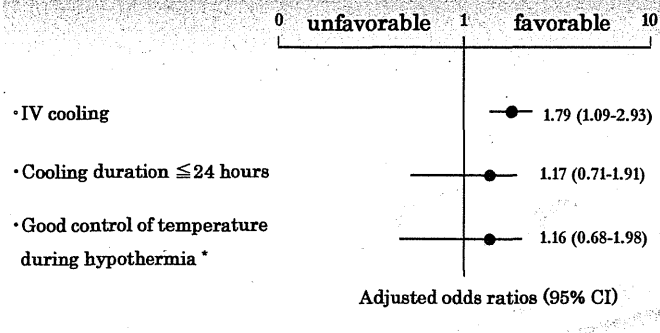
J-PULSE hypothermia registry

Study Endpoints



J-PULSE hypothermia registry

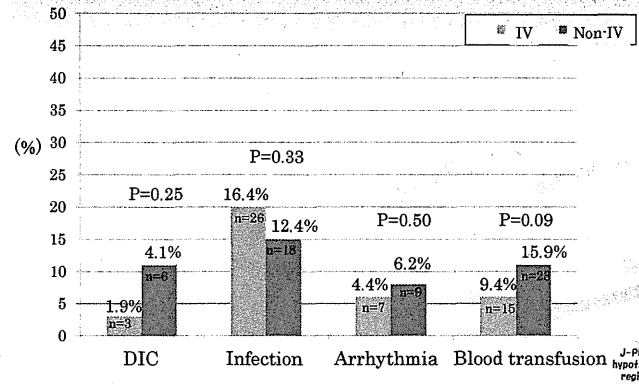
Multivariate Logistic Regression Analysis for Favorable Neurological Outcome (n=300)



* This shows the case that we were able to control at less than 34±1℃ from beginning to end.

J-PULSE hypothermia registry

Complications during hypothermia



J-PULSE hypothermia registry

Discussion

- Although the core temperature did not achieve at 34℃ during the infusion of ice-cold fluids, early induction of hypothermia using intravenous ice-cold fluids was superior to non-IV ice-cold fluids in terms of neurological benefit.
- A loss of time was caused because hypothermia for the patients of Non-IV group was often introduced after coronary arteriography (CAG), percutaneous coronary intervention (PCI), CT scan and so on in ICU.
- The proportion of patients with any complications did not differ significantly between the two groups.
- Because early induction of hypothermia with intravenous ice-cold fluids can be instituted rapidly, easily, safely and inexpensively, this method should be conducted positively.

J-PULSE hypothermia registry

Limitation

- The J-PULSE-Hypo Study was not a randomized control trial. The induction, maintenance and rewarming of hypothermia were placed under the protocols of each institutions.
- We could not conclude about the volume and the speed of optimal infusion therapy in this study.

J-PULSE hypothermia registry

Conclusion

Early induction of hypothermia using intravenous ice-cold fluids was associated with better neurological outcomes.

J-PULSE hypothermia registry

Prognostic significance of the combination of percutaneous cardiopulmonary assisted devices with mild hypothermia in patients with out-of-hospital cardiac arrest: Insights from J-Pulse Hypo-registry

Nobuaki Kokubu, Hiroyuki Yokoyama, Nobuhito Yagi, Mamoru Hase, Kazufumi Tsuchihashi, Tetsuji Miura, Naohiro Yonemoto, Ken Nagao, Hiroshi Nonogi

Background: Prognostic significance of therapeutic hypothermia (TH) in patients with cardiogenic shock who require percutaneous cardiopulmonary assisted devices (PCPS) is not clear. The aim of this study was to assess whether combination of PCPS with TH affords clinical benefits in terms of the 30-day mortality and favorable neurologic outcome (FNO).

Methods: Five years (2005-2009) data from 452 patients treated with TH were available in the multicenter registry in Japan (J-Pulse-Hypo registry), for analysis of efficacy of TH in out-of-hospital cardiac arrest patients. The patients with hemodynamic compromised states were treated with PCPS. FNO was defined as cerebral performance category 1 and 2.

Results: Of total 452 cases with out-of-hospital cardiac arrest patients, PCPS was used in 102 (22.6%) patients. Although there was no significant differences in age, gender, the presence of bystanders, initial ECG findings between PCPS group and non-PCPS group, severer hemodynamic derangements in the PCPS group compared with those in the non-PCPS group were indicated by inter-group differences in maximum blood pressure (BP), blood sugar, pH, and base excess of arterial blood gas at admission and rate of return of spontaneous circulation (ROSC) before admission. The PCPS group was more frequently treated with PCI and IABP than non-PCPS group. The 30-day mortality of PCPS group was significantly higher than that of non-PCPS group (42.6 % vs.13.5%, $p<0.01$). However, in 358 patients surviving at 30 days, FNO rate of PCPS group (n=58) was comparable to that of non-PCPS group (n=300) (60% vs. 72%, p=0.09), though hemodynamic and metabolic parameters upon admission predicted poorer prognosis in the subgroup of the PCPS group as those in total PCPS group. PCPS group with FNC was more often witnessed at cardiac arrest, more likely to use AED and showed higher rate of ROSC before admission than that with non-FNC.

Conclusions: In patients with out-of-hospital cardiac arrest requiring PCPS, improvement of FNO after surviving acute phase might be afforded by combination of TH with PCPS. Witnessed cardiac arrest, use of AED and ROSC before admission may be important factors of FNC for patients treated with PCPS under TH.

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Prognostic significance of the combination of percutaneous cardiopulmonary assisted devices with mild hypothermia in patients with out-of-hospital cardiac arrest: Insights from J-Pulse Hypo-registry

Nobuaki Kokubu, Hiroyuki Yokoyama#,
Nobuhito Yagi#, Mamoru Hase, Kazufumi Tsuchihashi,
Tetsuji Miura, Naohiro Yonemoto*,
Ken Nagao$, Hiroshi Nonogi#

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Presenter Disclosure Information

Nobuaki Kokubu, MD
Prognostic significance of the combination of percutaneous cardiopulmonary assisted devices with mild hypothermia in patients with out-of-hospital cardiac arrest:
Insights from J-Pulse Hypo-registry

FINANCIAL DISCLOSURE: None

UNLABELED/UNAPPROVED USES DISCLOSURE: None

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Backgrounds

Although it has been reported that therapeutic hypothermia (TH) improves neurological outcomes of patients with cardiac arrest, procedures of the hypothermia remain to be established.

Particularly, impact of cardiopulmonary assisted devices (PCPS) to treat the patients with prolonged cardiogenic shock under TH has not been sufficiently studied.

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Objective

The aim of this study was to assess whether combination of PCPS with TH affords clinical benefits in terms of the 30-day mortality and favorable neurologic outcome.

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Study Populations

452 consecutive patients after resuscitation from out-of-hospital cardiac arrest treated with TH in the multicenter registry in Japan (J-Pulse-Hypo registry) for 5 years (2005-2009).

<Inclusion criteria>
- Adult patients who remained unconscious after resuscitation from out-of-hospital cardiac arrest.
- Presented the stable hemodynamics with treatment or mechanical supporting system including IABP or cardiopulmonary bypass (CPB).

<Exclusion criteria>
- pregnancy
- acute aortic dissection
- pulmonary thromboembolism
- drug poisoning
- poor daily activity

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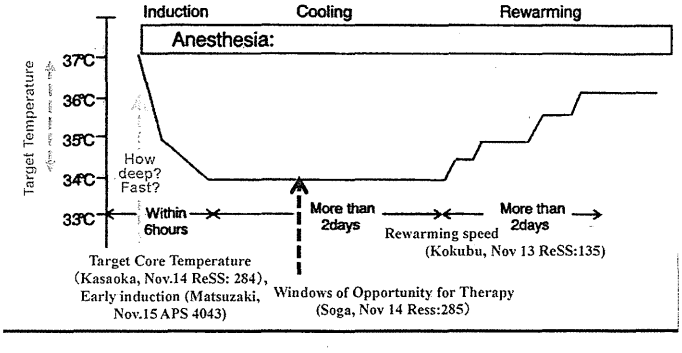
10 Clinical Questions from J-PULSE-Hypo in 2010

Patients characteristic

Initial Patients Evaluation (blood exam.) (Toh,Nov 13 ReSS:133, Kasai, Nov 14 ReSS:275, Kashiwase, Nov 14 Ress:282, Shirai, Nov 15 APS 4048),Non-VF (Tahara, Nov 13 ReSS: 137), PCPS with Hemodynamic Compromised State (Kokubu, Nov 14 Ress:262)



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Study Organization

Principle Investigator:
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Working members:
Ken Nagao, Hiroyuki Yokoyama, Yoshio Tahara, Shinichi Shirai, Shunji Kasaoka, Kazunori Kashiwase, Yuichi Motomura, Tomotaka Sawano, Mamoru Hase, Yuji Yasuga, Nobuaki Kokubu, Naoyuki Ohtani, Hideaki Arimoto, Yasuhiro Kuroda, Hiroshi Hazui

Biostatisticians:
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Participating institution:

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Hiroshima City Hospital	Osaka City General Hospital
Yamaguchi Univrsity Hospital	Mishima Emergency critical Center
Kagawa University Hospital	Sumitomo Hospital

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Methods-1

Selection of cooling procedure was left to each institution.

The patients with hemodynamic compromised state were treated with PCPS (PCPS group).

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Methods-2

452 patients were enrolled in the J-Pulse-Hypo registry

PCPS group: n=102 (23%) | **Non-PCPS group: n=350 (77%)**

TH in 18 patients were discontinued by any cause

TH in 20 patients were discontinued by any cause

PCPS group: n=84 | **Non-PCPS group: n=330**

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Methods-3

We evaluated clinical characteristics of the patients treated with PCPS under TH, and factors to influence on favorable neurologic outcome in patients treated with PCPS.

We used Pittsburg cerebral performance category (CPC) score to assess the favorable neurological outcomes.

<CPC score>

1. Good cerebral performance
2. Moderate cerebral disability
3. Severe cerebral disability
4. Coma or vegetative state
5. Brain death

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Clinical characteristics of patients treated with TH from J-pulse-hypo registry

	All patients (n = 414)
Age (years)	58± 13
Male	343 (83%)
Initial cardiac rhythm	
Ventricular fibrillation	290 (70%)
Pulseless electrical activity	58 (14%)
Asystole	34 (8%)
Unidentified	29 (7%)
Witnessed cardiac arrest	357 (86%)
AED use	52 (13%)
Bystander CPR	209 (50%)
ROSC before admission	399 (96%)
Acute coronary syndrome	248 (60%)
Emergency PCI	182 (44%)
PCPS use	84 (20%)
IABP use	165 (40%)
Survival rate at 30 days	348 (84%)

Data are presented as mean value ± SD or number (%) of patients.
AED, automated external defibrillator; CPR, cadiopulmonary resuscitation; IABP, intra aortic balloon pumping; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation

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Clinical characteristics between PCPS group and non-PCPS group

	PCPS group (n = 84)	Non-PCPS group (n = 330)	p value
Age (years)	59± 11	58 ± 14	0.58
Male	73 (87%)	270 (82%)	0.26
Initial cardiac rhythm			0.44
Ventricular fibrillation	55 (65%)	235 (71%)	
Pulseless electrical activity	15 (18%)	43 (13%)	
Asystole	6 (7%)	28 (8%)	
Unidentified	8 (10%)	21 (6%)	
AED use	13 (15%)	39 (12%)	0.41
Witnessed cardiac arrest	69 (82%)	288 (87%)	0.24
Bystander CPR	46 (55%)	163 (49%)	0.38
ROSC before admission	82 (98%)	317 (96%)	0.47
Acute coronary syndrome	59 (70%)	189 (57%)	0.03
Emergency PCI	50 (60%)	132 (40%)	<0.01
IABP use	65 (77%)	100 (30%)	<0.01

Data are presented as mean value ± SD or number (%) of patients.
AED, automated external defibrillator; CPR, cadiopulmonary resuscitation; IABP, intra aortic balloon pumping; PCI, percutaneous coronary intervention; ROSC, return of spontaneous circulation

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Cooling parameters and laboratory value on admission between PCPS group and non-PCPS group

	PCPS group (n = 84)	Non-PCPS group (n = 330)	p value
Maximam BP after ROSC	116± 29	131± 29	<0.01
Initiation cooling to target temperature (min)	101 ± 120	285± 233	<0.01
Cooling duration (hour)	30± 11	33 ± 14	0.09
Arterial blood pH	7.07± 0.20	7.16± 0.18	<0.01
Arterial blood base excess(mmol/l)	-16.1± 6.9	-11.5 ± 5.9	<0.01
Blood sugar(mg/dl)	304± 114	261± 87	<0.01
Creatinine(mg/dl)	1.3± 1.4	1.5± 1.9	0.29
Potassium(mEq/l)	4.1± 1.0	4.0± 0.9	0.27
Hemoglobin(g/dl)	13± 3	14 ± 2	0.03

Data are presented as mean value ± SD or number (%) of patients.

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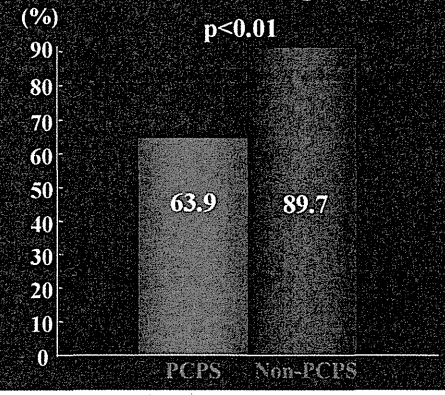
Survival rate at 30 days between PCPS group and non-PCPS group



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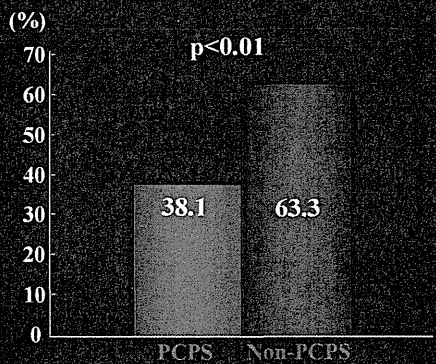
CPC 1 or 2 rate at 30 days



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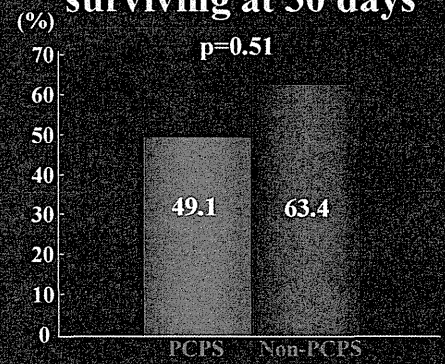
CPC 1 rate in 348 patients surviving at 30 days



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Comparison between CPC 1/2 category and CPC 3~5 category in PCPS group

	CPC 1/2 group (n = 32)	CPC 3~5 group (n = 52)	p value
Age (years)	58± 12	59 ± 10	0.72
AED use	9 (28%)	4 (8%)	0.01
Ventricular fibrillation	22 (69%)	33 (63%)	0.62
Witnessed cardiac arrest	30 (94%)	39 (75%)	0.02
Bystander CPR	17 (53%)	29 (56%)	0.81
ROSC before admission	32 (100%)	50 (96%)	0.16
Acute coronary syndrome	23 (72%)	36 (69%)	0.80
Emergency PCI	16 (50%)	34 (65%)	0.16
IABP use	19 (59%)	46 (88%)	<0.01
Maximam BP after ROSC(mmHg)	111 ± 30	87 ± 30	0.12
Initiation cooling to target temperature(min)	108 ± 157	96 ± 92	0.64
Cooling duration (hour)	31± 10	29 ± 11	0.43
Arterial blood pH	7.14± 0.18	7.02 ± 0.20	0.02
Arterial blood Base Excess(mmol/l)	-14.2± 7.4	-17.3 ± 6.3	0.06
Blood Sugar(mg/l)	274± 103	322± 118	0.07

Data are presented as mean value ± SD or number (%) of patients

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Sapporo Medical University

Summary

Although there was no significant differences in age, gender, the presence of bystanders, initial ECG findings between PCPS group and non-PCPS group, severer hemodynamic derangements in the PCPS group compared with those in the non-PCPS group were indicated by inter-group differences in maximum blood pressure, blood sugar, pH, and base excess of arterial blood gas at admission. The PCPS group was more frequently treated with PCI and IABP due to acute coronary syndrome than non-PCPS group.

The survival and CPC 1 or 2 rate in PCPS group at 30 days was significantly lower than that of non-PCPS group. However, in 348 patients surviving at 30 days, CPC 1 rate of PCPS group was comparable to that of non-PCPS group.

Patients with CPC 1 or 2 in PCPS group was more often witnessed at cardiac arrest, more likely to use AED than that with CPC 3~5.

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Conclusions

The patients treated with TH using PCPS, even who were in very ill condition, were reached CPC 1 or 2 rate at 30 days up to 38.1%.

Improvement of favorable neurologic outcome after surviving acute phase might be afforded by combination of TH with PCPS.

Witnessed cardiac arrest with use of AED may be important factors of favorable neurologic outcome for patients treated with PCPS under TH.

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Anemia, High LDH, Hyperglycemia, and Low pH on Admission Are Associated with Poor Neurological Outcome in Out-of-hospital Cardiac Arrest Patients Treated with Hypothermia Therapy from Multicenter Hypothermia Registry in Japan: J-PULSE- Hypo Registry

Kazunori Kashiwase, Yasunori Ueda, Naohiro Yonemoto, Hiroyuki Yokoyama, Ken Nagao, Hiroshi Nonogi and J-PULSE-Hypo Investigators.

Background: Although mild hypothermia (MH) has neurological benefits for patients with return of spontaneous circulation (ROSC) after out-of-hospital ventricular fibrillation cardiac arrest, there are limited data about predictors of good neurological outcome in these patients.
Method: Five years (2005-2009) data were available for 452 patients treated with MH in the multicenter registry in Japan (J-Pulse-Hypo). We included 389 patients with initial blood examination and atrial gas sampling. We examined the relationship between initial blood examination data and neurological outcome. Primary end point of this study was favorable neurologic outcome (cerebral performance category (CPC) 1 and 2) rate at 30 days.
Result: According to neurologic outcome at 30 days, we divided all cases into two groups: the favorable outcome group (n=221) and the unfavorable outcome group (n=168). Favorable outcome rate at 30 days was 56.8%. By the multiple logistic regression analysis, age, witness of cardiac arrest, ROSC before admission, hematocrit (HCT), lactate dehydrogenase (LDH), glucose (BS), and pH were revealed as the independent predictors of 30 days favorable outcome. Cutoff values of age, HCT, LDH, BS and pH were obtained by receiver operating characteristic (ROC) curve (shown in Table).
Conclusion: Anemia, high LDH, hyperglycemia, and low pH on admission were significantly associated with poor neurological outcome even among patients treated with hypothermia therapy.

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Abstract

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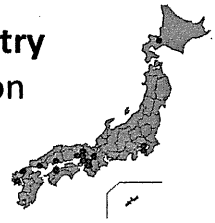
J-Pulse-Hypo registry
Study Organization



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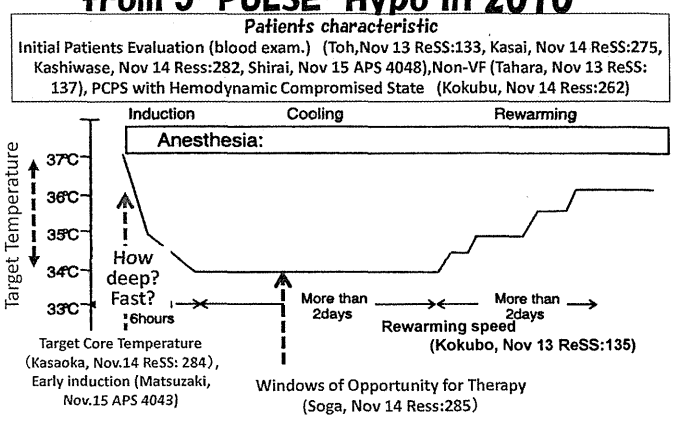
10 Clinical Questions from J-PULSE-Hypo in 2010



Background

Although mild hypothermia has neurological benefits for patients with return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest, there are limited data about predictors of good neurological outcome in these patients.

Objective

To clarify the relationship between initial blood examination data and neurological outcome in patients with ROSC after out-of-hospital cardiac arrest treated with mild hypothermia .

Methods: Population

452 patients — treated with mild hypothermia in the multicenter registry in Japan (**J-Pulse-Hypo registry**) in 2005 -2009.

↓

389 patients — Initial blood examination and gas sampling were available.

The exclusion criteria
1)less than 15 years old
2)pregnant woman
3)aortic dissection with or without cardiac tamponade
4)cerebral hemorrhage or subarachnoid hemorrhage
5)known terminal disease.

Methods: Mild hypothermia

After sedation with analgesia and in some cases, cold intravenous fluid (4 Celsius degree) was administered over 30-60 min to initiate hypothermia.

The methods of initiation or maintenance of hypothermia
1) Surface cooling
   a: Cooling Blanket (Blanketrol II)
   b: Cooling device with self-adhesive, hydrogel-coated pads (Arctic Sun)
2) Blood cooling
   c: Extracorporeal direct blood cooling (KTEK-III)
   d: Endovascular cooling device (CoolGard 3000)

Mild hypothermia (32-34 ° C) was maintained for 24-72hours. Rewarming was conducted slowly and gradually and took at least 24-72 hours. Protocol of hypothermia was determined in each institutional state.

Methods: Endpoint

All cases were divided into two groups by cerebral performance category (CPC) at 30 days.

The favorable neurologic outcome group: CPC 1 and 2

221 patients (56.8%)

The unfavorable neurologic outcome group: CPC 3 to 5

168 patients (43.2%)

Results (1) Baseline Characteristics

	the favorable outcome group (n = 221)	the unfavorable outcome group (n = 168)	p value
Age (y)	55 ± 14	62 ± 12	< 0.001
Witness of cardiac arrest	91%	83%	0.015
ROSC before admission (%)	77%	36%	< 0.001
VT/VF in initial rhythm (%)	78%	57%	< 0.001
Time interval from collapse to ROSC (min)	28± 38	43 ± 25	< 0.001

Results (2) Initial blood examination

	the favorable outcome group (n = 221)	the unfavorable outcome group (n = 168)	p value
WBC ($10^3/mm^3$)	12.4 ± 8.20	12.3 ± 5.90	0.865
Hematocrit (%)	42 ± 6.0	39 ± 6.8	< 0.001
Potassium (mEq/L)	3.9 ± 0.81	4.3 ± 1.1	< 0.001
Blood urea nitrogen (BUN) (mg/dL)	19 ± 12	22 ± 15	0.018
Creatinine (mg/dL)	1.4 ± 1.8	1.6 ± 1.7	0.271
Blood sugar (mg/dL)	252 ± 77.1	296 ± 108	< 0.001
Lactate dehydrogenase (LDH) (mg/dL)	379 ± 158	434 ± 194	0.002
pH	7.21 ± 0.147	7.03 ± 0.196	< 0.001
PaO_2 (mmHg)	287 ± 163	231 ± 169	0.01
$PaCO_2$ (mmHg)	45 ± 18	62 ± 29	< 0.001

Results (3) Multivariate analysis of 30 days favorable neurologic outcome

Variables	Good Outcome	Odds Ratio	95% C.I	p value
Age (per 10 years)	Low	1.411	1.147-1.737	0.001
Witness of cardiac arrest	Yes	2.241	1.036-4.8349	0.040
ROSC before admission	Yes	2.605	1.443-4.702	0.001
VT/VF in initial rhythm	Yes	1.410	0.795-2.499	0.240
Hematocrit (per 2%)	High	1.108	1.012-1.213	0.026
Potassium (per 0.1 mEq/L)	Low	1.022	0.989-1.056	0.196
BUN (per 1 mg/dL)	Low	1.007	0.984-1.032	0.544
Blood sugar (per 20 mg/dL)	Low	1.086	1.022-1.154	0.008
LDH (per 20 mg/dL)	Low	1.040	1.011-1.070	0.007
pH (per 0.1)	High	1.479	1.246-1.756	< 0.001
PaO_2 (per 10 mmHg)	High	1.002	0.986-1.019	0.806

Results (4) ROC curve analysis

Variables	Cutoff value	Sensitivity	Specificity	AUC
Age	60.5	60.7%	58.8%	0.634
Hematocrit	41.05	58.6%	57.1%	0.616
LDH	346.50	57.7%	56.1%	0.591
Blood sugar	260.50	60.7%	60.6%	0.635
pH	7.165	71.2%	70.7%	0.761

Summary

There were significant differences in hematocrit, potassium, LDH, blood sugar, pH, and PaCO2 between the favorable and the unfavorable outcome groups.

By the multiple logistic regression analysis, low hematocrit, high LDH, high blood sugar, and low pH were identified as the independent predictors of 30-day unfavorable outcome in addition to high age, no witness of cardiac arrest, and no ROSC before admission.

Discussion

Cardiac arrest and oxygen deficiency cause increase of LDH and blood sugar, and progression of acidosis. In this registry, these factors were also associated with poor neurologic outcome.

In patients with cardiogenic shock, high blood glucose level on ER arrival provides predictive information (the adjusted odd ratio for a glucose level of 165 mg/dL or more was 5.8 (95% confidence interval 1.0–32.8), p=0.047).

(Tada T et al. Circ J 2006; 70: 1064–1069)

Conclusion

Anemia, high LDH, hyperglycemia, and low pH on admission were significantly associated with poor neurological outcome even among patients treated with hypothermia therapy.

Presenter Financial Disclosure

Kazunori Kashiwase, MD

Title: Anemia, High LDH, Hyperglycemia, and Low pH on Admission Are Associated with Poor Neurological Outcome in Out-of-hospital Cardiac Arrest Patients Treated with Hypothermia Therapy from Multicenter Hypothermia Registry in Japan: J-PULSE- Hypo Registry

DISCLOSURE INFORMATION:
There is no relationship related to this presentation.

AHA 2010 Abstract

Title: Impact of Target Core Temperature on Neurological Outcome of Cardiac Arrest Patients Treated with Therapeutic Hypothermia

Shunji Kasaoka, Ryosuke Tsuruta, Ken Nagao, Naohiro Yonemoto, Hiroyuki Yokoyama, Hiroshi Nonogi and the J-PULSE-Hypo Investigators

Introduction: Therapeutic hypothermia improves neurological outcome in patients with out-of-hospital cardiac arrest. However, ideal target core temperature remains unclear. We investigated the effects of target core temperature on neurological outcome of cardiac arrest patients treated with therapeutic hypothermia.

Methods: We conducted a multi-center registry at 14 institutions to evaluate the effect of therapeutic hypothermia on out-of-hospital cardiac arrest between January 2005 and December 2009. The study committee entrusted each hospital with the timing of cooling, cooling methods, target temperature, duration, and rewarming rate. Enrolled patients were divided into the L group (32-33°C) and the M group (34-35°C) according to target core temperature, and neurological outcome was compared at hospital discharge. A favorable outcome was defined as a Cerebral Performance Category (CPC) of 1-2.

Results: A total of 452 patients were enrolled into the registry. Two patients were excluded because target temperature was unknown. The median interval from collapse to return of spontaneous circulation was 25 minutes. Between the L group (n=43) and the M group (n=407), the rates of survivors (77% vs. 77%) and favorable outcomes (60% vs. 55%) were not statistically different. As compared with the M group, the L group had significantly longer cooling time (43 hrs vs. 25 hrs, p=0.0005) and lower rate of core cooling method (28% vs. 50%, p=0.0056). The L group had significantly higher rates of inadequately controlled core temperature (49% vs. 29%, p=0.0073) and side effects of hypothermia (48% vs. 29%, p=0.014). Of the side effects, the rate of arrhythmia was significantly different (19% vs. 5%, p=0.0004).

Conclusions: This study indicated that target core temperature did not affect neurological outcome of cardiac arrest patients. In addition, the lower target core temperature may cause increase of side effects. To control core temperature adequately, further studies of cooling methods and management are needed.