J-PULSE hypothermia registry
UMIN：臨床試験登録

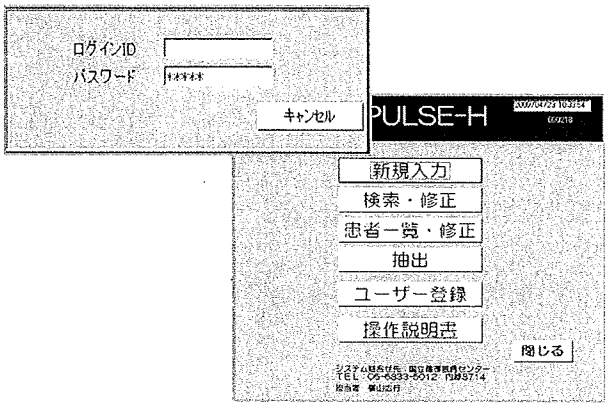
選択基準	2005年から2009年までの5年間の各施設で心原性心停止後に低体温療法を施行した患者 心拍再開した病院外あるいは院内心停止症例のうち、 1. 18歳以上の症例 2. 心拍再開後に循環動態が安定している（薬物あるいは補助循環で安定していても可） 3. 心拍再開後も昏睡状態にある患者で、低体温療法を施行した患者
除外基準	妊婦、大動脈解離、肺動脈塞栓症、薬物中毒発症前ADL不良の患者

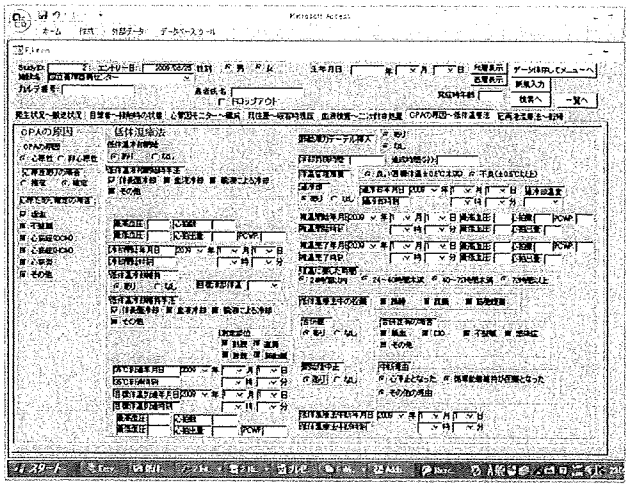
J-PULSE hypothermia registry

共同研究医療機関（16施設）

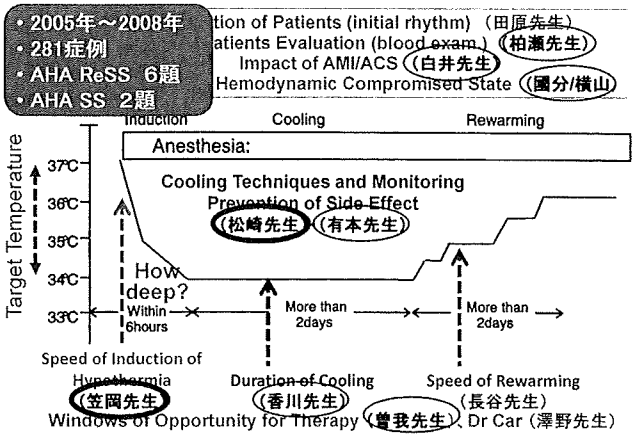
- 札幌医大付属病院　救急集中治療部
- 駿河台日本大学病院　循環器科（長尾）
- 横浜市立大学付属市民総合医療センター 高度救命救急センター
- 北里大学病院　救急救命センター
- 国立循環器病センター　心臓血管内科・CCU（野々木、横山）
- 大阪府三島救命救急センター
- 大阪市立総合医療センター　救命救急センター
- 大阪警察病院
- 大阪府済生会千里病院
- 住友病院　循環器内科
- 神戸市立医療センター中央市民病院 救命救急センター
- 広島市民病院　循環器科
- 香川大学医学部付属病院
- 山口大学医学部付属病院 先進救急医療センター
- 佐賀大学医学部附属病院 救命救急センター
- 小倉記念病院循環器科

J-PULSE hypothermia registry





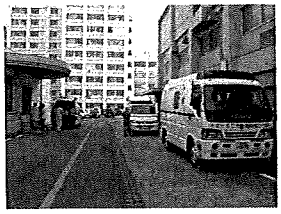
Clinical Question



	Presentation		Session
☑	3309/5052 - Impact of Target Core Temperature on Neurological Outcome of Cardiac Arrest Patients Treated With Therapeutic Hypothermia 目標温度について検討	Shunji Kasaoka, Ryosuke Tsuruta, Tsuyoshi Maekawa, Yamaguchi Univ Hosp, Ube, Japan; Ken Nagao, Nihon Univ, Tokyo, Japan; Naohiro Yonemoto, Hiroyuki Yokoyama, Hiroshi Nonogi, Natl Cardiovascular Ctr, Osaka, Japan; the J-PULSE-Hypo Investigators	Abstract Poster Session APS.509.01. Pulmonary Circulation and Critical Care: Advances in Hypothermia and Cellular Injury Mon, Nov 16, 9:00 AM - 5:00 PM

☑	P93 - Impact of Target Core Temperature on Neurological	Shunji Kasaoka, Ryosuke Tsuruta, Tsuyoshi Maekawa, Yamaguchi Univ Hosp,	ReSS - Saturday VI. Best Original Resuscitation Science, Moderated Poster

山口大学病院における低体温療法

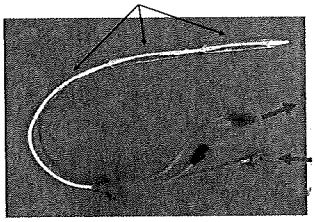


山口大学における低体温療法

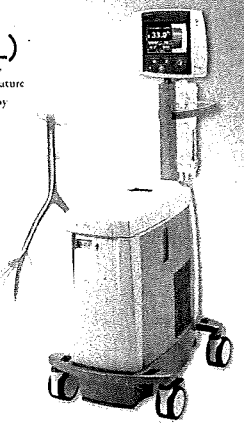
COOLGARD (ALSIUS)
↓
THERMOGARD (ZOLL)

Use Of Temperature Control Therapy

冷却用バルーン



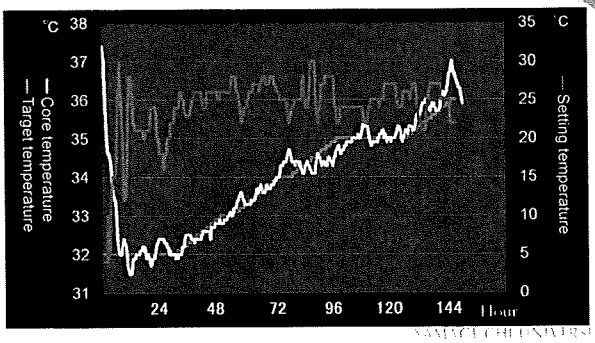
血管内冷却カテーテル
(Icy Catheter™)
8.5Fr, 38cm



心停止蘇生後の低体温療法①

体表冷却法
症例: 49歳 女性 肺塞栓症

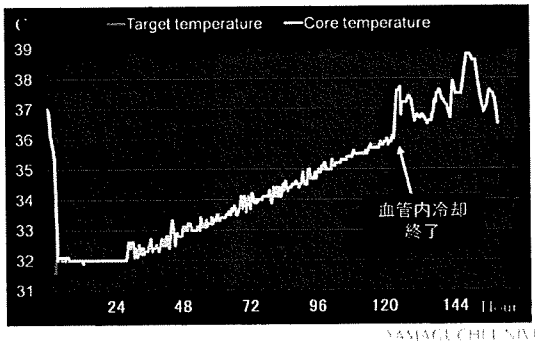
BLANKETROL™
20分毎に水温設定を調節



心停止蘇生後の低体温療法②

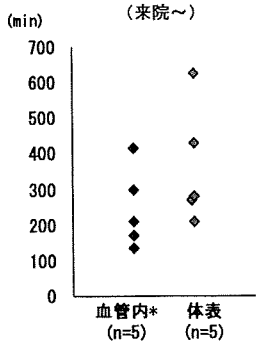
血管内冷却法
症例: 25歳 女性 VF

COOLGARD™
2時間毎に目標温度設定

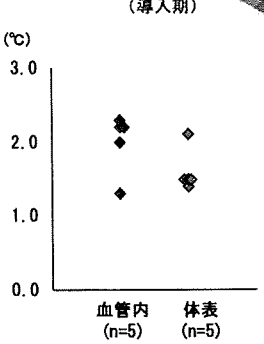


冷却法による比較 (1)

目標温度到達時間
(来院～)

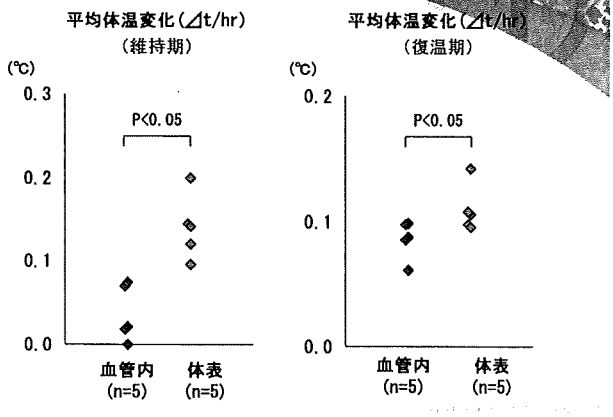


最大体温変化(max⊿t/hr)
(導入期)



＊ICに要した時間を含む

冷却法による比較 (2)



血管内冷却法の利点

優れた体温調節性

↓

低体温管理における施設間格差の減少

↓

低体温療法に関する多施設共同研究に有用

山口大学における 軽度低体温療法中の全身管理

麻　酔: Droperidol・Fentanyl, Muscle relaxant
　　血管拡張と容量負荷 (初期冷却輸液)
呼　吸: PaO_2 >100 mmHg, $PaCO_2$ 35～40 mmHg
循　環: 心係数 CI ≥ 3.0 L/min/m^2
　　脳潅流圧 CPP ≥ 60～70 mmHg
　　頭蓋内圧 ICP < 20 mmHg
代　謝: 血糖 BS 100～150 mg/dL
　　内頸静脈血 $SjvO_2$ ≥ 50～60 %
電解質: 血清 K^+ 3.5～4.5 mEq/L
血　液: 血小板 plt ≥ 5 x $10^4/\mu L$
復　温: 緩徐に行う (過剰なラジカル産生抑制)

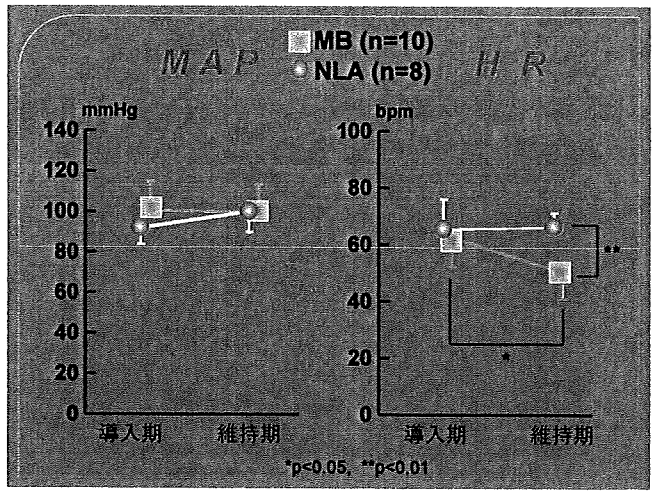
麻酔薬の特徴

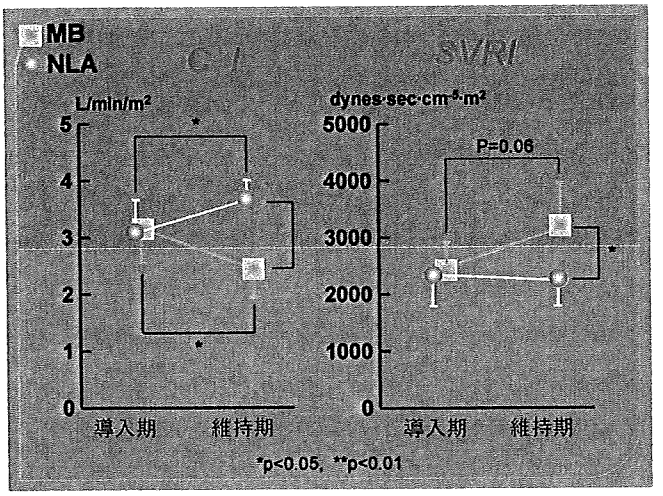
- Midazolam
  GABAアゴニスト。抑制性GABAニューロンの作用を特異的に増強して脳酸素代謝率を抑制。GABA放出を介するNaイオン細胞内取込みを抑制して脳虚血後の神経細胞の膨化を抑制。
- Doroperidol
  ブチロフェノン系神経遮断薬。鎮静作用。α-受容体遮断による血管拡張作用。
- Fentanyl
  麻薬。強力な鎮痛効果。交感神経の緊張抑制。体温中枢に作用して寒冷反応(シバリング)を抑制。
- Butorphanol
  麻薬拮抗性鎮痛薬。体温中枢に作用して寒冷反応(シバリング)を抑制。

麻　酔　法

上段:導入量
下段:維持量

	MB群	NLA群
droperidol	—	0.5 mg/kg 0.025 mg/kg/hr
fentanyl	—	5-10 μg/kg 0.02 mg/kg/day
midazolam	0.1 mg/kg 0.1-0.2 mg/kg/hr	(必要時)
butorphanol	0.01 mg/kg 0.01-0.02 mg/kg/hr	—
vecuronium	0.1 mg/kg 0.05 mg/kg/hr	0.1 mg/kg 0.05 mg/kg/hr

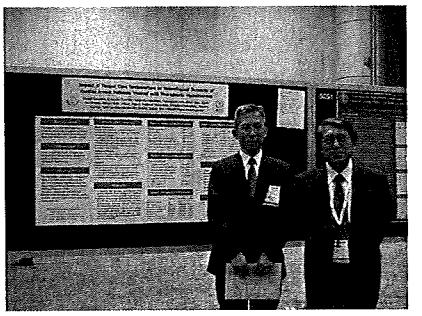




American Heart Association | ReSS
TWO-DAY EVENT | FOUR-DAY EVENT

American Heart Association | SCIENTIFIC SESSIONS 2009
Exhibits: November 15-17 | Sessions: November 14-18 | Orlando, Florida

AHAのポスター発表



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

Shunji Kasaoka, Ryosuke Tsuruta, Tsuyoshi Maekawa, Yamaguchi Univ Hosp, Ube, Japan; Ken Nagao, Nihon Univ, Tokyo, Japan; Naohiro Yonemoto, Hiroyuki Yokoyama, Hiroshi Nonogi, Natl Cardiovascular Ctr, Osaka, Japan; the J-PULSE-Hypo Investigators

AMEC

山口大学

Objective

To investigate the effects of target core temperature on neurological outcome of cardiac arrest patients treated with therapeutic hypothermia.

Methods

We conducted a multi-center retrospective study at 16 institutions to evaluate the effect of therapeutic hypothermia on out-of-hospital cardiac arrest between January 2005 and December 2008.
The study committee entrusted each hospital with the timing of cooling, cooling methods, target temperature, duration, and rewarming rate.

Methods (cont'd)

Study Population
Patients with therapeutic hypothermia after cardiac arrest from 2005 to 2008 in each hospital.

Inclusion Criteria
- Adult patients who remained unconscious after resuscitation from out-of-hospital 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, and poor daily activity.

Methods (cont' d)

Analysis

- Patients were divided into the L group (32~33°C) and the M group (34~35°C) according to target core temperature.

- Neurological outcome was compared at hospital discharge. A favorable outcome was defined as a Cerebral Performance Category (CPC) of 1-2.

Table 1. Baseline Characteristics

Number of patients	281
Age (years)	60 (51-68)
Male (%)	235 (84%)
Witnessed cardiac arrest (%)	247 (88%)
Performed bystander CPR (%)	145 (52%)
Time from collapse to ROSC (min)	18 (12-29)
Initial arrest rhythm: VF/VT (%)	226 (80%)

Table 2. Method of Hypothermia

Cooling methods	
- Surface cooling (%)	159 (57%)
- Extracorporeal circulation (%)	102 (36%)
- Intravascular catheter (%)	8 (3%)
- Infusion of ice-cold fluid (%)	135 (48%)
Duration of cooling (hours)	27 (24-48)
Target core temperature (°C)	
- 32.0 ~ 33.9 °C	35 (12%)
- 34.0 ~ 35.0 °C	246 (88%)

Table 3. Comparison of Outcome

	L group	M group	*p* Value
Number of patients	35	246	
Age (years)	52 (45-61)	61 (52-69)	0.0014
Target temperature (°C)	33 (33-33)	34 (34-34)	<0.0001
Duration of cooling (hrs)	49 (26-51)	26 (24-46)	0.0009
Surface cooling (%)	25 (71%)	134 (54%)	0.0688
Survival (%)	**26 (74%)**	**195 (79%)**	**0.5110**
Favorable outcome (%)	**18 (51%)**	**139 (57%)**	**0.5897**

Table 4. Side Effects of Hypothermia

	L group	M group	*p* Value
Inadequately controlled core temperature (%)	21 (60%)	82 (35%)	0.0050
Over-cooling (%)	**14 (40%)**	**53 (22%)**	**0.0326**
Side effects (%)	**17 (50%)**	**64 (26%)**	**0.0079**
- Arrhythmia	6 (17%)	14 (6%)	0.0256
- Infection	6 (17%)	43 (17%)	0.9608
- Blood transfusion	7 (20%)	26 (11%)	0.1541

Table 4 (cont' d) Side Effects of Hypothermia

Definition

1) Inadequately controlled core temperature:
Core temperature exceeds target temperature ± 0.5 °C

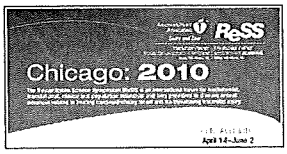
2) Over-cooling:
Core temperature decreases more than 0.5 °C from target temperature

Conclusions

1. **Target core temperature did not affect neurological outcome of cardiac arrest patients.**
2. **The lower target core temperature might cause increase of side effects.**
3. **To control core temperature adequately, further studies of cooling methods and managements are needed.**

結　語

■心原性心停止蘇生後患者に対する低体温療法は有効な治療法であるが、適応、至適温度、低体温管理法などについてさらなる検討が必要である。



4. 最重症例へのチャレンジ
低体温療法 (J-PULSE Hypothermia)
補助循環と低体温療法 (SAVE-J)

J-PLUSE Hypo & SAVE-J
日本大学医学部・駿河台日本大学病院:長尾 建
2010 Feb. 23

Disclosures
2009年12月

- 日本循環器学会・日本救急医学会など
  - 循環器救急医療委員会委員（蘇生科学委員長・AED委員・救急医療委員）
  - 救命救急法検証委員会委員、循環器終末医療委員会委員
  - 循環器病の診断と治療に関するガイドライン班員
    - AED、心筋梗塞二次予防、急性心筋梗塞(ST上昇型)、
    - 心肺蘇生・心血管救急
- 厚生労働科学研究・循環器疾患等生活習慣病対策総合研究事業
  1. 超急性期診療体制の構築の研究委員
  2. AEDを用いた心疾患の救命率向上の研究委員
  3. 高度救命処置の効果と費用の研究委員
- 総務省消防庁
  - ウツタイン統計調査部会委員
- 救急医療財団
  - AED 普及・啓発委員会委員
- 東京CCU ネットワーク学術委員会委員長

概　要

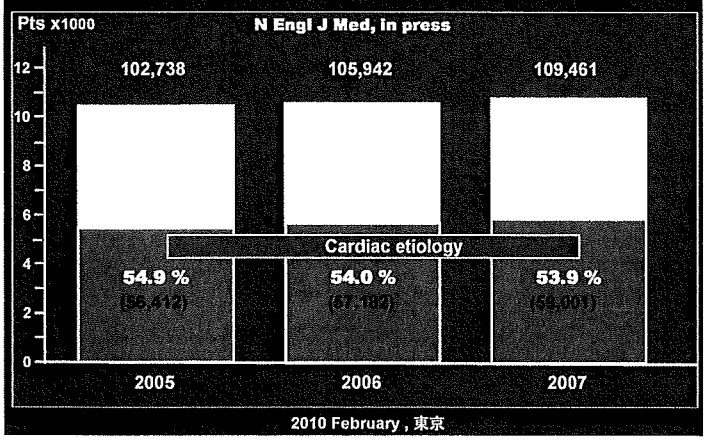
- わが国の院外心停止患者の現況
- 心停止患者に対する低体温療法のEBMとその機序
- **J-PLUSE Hypothermia**
  心停止後心拍再開するも昏睡状態にある患者に対する低体温療法; **Post-ROSC cooling**
- **SAVE-J**
  標準的蘇生法が無効な心停止患者に対するPCPSを用いた低体温療法; **Intra arrest cooling**

2010 February , 東京

●わが国の院外心停止患者の現況

2010 February , 東京

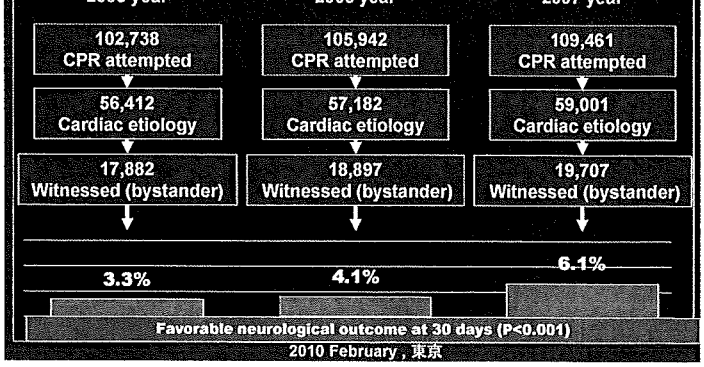
わが国の Utstein style statistical working group



2010 February , 東京

わが国の Utstein style statistical working group　N Engl J Med, in press

目撃された院外心疾性心停止30日後の良好な神経学的転帰



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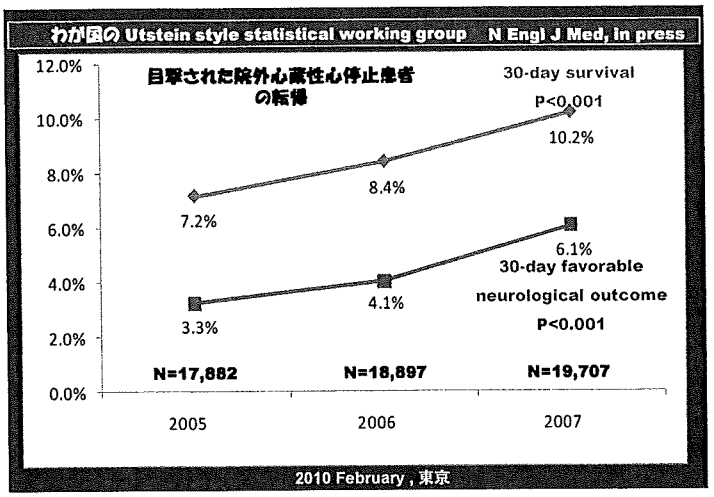
わが国の Utstein style statistical working group　N Engl J Med, in press
目撃された院外心臓性心停止患者の転帰
30-day survival
P<0.001
12.0%
10.0%
8.0%
6.0%
4.0%
2.0%
0.0%
7.2%
8.4%
10.2%
3.3%
4.1%
6.1%
30-day favorable neurological outcome
P<0.001
N=17,882
N=18,897
N=19,707
2005
2006
2007
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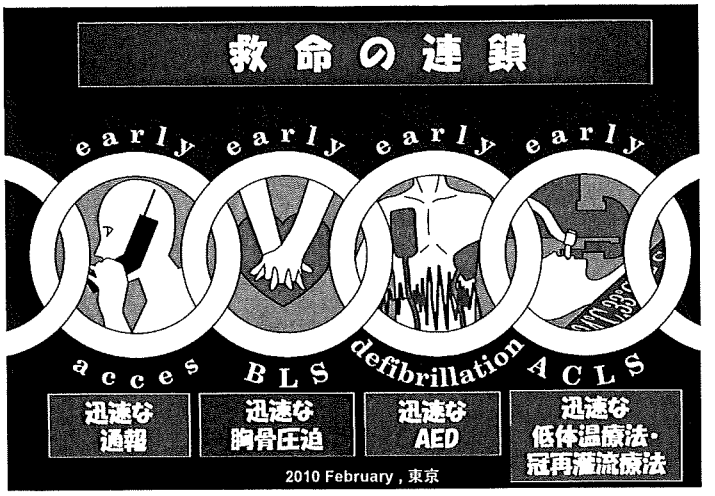
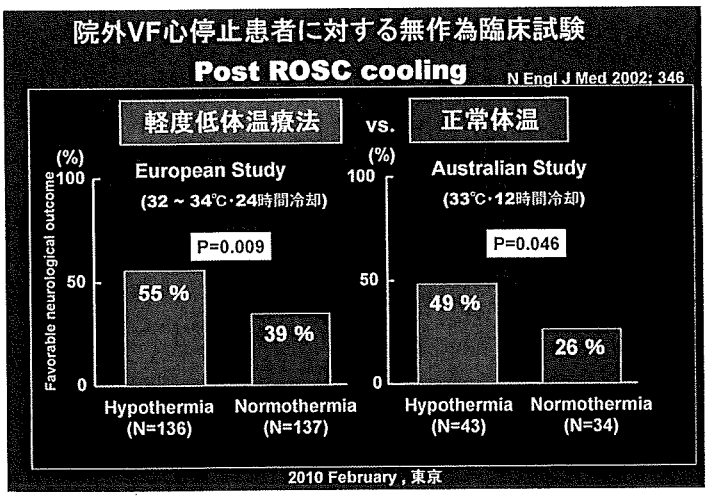
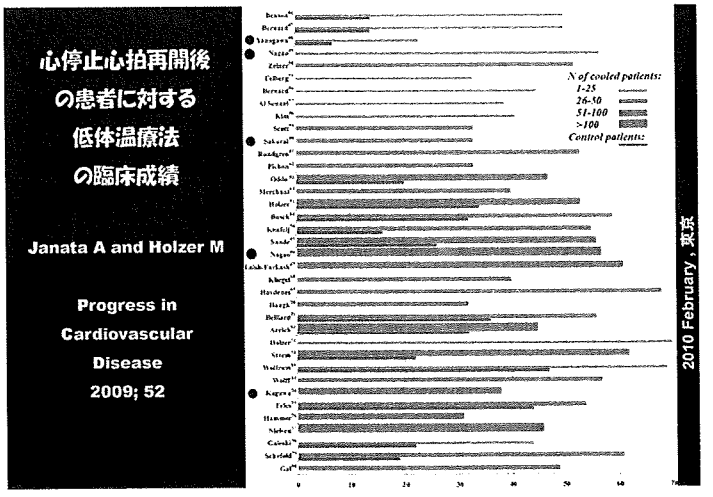

救命の連鎖
early early early early
acces
BLS
defibrillation
ACLS
迅速な通報
迅速な胸骨圧迫
迅速なAED
迅速な低体温療法・冠再灌流療法
2010 February , 東京


●2010年現在の低体温療法のEBMとその機序
2010 February , 東京


2009 May 3 ペンシルバニア 国際E-CPR協議会
Lance Becker, Robert Berg, Michael Holzer らと共に
2010 February , 東京


院外VF心停止患者に対する無作為臨床試験
Post ROSC cooling
N Engl J Med 2002; 346
軽度低体温療法
vs.
正常体温
Favorable neurological outcome
(%)
100
50
0
European Study
(32 ~ 34℃・24時間冷却)
P=0.009
55 %
39 %
Hypothermia (N=136)
Normothermia (N=137)
Australian Study
(33℃・12時間冷却)
P=0.046
49 %
26 %
Hypothermia (N=43)
Normothermia (N=34)
2010 February , 東京


心停止心拍再開後の患者に対する低体温療法の臨床成績
Janata A and Holzer M
Progress in Cardiovascular Disease
2009; 52
N of cooled patients:
1-25
26-50
51-100
>100
Control patients:
2010 February , 東京

心肺蘇生と救急心血管治療のための ILCOR/AHA ガイドライン 2005

●心停止後心拍再開患者に対する軽度低体温療法

・Class 2a:　院外初回ECGがVF/VT心停止で心拍再開後も昏睡状態にある成人は、32-34 ℃, 12-24 時間の低体温療法を施行すべきである。

・Class 2b:　かかる低体温療法は、院外非VF/VT心停止または院内心停止成人で、心拍再開後も昏睡状態にある場合も有益・有用・有効であろう。

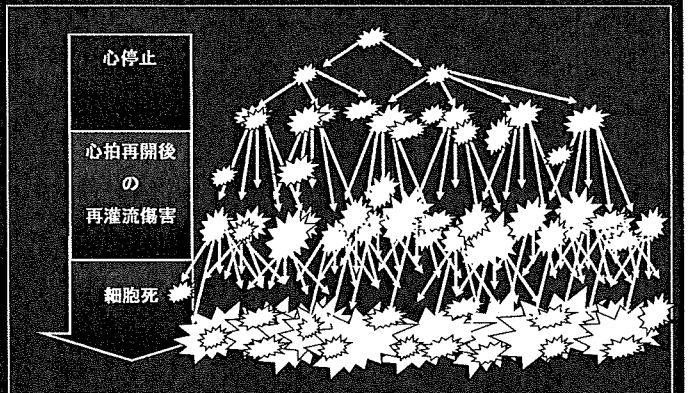
2010 February , 東京

低体温療法の脳保護

- 脳代謝を抑制 ：Rosomoff HL, 1954. Steen PA, 1983. Oku K, 1993. Lanier WL, 1995. Safar PJ, 1997. etc
- 細胞内Ca^{2+}蓄積を防止：Siesjo BK, 1989. Safar PJ, 1997 etc
- 脳温上昇を防止：Hayashi, 1993. etc
- 神経伝達物質の放出を抑制 (glutamate, dopamine, et al) ：Busto R, 1989. Illievich UM, 1994. Safar PJ, 1997 Hachimi-Idrissi S, 2004. Berger C, 2004. Vosler PS, 2005.
- ラジカル産生の抑制 ：Grinsberg MD, 1992. Lei B, 1994. Globus MY, 1995. Maier CM, 2002. Horiguchi T, 2003.
- サイトカイン関連 ：Akriotis V, 1985. Dempsey RJ, 1987. Kumar K, 1997. Wang GJ, 2002. Yanagawa Y, 2002. Kimura A, 2002. Callaway CW, 2008.
- アポトーシスの防止：Colbourne F, 1997. Fukuda H, 2001. Zhang Z, 2001. Xu L, 2002. Zhao H, 2005. Eberspacher E, 2005.

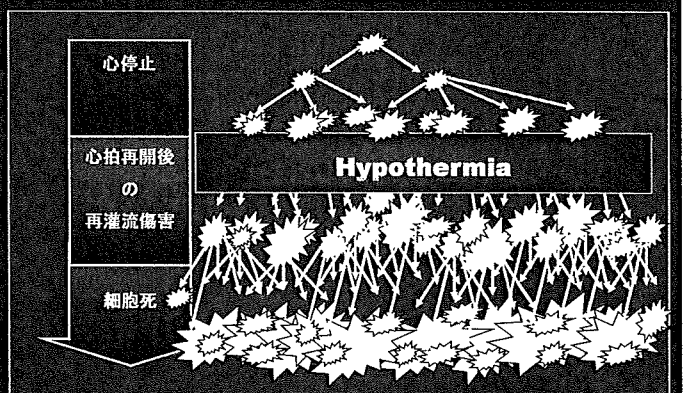
2010 February , 東京

Resuscitative Hypothermia の効果



2010 February , 東京

Resuscitative Hypothermia の効果



2010 February , 東京

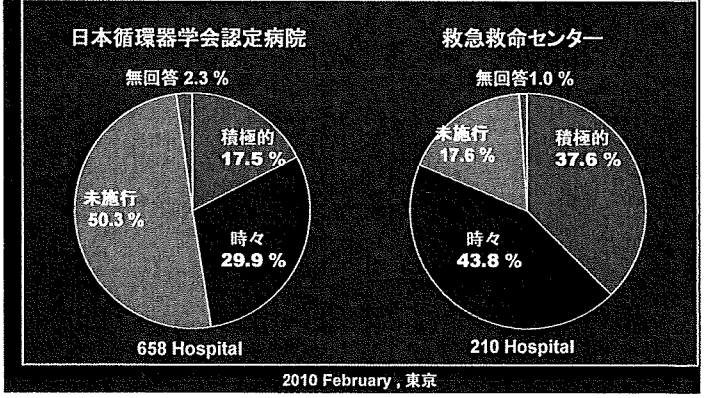
2010年1月現在の低体温療法のEBM

国際蘇生連絡協議会(**International Liaison Committee on Resuscitation; ILCOR**) は、低体温療法の**EBM**を、**2003**年・**2005**年・**2008**年に検証し、下記ごとく報告している。

- **自己心拍再開後の低体温療法**は、有用・有効・有益である。
- 動物実験では、低体温療法の導入(自己心拍再開後; **post-ROSC cooling**、心停止中; **Intra arrest cooling**)、**早ければ早い程、その効果は大**である。
- **しかし、至適深部体温・冷却持続時間・復温時間・冷却方法などは、明らかではない。**

2010 February , 東京

日本の循環器学会認定病院と救命救急センターにおける低体温療法施行施設の割合 2009



2010 February , 東京

心停止患者に対する低体温療法の戦略

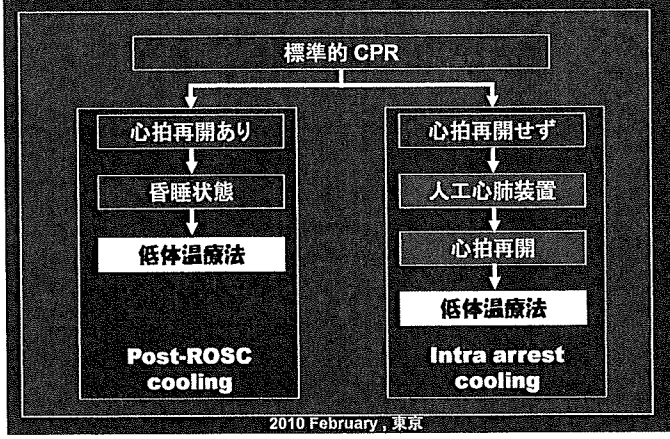
Nagao,et al. AHA 2005,2006,2007

1. 心拍再開後に低体温療法を導入
   Post-ROSC cooling

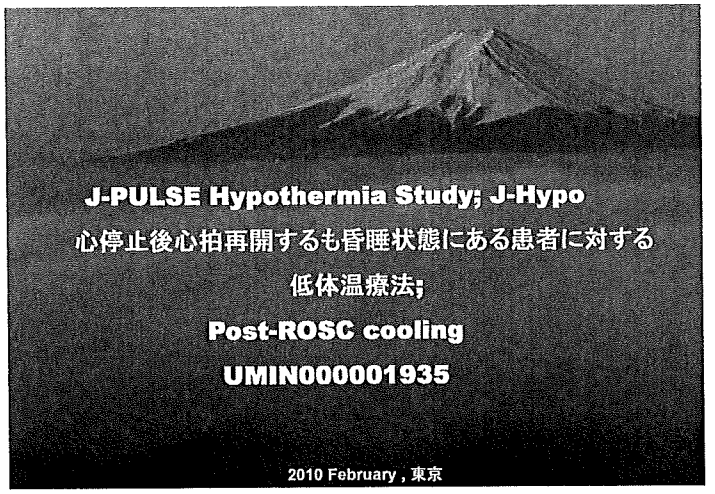
2. 心停止中から低体温療法を導入
   Intra arrest cooling

2010 February , 東京

心停止患者に対する低体温療法の戦略



2010 February , 東京



J-PULSE Hypothermia Study; J-Hypo

心停止後心拍再開するも昏睡状態にある患者に対する低体温療法;

Post-ROSC cooling

UMIN000001935

2010 February , 東京

J-Hypo ; J-PULSE Hypothermia Study

- 多施設共同臨床観察研究
- 対象 1. 院外心停止
  2. 心蔵性
  3. 標準的CPRで心拍再開
  4. 心拍再開後も昏睡状態
- 主要エンドポイント
  30日後の良好な神経学的転帰
- 目標症例;500例

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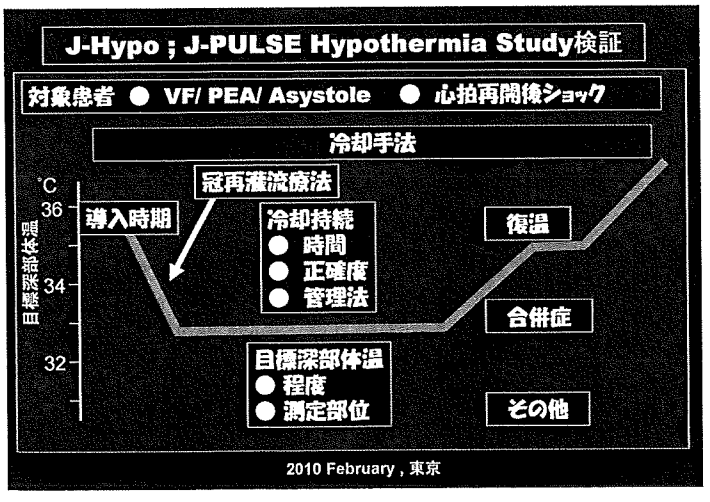
J-Hypo ; J-PULSE Hypothermia Study検証



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J Hypo "post-ROSC cooling" 多施設観察研究

281 patients treated with post-ROSC cooling were enrolled.

Data are median (IQR) and %

- Age (years); 60 (51 to 68)
- Collapse-to-ROSC interval (min); 25 (17 to 40)
- Cooling methods; Surface cooling (58 %)
- Induction interval (minutes); 187 (95 to 363)
- Target core temperature (℃);
- Cooling duration (hours) ; 24 or shorter (39 %)
  24 to 48 (34 %)
  longer than 48 (26 %)
- Rewarming duration (hours) ; 24 or shorter (22 %)
  24 to 48 (33 %)
  longer than 48 (45 %)

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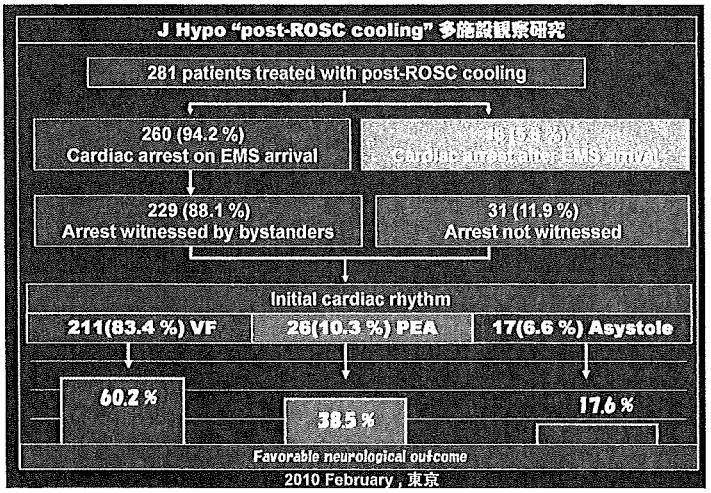
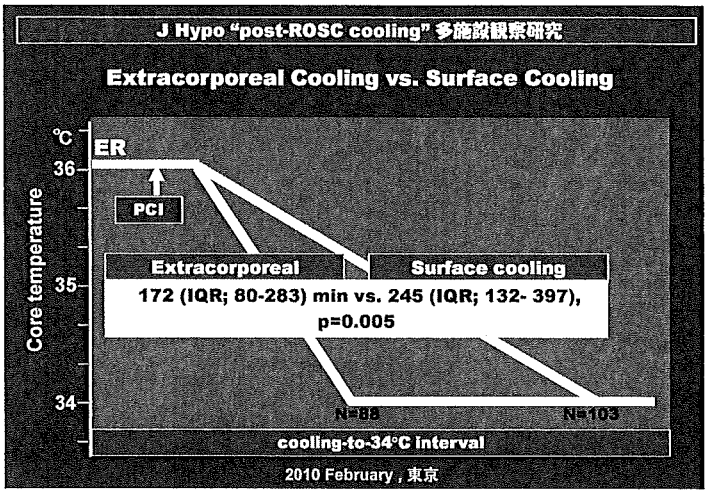
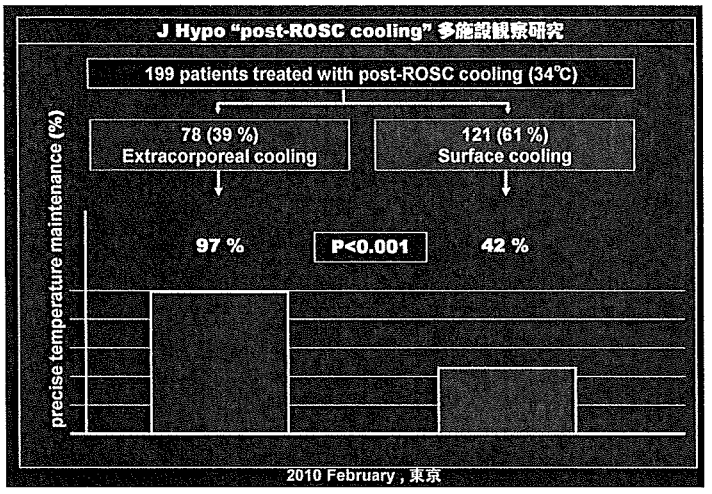
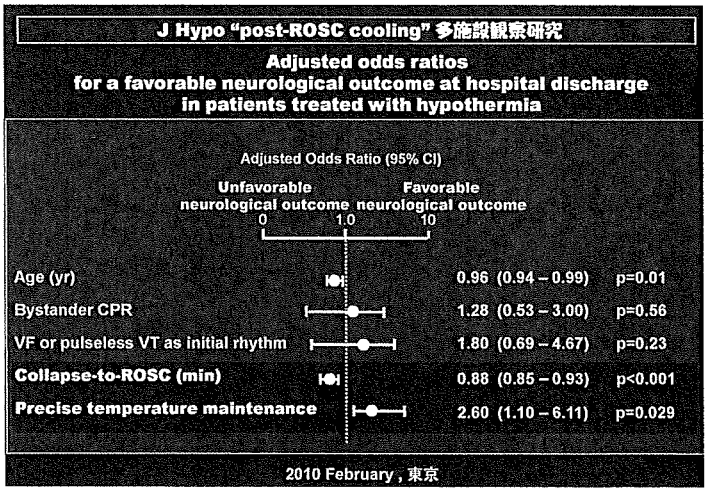
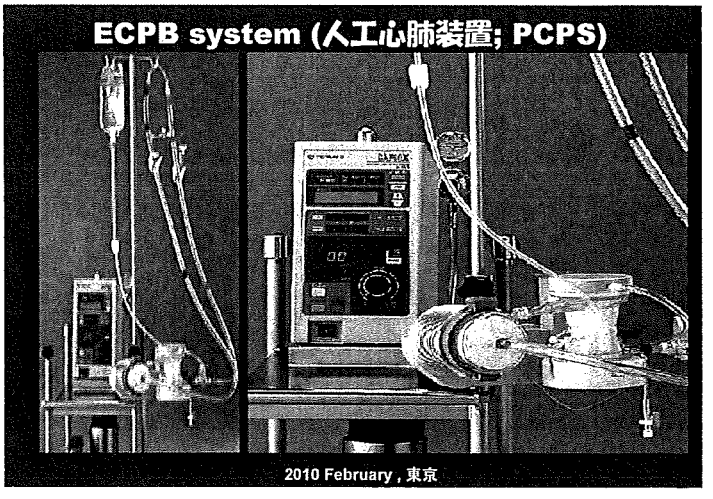

J Hypo "post-ROSC cooling" 多施設観察研究
281 patients treated with post-ROSC cooling
260 (94.2 %)
Cardiac arrest on EMS arrival
16 (5.8 %)
Cardiac arrest after EMS arrival
229 (88.1 %)
Arrest witnessed by bystanders
31 (11.9 %)
Arrest not witnessed
Initial cardiac rhythm
211(83.4 %) VF
26(10.3 %) PEA
17(6.6 %) Asystole
60.2 %
38.5 %
17.6 %
Favorable neurological outcome
2010 February , 東京


J Hypo "post-ROSC cooling" 多施設観察研究
Extracorporeal Cooling vs. Surface Cooling
℃
ER
36
PCI
Core temperature
35
Extracorporeal
Surface cooling
172 (IQR; 80-283) min vs. 245 (IQR; 132- 397), p=0.005
34
N=88
N=103
cooling-to-34°C interval
2010 February , 東京


J Hypo "post-ROSC cooling" 多施設観察研究
199 patients treated with post-ROSC cooling (34℃)
78 (39 %)
Extracorporeal cooling
121 (61 %)
Surface cooling
precise temperature maintenance (%)
97 %
P<0.001
42 %
2010 February , 東京


J Hypo "post-ROSC cooling" 多施設観察研究
Adjusted odds ratios
for a favorable neurological outcome at hospital discharge
in patients treated with hypothermia
Adjusted Odds Ratio (95% CI)
Unfavorable neurological outcome
Favorable neurological outcome
0
1.0
10
Age (yr) 0.96 (0.94 – 0.99) p=0.01
Bystander CPR 1.28 (0.53 – 3.00) p=0.56
VF or pulseless VT as initial rhythm 1.80 (0.69 – 4.67) p=0.23
Collapse-to-ROSC (min) 0.88 (0.85 – 0.93) p<0.001
Precise temperature maintenance 2.60 (1.10 – 6.11) p=0.029
2010 February , 東京


● ER収容時も
心停止状態にある患者
に対する低体温療法;
Intra arrest cooling
February , 東京


ECPB system (人工心肺装置; PCPS)
2010 February , 東京

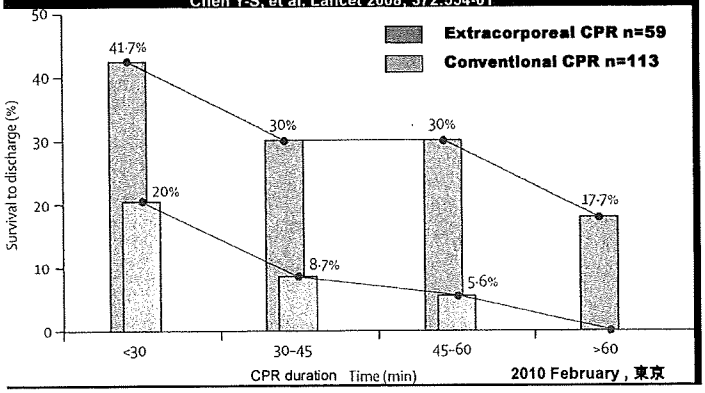
CPBの臨床報告とIntra-arrest coolingの動物研究

- **CPB, 低体温療法なし**
  - ❶ Nagao, et al. Intern Med 1999.
  - ❷ Martin et al. Chest 1998
  - ❸ Younger et al. Acad Emerg Med 1999
  - → 神経学的転帰改善効果？
  - ❹ Chen et al. J Am Coll Cardiol 2003
  - ❺ Hase et al. Circ J 2005
  - ❻ Kano et al. Circulation 2006
  - ❼ Chen et al. Lancet 2008
  - ❽ Aoyama et al. Circ J 2009
  - → 効果あり; CPB駆動までの時間
    <45 mins Hase
    <60 mins Chen, Kano
- **CPB, 低体温療法 (Post ROSC cooling)**
  - ❶ Nagao, et al. J Am Coll Cardiol 2000 → 効果ありそうだ
- **動物研究: Intra-arrest cooling**
  - ❶ Abella et al. Circulation 2004
  - ❷ Nozari et al. Circulation 2004
  - ❸ Nozari et al. Circulation 2006
  - → 効果あり

2010 February , 東京

CPR with assisted extracorporeal life-support vs. conventional CPR in adults with in-hospital cardiac arrest : an observational study and propensity analysis

Chen Y-S, et al. Lancet 2008; 372:554-61



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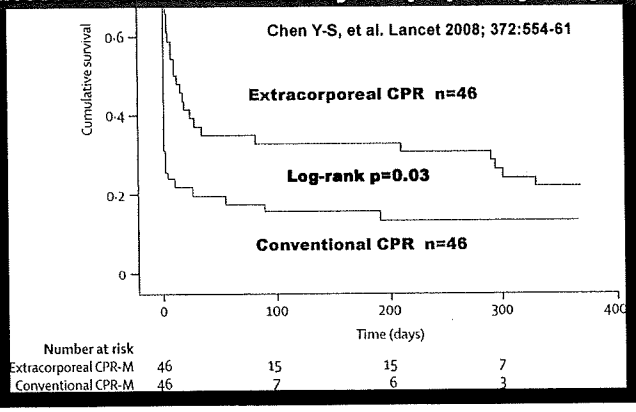
CPR with assisted extracorporeal life-support vs. conventional CPR in adults with in-hospital cardiac arrest : an observational study and propensity analysis



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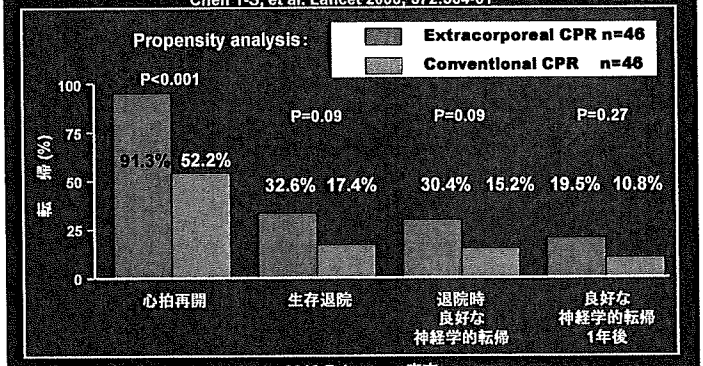
CPR with assisted extracorporeal life-support vs. conventional CPR in adults with in-hospital cardiac arrest : an observational study and propensity analysis

Chen Y-S, et al. Lancet 2008; 372:554-61



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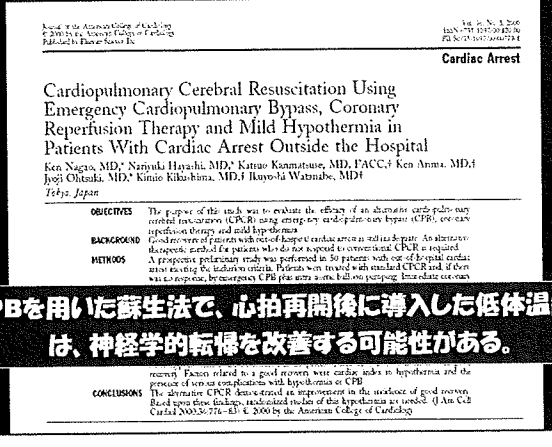
● CPBを用いた蘇生+低体温療法 JACC 2000



Cardiac Arrest

Cardiopulmonary Cerebral Resuscitation Using Emergency Cardiopulmonary Bypass, Coronary Reperfusion Therapy and Mild Hypothermia in Patients With Cardiac Arrest Outside the Hospital

Ken Nagao, MD,* Nariyuki Hayashi, MD,* Katsuo Kanmatsuse, MD, FACC,† Ken Anma, MD,† Jyoji Okitsuki, MD,* Kinzo Kikushima, MD,† Ikuyoshi Watanabe, MD†

Tokyo, Japan

OBJECTIVES The purpose of this study was to evaluate the efficacy of an alternative cardiopulmonary cerebral resuscitation (CPCR) using emergency cardiopulmonary bypass (CPB), coronary reperfusion therapy and mild hypothermia.

BACKGROUND Good recovery of patients with out-of-hospital cardiac arrest is still inadequate. An alternative therapeutic method for patients who do not respond to conventional CPCR is required.

METHODS A prospective preliminary study was performed in 50 patients with out-of-hospital cardiac arrest meeting the inclusion criteria. Patients were treated with standard CPCR and, if they were not responsive, by emergency CPB plus intracoronary balloon pumping. Immediate coronary

CPBを用いた蘇生法で、心拍再開後に導入した低体温療法は、神経学的転帰を改善する可能性がある。

recovery. Factors related to a good recovery were cardiac index in hypothermia and the presence of less complications with hypothermia or CPB.

CONCLUSIONS The alternative CPCR limits extend an improvement in the incidence of good recovery. Based upon these findings, randomized studies of this hypothermia are needed. (J Am Coll Cardiol 2000;36:776–83) © 2000 by the American College of Cardiology

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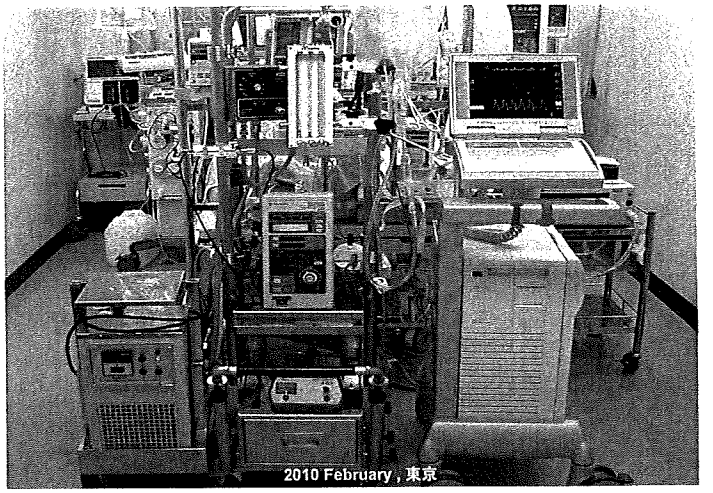

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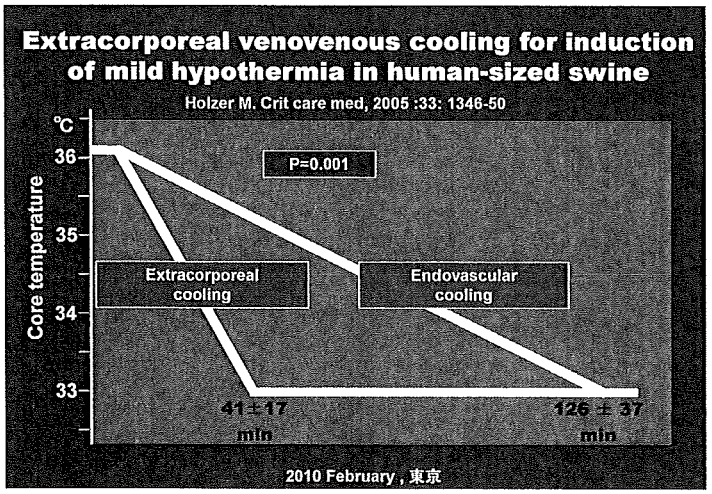
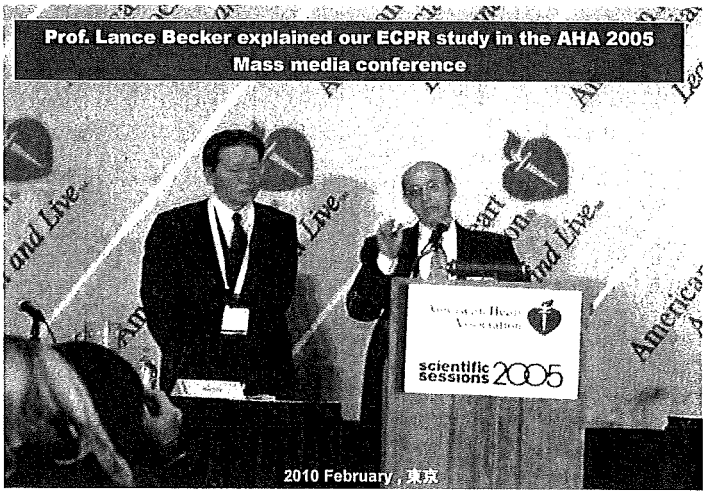
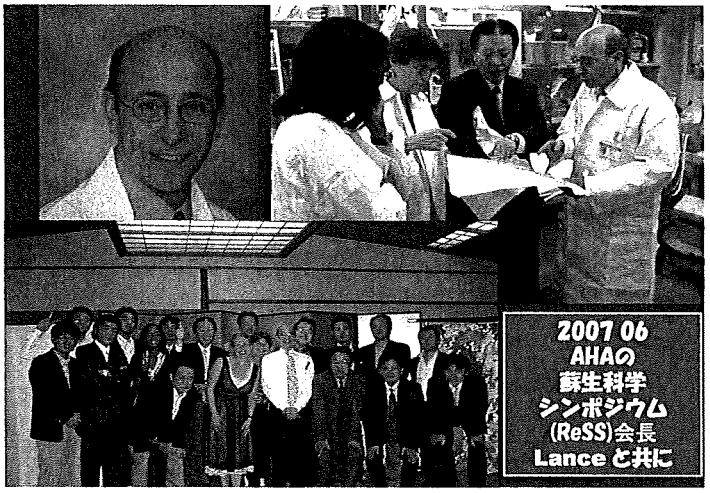
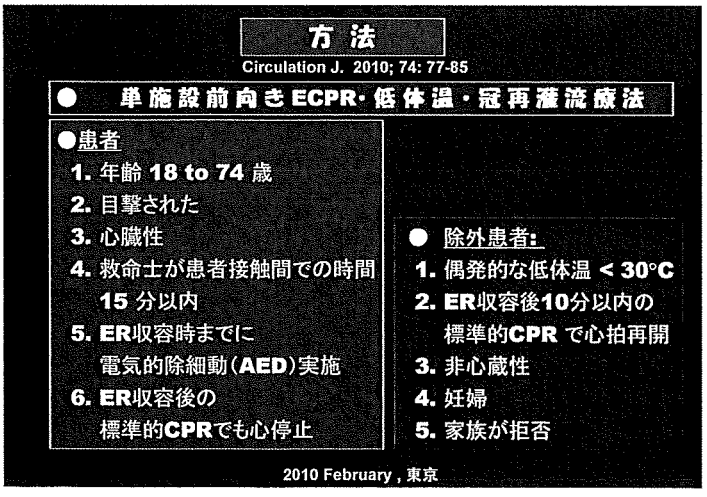
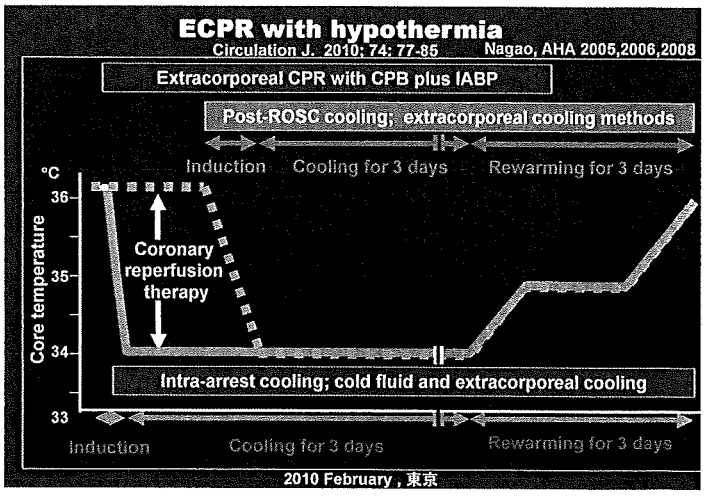

Extracorporeal venovenous cooling for induction of mild hypothermia in human-sized swine
Holzer M. Crit care med, 2005 :33: 1346-50
℃
36
35
34
33
Core temperature
P=0.001
Extracorporeal cooling
Endovascular cooling
41±17 min
126 ± 37 min
2010 February , 東京


Prof. Lance Becker explained our ECPR study in the AHA 2005 Mass media conference
scientific sessions 2005
2010 February , 東京


2007 06 AHAの 蘇生科学 シンポジウム (ReSS)会長 Lance と共に

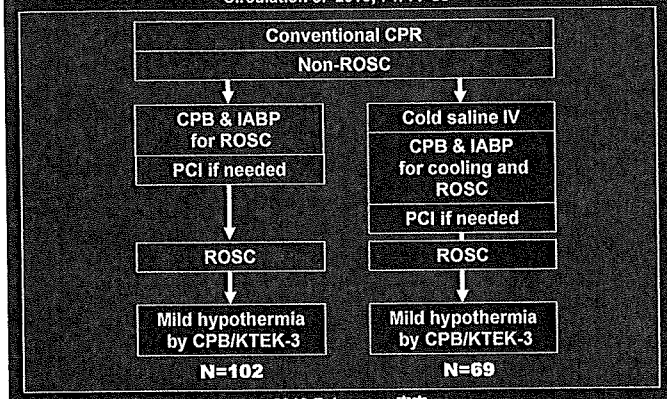

DAILY NEWS
Welcome to Scientific Sessions 2006
Our ECPR study was reported in the Daily Newspaper, AHA 2006.
Opening Session will include presiden address, Conner lecturer, award prese
Existing technology, new applications improve survival in cardiac arrest
2010 February 東京


方 法
Circulation J. 2010; 74: 77-85
● 単施設前向きECPR・低体温・冠再灌流療法
●患者
1. 年齢 18 to 74 歳
2. 目撃された
3. 心臓性
4. 救命士が患者接触間での時間 15 分以内
5. ER収容時までに 電気的除細動(AED)実施
6. ER収容後の 標準的CPRでも心停止
● 除外患者:
1. 偶発的な低体温 < 30°C
2. ER収容後10分以内の 標準的CPR で心拍再開
3. 非心蔵性
4. 妊婦
5. 家族が拒否
2010 February , 東京

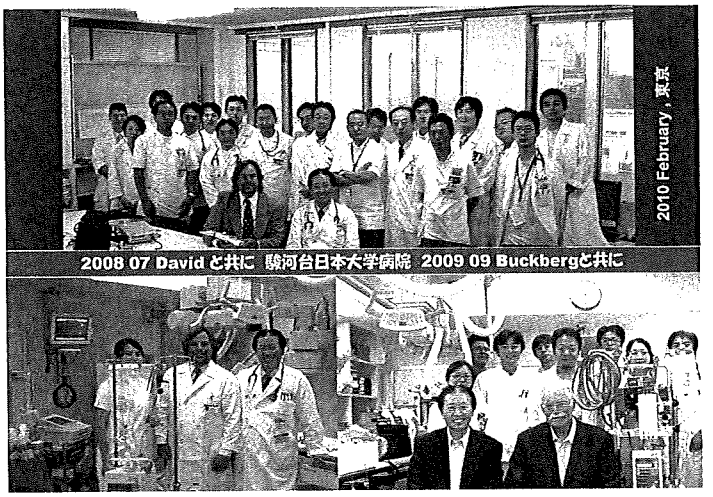

ECPR with hypothermia
Circulation J. 2010; 74: 77-85
Nagao, AHA 2005,2006,2008
Extracorporeal CPR with CPB plus IABP
Post-ROSC cooling; extracorporeal cooling methods
Induction
Cooling for 3 days
Rewarming for 3 days
℃
36
35
34
33
Core temperature
Coronary reperfusion therapy
Intra-arrest cooling; cold fluid and extracorporeal cooling
Induction
Cooling for 3 days
Rewarming for 3 days
2010 February , 東京

結 果

Circulation J. 2010; 74: 77-85

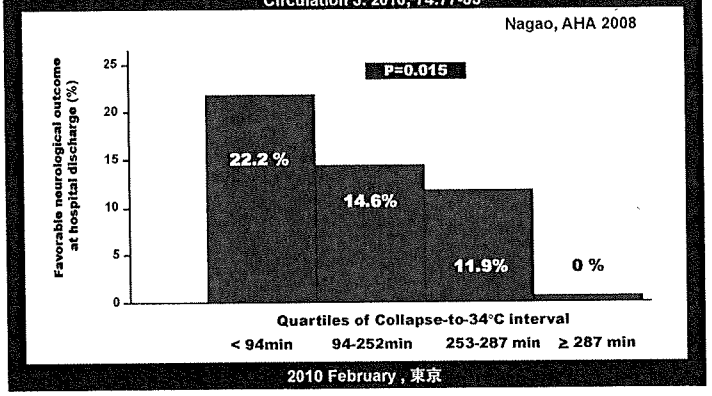


2010 February , 東京



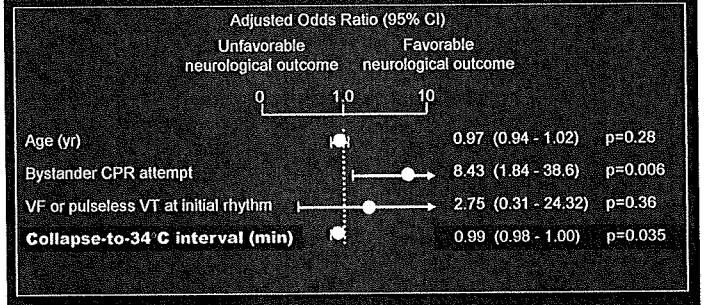
Association between the quartiles of collapse-to-34°C interval and the frequency of a favorable neurological outcome at hospital discharge

Circulation J. 2010; 74:77-85



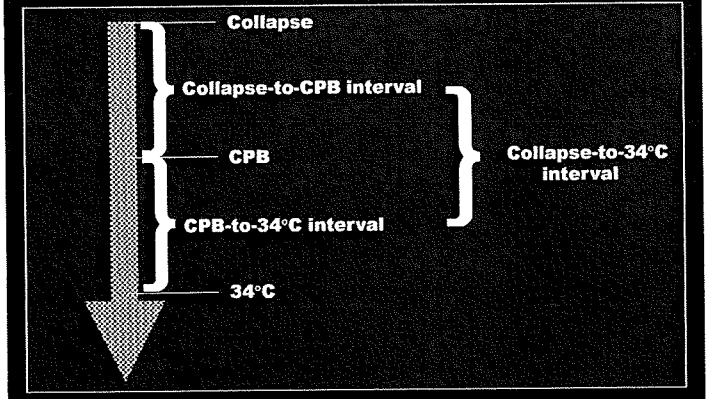
2010 February , 東京

Adjusted odds ratios for a favorable neurological outcome at hospital discharge associated with selected factors



Circulation J. 2010; 74:77-85

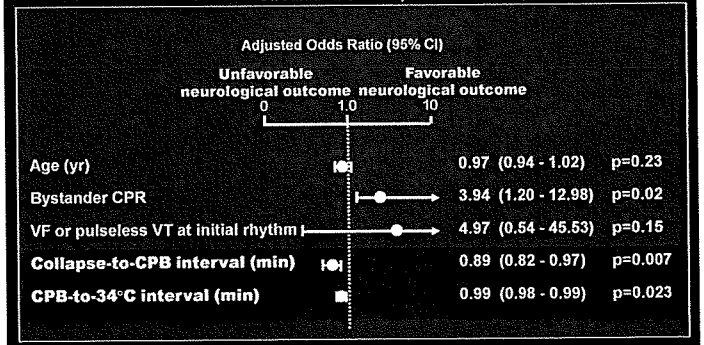
Time interval between collapse and 34°C



Circulation J. 2010; 74:77-85

Adjusted odds ratios for favorable neurological outcome at hospital discharge

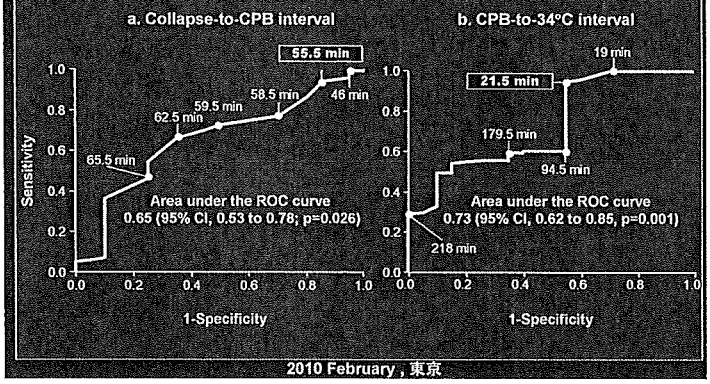
Circulation J. 2010; 74:77-85



2010 February , 東京

ROC curves for various cutoff levels of collapse-to-CPB interval and CPB-to-34°C interval to differentiate favorable neurological outcome and unfavorable neurological outcome at hospital discharge

Circulation J. 2010; 74:77-85



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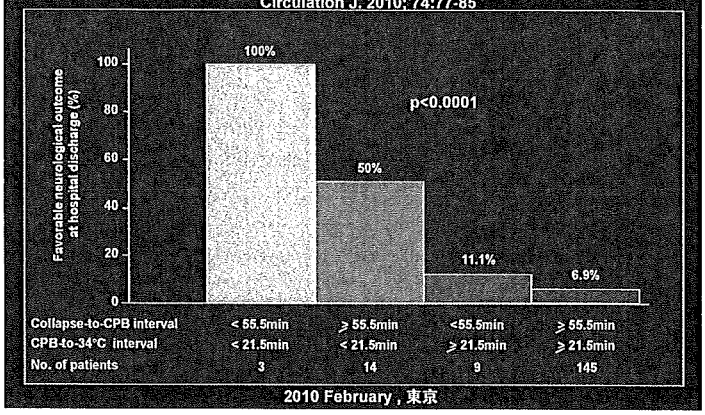
Frequencies of favorable neurological outcome among four subsets of patients who were classified the two cutoff values

Circulation J. 2010; 74:77-85



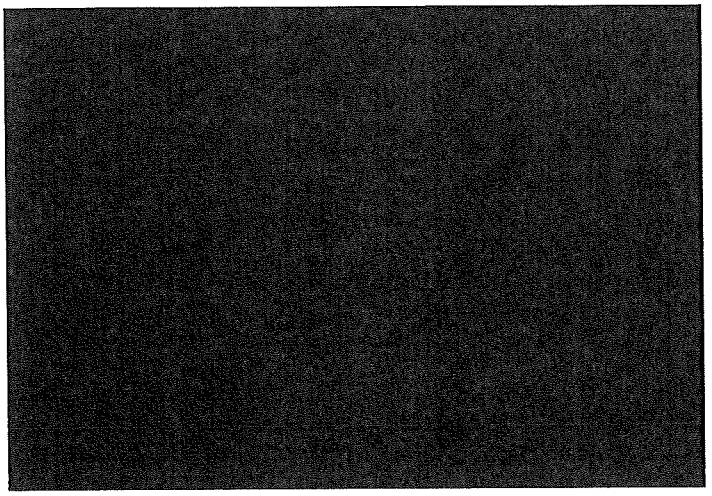
2010 February , 東京

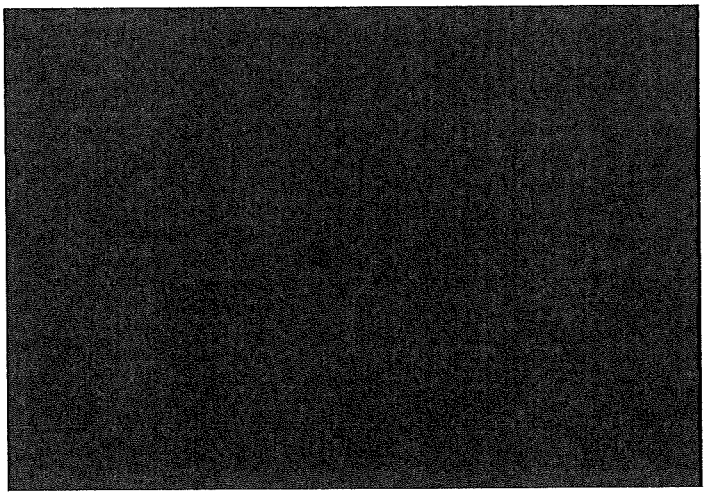
Study of Advanced life support for Ventricular fibrillation with Extracorporeal circulation in Japan

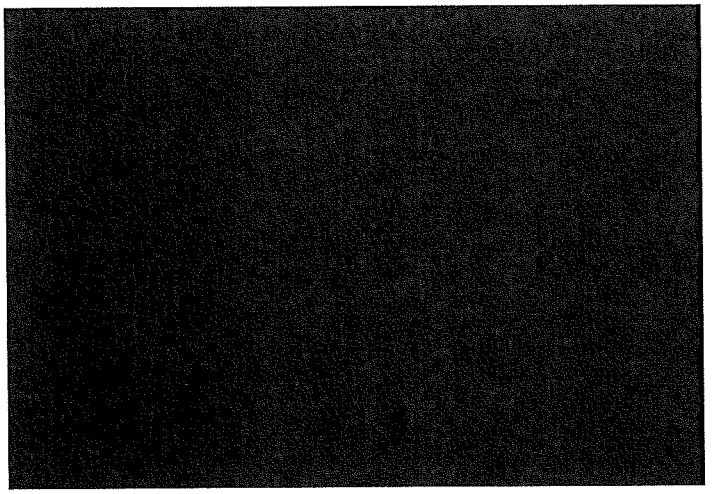
UMIN000001403

SAVE J

2010 February , 東京







J-PULSE-Hypo registry: Mild Hypothermia Therapy for Acute Coronary Syndrome

Shinichi Shirai [1], M.D., Ken Nagao [2], M.D., Hiroshi Nonogi [3], M.D., Naohiro Yonemoto [3], M.D., Hiroyuki Yokoyama [3], M.D., Mamoru Hase [4], M.D., Yoshio Tahara [5], M.D., Kazunori Kashiwase [6], M.D., Yuji Yasuga [7], M.D., Hideki Arimoto [8], M.D., Soma Kazui [9], M.D., Hirotaka Sawano [10], M.D., Hiroshi Hazui [11], M.D., Takuro Hayashi [12], M.D.,Tatsuya Maruhashi [13], M.D., Yasuhiro Kuroda [14], M.D., Yuichi Motomura [15], M.D. and for the J-PULSE Hypo registry Investigators.

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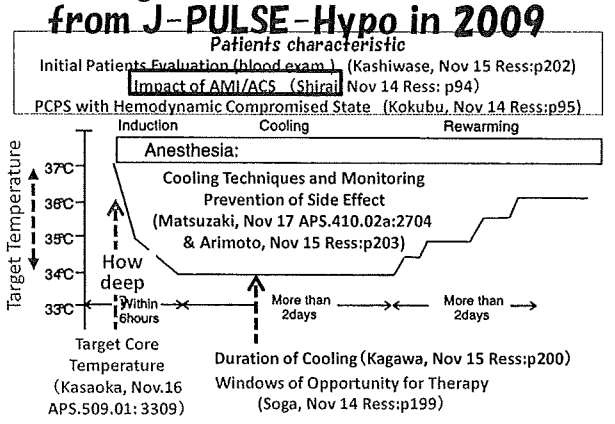
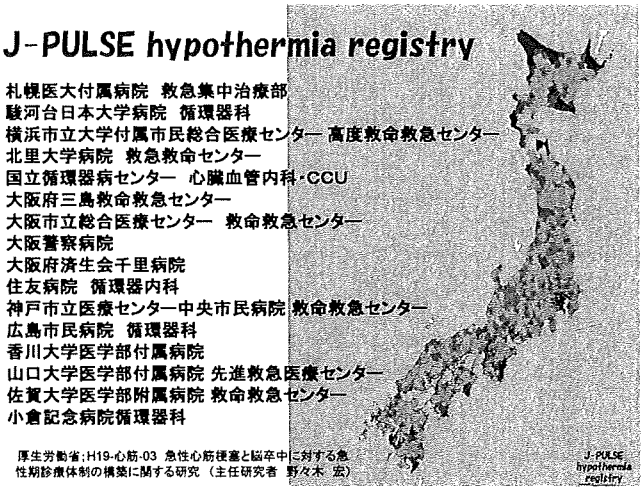
8 Clinical Questions from J-PULSE-Hypo in 2009



Courtesy of Hiroyuki Yokoyama

J-PULSE hypothermia registry

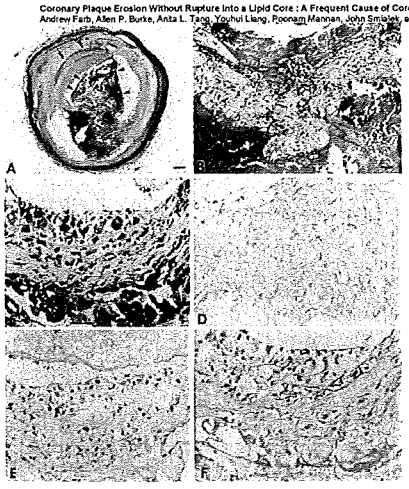


Introduction

Resuscitated patients from sudden cardiac death (SCD) had a poor prognosis because of not only high mortality but also severe neurologic disability (1)

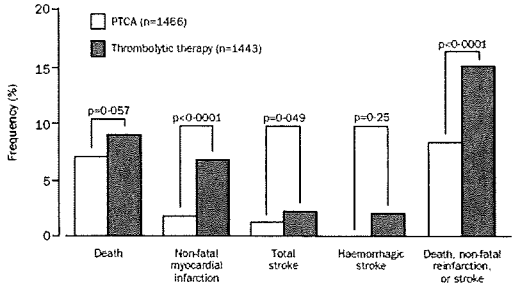
Ischemic heart disease was reported to be the main causes of SCD. Myocardial infarction was the main causes of SCD (2,3), therefore, emergency revascularization therapy might be the most effective for improving the mortality for the patients with cardiac arrest due to acute ischemic coronary artery disease, even without ST segment elevation in ECG (3).

For the patients with post cardiac arrest syndrome (PCAS), 'bundled' therapy was recommended, that is ,early coronary revascularization (3-5), temperature control (6,7) was mandatory treatment strategy (8). Percutaneous coronary intervention (PCI) with mild hypothermia therapy (MHT) was effective for the cardiac arrest patients with ST elevation MI (9).



Acute thrombosis of the left anterior descending coronary artery was found in this 54-year-old man with witnessed cardiac arrest and death 2.5 hours after the onset of chest pain. A, Concentric plaque with a large hemorrhagic lipid core (L) and focal calcification (arrows) is seen at low power; an occlusive thrombus (arrowheads) is present. B, The platelet-rich thrombus (T) is adjacent to the rupture of the fibrous cap (high power). Immunohistochemical staining demonstrates abundant macrophages (in C), an absence of smooth muscle cells (in D), and scattered T cells (in E) with HLA-DR–positive macrophages and T cells (in F).

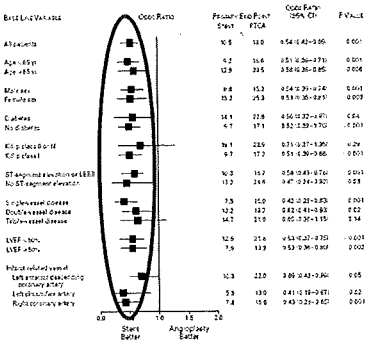
PCI was the main stream for the treatment of STEMI.



Short-term clinical outcomes in individuals treated with on-site thrombolysis or after emergent transfer for primary PTCA

Lancet 2003;361:13-20.

COMPARISON OF ANGIOPLASTY WITH STENTING, WITH OR WITHOUT ABCIXIMAB, IN ACUTE MYOCARDIAL INFARCTION



N Engl J Med 2002;346:957-66.

Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest

Characteristic	No significant CAD (n = 26)	Significant CAD (n = 46)	P	Total (n = 72)
Electrographic patterns on admission*				
ST-segment elevation	2 (7.7)	21 (45.7)	0009	23 (31.9)
ST-segment depression	6 (230.)	15 (32.6)	.4	21 (29.2)
Left bundle branch block	4 (15.4)	8 (17.4)	1.0	12 (16.7)
Unspecific ST or T changes	8 (30.7)	4 (8.7)	02	12 (16.7)
Normal	6 (23)	5 (10.9)	2	11 (15.3)

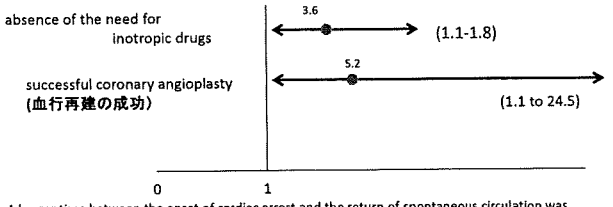
Pattern of ECG change immediately after ROSC.

ECG did not reflect the severity of coronary lesion.: in some cases, no significant change or normal pattern was found in the case of coronary block. Therefore, no ECG change immediately after ROSC could not conclude that the reason of cardiac arrest was due to the coronary ischemia.

⇒Emergency coronary angiography immediately after ROSC should be performed to establish the adequate diagnosis and treatment in order to improve the prognosis

Am Heart J 2009;157:312-8.

IMMEDIATE CORONARY ANGIOGRAPHY IN SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST

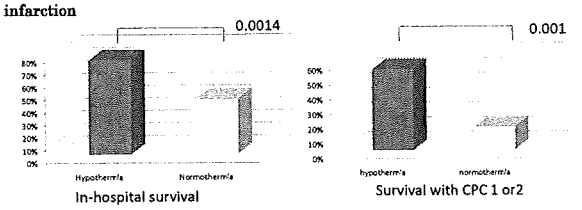


A longer time between the onset of cardiac arrest and the return of spontaneous circulation was associated with a lower rate of survival, with an odds ratio for mortality of 1.1 per minute of delay (95 percent confidence interval, 1.02 to 1.12; P=0.003).

心肺停止患者において生存の条件は血行再建の成功であるといわれている。

N Engl J Med 1997;336:1629-33.

Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction



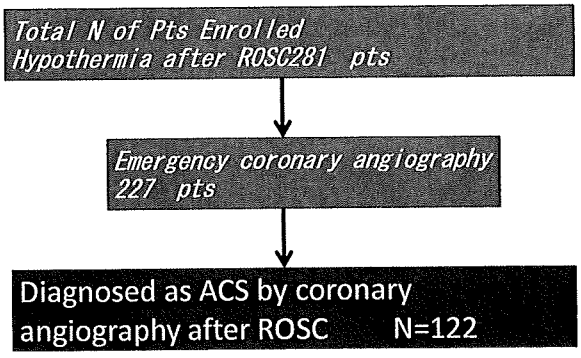
(Conclusion)

Our preliminary experience indicates that primary PCI and MIH are feasible and may be combined safely in comatose survivors of ventricular fibrillation with signs of STEMI. Such a strategy may improve survival with good neurological recovery.

VfによるⅡ心肺停止を発症したST上昇型心筋梗塞患者に対してPCIおよび低体温療法を施行することは生存率およびCPC1,2という神経学的予後の改善をもたらすことが可能である。

Resuscitation (2007) **74, 227—234**

Results



From 2005 to 2008, two hundred eighty one patients were enrolled with fulfillment of the inclusion criteria. Of those 281 patients, emergency coronary angiography was attempted in 227 patients. For this current analysis of this sub-study of J-PULSE Hypo registry, one hundred twenty two patients were evaluated for the efficacy of hypothermia with emergency percutaneous coronary intervention (PCI).

Baseline Characteristics (1)

Man (%)	95.1
Age	60+/−11
Bystander CPR (%)	54.1
Shockable Rhythm (%)	82.8
Mean no flow time (min)	3.0
OMI (%)	2.5
History of Heart Failure (%)	4.9
Stroke (%)	5.7
Hypertension (%)	35.0
Diabetes (%)	15.6
Mean GCS	3.8
ROSC before ER (%)	55.7
Hb (mean g/dl)	14.0+/−1.6
Serum K (mEq/l)	4.1+/−0.9
Cre>1.5 (%)	12.3

Baseline Characterstics (2)

mean B.E	−12.9
mean CA-ROSC	30 +/− 24
Cold saline use (%)	52.7
Surface cooling (%)	56.0
Over cooling during Tx (%)	28.6
cooling start to target temperature (min)	239.8+/− 211.4
Mean cooling time (hrs)	32.6+/−14.0
Rewarming	
24 hours>= (%)	24.6
24-48 hours (%)	30.3
48-72 hours (%)	33.6
72 hours<	9.0
Multivessel disease (%)	41.0
Anterior MI (%)	63.1
Left main culprit (%)	4.0
IABP use (%)	61.5
PCPS use (%)	29.5

Clinical Outcomes

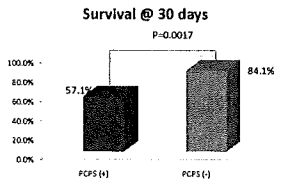
Alive @ 30days 77.0%

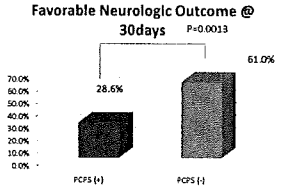
Favorable Neurologic Outcome @ 30days 52.0%

Including cardiogenic shock required PCPS

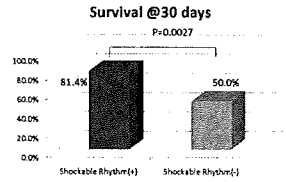
Clinical Outcomes (2)

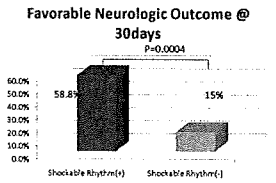
PCPS use





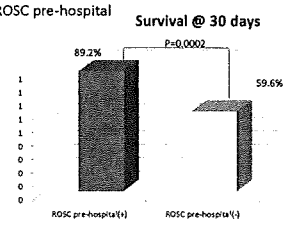
Shockable Rhythm

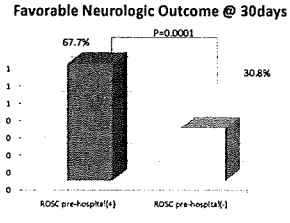




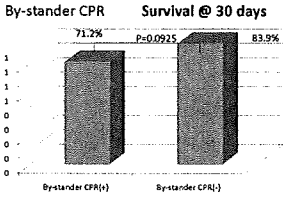
Clinical Outcomes (2)

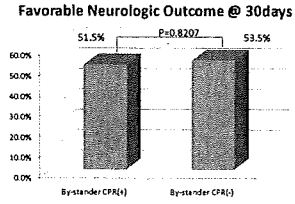
ROSC pre-hospital





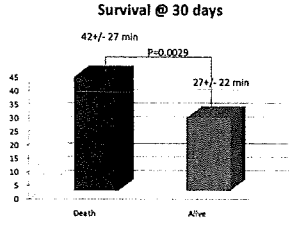
By-stander CPR

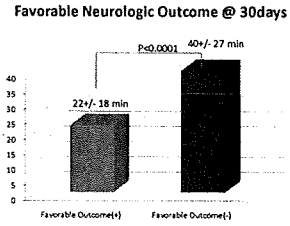




Clinical Outcomes (3)

Correlation Between Collapse to ROSC time and Clinical Outcomes





Which is better: PCI first or Hypothermia first?

Merits of early PCI for the cardiac arrest patients with acute coronary events were improving mortality. On the other hand, these procedure needed anticoagulation and anti-platelet therapy, therefore, increased risk for bleeding.

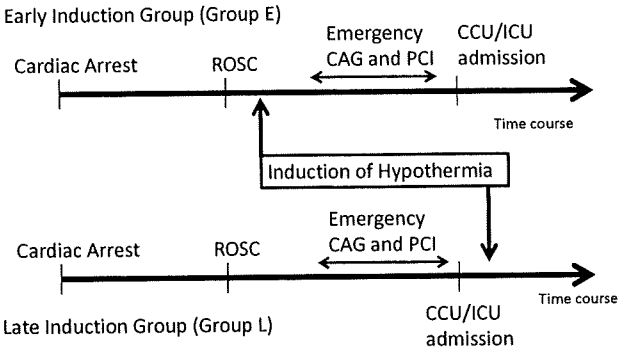
Early induction of hypothermia was recommended (10,11), however, it remained unknown which procedure should be initiate, PCI or MHT in case of acute ischemic coronary event that was indication for emergency revascularization therapy.

Our study examined clinical outcomes and efficacies of early induction of MHT prior to PCI group (Early induction group: Group E) compared with late induction of MHT after PCI (Late Induction group: Group L).

Complication	Normothermia	Hypothermia
	no./total no. (%)	
Bleeding of any severity†	26/138 (19)	35/135 (26)
Need for platelet transfusion	0/138	2/135 (1)
Pneumonia	40/137 (29)	50/135 (37)
Sepsis	9/138 (7)	17/135 (13)
Pancreatitis	2/138 (1)	1/135 (1)
Renal failure	14/138 (10)	13/135 (10)
Hemodialysis	6/138 (4)	6/135 (4)
Pulmonary edema	5/133 (4)	9/136 (7)
Seizures	11/133 (8)	10/136 (7)
Lethal or long-lasting arrhythmia	44/138 (32)	49/135 (36)
Pressure sores	0/133	0/136

N Engl J Med 2002;346:549-56.

Figure-2



	Late Induction (L) (N=70)	Early Induction (E) (N=42)	p-value
Age	61+/-1	58+/-2	0.0788
Man (%)	94.3	95.2	0.8284
Witness (%)	90.0	88.1	0.7524
By-stander CPR (%)	54.2	50.0	0.6601
Shockable Rhythm (%)	82.9	83.3	0.9482
No flow time (min)	2.8+/-0.8	4.6+/-1.1	0.2025
Prior MI (%)	3.2	2.5	0.8427
History of heart failure (%)	6.3	5.0	0.7757
History of Stroke (%)	6.3	5.0	0.7757
Hypertension (%)	27.0	35.0	0.3874
Diabetes	19.0	15.0	0.5981
Hemoglobin (g/dl)	13.7+/-2.0	14.2+/-2.0	0.1546
Serum creatinine (mg/dl)	1.47+/-0.25	1.74+/-0.32	0.5312
Serum potassium (mEq/l)	4.0+/-0.1	4.0+/-0.1	0.9101
Serum glucose (mg/dl)	286+/-12	277+/-15	0.6558
Collapse to ROSC (min)	31.3+/-2.9	28.2+/-4.0	0.5312
Hemodynamic compromise (%)	15.1	22.9	0.3356

Table-1 Baseline patient characteristics. CPR: cardiopulmonary resuscitation, MI: myocardial infarction. ROSC: recovery of spontaneous circulation.

	Late Induction (L) (N=70)	Early Induction (E) (N=42)	p-value
Target temperature (%)			
33 Celsius degree	25.7	0.0	<0.0001
34 Celsius degree	72.8	90.5	
35 Celsius degree	1.4	9.5	
Cold fluid infusion at Initiation of MHT (%)	32.4	82.6	<0.0001
Blood cooling methods for maintenance of hypothermia (%)	30.0	66.6	<0.0001
Collapse to Initiation of hypothermia (min)	168+/-9	52+/-13	<0.0001
Collapse to target temperature (min)	422+/-28	230+/-38	<0.0001
Initiation to target temperature (min)	278+/-25	173+/-32	0.0106
Cooling duration (hours)	33.3+/-1.8	31.3+/-2.4	0.5107
Rewarming time (%)			
24hours>=	25.0	26.8	0.0125
25-48	32.4	22.0	
49-72	27.9	51.2	
72=<	14.7	0.0	
Excessive cooling (%)	37.1	11.9	0.0039

Table-2 hypothermia data. MHT: Mild Hypothermia Therapy

	Late Induction (L) (N=70)	Early Induction (E) (N=42)	p-value
Anterior Myocardial infarction (%)	57.1	78.6	0.0212
Multi-vessel disease (%)	38.6	42.9	0.6542
Use of IABP (%)	60.0	61.9	0.8416
Use of PCPS (%)	25.7	33.3	0.3875
Pre TIMI (n)			
0	45	22	0.6174
1	10	7	
2	7	4	
3	8	8	
Post TIMI			
0	0	1	0.1947
1	0	0	
2	4	5	
3	66	35	
Stent use (%)	92.3	93.0	0.9001

Table-3 Angiographic and Intervention data.