

低体温療法について

2014.10.7 戦略会議

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低体温療法の定義

- 低体温療法(therapeutic hypothermia)や常温療法(antihyperthermia, fever control, induced normothermia)などの言葉があるが、過去の報告を見ても目標体温や維持期間、復温速度なども含めて方法が多様すぎる。
- おそらくはAHAのガイドラインにある「 32°C ～ 34°C を12～24時間」というのが最も一般的になっているのではないか？

低体温療法の定義

2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science

In summary, we recommend that comatose (ie, lack of meaningful response to verbal commands) adult patients with ROSC after out-of-hospital VF cardiac arrest should be cooled to 32°C to 34°C (89.6°F to 93.2°F) for 12 to 24 hours (Class I, LOE B). Induced hypothermia also may be considered for comatose adult patients with ROSC after in-hospital cardiac arrest of any initial rhythm or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electric activity or asystole (Class IIb, LOE B). Active rewarming should be avoided in comatose patients who spontaneously develop a mild degree of hypothermia ($.32^{\circ}\text{C}$ [89.6°F]) after resuscitation from cardiac arrest during the first 48 hours after ROSC. (Class III, LOE C).

もう低体温療法とは呼ばせない？

- 2009年に集中治療に関連する5学会(American Thoracic Society, European Respiratory Society, European Society of Intensive Care Medicine, Society of Critical Care Medicineなど)によって開催されたコンセンサスカンファレンスでは用語の混乱を解決するためにこれまでの「低体温療法 therapeutic hypothermia」という用語の使用をやめ、“targeted temperature management(TTM)”という用語で統一し導入・維持・復温についてのプロファイルを詳細に示すように強く推奨している。

現状で体温管理されている病態

- 心停止後症候群
- 頭部外傷
- 脳梗塞
- くも膜下出血・脳出血
- 脳炎・けいれん重積

心停止後症候群

- 唯一、低体温療法のエビデンスが認められているのは「目撃のある心肺停止症例で、心拍再開後も昏睡が続き、初回心電図がVF/VTの症例」に限られる。
- ではそれ以外のものはしないのか？

心停止後症候群

2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science

Induced hypothermia also may be considered for comatose adult patients with ROSC after in-hospital cardiac arrest of any initial rhythm or after out-of-hospital cardiac arrest with an initial rhythm of pulseless electric activity or asystole (Class IIb, LOE B).

心停止後症候群

日本蘇生協議会(JRC)ガイドライン2010

院外でのVFによる心停止後、ROSC後昏睡状態(質問に対して意味のある応答がない)の成人患者に対しては、低体温療法(12～24時間、 32°C ～ 34°C)を施行すべきである(Class I)。低体温療法は、院外でのPEA、心静止による心停止後もしくは院内心停止後に成人のROSC後昏睡状態の患者においても有益かもしれない(Class II b)。

心停止後症候群

	院外心停止		院外心停止	
	VF/VT	PEA/Asys	VF/VT	PEA/Asys
JRC	Class I	Class II b	Class II b	Class II b
AHA	Class I LOE B	Class II b LOE B	Class II b LOE B	Class II b LOE B

JRC: Japanese Resuscitation Council

AHA: American Heart Association

Class I : 強く推奨される

Class II b: 考慮する価値がある

Class I LOE B: this treatment is useful/effective,
evidence from single randomized trial
or nonrandomized studies

Class II LOE B: recommendation's usefulness/efficacy
less well established, greater conflicting evidence from
single randomized trial or nonrandomized studies

The New England Journal of Medicine

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MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

THE HYPOTHERMIA AFTER CARDIAC ARREST STUDY GROUP*

N Engl J Med 2002;346:549-556

TREATMENT OF COMATOSE SURVIVORS OF OUT-OF-HOSPITAL CARDIAC ARREST WITH INDUCED HYPOTHERMIA

N Engl J Med 2002;346:557-563

ガイドラインの根拠としてはこれら2つのRCT

MILD THERAPEUTIC HYPOTHERMIA TO IMPROVE THE NEUROLOGIC OUTCOME AFTER CARDIAC ARREST

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- 目撃のある、心原性と推定される、初期波形がVF/VTのCPA蘇生後を対象としたRCT
- 目標体温は32～34℃で冷却期間は24時間

MILD THERAPEUTIC HYPOTHERMIA AFTER CARDIAC ARREST

TABLE 2. NEUROLOGIC OUTCOME AND MORTALITY AT SIX MONTHS.

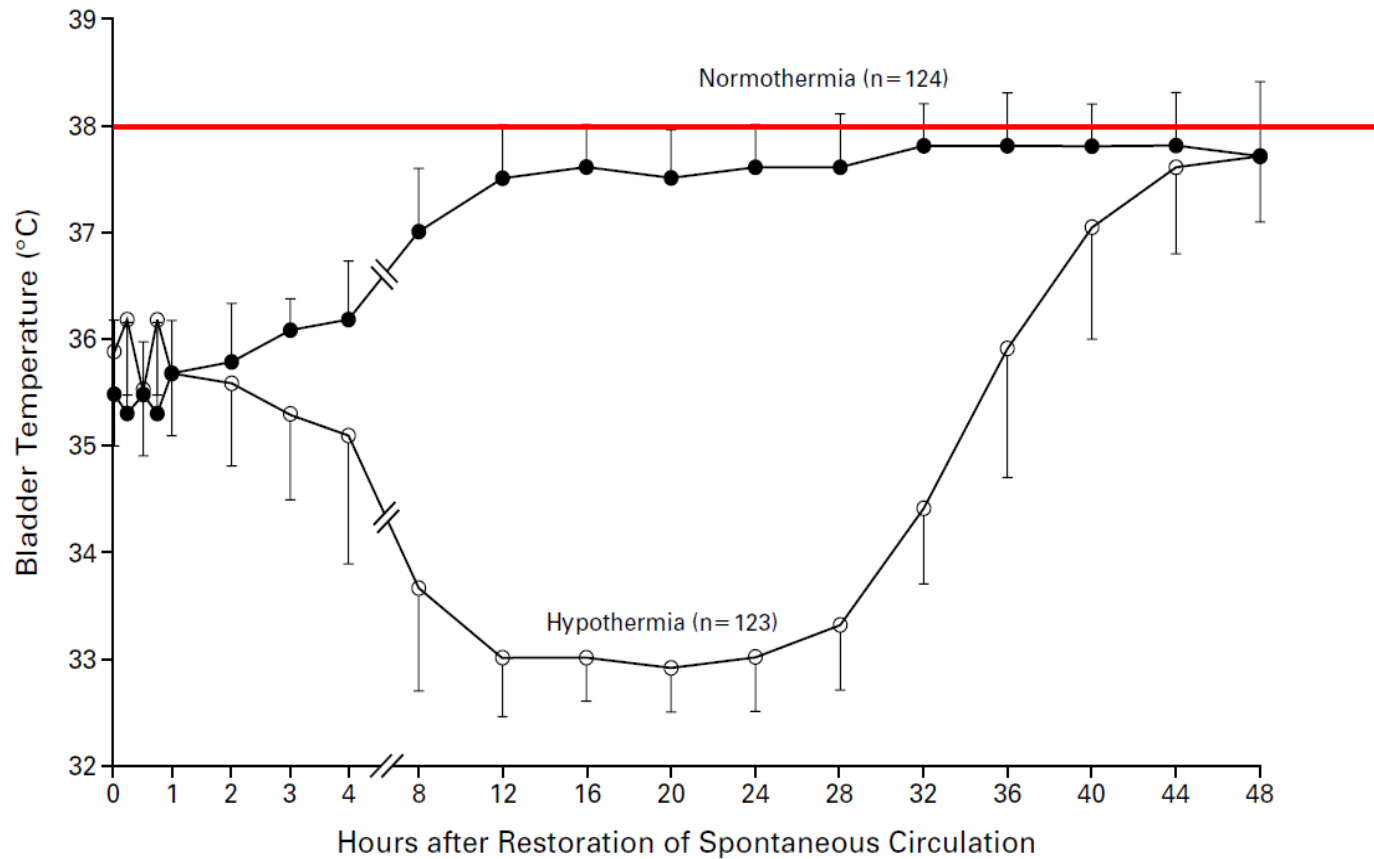
OUTCOME	NORMOTHERMIA	HYPOTHERMIA	RISK RATIO (95% CI)*	P VALUE†
	no./total no. (%)			
Favorable neurologic outcome‡	54/137 (39)	75/136 (55)	1.40 (1.08–1.81)	0.009
Death	76/138 (55)	56/137 (41)	0.74 (0.58–0.95)	0.02

神経学的予後も
死亡率も改善!!

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- 初期波形がVFのCPA蘇生後を対象にしたRCT
- 目標体温は33°Cで冷却期間は12時間

TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.

OUTCOME*	HYPOTHERMIA (N=43)	NORMOTHERMIA (N=34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely dependent (discharged to a long-term nursing facility)	0	1
Severe disability, unconscious (discharged to a long-term nursing facility)	0	1
Death	22	23

神経学的予後が
改善!!

しかし

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

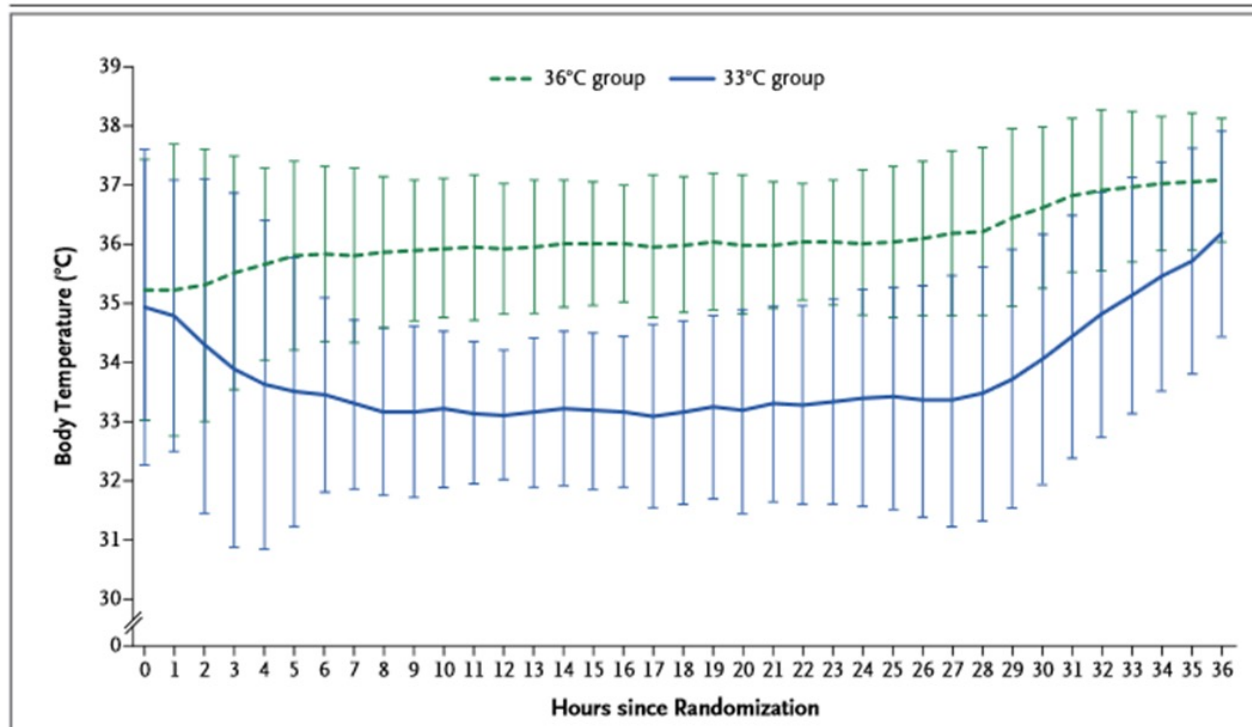
N Engl J Med 2013;369:2197-2206

院外心肺停止蘇生後939例を対象とした2つの目標体温の比較
Hypothermia(33°C) vs. Normothermia(36°C)
両群間の6か月転帰に差は認められなかった

ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

N Engl J Med 2013;369:2197-2206



ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

N Engl J Med 2013;369:2197-2206

Table 2. Outcomes.

Outcome	33°C Group	36°C Group	Hazard Ratio or Risk Ratio (95% CI)*	P Value
	<i>no./total no. (%)</i>			
Primary outcome: deaths at end of trial	235/473 (50)	225/466 (48)	1.06 (0.89–1.28)	0.51
Secondary outcomes				
Neurologic function at follow-up†				
CPC of 3–5	251/469 (54)	242/464 (52)	1.02 (0.88–1.16)	0.78
Modified Rankin scale score of 4–6	245/469 (52)	239/464 (52)	1.01 (0.89–1.14)	0.87
Deaths at 180 days	226/473 (48)	220/466 (47)	1.01 (0.87–1.15)	0.92

ORIGINAL ARTICLE

Targeted Temperature Management
at 33°C versus 36°C after Cardiac Arrest

N Engl J Med 2013;369:2197-2206

国際蘇生連絡委員会はこの報告に対して2013年12月に異例の勧告を行った。この研究で重要なのは低体温療法の否定ではなく、**体温管理が重要であること**。また、さらなる研究の必要性を示唆しており、**ガイドライン改訂まで低体温療法の推奨度を変更しない方針を示した**。

現時点では

- 院外の心停止かつ目撃ありかつ初期波形がVF/VTの蘇生後で昏睡状態であれば積極的に体温管理を行うべき。
- それ以外の心停止、(院内外/目撃の有無/Asys・PEA)ではエビデンスレベルは低いものの現状では体温管理を行うという方針で良いだろう。(エビデンスレベル・推奨度が低いのは真の心原性心停止の割合が少ないことが一因)

→(突然のVF/VTのほとんどが心原性であると思われ、また原因の特定が出来ないものも心原性心停止となる)

つまり心原性心停止蘇生後で昏睡状態であれば体温管理を行う。

注:心原性心停止/ウツタイン様式では原因の特定できないものも心原性として扱うため、明らかな心原性と原因が特定できないものも合わせたものと定義される。

では非心原性心停止は？

非心原性心停止の原因や病態は？

- 脳血管障害
- 窒息
- 溺水
- 外傷
- 中毒
- 偶発性低体温
などか？

では非心原性心停止は？

- 現時点で非心原性心停止に対する体温管理の効果は証明されていない。
- 予後を改善したという症例報告もあるが数が少ない。

→原因や蘇生に要した時間などを十分に考察し神経学的予後が期待できると判断された症例にのみ導入を考えるのが現実的ではないか。

ただし、現時点で回復の可能性を否定できる臨床的神経所見や検査方法はない。

頭部外傷の体温管理

重症頭部外傷 治療・管理のガイドライン



1. 低体温療法を考慮してよい症例がある。
2. 若年者では転帰改善効果が高いが、高齢者では限界がある。
3. evacuated mass lesion で転帰が改善する可能性がある。
4. 感染症、不整脈、低カリウム血症、血小板減少、凝固異常、高血糖などの発生頻度が高くなる可能性がある。
5. 復温に際し頭蓋内圧の再上昇する例では、復温の一時中止が勧められる。

頭部外傷の体温管理

重症頭部外傷 治療・管理のガイドライン



施行に当たっては、下記の条件が考慮される

1. 呼吸循環動態が安定している
2. GCSスコア3~4に対する適応に関して一定の見解はない
3. 若年者では転帰改善効果が高く、50歳以下でも有効であるが、高齢者では限界がある
4. 手術された占拠性病変においては転帰不良率が減少したが、びまん性脳損傷では転帰不良率に差はない
5. 受傷後できるだけ早期に導入し、6時間以内の目標温度達成が勧められる
6. 頭蓋内圧、脳組織酸素分圧、頸静脈球酸素飽和度などのモニタリングが望ましい
7. 目標体温は定まっていない
8. 期間は48~72時間、あるいは正常頭蓋内圧に至るまで
9. 復温速度は定まっていないが本邦では0.5~1°C/日が多い

Guidelines for the Management of Severe Traumatic Brain Injury 3rd Edition

SUMMARY

Evidence from six moderate quality RCTs did not clearly demonstrate that hypothermia was associated with consistent and statistically significant reductions in all-cause mortality. However, patients treated with hypothermia were more likely to have favorable neurological outcomes, defined as GOS scores of 4 or 5.

Preliminary findings suggest that hypothermia may have higher chances of reducing mortality when cooling is maintained for more than 48 hours. Interpretation of results from this and other subgroup analyses based on different aspects of the hypothermia treatment protocols were limited due to small sample sizes. Potential confounding and effect modifying factors that are not accounted for in the trials included in this analysis, such as patients' temperature at admission, limit these recommendations to Level III.

Hypothermia for traumatic head injury

Sydenham E, et al; Cochrane Database Syst Rev. 2009 Apr 15;(2):CD001048



THE COCHRANE
COLLABORATION®

- Cochrane systematic reviews
- 非開放性の頭部外傷患者に対して
低体温療法(35°C以下、12時間以上)と常温療法を比較したRCT
- 1614名、23研究
- 死亡率、機能的予後、合併症の発生頻度について解析

Authors' conclusions

There is no evidence that hypothermia is beneficial in the treatment of head injury.

Hypothermia may be effective in reducing death and unfavorable outcomes for traumatic head injured patients, but significant benefit was only found in low quality trials. Low quality trials have a tendency to overestimate the treatment effect. The high quality trials found no decrease in the likelihood of death with hypothermia, but this finding was not statistically significant and could be due to the play of chance. Hypothermia should not be used except in the context of a high quality randomized controlled trial with good allocation concealment.

The New England Journal of Medicine

LACK OF EFFECT OF INDUCTION OF HYPOTHERMIA AFTER ACUTE BRAIN INJURY

N Engl J Med 2001;344:556-63

頭部外傷に対しての低体温療法に関して最大規模のもの

- 多施設RCT
- 16-65歳の非開放性の頭部外傷392名
- 低体温群→33°Cで48時間持続
- 平温群→通常治療
- Outcome : 死亡率、6ヶ月後の転帰、合併症

The New England Journal of Medicine

LACK OF EFFECT OF INDUCTION OF HYPOTHERMIA AFTER ACUTE BRAIN INJURY

N Engl J Med 2001;344:556-63

TABLE 4. RATES OF POOR OUTCOME AND DEATH SIX MONTHS AFTER SEVERE BRAIN INJURY IN PATIENTS TREATED WITH INDUCTION OF HYPOTHERMIA OR NORMOTHERMIA.

TREATMENT GROUP	TOTAL No.	No. (%) WITH POOR OUTCOME*	RELATIVE RISK (95% CI)†	P VALUE	No. (%) WHO DIED	RELATIVE RISK (95% CI)†	P VALUE
All patients‡	368		1.0 (0.8–1.2)	0.99		1.0 (0.7–1.4)	0.79
Hypothermia	190	108 (57)			53 (28)		
Normothermia	178	102 (57)			48 (27)		
Patients with Glasgow coma scores of 3–4 on admission	87		1.1 (0.8–1.4)	0.64		1.4 (0.4–2.4)	0.35
Hypothermia	50	39 (78)			22 (44)		
Normothermia	37	27 (73)			13 (35)		
Patients with Glasgow coma scores of 5–8 on admission	281		0.9 (0.7–1.2)	0.55		1.0 (0.6–1.5)	0.71
Hypothermia	140	69 (49)			30 (21)		
Normothermia	141	75 (53)			32 (23)		
Patients >45 years old	52		1.3 (1.0–1.7)	0.08		1.0 (0.3–2.0)	1.00
Hypothermia	26	23 (88)			10 (38)		
Normothermia	26	18 (69)			10 (38)		

poor outcome率、
及び死亡率に
有意差なし

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

Guy L Clifton, Alex Valadka, David Zygun, Christopher S Coffey, Pamala Drever, Sierra Fourwinds, L Scott Janis, Elizabeth Wilde, Pauline Taylor, Kathy Harshman, Adam Conley, Ava Puccio, Harvey S Levin, Stephen R McCauley, Richard D Bucholz, Kenneth R Smith, John H Schmidt, James N Scott, Howard Yonas, David O Okonkwo

Lancet Neurol 2011; 10: 131-39

- 多施設RCT
- 非開放性の頭部外傷、意識不明患者
低体温群：受傷2.5時間以内に冷却開始、33°Cを48時間継続
常温群：37°C、通常治療
- Primary outcome：6ヶ月後のGlasgow outcome scale

Glasgow Outcome Scale (GOS)

1: DEAD

2: VEGETATIVE STATE

3: SEVERE DISABILITY

Able to follow commands/ unable to live independently

4: MODERATE DISABILITY

Able to live independently; unable to return to work or school

5: GOOD RECOVERY

Able to return to work or school

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

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Lancet Neurol 2011; 10: 131–39

	Poor outcome			Died		
	n (%)	RR (95% CI)	p value	n (%)	RR (95% CI)	p value
Primary analysis						
All patients (n=97)	56 (58%)	20 (21%)
Hypothermia (n=52)	31 (60%)	1.08 (0.76–1.53)	0.67	12 (23%)	1.30 (0.58–2.89)	0.52
Normothermia (n=45)	25 (56%)	8 (18%)

poor outcome率、死亡率ともに改善認められない

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

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Lancet Neurol 2011; 10: 131-39

	Hypothermia (n=52)	Normothermia (n=45)	p value
Received morphine	49 (94%)	39 (87%)	0.30
Morphine dose (mg/h)*	6.5 (2.4)	6.6 (3.0)	0.88
Received any paralytic	51 (98%)	37 (82%)	0.01
Received pancuronium bromide	39 (75%)	26 (58%)	0.07
Pancuronium bromide dose (mg/h)	4.9 (2.7)	6.8 (9.0)	0.30
Received mannitol	39 (75%)	27 (60%)	0.11
Mannitol dose (g/day)*	59 (3)	51 (60)	0.27
Received phenytoin	47 (90%)	42 (93%)	0.72
Phenytoin dose (mg/day)*	224 (251)	283 (311)	0.33
Administered vasopressors*	42 (81%)	32 (71%)	0.26
Daily therapeutic intervention score in ICU*	46 (8)	40 (7)	0.0006
Daily therapeutic intervention score after ICU discharge	17 (18)	15 (15)	0.46
Daily therapeutic intensity level *†	5.4 (2.3)	4.0 (2.0)	0.002
Fluids administered (mL)	2375 (1240)	1159 (999)	<0.0001
Cumulative fluid balance (mL)*	5285 (4285)	3099 (4080)	0.01
Negative fluid balance*	4 (8%)	9 (20%)	0.08
Caloric intake on day 5 (kcal)	761 (732)	704 (800)	0.71

Data are mean (SD) or number (%). ICU=intensive care unit. *For the first 96 h after injury. †Calculated for treatments administered to each patient in each 24-h period and mean values over 4 days were taken for each patient.

Table 3: Factors associated with medical treatment after hospitalisation

低体温群でICUでの治療介入が多い
輸液も多く、プラスバランスになった

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

Guy L Clifton, Alex Valadka, David Zygun, Christopher S Coffey, Pamala Drever, Sierra Fourwinds, L Scott Janis, Elizabeth Wilde, Pauline Taylor, Kathy Harshman, Adam Conley, Ava Puccio, Harvey S Levin, Stephen R McCauley, Richard D Bucholz, Kenneth R Smith, John H Schmidt, James N Scott, Howard Yonas, David O Okonkwo

Lancet Neurol 2011; 10: 131–39

	Hypothermia (n=52)	Normothermia (n=45)	p value
Serum sodium (mmol/L)	143 (5)	143 (6)	0.80
Serum potassium (mmol/L)	3.6 (0.3)	3.8 (0.2)	0.0005
Blood urea nitrogen (mmol/L)	4.3 (2.9)	3.9 (1.4)	0.28
Serum creatinine (µmol/L)	74 (36)	72 (18)	0.66
Prothrombin time (s)*	15 (2)	14 (3)	0.73
Partial thromboplastin time (s)†	34 (7)	31 (5)	0.004
Haemoglobin (g/L)	110 (10)	110 (10)	0.28
Platelet count (cells per µL)‡	189 (77)	209 (74)	0.2
Serum magnesium (mmol/L)§	0.8 (0.1)	0.8 (0.1)	0.46
Partial pressure of brain oxygen <6 mm Hg	19 (39%)	18 (45%)	0.55
Partial pressure of arterial carbon dioxide (mm Hg)¶	36 (4)	37 (3)	0.75
Partial pressure of arterial carbon dioxide <30 mm Hg	43 (83%)	28 (62%)	0.02
Serum glucose (mmol/L)	7.6 (2.0)	7.1 (0.8)	0.12

低体温群で低K血症、
APTT延長が多い

Data are mean (SD) or number (%). Mean values were calculated for each patient who had a value recorded from the time of admission until discharge from the intensive care unit. Mean values are not corrected for the duration of intensive care stay or the number of values collected for each patient. *Data missing for 11 patients in the hypothermia group and 12 in the normothermia group. †Data missing for two patients in the hypothermia group. ‡Data missing for two patients in the hypothermia group. §Data missing for one patient in the hypothermia group. ¶Not corrected for temperature (alpha stat).

Table 4: Laboratory findings

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

Guy L Clifton, Alex Valadka, David Zygun, Christopher S Coffey, Pamala Drever, Sierra Fourwinds, L Scott Janis, Elizabeth Wilde, Pauline Taylor, Kathy Harshman, Adam Conley, Ava Puccio, Harvey S Levin, Stephen R McCauley, Richard D Bucholz, Kenneth R Smith, John H Schmidt, James N Scott, Howard Yonas, David O Okonkwo

Lancet Neurol 2011; 10: 131-39

	Hypothermia (n=52)		Normothermia (n=45)		p value		Number of episodes		p value
	Total	Critical	Total	Critical	Total	Critical	Hypothermia	Normothermia	
Neurological complications*	43 (83%)	26 (50%)	31 (69%)	18 (40%)	0.11	0.32	428	208	0.01
Increased ICP	37 (71%)	14 (27%)	27 (60%)	9 (20%)	0.25	0.42	335	148	0.003
Decreased CPP	24 (46%)	21 (40%)	16 (36%)	13 (29%)	0.29	0.24	82	54	0.27
Hydrocephalus	4 (8%)	0 (0%)	2 (4%)	0 (0%)	0.68	0.99	4	2	0.13
New subdural haemorrhage	2 (4%)	1 (2%)	2 (4%)	1 (2%)	0.99	0.99	2	2	0.97

低体温群でICPの上昇回数が増加

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial

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Lancet Neurol 2011; 10: 131–39

	Poor outcome			Died		
	n (%)	RR (95% CI)	p value	n (%)	RR (95% CI)	p value
Subgroup analysis						
Diffuse brain injury (n=69)	42 (61%)	13 (19%)
Hypothermia (n=37)	26 (70%)	<u>1.44 (0.95–2.17)</u>	<u>0.09</u>	10 (27%)	2.88 (0.87–9.57)	0.08
Normothermia (n=32)	16 (50%)	3 (9%)
Surgically removed haematomas (n=28)	14 (50%)	7 (25%)
Hypothermia (n=15)	5 (33%)	<u>0.44 (0.22–0.88)</u>	<u>0.02</u>	2 (13%)	0.35 (0.08–1.50)	0.16
Normothermia (n=13)	9 (69%)	5 (39%)

Data are number (%). RR=relative risk.

Table 2: Outcome and mortality rates

血腫除去＋低体温療法でpoor outcome率の低下

Diverse effects of hypothermia therapy in patients with severe traumatic brain injury based on the CT classification of the Traumatic Coma Data Bank

Journal of Neurotrauma. -Not available-, ahead of print. doi:10.1089/neu.2014.3584.

Online Ahead of Editing: September 18, 2014

- 多施設RCT
- 重症頭部外傷に対して低体温療法群と常温療法の比較
(目標体温・冷却期間はabstractからは不明)
- 治療効果はどちらの群でも有意差はなかった
- 二次解析では血腫除去を行った50歳未満で有意にfavorable outcome率が上昇
(低体温77.8%、常温療法33.3%)
- しかし、低体温療法を行ったびまん性脳損傷では有意に死亡率が上昇

Glasgow Outcome Scale (GOS)

1: DEAD

2: VEGETATIVE STATE

3: SEVERE DISABILITY

Able to follow commands/ unable to live independently

4: MODERATE DISABILITY

Able to live independently; unable to return to work or school

5: GOOD RECOVERY

Able to return to work or school

Prolonged mild therapeutic hypothermia versus fever control with tight hemodynamic monitoring and slow rewarming in patients with severe traumatic brain injury: a randomized controlled trial

Journal of Neurotrauma. -Not available-, ahead of print.
doi:10.1089/neu.2013.3197.

- **多施設RCT**
- **重症頭部外傷に対しての低体温療法群と常温療法の比較**
低体温療法: 32~34°C、72時間、復温は1°C/日、n=98
常温療法 : 35.5°C~37°C、n=50
- **Poor outcome率及び死亡率に有意差なし**
低体温療法53%、常温療法48%

ORIGINAL ARTICLE

Hypothermia Therapy after Traumatic Brain Injury in Children

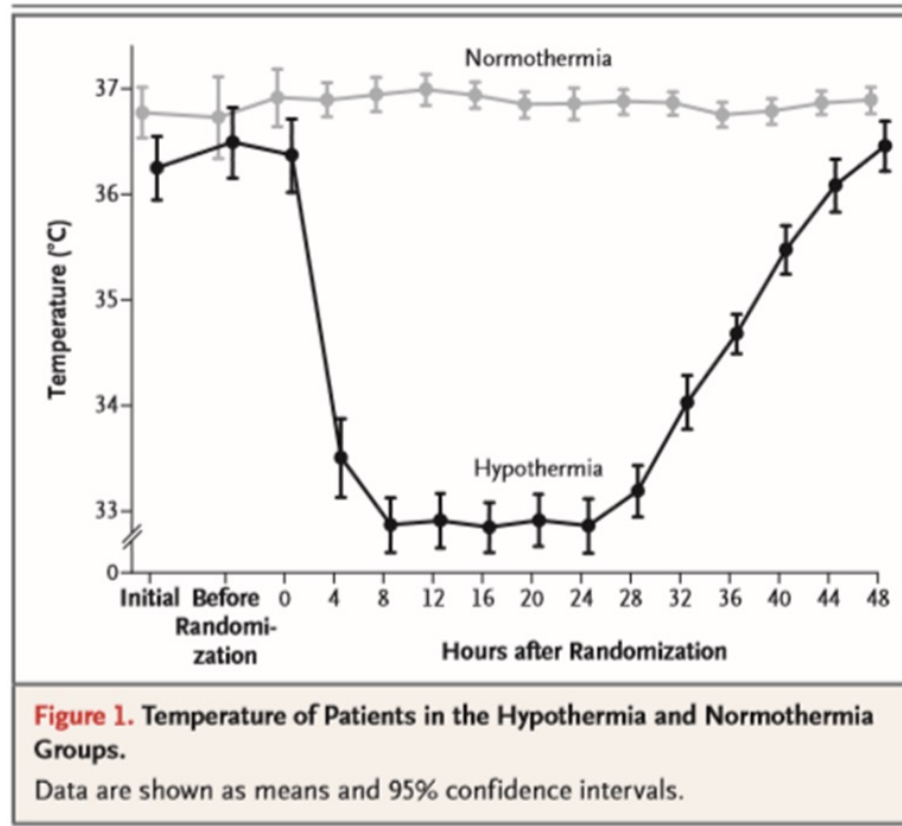
N Engl J Med 2008;358:2447-2256.

- 多施設RCT
- 小児重症頭部外傷
- Hypothermia vs. Normothermia
32.5°C 37度
- Primary outcomeはunfavorable outcome率
- Hypothermia群で32%、Normothermia群で23%

ORIGINAL ARTICLE

Hypothermia Therapy after Traumatic Brain Injury in Children

N Engl J Med 2008;358:2447-2256.



ORIGINAL ARTICLE

Hypothermia Therapy after Traumatic Brain Injury in Children

N Engl J Med 2008;358:2447-2256.

Table 3. Primary and Secondary Outcomes.*

Outcome	Hypothermia Group (N=108)	Normothermia Group (N=117)	Relative Risk or Absolute Difference (95% CI)	P Value
Primary				
PCPC score 4–6 — no./total no. (%)	32/102 (31)	23/103 (22)	1.41 (0.89 to 2.22)	0.14
Secondary				
Overall mortality — no. (%)	23 (21)	14 (12)	1.40 (0.90 to 2.27)	0.06

poor outcome率、死亡率ともに改善を認めなかった

Comparison of hypothermia and normothermia after severe traumatic brain injury in children (Cool Kids): a phase 3, randomised controlled trial

P David Adelson, Stephen R Wisniewski, John Beca, S Danielle Brown, Michael Bell, J Paul Muizelaar, Pamela Okada, Sue R Beers, Goundappa K Balasubramani, Deborah Hirtz, for the Paediatric Traumatic Brain Injury Consortium

Lancet Neurol 2013; 12: 546–53

- 多施設RCT
- 18歳未満の重症頭部外傷
- Hypothermia vs. Normothermia
- Hypothermia: 32–33°C for 48–72 h, rewarmed by 0.5–1.0°C every 12–24 h)
- Normothermia: maintained at 36.5–37.5°C
- Primary outcomeは3か月時点の死亡率
- 6 /39(15%) vs 2/38(5%) p=0.15

Comparison of hypothermia and normothermia after severe traumatic brain injury in children (Cool Kids): a phase 3, randomised controlled trial

P David Adelson, Stephen R Wisniewski, John Beca, S Danielle Brown, Michael Bell, J Paul Muizelaar, Pamela Okada, Sue R Beers, Goundappa K Balasubramani, Deborah Hirtz, for the Paediatric Traumatic Brain Injury Consortium

Lancet Neurol 2013; 12: 546–53

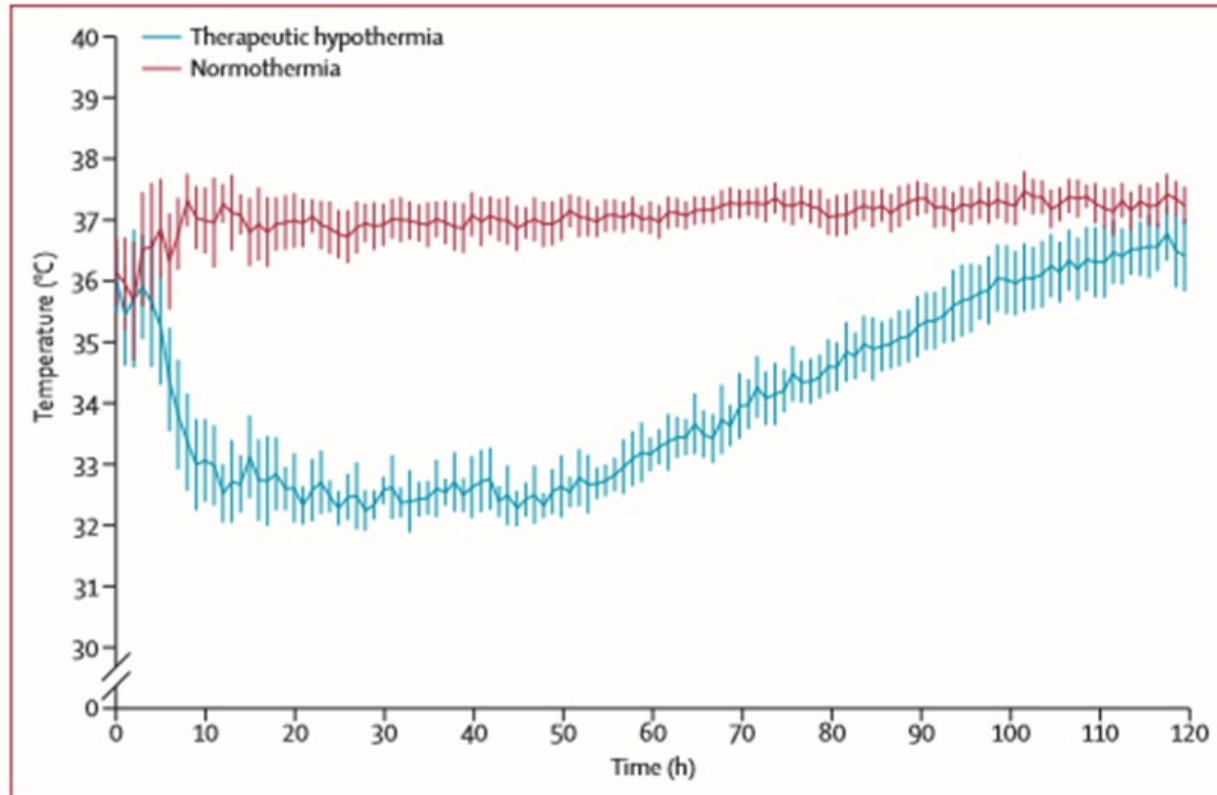
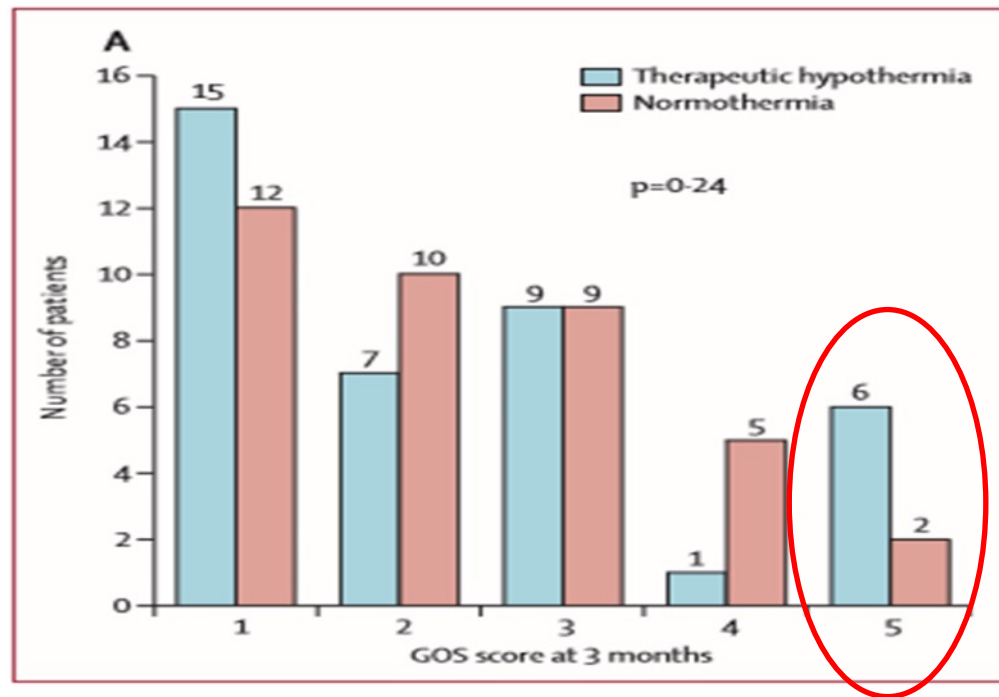


Figure 3: Temperatures of patients during the first 5 days after randomisation
Error bars are SDs.

Comparison of hypothermia and normothermia after severe traumatic brain injury in children (Cool Kids): a phase 3, randomised controlled trial

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Lancet Neurol 2013; 12: 546–53

	Total	Hypothermia	Normothermia
Glasgow outcome scale*			
Good outcome (scores 1–2)	44/76 (59%)	22/38 (58%)	22/38 (58%)
Poor outcome (scores 3–5)	32/76 (41%)	16/38 (42%)	16/38 (42%)
Glasgow outcome scale-extended pediatrics†			
Good outcome (scores 1–4)	38/75 (51%)	20/38 (53%)	18/37 (49%)
Poor outcome (scores 5–8)	37/75 (49%)	18/38 (47%)	19/37 (51%)

Data are number of patients (%). *Between-group difference (p value=0.90). †Between-group difference (p value=0.73). Despite random assignment, there were missing data for two patients: one patient was lost to follow-up at 3 months, and Glasgow outcome scale-extended pediatrics data were missing for one patient in the normothermia group.

Table 3: Secondary outcomes at 3 months after injury

Is therapeutic hypothermia beneficial for pediatric patients with traumatic brain injury? A meta-analysis

Child's Nervous System

June 2013, Volume 29, Issue 6, pp 979-984

- 小児頭部外傷で低体温vs常温の研究を抽出
- 死亡率、有害事象を解析
- 6研究
- 366症例

Conclusions

Hypothermia may slightly increase the risk of mortality in children with traumatic brain injury and the ratio of cardiac arrhythmia after this hypothermia therapy is slightly higher than that in normothermia groups. In the future, more randomized controlled trials and multicenter studies on the mechanism of therapeutic hypothermia are required.

頭部外傷の体温管理

- 以上から、現時点では頭部外傷に対しての低体温療法を積極的に行うに十分なエビデンスはない
- 高体温はおそらく悪いので目標体温を 36°C 前後に設定したTTMを行うのが現実的ではないか？
- ただし、血腫除去を行った症例では考慮してもいいかもしれない