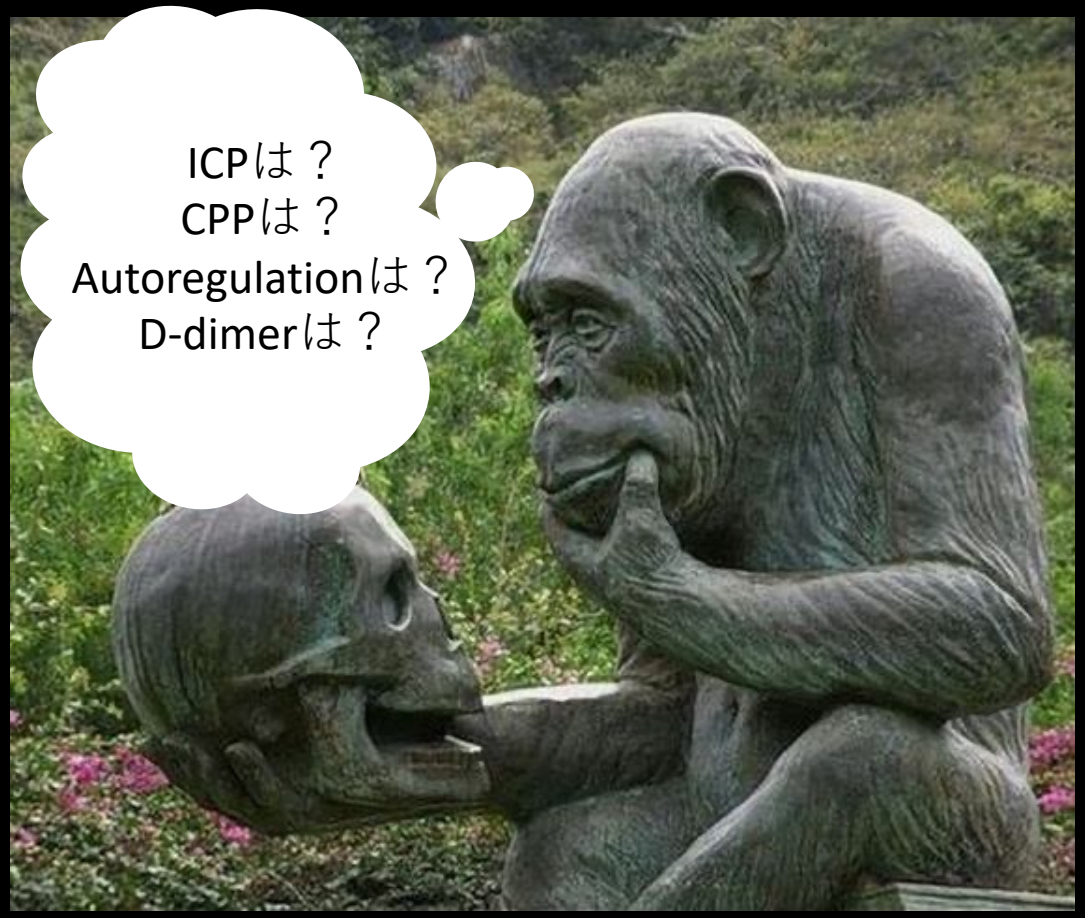
重症頭部外傷治療戦略会議

脳外チーム

令和2年7月

今回の戦略会議の目的

- 治療戦略の周知
- 脳外科医が考えていることを知っていただきたい
- 初療、ICU管理それぞれの戦略



初療で気にしていること

低血圧

低酸素

凝固障害

循環管理

- 数値目標

sBP > 110 mmHg or MAP > 90 mmHg

(1) *Level III*　(2) グレードA

手術時Hb > 10 g/dL　非手術時> 7 g/dL

(2) グレードA

1. Brain trauma foundation
   Guideline for the Management of Severe Brain Traumatic Injury 4th edition
2. 頭部外傷治療・管理のガイドライン　第4版

高血圧の是正

- 数値目標

sBP < 160 mmHg

⬇

エビデンスなし！！

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 20, 2013 VOL. 368 NO. 25

Rapid Blood-Pressure Lowering in Patients with Acute Intracerebral Hemorrhage

Craig S. Anderson, M.D., Ph.D., Emma Heeley, Ph.D., Yining Huang, M.D., Jiguang Wang, M.D., Christian Stapf, M.D., Candice Delcourt, M.D., Richard Lindley, M.D., Thompson Robinson, M.D., Pablo Lavados, M.D., M.P.H., Bruce Neal, M.D., Ph.D., Jun Hata, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Mark Parsons, M.D., Ph.D., Yuechun Li, M.D., Jinchao Wang, M.D., Stephane Heritier, Ph.D., Qiang Li, B.Sc., Mark Woodward, Ph.D., R. John Simes, M.D., Ph.D., Stephen M. Davis, M.D., and John Chalmers, M.D., Ph.D., for the INTERACT2 Investigators*

sBP <140mmHg
予後改善

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October 21, 2014; 83 (17) ARTICLE

Intensive blood pressure reduction in acute intracerebral hemorrhage

A meta-analysis

Georgios Tsivgoulis, Aristeidis H. Katsanos, Kenneth S. Butcher, Efstathios Boviatsis, Nikos Triantafyllou, Ioannis Rizos, Andrei V. Alexandrov

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Intensive Blood-Pressure Lowering in Patients with Acute Cerebral Hemorrhage

Adnan I. Qureshi, M.D., Yuko Y. Palesch, Ph.D., William G. Barsan, M.D., Daniel F. Hanley, M.D., Chung Y. Hsu, M.D., Renee L. Martin, Ph.D., Claudia S. Moy, Ph.D., Robert Silbergleit, M.D., Thorsten Steiner, M.D., Jose I. Suarez, M.D., Kazunori Toyoda, M.D., Ph.D., Yongjun Wang, M.D., Haruko Yamamoto, M.D., Ph.D., and Byung-Woo Yoon, M.D., Ph.D., for the ATACH-2 Trial Investigators and the Neurological Emergency Treatment Trials Network*

sBP <140mmHg
予後改善効果なし

British Journal of Anaesthesia **113** (5): 832–9 (2014)
Advance Access publication 25 June 2014 · doi:10.1093/bja/aeu185

BJA

NEUROSCIENCES AND NEUROANAESTHESIA

Flurbiprofen and hypertension but not hydroxyethyl starch are associated with post-craniotomy intracranial haematoma requiring surgery

M. Jian[1†], X. Li[1†], A. Wang[1], L. Zhang[2], R. Han[1*] and A. W. Gelb[3]

[1] Department of Anaesthesiology, Beijing Tiantan Hospital, Capital Medical University, No. 6 Tiantan Xili, Beijing 100050, China
[2] Department of Epidemiology and Biostatistics, School of Public Health and Family Medicine, Capital Medical University, Beijing, China
[3] Department of Anaesthesia and Perioperative Care, University of California San Francisco, San Francisco, CA, USA

* Corresponding author. E-mail: ruquan.han@gmail.com

Results. A total of 202 patients suffered post-craniotomy intracranial haematoma during the study period, for an incidence of 0.48% (95% CI=0.41–0.55). Haematoma requiring surgery was associated with an intraoperative systolic blood pressure of >160 mm Hg (OR=2.618, 95% CI=2.084–2.723, *P*=0.007), an intraoperative mean blood pressure of >110 mm Hg (OR=2.600, 95% CI=2.312–3.098, *P*=0.037), a postoperative systolic blood pressure of >160 mm Hg (OR=2.060, 95% CI= 1.763–2.642, *P*=0.022), a postoperative mean blood pressure of >110 mm Hg (OR=3.600, 95% CI= 3.226–4.057, *P*=0.001), and the use of flurbiprofen during but not after the surgery (OR=2.256, 95% CI=2.004–2.598, *P*=0.005). The intraoperative infusion of HES showed no significant difference between patients who had a haematoma and those who did not.

sBP ＞160mmHg
再開頭を要する

呼吸管理

- 数値目標

SpO_2 ≧ 98%　PaO_2 > 80 mmHg
$PaCO_2$ 35 mmHg付近(手術待機中に25 mmHgまでは可)

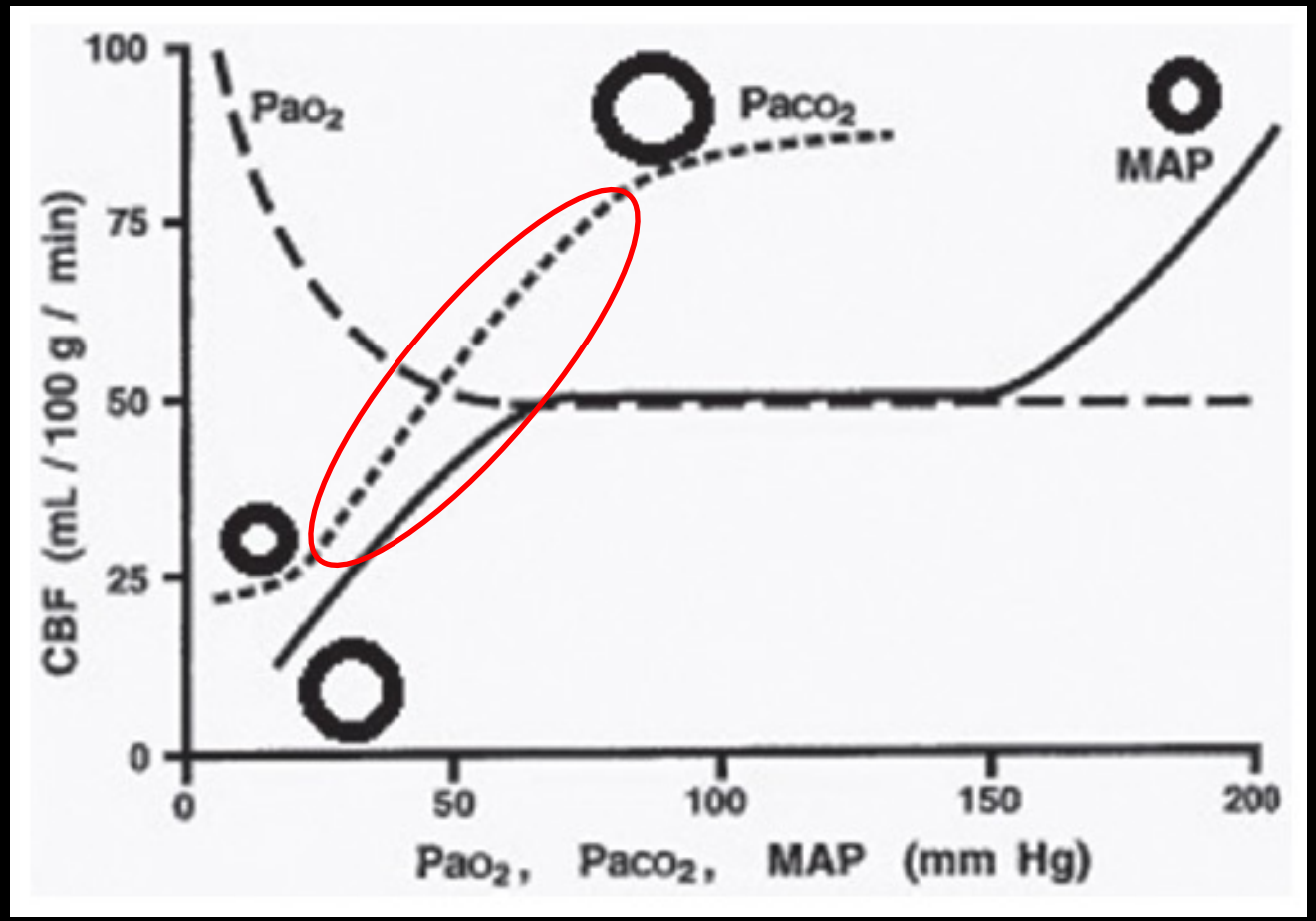
(2) グレードA

※予防的過換気(25 mmHg以下)を続けることは推奨されない

(1) *Level IIB*

1. Brain trauma foundation
   Guideline for the Management of Severe Brain Traumatic Injury 4th edition
2. 頭部外傷治療・管理のガイドライン　第4版

PCO_2は強力なICP規定因子



Rameshkumar et al. J Pediatr Crit Care. 2(3): 13-24. 2015

凝固障害

- 達成行動目標

速やかなMTP発動（原則手術症例）

受傷後1,2,3,4,5,6時間後のFibrinogenとD-dimerフォロー

受傷３時間以内であればトラネキサム酸1g

FFPオーダー

MTP発動症例 ≒ 手術症例

- 確実例

  JCS III-100以上　かつ　瞳孔不同 2mm以上[1)]

- 危険症例

  Dr 接触時GCS と院着時GCS に 2 以上の悪化がある[2)]

  JCS III-100以上　かつ　Cushing徴候 (sBP ≧ 180 mmHg　HR < 60)[3)]

1. Chesnut RM et al. Neurosurgery 34: 840-845, 1994
2. Majidi S et al. Am J Emerg Med 31: 1215-1219, 2013
3. Yumoto T et al. Scand J Trauma Resusc Emerg Med 24: 147-153, 2016

MTP発動

最低1h毎のABG、凝固、血算

6時間継続！

1.1＜iCa＜1.25mmol/Lを保つ

凝固製剤

異型O型RBC6U＋Fib3g

初回INR＞1.5　or　経過中　INR>1.5

ケイセントラ25U/kg

経過中　Fib>150mg/dl継続

150以上Keep！

Fib3g　＋フィブロガミン15U/kg

RBC、FFP
（volume　replace）

止血完了まで投与

PC

初回採血の血小板数

血小板＜6万

血小板＞10万

PCオーダー

オーダー開始

オーダー待ち

FFP8U以上投与
PCオーダー開始

上記戦略を初療室からZeego、Ope室でも一貫して行う　ICU入室まででMTP完結とする

D-dimerとTBI

Takayama et al. 脳外誌 22: 837-841, 2013

57 years under

GCS	50	D-dimer
7	0/68 0%	1/7 14.3%
	1/36 2.7%	11/22 50%

57 years over

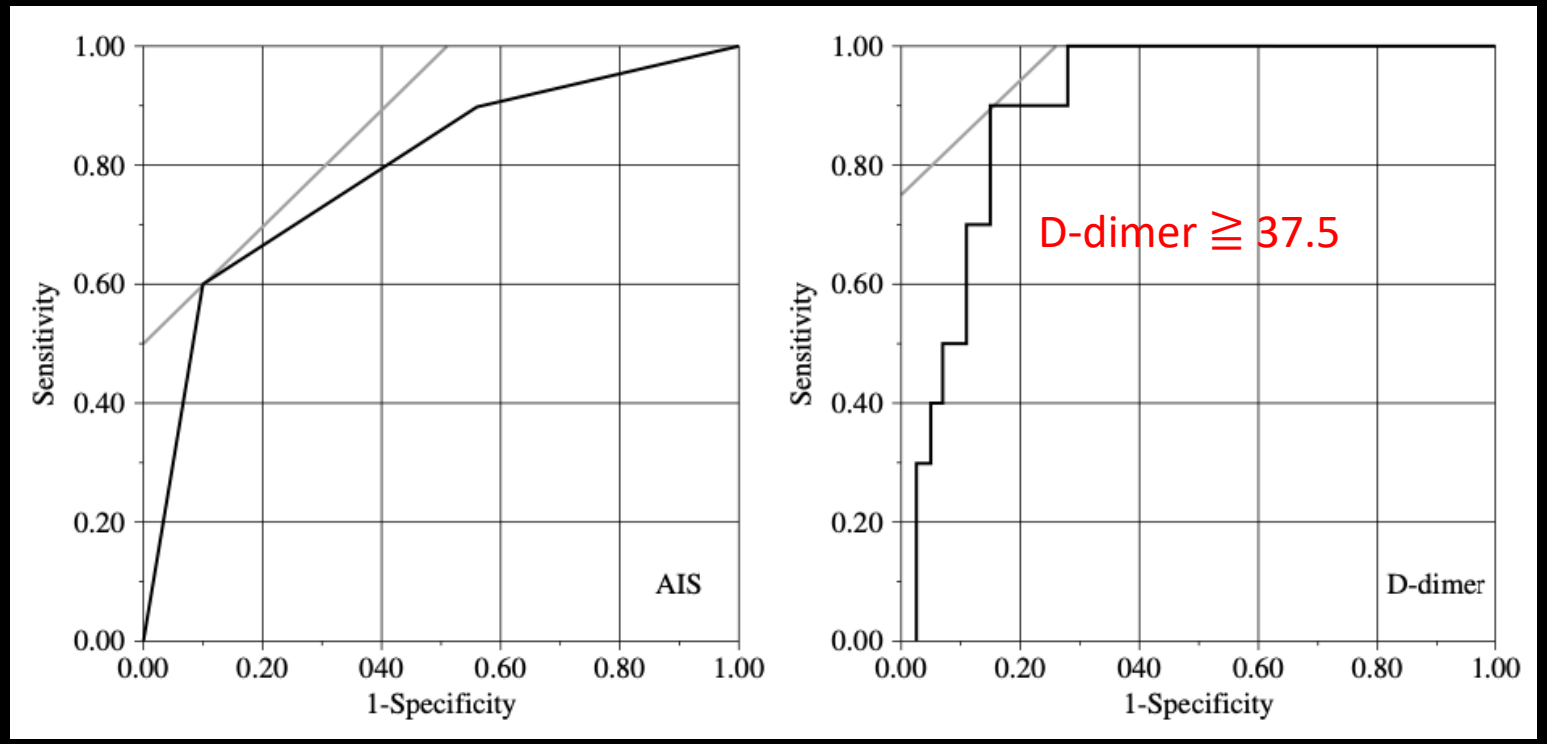
GCS	50	D-dimer
7	0/42 20%	5/20 25%
	3/18 16.7%	32/34 94.1%

➡ 50は1つの指標（手術の目安、ICPセンサー挿入）

D-dimerとTBI

Factor	p Value	Odds ratio	95% CI
AIS	0.02	7.21	1.31 - 47.01
D-dimer	<0.001	37.31	5.77 - 740.13

AIS: abbreviated injury score, 95% CI: 95% confidence interval.



D-dimer ≧ 35

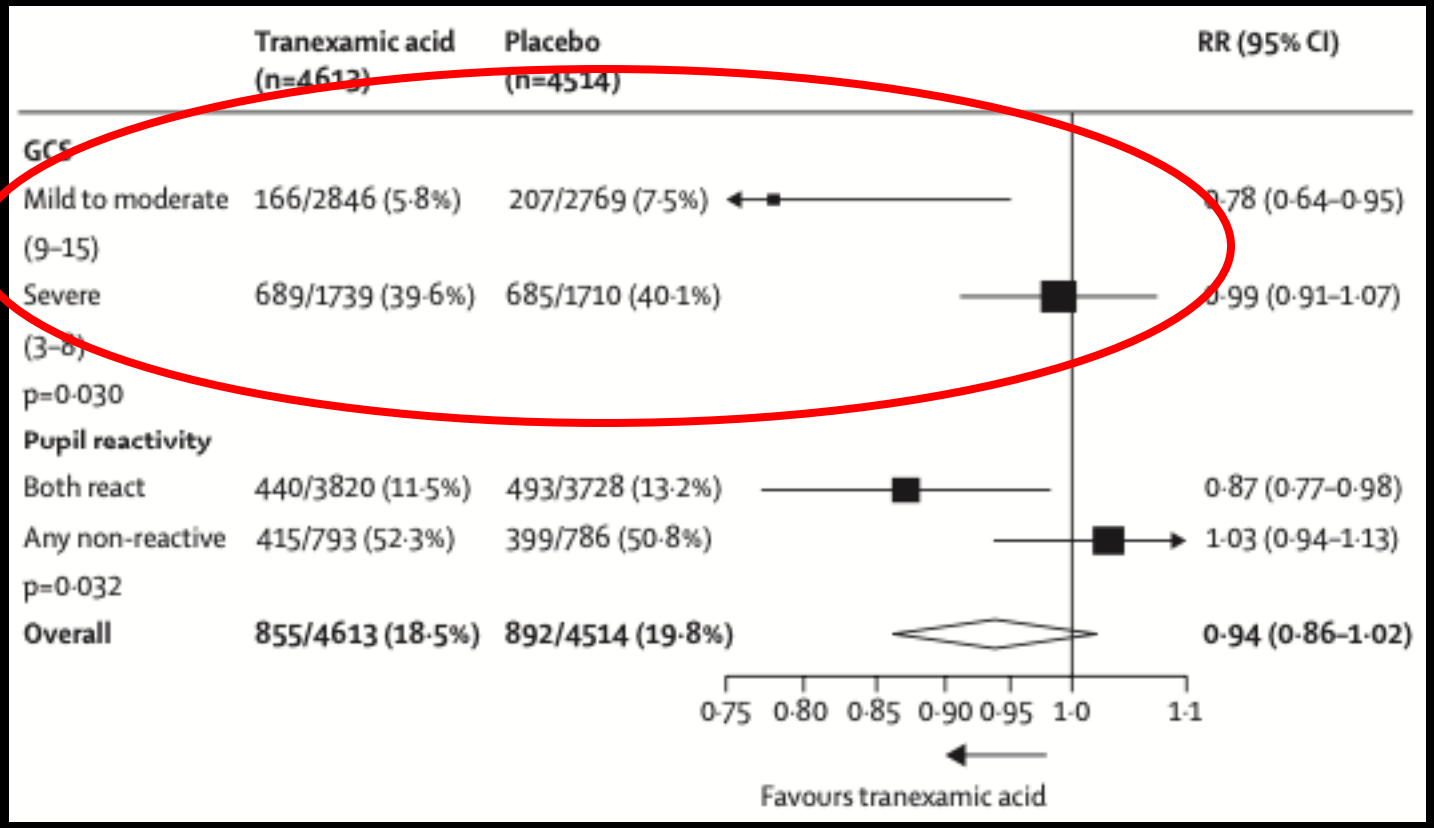
は３時間後CT検討

中江竜太. 他 日救急医会誌 25: 247-253, 2014

トラネキサム酸　～CRASH 3 trial～

Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial

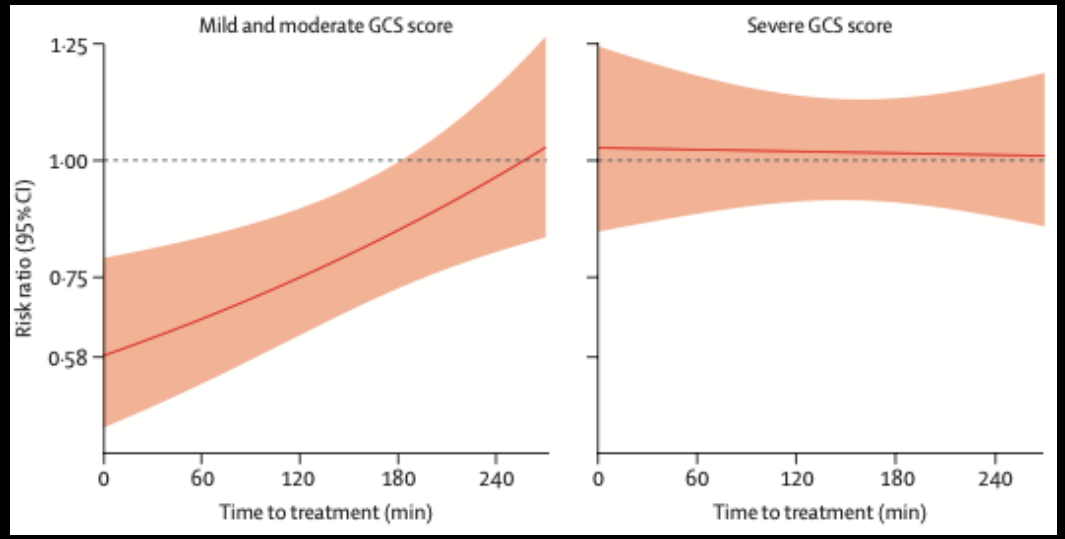
*The CRASH-3 trial collaborators**



受傷 3 時間以内

GCS 9-15

死亡率低下12.5% vs 14.0%



ICPセンサー挿入の適応

※血腫、脳挫傷、脳腫脹、脳ヘルニア 、基底槽の圧迫

- 原則

  GCS ≦ 8 （原則）　かつ　CTで異常所見(※)　(1) グレードA

- ありうる例

  GCS ≦ 8　かつ　CT正常　40歳以上　異常肢位　sBP ≦ 90 mmHg

  (1) グレードA

  他部位損傷に対する手術が必要な症例　(1) グレードB

  Talk and deteriorateのリスクの高い症例

  超重症例に対する姑息的介入

1. 頭部外傷治療・管理のガイドライン　第4版

BTF Guideline 4th editionでのICP

RECOMMENDATIONS

Level I and II A

Level IやIIでの推奨のエビデンスなし

- There was insufficient evidence to support a Level I or II A recommendation for this topic.

Level II B

院内死亡率・受傷2週間後死亡率を下げるために推奨

- Management of severe TBI patients using information from ICP monitoring is recommended to reduce in-hospital and 2-week post-injury mortality.

ICPのエビデンス

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 27, 2012 VOL. 367 NO. 26

A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury

Class 1

BEST TRIP → 有効性を示せず

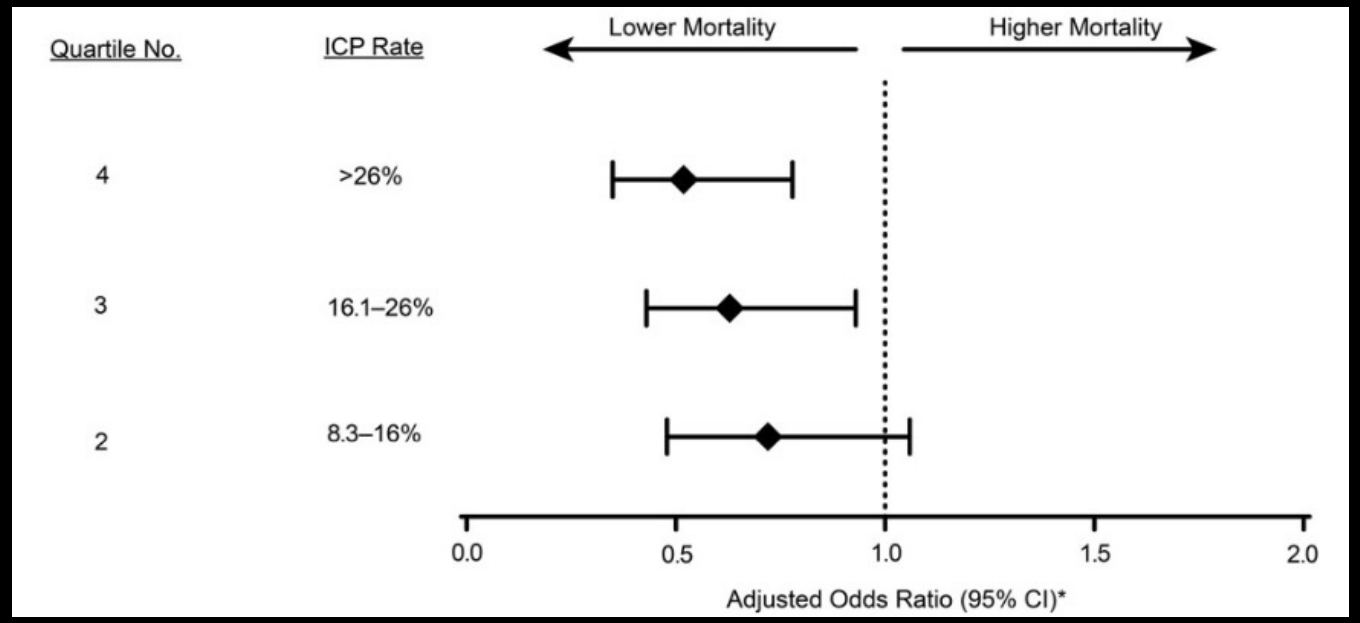
Class 2

Intracranial Pressure Monitoring in Severe Traumatic Brain Injury: Results from the American College of Surgeons Trauma Quality Improvement Program

Aziz S. Alali,[1–3] Robert A. Fowler,[1,2,4,5] Todd G. Mainprize,[6] Damon C. Scales,[1,2,4,5] Alexander Kiss,[1,2,7] Charles de Mestral,[1,10] Joel G. Ray,[2,8,9] and Avery B. Nathens[1,2,8,10]

J Neurotrauma. 2013;30(20):1737-1746.

Covariate	*Adjusted OR*	*95% CI*	p *value*
Patient-level characteristics			
ICP monitoring (yes)	0.44	0.31–0.63	<0.0001



ICPモニタリングは
死亡率低下と有意に関連

J Neurosurg 117:729–734, 2012

Class 2

Increased mortality in patients with severe traumatic brain injury treated without intracranial pressure monitoring

Clinical article

Arash Farahvar, M.D., Ph.D.,[1] Linda M. Gerber, Ph.D.,[2] Ya-Lin Chiu, M.S.,[2] Nancy Carney, Ph.D.,[3] Roger Härtl, M.D.,[4] and Jamshid Ghajar, M.D., Ph.D.[4,5]

Predictor Variable	Adults		All Ages	
	Adjusted OR (95% CI)	p Value	Adjusted OR (95% CI)	p Value
ICP monitoring				
yes	0.64 (0.41–1.00)	0.05	0.63 (0.41–0.94)	0.02
no	reference		reference	
age (yrs)				
≥60	2.43 (1.56–3.79)	<0.0001	2.50 (1.65–3.78)	<0.0001
<60	reference		reference	
initial GCS score				
6–8	0.46 (0.37–0.57)	<0.0001	0.44 (0.36–0.53)	<0.0001
3–5	reference		reference	
hypotension present on Day 1				
yes	2.08 (1.48–2.92)	<0.0001	2.08 (1.54–2.82)	<0.0001
no	reference		reference	
CT scan findings				
abnormal	2.45 (1.05–5.75)	0.04	2.71 (1.11–6.60)	0.03
normal	reference		reference	
pupil abnormalities on Day 1				
yes	1.38 (0.99–1.91)	0.05	1.40 (0.98–2.00)	0.07
no	reference		reference	

後向きコホート研究

N=1,307

アメリカ外傷センター20施設

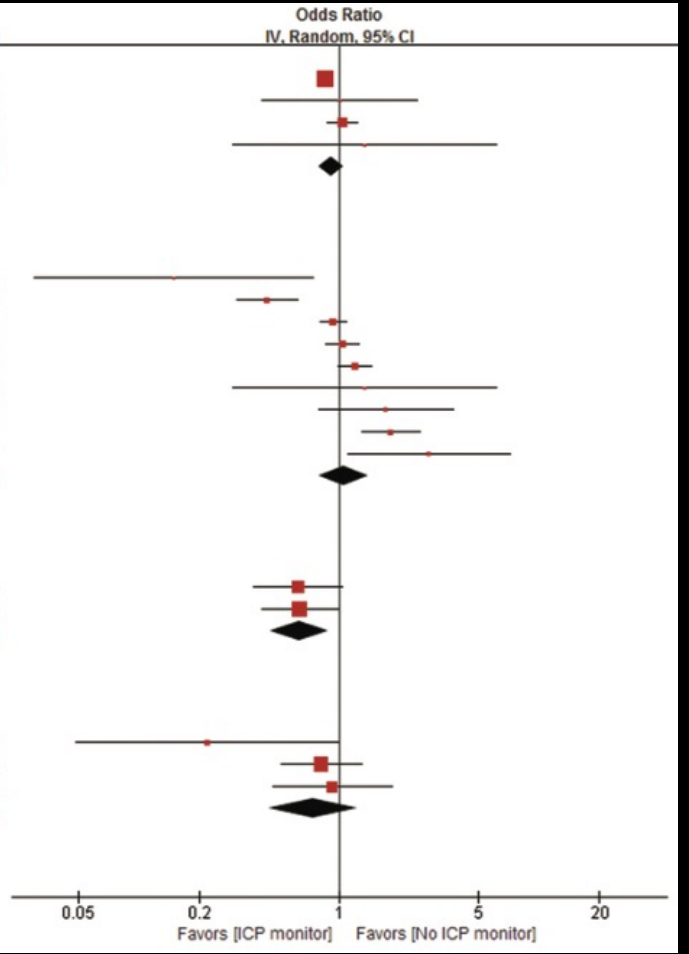
ICPモニターは死亡率を低下

Impact of intracranial pressure monitoring on mortality in patients with traumatic brain injury: a systematic review and meta-analysis

*Qiang Yuan, MD, Xing Wu, MD, PhD, Yirui Sun, MD, PhD, Jian Yu, MD, PhD, Zhiqi Li, MD, Zhuoying Du, MD, PhD, Ying Mao, MD, PhD, Liangfu Zhou, MD, PhD, and Jin Hu, MD, PhD

J Neurosurg. 122:574–587, 2015.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.5.1 ICU mortality				
Mauritz et al 2007	-0.157	0.011	64.0%	0.85 [0.84, 0.87]
Haddad et al 2011	0.01	0.456	2.5%	1.01 [0.41, 2.47]
Mauritz et al 2008	0.042	0.092	32.5%	1.04 [0.87, 1.25]
Gao et al 2013	0.3	0.774	0.9%	1.35 [0.30, 6.15]
Subtotal (95% CI)			100.0%	0.92 [0.79, 1.06]
Heterogeneity: Tau² = 0.01; Chi² = 5.09, df = 3 (P = 0.17); I² = 41%				
Test for overall effect: Z = 1.13 (P = 0.26)				
1.5.2 Hospital mortality				
Talving et al 2013	-1.897	0.818	2.7%	0.15 [0.03, 0.75]
Alali et al 2013	-0.821	0.181	14.3%	0.44 [0.31, 0.63]
Thompson et al 2008	-0.062	0.076	17.4%	0.94 [0.81, 1.09]
Mauritz et al 2008	0.039	0.096	16.9%	1.04 [0.86, 1.26]
Lane et al 2000	0.182	0.099	16.8%	1.20 [0.99, 1.46]
Gao et al 2013	0.3	0.774	3.0%	1.35 [0.30, 6.15]
Haddad et al 2011	0.536	0.394	7.9%	1.71 [0.79, 3.70]
Shafi et al 2008	0.598	0.17	14.7%	1.82 [1.30, 2.54]
Griesdale et al 2010	1.03	0.476	6.3%	2.80 [1.10, 7.12]
Subtotal (95% CI)			100.0%	1.06 [0.80, 1.42]
Heterogeneity: Tau² = 0.12; Chi² = 48.83, df = 8 (P < 0.00001); I² = 84%				
Test for overall effect: Z = 0.41 (P = 0.68)				
1.5.3 2-week mortality				
Chesnut et al 2012	-0.474	0.259	43.4%	0.62 [0.37, 1.03]
Farahvar et al 2012	-0.446	0.227	56.6%	0.64 [0.41, 1.00]
Subtotal (95% CI)			100.0%	0.63 [0.45, 0.88]
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%				
Test for overall effect: Z = 2.68 (P = 0.007)				
1.5.4 6-month mortality				
Zeng et al 2013	-1.514	0.769	10.4%	0.22 [0.05, 0.99]
Chesnut et al 2012	-0.202	0.236	54.0%	0.82 [0.51, 1.30]
Biersteker et al 2012	-0.073	0.35	35.5%	0.93 [0.47, 1.85]
Subtotal (95% CI)			100.0%	0.75 [0.45, 1.25]
Heterogeneity: Tau² = 0.07; Chi² = 3.00, df = 2 (P = 0.22); I² = 33%				
Test for overall effect: Z = 1.11 (P = 0.27)				



2012年以降のStudy
ICPは死亡率低下に関連
ただしICU滞在日数、
入院日数が有意に伸びる

ICPの適応

Acta Neurochir (2014) 156:1615–1622

Clinical applications of intracranial pressure monitoring in traumatic brain injury

Report of the Milan consensus conference

Nino Stocchetti · Edoardo Picetti · Maurizio Berardino · Andràs Buki · Randall M. Chesnut · Kostas N. Fountas · Peter Horn · Peter J. Hutchinson · Corrado Iaccarino · Angelos G. Kolias · Lars-Owe Koskinen · Nicola Latronico · Andrews I. R. Maas · Jean-François Payen · Guy Rosenthal · Juan Sahuquillo · Stefano Signoretti · Jean F. Soustiel · Franco Servadei

- Monitoring the ICP of comatose TBI patients with a normal initial CT is generally not recommended.
  - However, due to the occurrence of early negative CT scans which may subsequently worsen, a second CT scan is recommended. In case of further neurological worsening, the second CT scan should be performed urgently.

ICPセンサーは症例を選んで入れるべし！

抗てんかん薬の予防投与

Brain trauma foundation Guideline for the Management of Severe Brain Traumatic Injury 4th edition

Level II A

- Prophylactic use of phenytoin or valproate is not recommended for preventing late PTS.
- Phenytoin is recommended to decrease the incidence of early PTS (within 7 days of injury), when the overall benefit is felt to outweigh the complications associated with such treatment. However, early PTS have not been associated with worse outcomes.

At the present time there is insufficient evidence to recommend levetiracetam over phenytoin regarding efficacy in preventing early post-traumatic seizures and toxicity.

初療で気づいたらイーケプラを投与してください

他の部位の損傷で手術　ご相談ください！

- CT所見が軽微　かつ　凝固問題なし　➡　手術可

※ 少量のSAH
厚さ1mmのASDHなど

※ Fib, Plt, INR正常 かつ
D-dimer <20など(骨折による上昇)

- CT所見に後々増大しそうな病変 or 凝固異常

※ 明らかに分かる脳挫傷
軽度のMLSのあるASDHなど

※ 低Fib, 低Plt, D-dimer 35程度
WfやDOAC内服中　APT中

➡　3時間後CTを確認させてください

頭蓋内圧亢進例はICP入れて手術も

Anaesth Crit Care Pain Med 37 (2018) 171–186

ELSEVIER

SFAR
Société Française d'Anesthésie et de Réanimation

Guidelines

Management of severe traumatic brain injury (first 24 hours)☆,☆☆

CrossMark

R8.3 – We suggest measuring intracranial pressure during extracranial surgical procedure in severe TBI patients.

Grade 2+, Strong Agreement

Argument:

The neurological monitoring of these patients is essential to limit episodes of decreased cerebral perfusion pressure.

Pietropaoli et al. studied the haemodynamic effects of extracranial surgery in the first 72 hours after severe TBI [207]. Thirty-two percent of patients had episodes of intraoperative arterial hypotension (systolic blood pressure < 90 mmHg). These patients had a mortality of 82%, whereas patients without intraoperative arterial hypotension had a mortality of 32%.

sBP ＜ 90 mmHg
死亡率82%(50%増)

手術の際の注意事項

- 体位
  仰臥位　→ 可能な限り頭部挙上
  腹臥位　→ Concorde position

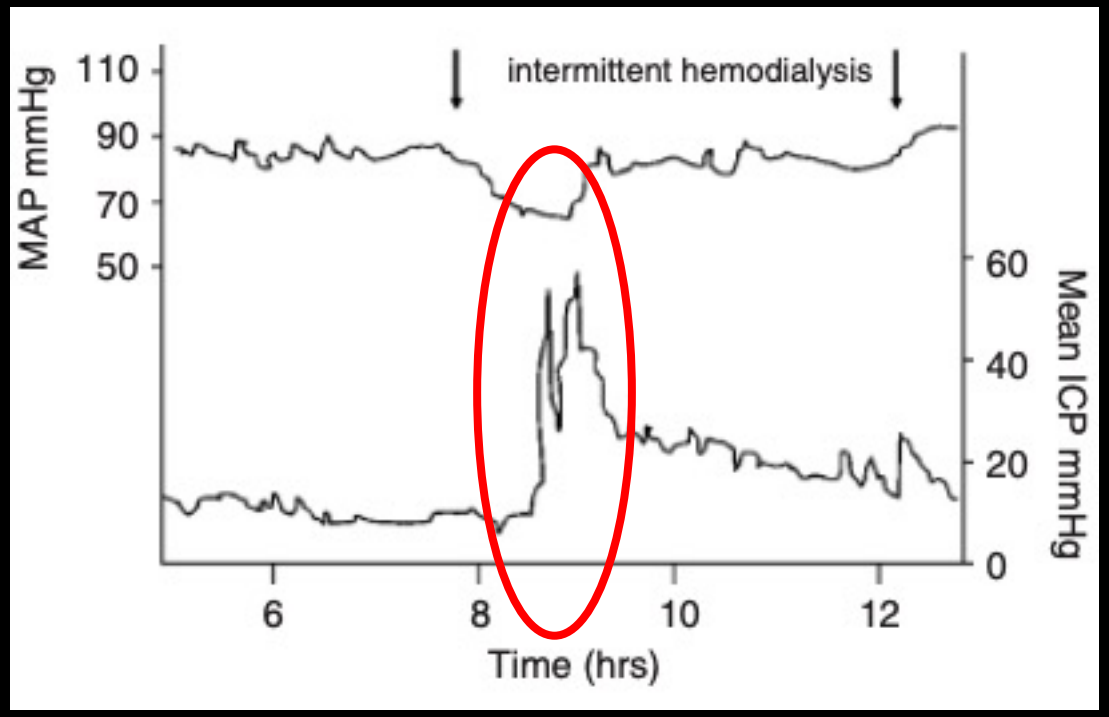
- ICPセンサーを入れているとき
  CPP ≧ 50　(CPP = MAP – ICP)　を目標に

- sBP > 90mmHg　体温36℃を目標に

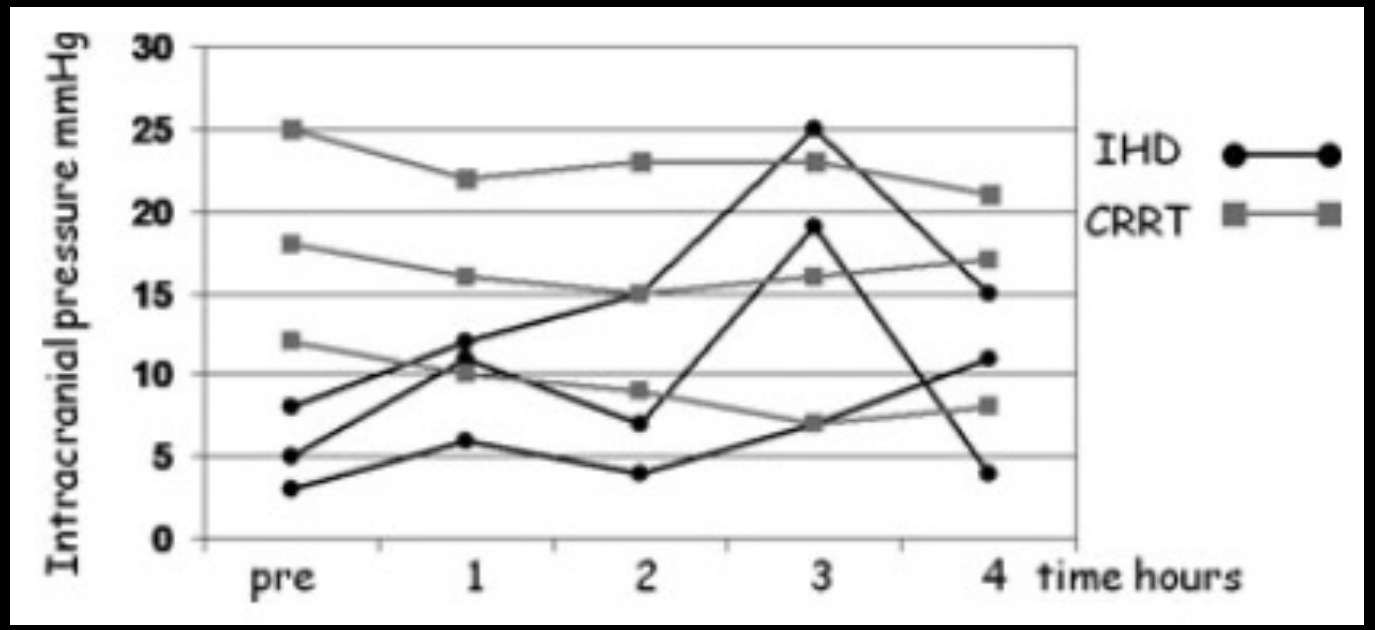
➡ 麻酔科の先生にお伝えを！術後にCTをお願いします

頭部外傷と人工透析

透析すると浮腫む！

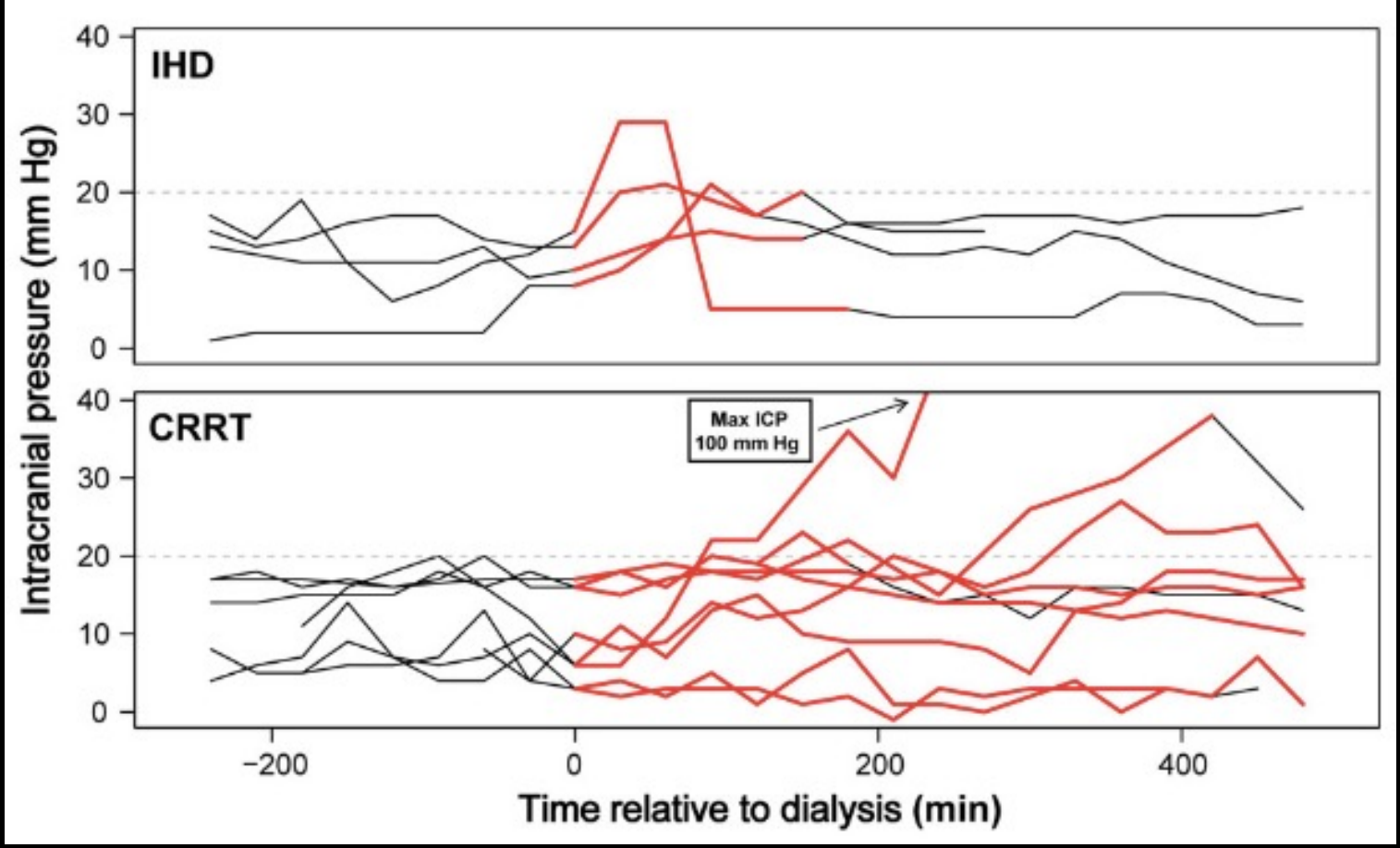


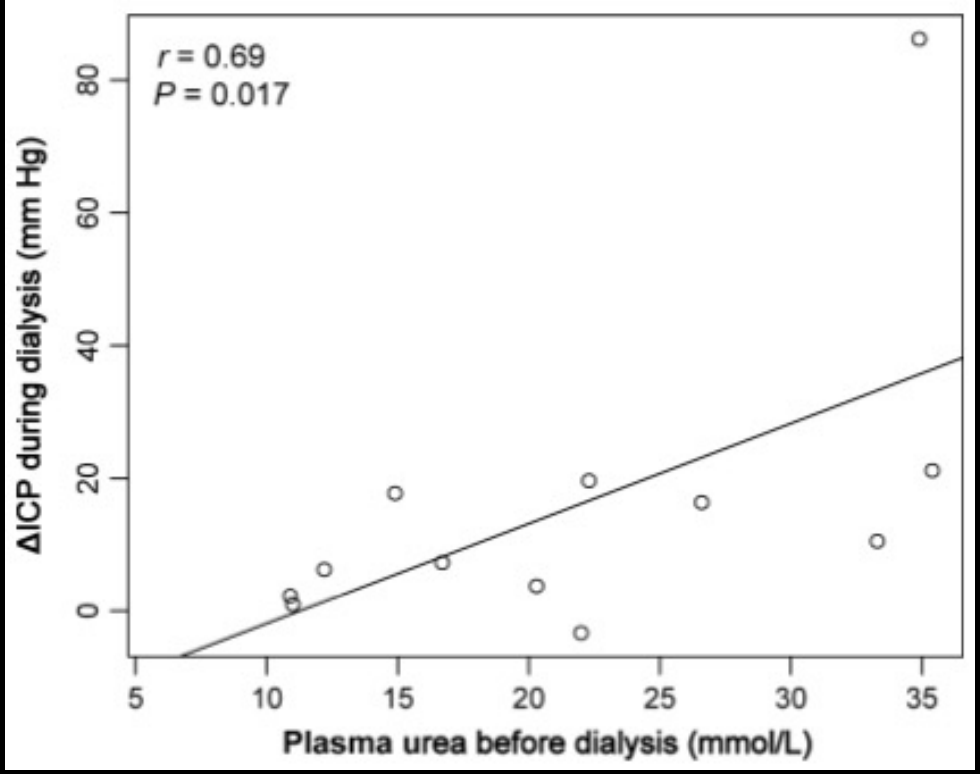
Davenport. Hemodial Int. 2008 Jul;12(3):307-12.



Davenport.Semin Dial. Mar-Apr 2009;22(2):165-8.

CHDFでもICPは上昇する





Lund et al. Acta Anaesthesiol Scand. 2019 Apr;63(4):493-499.

重症頭部外傷患者における腎代替療法

- 原則的に導入禁忌！！
- 待てるなら可能な限り待ってください
- どうしてもの時はCHD(F)
- その際は血液流量と透析液流量は低め
- ナファモスタットの使用

呼吸

SpO_2 > 98%
PCO2 35 mmHg

循環

110 mmHg< sBP < 160 mmHg
MAP > 90 mmHg

凝固障害

受傷後 3 h以内
トラネキサム酸 1g

開頭手術

Yes

- MTP発動（していなければ）
- Fibrinogen D-dimer 1時間毎フォロー
- Hb > 10 g/dL　FFP・Pltオーダー

NO

ICPセンサー挿入？

- D-dimer > 35 を目安に3時間後CT

※ tSAH以外はイーケプラ500mg投与

Take home message

- 初療においては低血圧、適切な換気、凝固障害への対応が重要

- 血圧は 110mmHg ≦ sBP ≦ 160mmHg　Hb 10を目標に
- 呼吸管理はSpO2 ≧ 98%　PCO2 35mmHgを目標に
- Fibrinogen 3g、トラネキサム酸1gの投与
- D-dimer、Fibrinogenを1-6時間 1時間おきにフォロー

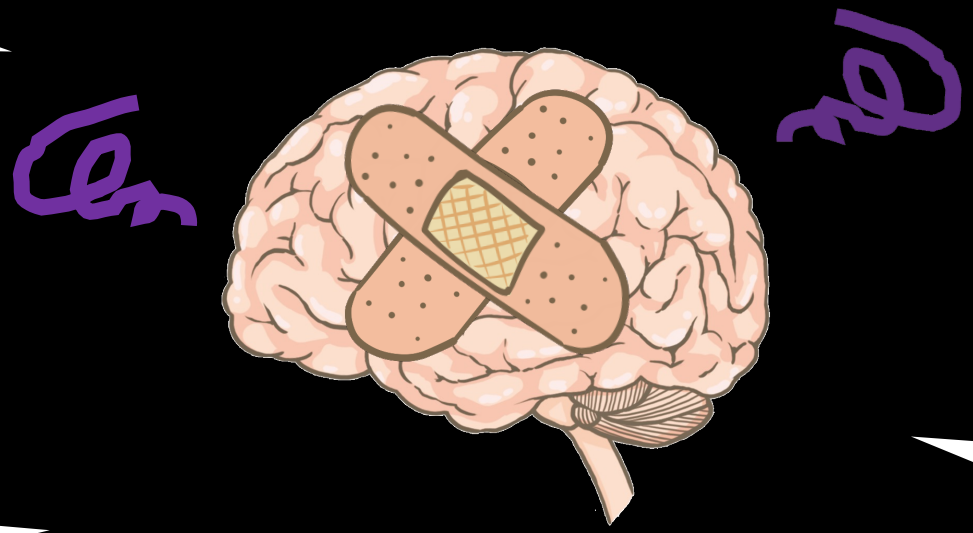
- D-dimer ≧ 35は異常がなくても3時間後CTを検討
- 余裕があればイーケプラ500mg投与
- 血液透析、特にAKIでの導入は原則禁忌

術後管理の原則

高体温

低血圧

凝固障害



低酸素

てんかん

脳腫脹

酸素と血流！！

局所酸素飽和度
rSO_2

脳組織酸素分圧
$PbtO_2$

$$SjO_2 = SaO_2 - \frac{CMRO_2}{CBF \times 1.34 \times Hb}$$

酸素供給
SaO_2

脳酸素代謝率
$CMRO_2$

内頸静脈血酸素飽和度
SjO_2

脳血流
CBF

低下の原因
①MAPの低下
②ICPの上昇

上昇の原因
①発熱
②異常興奮(てんかん)
③シバリング

術後　ICU管理

Brain Trauma FOUNDATION

Guidelines for the Management of Severe Traumatic Brain Injury
4th Edition

治療手順ではない!!

- 治療
- モニタリング
- 閾値

3つのカテゴリー
18のTopics
それぞれのrecommendation

CONFERENCE REPORTS AND EXPERT PANEL

A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC)

Check for updates

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

体系だった治療アルゴリズム
複数医師の意見集約で合意形成

早期に行うべき一般的なケア

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Tier Zero (Basic Severe TBI Care - Not ICP Dependent)

Expected Interventions:

- ICU入室
- 挿管・呼吸器管理
- 連続的な神経学的評価
- 30-45°のギャッジアップ
- 鎮痛
- 鎮静
- 体温管理
  38℃以下を目標
- 1週間抗てんかん薬投与を考慮
- CPP ≧ 60
- Hb ≧ 7 g/dL
- 低Na血症の回避
- 静脈還流の最適化
- A line挿入
- SpO_2 ≧ 94%

Recommended Interventions:

- CV挿入
- $EtCO_2$モニタリング

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Tier 1

- Maintain CPP 60–70 mmHg
- Increase analgesia to lower ICP
- Increase sedation to lower ICP
- Maintain P_aCO_2 at low end of normal (35–38 mmHg/4.7–5.1 kPa)
- Mannitol by intermittent bolus *(0.25–1.0 g/kg)*
- Hypertonic saline by intermittent bolus*
- CSF drainage if EVD *in situ*
- Consider placement of EVD to drain CSF if parenchymal probe used initially
- Consider anti-seizure prophylaxis for 1 week only (unless indication to continue)
- Consider EEG monitoring

Principles for Using Tiers:

- When possible, use lowest tier treatment
- There is no rank order within a tier
- It is not necessary to use all modalities in a lower tier before moving to the next tier
- If considered advantageous, tier can be skipped when advancing treatment

Tier 2

- Mild hypocapnia range 32–35 mmHg/4.3–4.6 kPa)
- Neuromuscular paralysis in adequately sedated patients if efficacious**
- **Perform MAP Challenge to assess cerebral autoregulation and guide MAP and CPP goals in individual patients†**
  - *Should be performed under direct supervision of a physician who can assess response and ensure safety*
  - *No other therapeutic adjustments (ie. sedation) should be performed during the MAP Challenge*
  - *Initiate or titrate a vasopressor or inotrope to increase MAP by 10 mmHg for not more than 20 minutes*
  - *Monitor and record key parameters (MAP, CPP, ICP and $P_{bt}O_2$) before during and after the challenge*
  - *Adjust vasopressor/inotrope dose based on study findings*
- Raise CPP with fluid boluses, vasopressors and/or inotropes to lower ICP when autoregulation is intact

- Re-examine the patient and consider repeat CT to re-evaluate intracranial pathology
- Reconsider surgical options for potentially surgical lesions
- Consider extracranial causes of ICP elevation
- Review that basic physiologic parameters are in desired range (e.g. CPP, blood gas values)
- Consider consultation with higher level of care if applicable for your health care system

Tier 3

- Pentobarbital or Thiopentone coma titrated to ICP control if efficacious‡
- Secondary decompressive craniectomy
- Mild hypothermia (35–36°C) using active cooling measures

Not recommended !

- マンニトールの持続投与
- 4-6時間毎の高浸透圧液の定期投与
- 腰椎穿刺ドレナージ
- フロセミド投与
- ルーチンでのステロイド投与
- ルーチンでの35℃以下の低体温療法
- Burst suppressionを目指した高容量propofol
- ルーチンで$PaC0_2$ < 30 mmHgにする
- ルーチンでCPP > 90 mmHgにする

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

大前提

1. Brain trauma foundation
   Guideline for the Management of Severe Brain Traumatic Injury 4th edition
2. 頭部外傷治療・管理のガイドライン　第4版

CPP: cerebral perfusion pressure
MAP: mean arterial pressure
ICP: Intracranial pressure

CPP ＝ MAP ― ICP

60-70 (1) *Level IIB* (2) グレードA

> 22 (1) *Level IIB* (2) グレードA

- ICP > 20 mmHgが5分以上持続がICP亢進の定義
- CPP <50は予後不良　> 70はARDSのリスク (1) *Level III* (2) グレードA
- CPPの最適値は症例により異なる (1) *Level IIB* (2) グレードA
- ICP-orientedとCPP-oriented

鎮静

- 挿管(+)　＋　ICPコントロール(+)

  RASS -4～-5 目標（48-72時間程度）

  ※筋弛緩薬投与中はICP、MAP、CPPを勘案して調整

- 挿管(+)　＋　ICPコントロール(-)

  RASS -2～0 目標

※その他ICPを入れていない頭部外傷ありの不穏患者など

鎮静とVAP

III. 適切な鎮静・鎮痛をはかる。特に過鎮静を避ける。

背景

人工呼吸中には鎮静・鎮痛薬を適切に用いる。過鎮静は人工呼吸期間延長の原因となり、VAP の発生頻度を増す。

実施方法

(1) 鎮静スケールとしてはRichmond Agitation-Sedation Scale（RASS）の使用を推奨する。
(2) RASS のスコアは−3〜0 となるように投与量を調節する。
(3) カルテ（看護記録など）に、鎮静・鎮痛薬の使用状況と、鎮静評価の記載欄を設ける。評価は毎日数回行う。
(4) 日中の鎮静薬中断・減量を検討し、RASSを用い鎮静レベルを評価する。必要時は、1/2量での鎮静薬投与を再開する。なお、鎮痛薬に関しては中断しない。
(5) 筋弛緩薬は特別な理由がある時以外には持続投与しない。
(6) 医療チームの中で鎮静の目的と目標スコアについての協議・評価を行い共通認識を持つ。

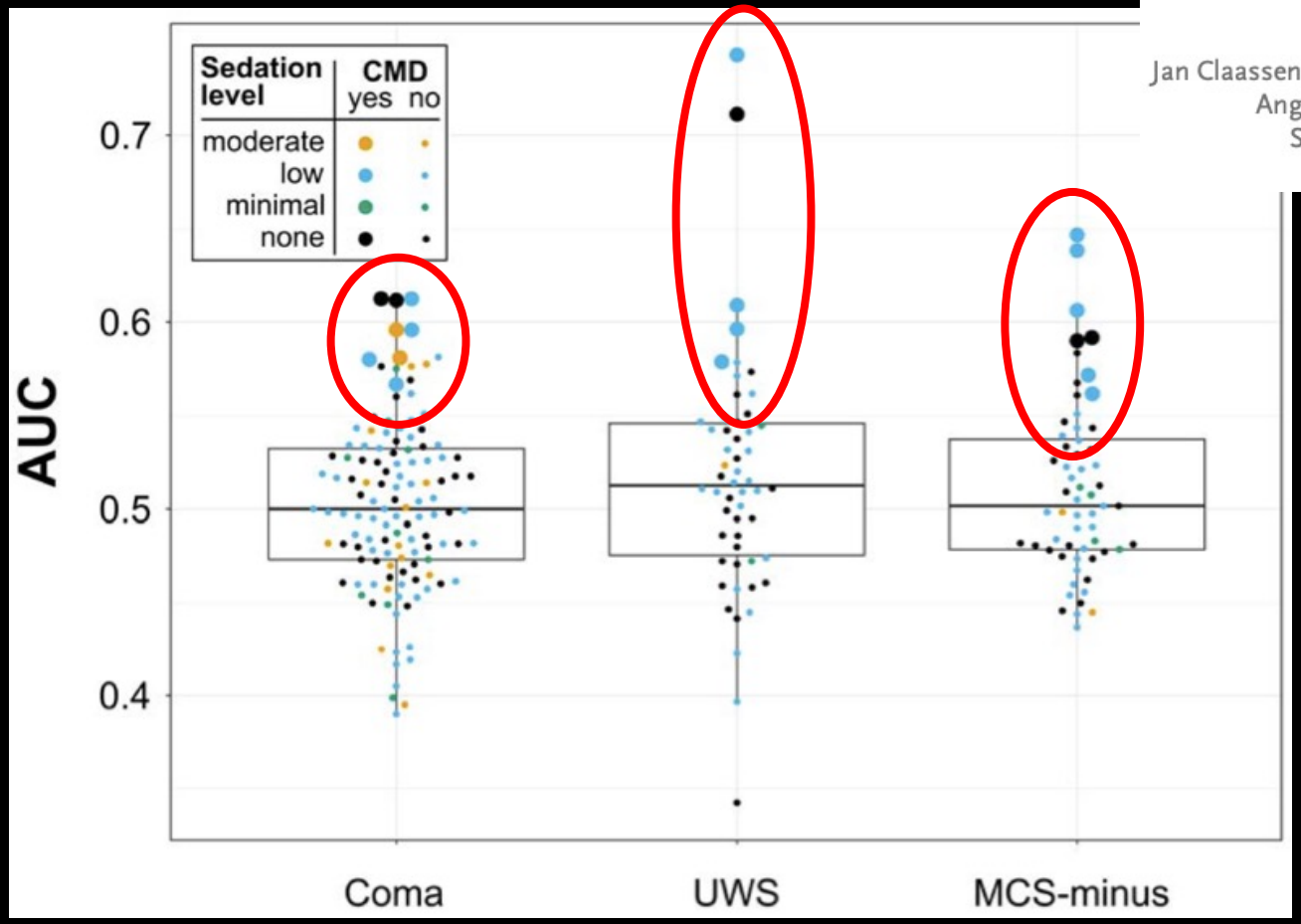
日本集中治療医学会 人工呼吸関連肺炎予防バンドル 2010改訂版 P4

Table 1 Problems potentially associated with deep sedation

Loss of human contact
Respiratory depression
Inactivity-induced diaphragm dysfunction
Myocardial depression and haemodynamic instability
Microvascular alterations
Altered gut function—ileus
Airway (micro)aspiration
Increased risk of pneumonia
Increased risk of thrombophlebitis
Risk of decubitus ulcers
Delirium
Risk of ICU-acquired weakness
Peripheral muscle weakness
Immunosuppression
Prolonged mechanical ventilation/weaning
Prolonged ICU and hospital stay
Permanent cognitive deficits
Chronic psychological illnesses
Costs

Vincent et al. Intensive Care Med (2016) 42:962–971

- 意識障害患者で刺激に対する脳波の反応を測定
- CMD(Cognitive-motor dissociation)
- 中等度の鎮静でもCMDあり
- 鎮静深度が浅いとCMDが増える



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 27, 2019 VOL. 380 NO. 26

Detection of Brain Activation in Unresponsive Patients with Acute Brain Injury

Jan Claassen, M.D., Kevin Doyle, M.A., Adu Matory, B.A., Caroline Couch, B.A., Kelly M. Burger, B.A., R.E.E.G.T., Angela Velazquez, M.D., Joshua U. Okonkwo, M.D., Jean-Rémi King, Ph.D., Soojin Park, M.D., Sachin Agarwal, M.D., David Roh, M.D., Murad Megjhani, Ph.D., Andrey Eliseyev, Ph.D., E. Sander Connolly, M.D., and Benjamin Rohaut, M.D.

植物状態でも脳は反応する！！

どんな患者でも脳の保護には鎮静を

Sedation holiday

ICP安定してから72時間

Consideration of Sedation Holiday in Patients with ICP Controlled *on Tier 2 or 3 Therapy*

Marshall Classification of Most Recent CT		GCS_M 6		GCS_M 5		GCS_M 4		GCS_M 1-3	
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for 24 hrs with Tier 2/3 Treatment	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for 48 hrs with Tier 2/3 Treatment	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for 72 hrs with Tier 2/3 Treatment	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for > 72 hrs with Tier 2/3 Treatment	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

鎮痛

CPOT (Critical-Care Pain Observation Tool）

３点以下

指標	説明	スコア	
表情	・リラックスした表情で、表情筋の緊張なし ・しかめ面、眉毛がさがる、眉間のしわ、表情筋緊張 ・上記の表情に加え、眼瞼を強く閉じている	リラックス 緊張 顔をゆがめる	0 1 2
体動	・動きはない（必ずしも痛みがないわけではない） ・ゆっくりとした、慎重な動き、痛む部位に触れたりする、動きで注意をひく ・チューブを引っ張る、座ろうとする、手足を動かしたり殴ろうとする、指示に従わない、スタッフを叩く、ベッドから降りようとする	動きなし 防御 落ち着きがない	0 1 2
筋緊張 上肢の受動運動（屈曲・伸展）による評価	・受動的な動きに抵抗しない ・受動的な動きに抵抗する ・受動的な動きに強く抵抗し、完全には動かせない	リラックス 緊張、硬直 強い緊張または硬直	0 1 2
人工呼吸器への同調（挿管患者） or 発語（非挿管患者）	・アラームが多くなく、換気が容易 ・アラームが自動的に止まる ・同調不良：換気の中断、頻繁なアラーム	人工呼吸器との同調 バッキングはあるが同調 ファイティング	0 1 2
	・通常の調子での会話、または訴えなし ・うめき声、ため息 ・泣く、叫ぶ	通常の調子の会話または訴えなし うめき声、ため息 泣く、叫ぶ	0 1 2
		総合得点	0～8点

Fillion L et al. *Am J Crit Care* 2006;15:420-427.

筋弛緩

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Tier 2

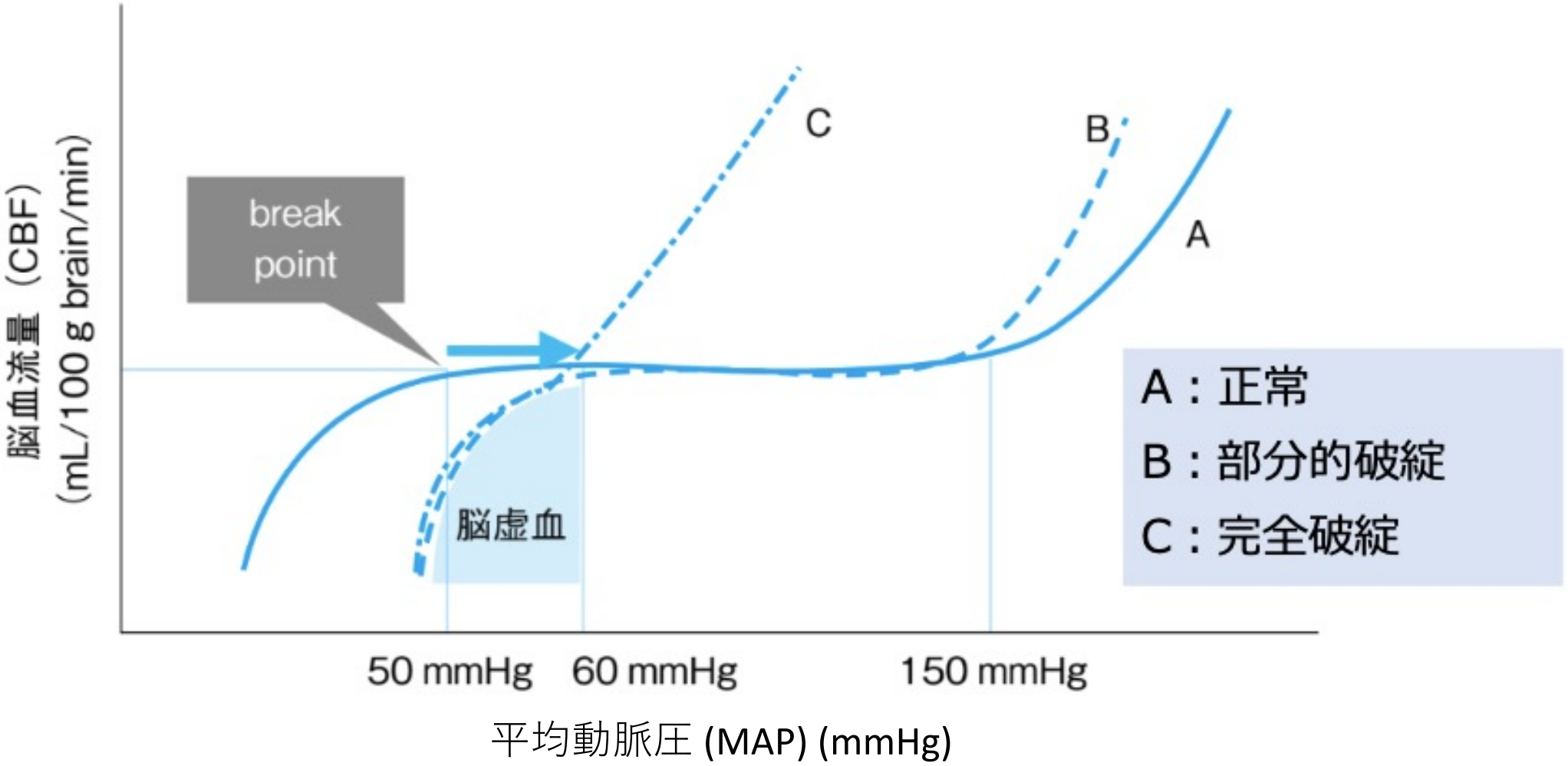
- Mild hypocapnia range 32–35 mmHg/4.3–4.6 kPa)
- Neuromuscular paralysis in adequately sedated patients if efficacious**
- **Perform MAP Challenge to assess cerebral autoregulation and guide MAP and CPP goals in individual patients†**
  - *Should be performed under direct supervision of a physician who can assess response and ensure safety*
  - *No other therapeutic adjustments (ie. sedation) should be performed during the MAP Challenge*
  - *Initiate or titrate a vasopressor or inotrope to increase MAP by 10 mmHg for not more than 20 minutes*
  - *Monitor and record key parameters (MAP, CPP, ICP and $P_{bt}O_2$) before during and after the challenge*
  - *Adjust vasopressor/inotrope dose based on study findings*
- Raise CPP with fluid boluses, vasopressors and/or inotropes to lower ICP when autoregulation is intact

➡ ルーチンでは行わない　その都度ご相談

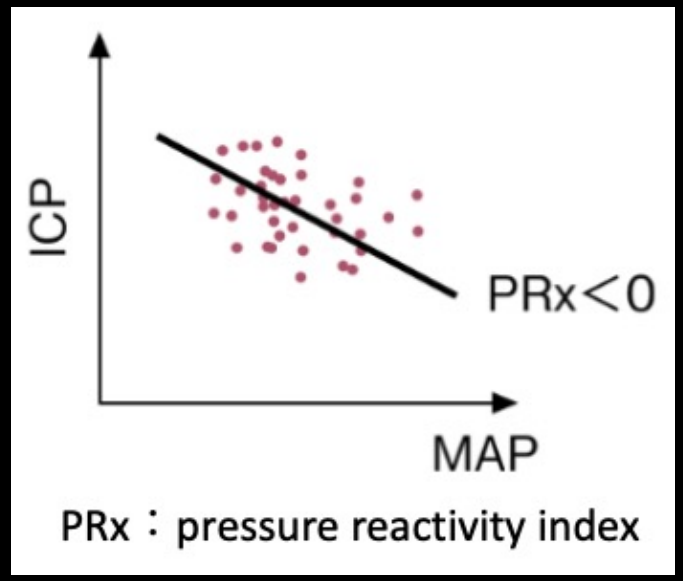
循環

- sBP > 110 mmHg
- sBP上限は140mmHg、160mmHg、180mmHgからその時の患者の状態を勘案して決定
- 脳外科チームでAuto regulationが保たれているか判断してお伝え
- Hb > 7 g/dL

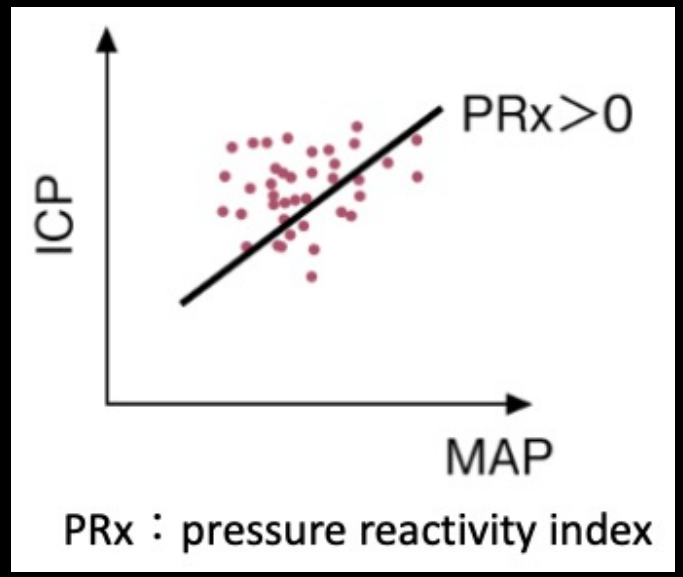
Auto regulation

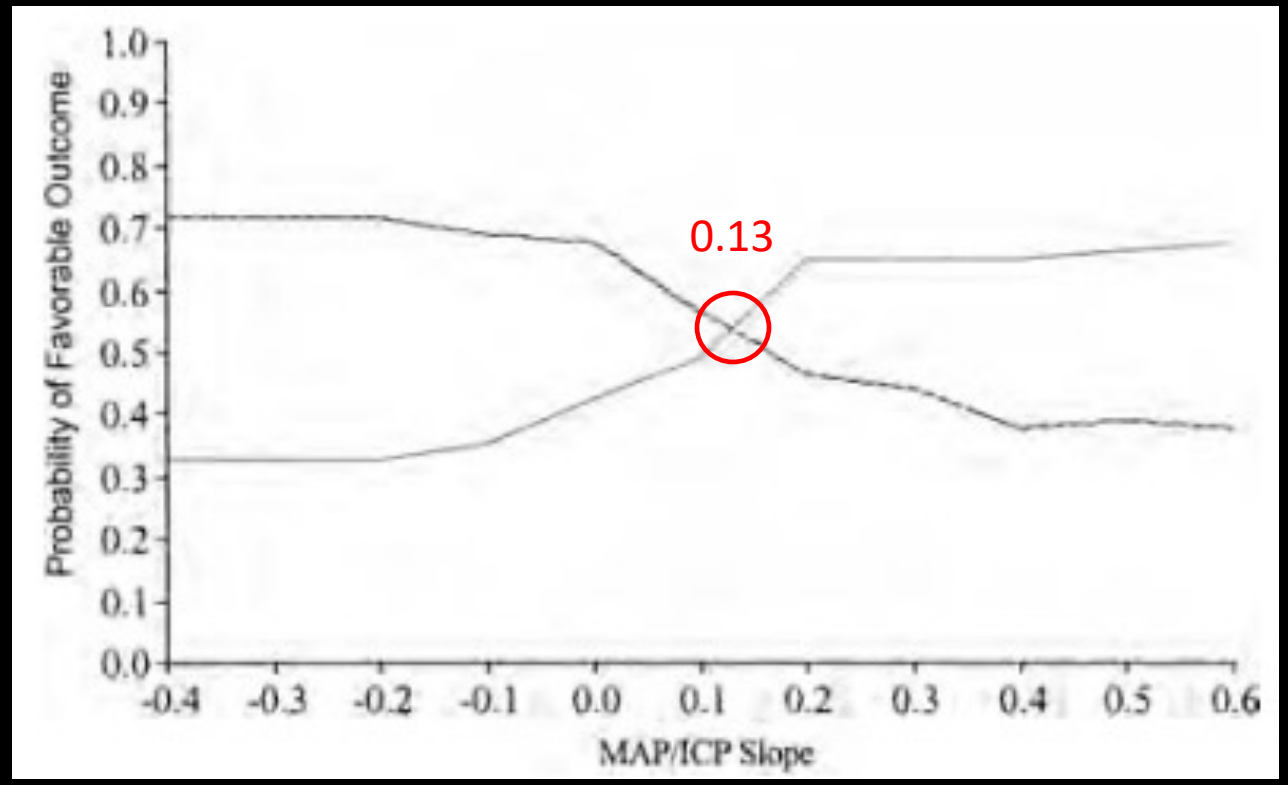


- Auto regulationが保たれている場合



- Auto regulationが破綻している場合





Howells, et al. *J Neurosurg* 102:311–317, 2005

MAP challenge

Tier 2

- Mild hypocapnia range 32–35 mmHg/4.3–4.6 kPa)
- Neuromuscular paralysis in adequately sedated patients if efficacious**
- **Perform MAP Challenge to assess cerebral autoregulation and guide MAP and CPP goals in individual patients†**
  - 結果の解釈が可能な医師の直接観察下で行う
  - MAP challenge中は他の治療は行わない
  - 昇圧剤や陽性変力薬で20分以内にMAPを10mmHg上昇させる
  - MAP、CPP、ICPの値をモニタリングする
  - 結果に基づき昇圧剤や陽性変力薬の投与量を調節する
- **Raise CPP with fluid boluses, vasopressors and/or inotropes to lower ICP when autoregulation is intact**

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

呼吸と体位

- $PaCO_2$
  ベース：35-40 mmHg　ICPコントロール不良時：30-35 mmHg

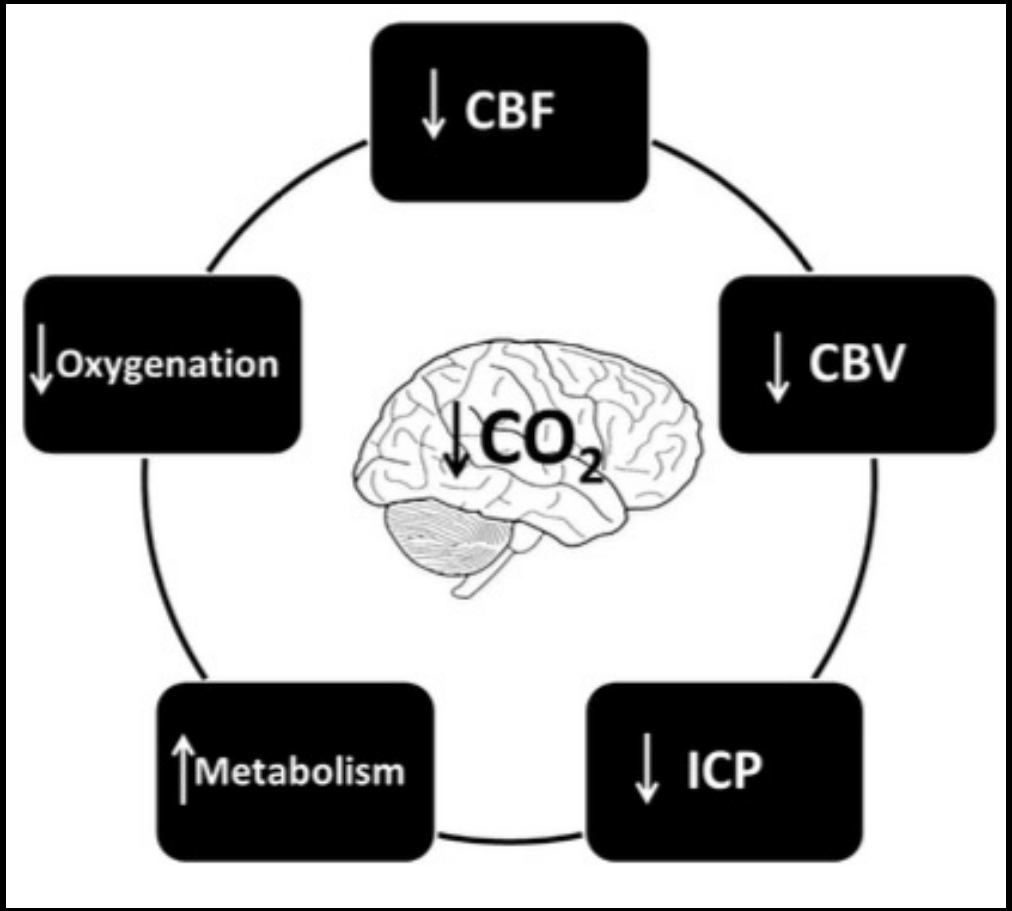
- SpO_2 > 98 %

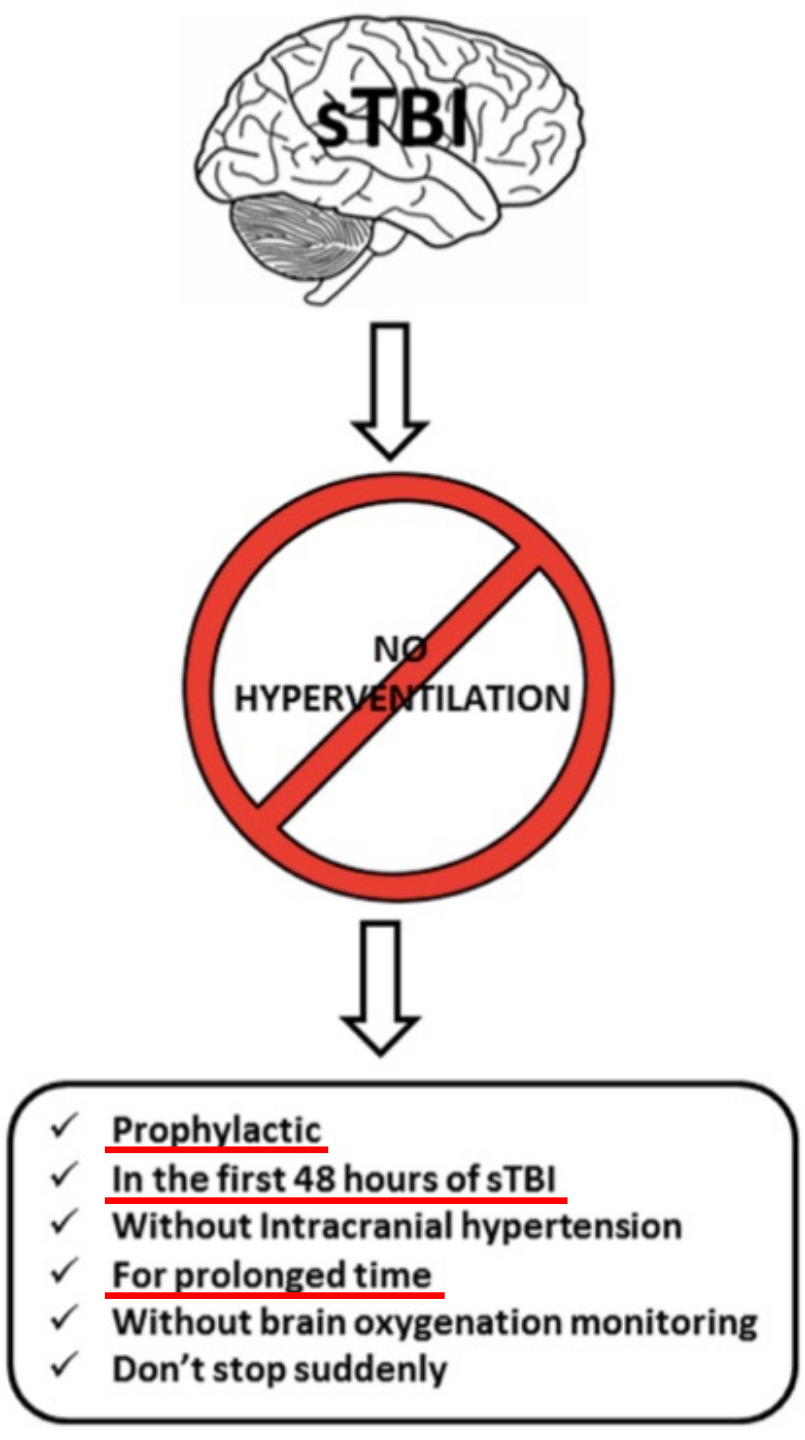
- 頭位
  ベース：30度　ICPコントロール不良時：45度まで

Front Neurol. 2017 Jul 17;8:250.

Hyperventilation Therapy for Control of Posttraumatic Intracranial Hypertension

Daniel Agustín Godoy[1,2], Ali Seifi[3], David Garza[4], Santiago Lubillo-Montenegro[5] and Francisco Murillo-Cabezas[6]*





Tier 1

- Maintain CPP 60–70 mmHg
- Increase analgesia to lower ICP
- Increase sedation to lower ICP
- Maintain P_aCO_2 at low end of normal (35–38 mmHg/4.7–5.1 kPa)
- Mannitol by intermittent bolus *(0.25–1.0 g/kg)*

Tier 2

- Mild hypocapnia range 32–35 mmHg/4.3–4.6 kPa)

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Level II B

- Prolonged prophylactic hyperventilation with partial pressure of carbon dioxide in arterial blood ($PaCO_2$) of 25 mm Hg or less is not recommended.

Brain trauma foundation Guideline for the Management of Severe Brain Traumatic Injury 4th edition

$PaCO_2$ 33 – 37 mmHgで予後良好という報告あり

Mauritz et al. Wien Klin Wochenschr (2007) 119/1–2: 46–55

高浸透圧療法

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Tier 1

- Maintain CPP 60–70 mmHg
- Increase analgesia to lower ICP
- Increase sedation to lower ICP
- Maintain P_aCO_2 at low end of normal (35–38 mmHg/4.7–5.1 kPa)
- Mannitol by intermittent bolus *(0.25–1.0 g/kg)*
- Hypertonic saline by intermittent bolus*
- CSF drainage if EVD *in situ*
- Consider placement of EVD to drain CSF if parenchymal probe used initially
- Consider anti-seizure prophylaxis for 1 week only (unless indication to continue)
- Consider EEG monitoring

Level I, II, and III

- Although hyperosmolar therapy may lower intracranial pressure, there was insufficient evidence about effects on clinical outcomes to support a specific recommendation, or to support use of any specific hyperosmolar agent, for patients with severe traumatic brain injury.

Brain trauma foundation Guideline for the Management of Severe Brain Traumatic Injury 4th edition

➡ 明確なエビデンスはない

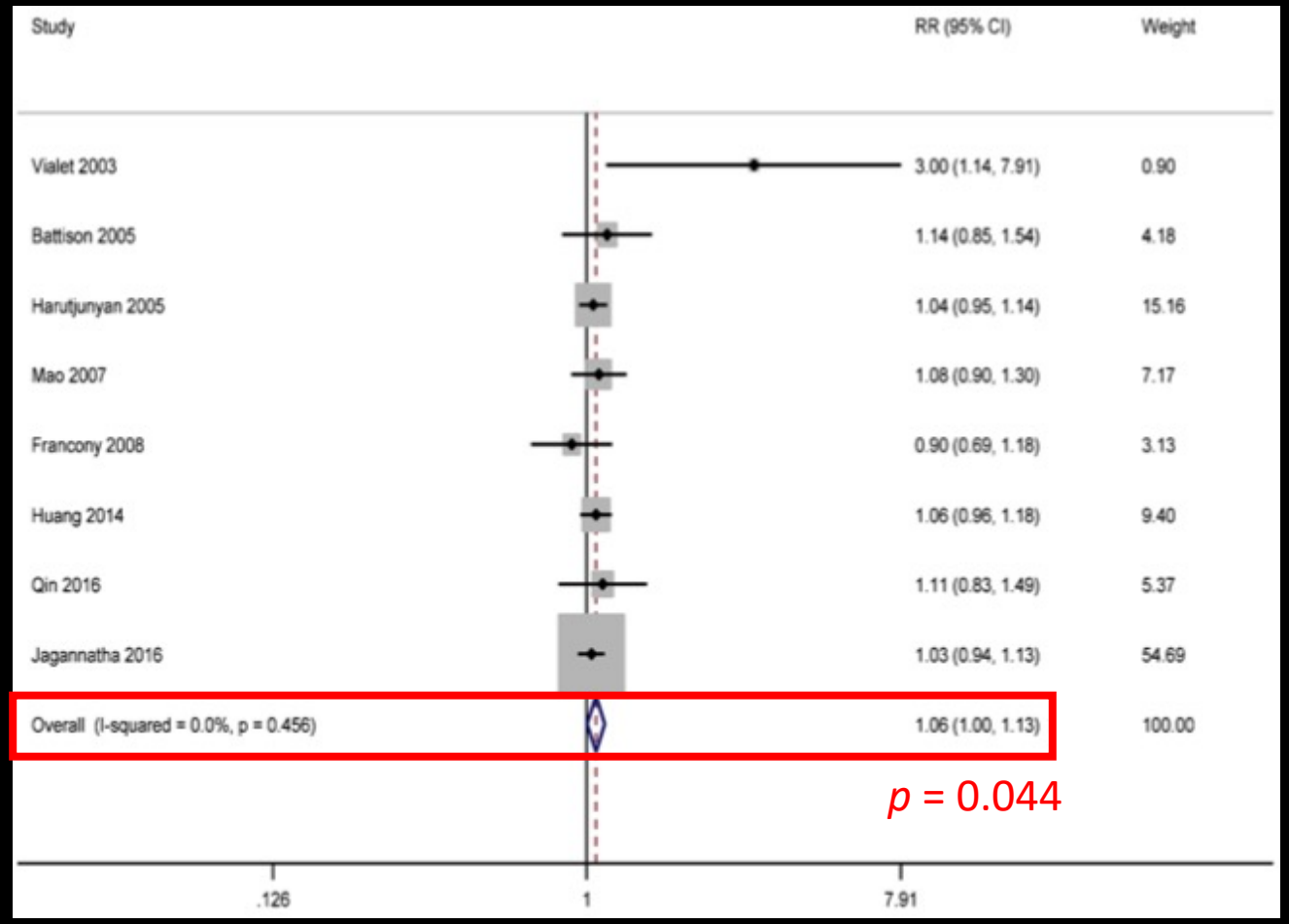
Hypertonic saline or mannitol for treating elevated intracranial pressure in traumatic brain injury: a meta-analysis of randomized controlled trials

Jiajie Gu[1] · Haoping Huang[1] · Yuejun Huang[2] · Haitao Sun[3] · Hongwu Xu[4]

Neurosurgical Review (2019) 42:499–509

HS vs Mannitol

若干HSに軍配



Cochrane Database Syst Rev. 2020 Jan 17;1(1):CD010904.

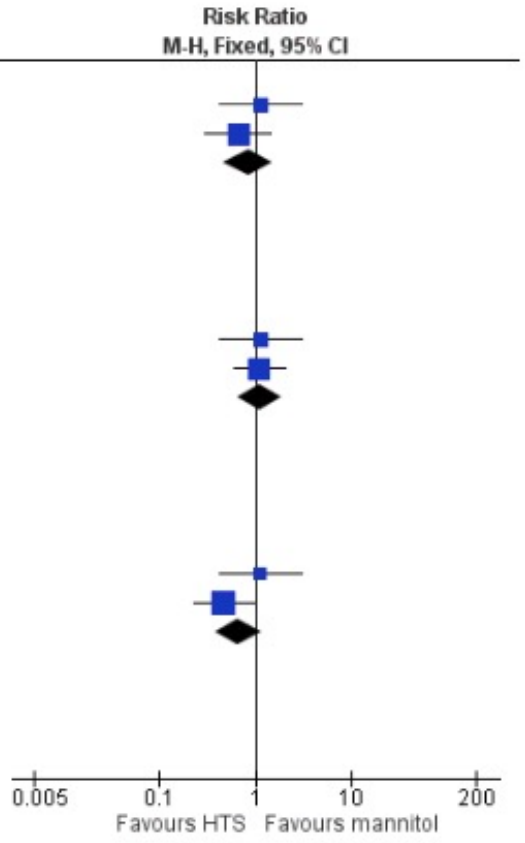
Hypertonic saline versus other intracranial pressure–lowering agents for people with acute traumatic brain injury (Review)

Chen H, Song Z, Dennis JA

Cochrane Library

Cochrane Database of Systematic Reviews

Study or Subgroup	HTS Events	HTS Total	Mannitol Events	Mannitol Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.1 Mortality at 6 months' follow-up (available data for Jagannatha)						
Cottenceau 2011	6	22	6	25	37.2%	1.14 [0.43, 3.02]
Jagannatha 2016	6	18	10	20	62.8%	0.67 [0.30, 1.46]
Subtotal (95% CI)		**40**		**45**	**100.0%**	**0.84 [0.46, 1.55]**
Total events	12		16			
Heterogeneity: Chi² = 0.70, df = 1 (P = 0.40); I² = 0%						
Test for overall effect: Z = 0.56 (P = 0.58)						
1.2.2 Mortality at 6 months' follow-up (worst case for HTS data for Jagannatha)						
Cottenceau 2011	6	22	6	25	37.2%	1.14 [0.43, 3.02]
Jagannatha 2016	10	18	10	20	62.8%	1.11 [0.61, 2.03]
Subtotal (95% CI)		**40**		**45**	**100.0%**	**1.12 [0.66, 1.89]**
Total events	16		16			
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.97); I² = 0%						
Test for overall effect: Z = 0.42 (P = 0.67)						
1.2.3 Mortality at 6 months' follow-up (best case for HTS data for Jagannatha)						
Cottenceau 2011	6	22	6	25	29.8%	1.14 [0.43, 3.02]
Jagannatha 2016	6	18	14	20	70.2%	0.48 [0.23, 0.97]
Subtotal (95% CI)		**40**		**45**	**100.0%**	**0.67 [0.38, 1.18]**
Total events	12		20			
Heterogeneity: Chi² = 2.01, df = 1 (P = 0.16); I² = 50%						
Test for overall effect: Z = 1.37 (P = 0.17)						



Test for subgroup differences: Chi² = 1.70, df = 2 (P = 0.43), I² = 0%

HS vs Mannitol

有意差なし

今後の高浸透圧療法

- グリセロールの定時投与は行わない　ICP > 20 mmHgが5分以上の時投与

- 基本は高張食塩水　マンニトール併用
- CV: 10%NaCl 60 mL(1 mL/kg)、末梢: 3%NaCl 260 mL(5 mL/kg)
- マンニトール 150 ml – 300 mL(0.25– 1 g/kg)　4-6 hあけて

- 4 h毎の採血でNaチェック、浸透圧チェック（夜間は手計算(Dr)）
- 血清浸透圧 > 320 mOsm/L、Na > 160 mEq/Lは投与中止

体温管理

Tier 3

- Pentobarbital or Thiopentone coma titrated to ICP control if efficacious‡
- Secondary decompressive craniectomy
- Mild hypothermia (35–36°C) using active cooling measures

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Level II B

- Early (within 2.5 hours), short-term (48 hours post-injury) prophylactic hypothermia is not recommended to improve outcomes in patients with diffuse injury.

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➡ 38℃を超えないように
低体温を支持する明確なエビデンスはない

Lancet Neurol. 2011 Feb;10(2):131-9.

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

Class I

➡ Evacuated mass lesion症例のみ有効

Effect of Early Sustained Prophylactic Hypothermia on Neurologic Outcomes Among Patients With Severe Traumatic Brain Injury
The POLAR Randomized Clinical Trial

D. James Cooper, MD; Alistair D. Nichol, MB, PhD; Michael Bailey, PhD; Stephen Bernard, MBBS, MD; Peter A. Cameron, MD; Sébastien Pili-Floury, MD, PhD; Andrew Forbes, PhD; Dashiell Gantner, MBBS; Alisa M. Higgins, MPH; Olivier Huet, MD, PhD; Jessica Kasza, PhD; Lynne Murray, BAppSci; Lynette Newby, MHSc; Jeffrey J. Presneill, MBBS, PhD; Stephen Rashford, MBBS; Jeffrey V. Rosenfeld, MD, MS; Michael Stephenson, BHSc; Shirley Vallance, MClinRes; Dinesh Varma, MD; Steven A. R. Webb, MD, PhD; Tony Trapani, BEmergHealth; Colin McArthur, MB, ChB; for the POLAR Trial Investigators and the ANZICS Clinical Trials Group

JAMA. 2018 Dec 4;320(21):2211-2220.

➡ 転期も変えない　肺炎も出血増大も変わらない

今後の体温管理方針

- 36℃台を維持する
- 症例によって35℃台をお願いすることがあるかもしれません
- Arctic SunからThermogardへ
- 体温管理デバイス使用期間の短縮化　７２時間以内
- シバリング対応のプロトコル化

Thermogard System

カテーテルを介した体温調節

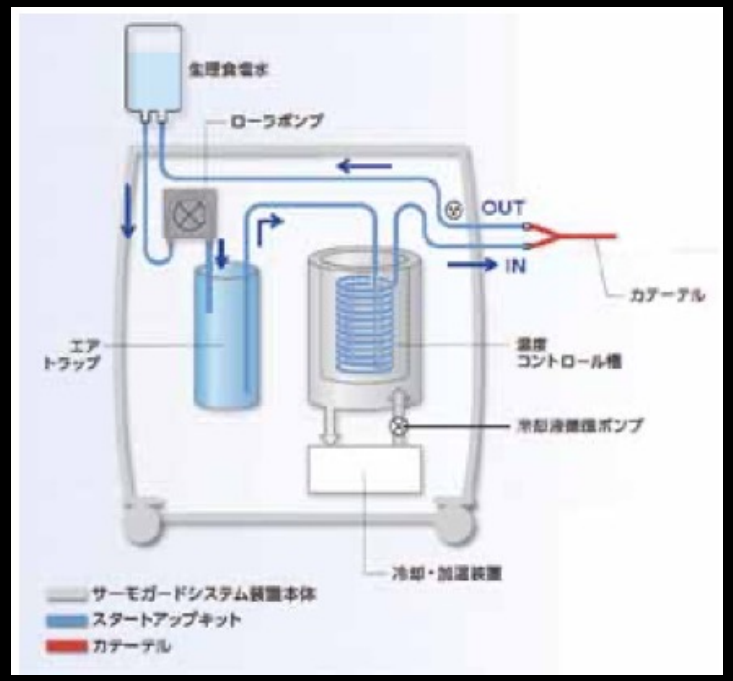
中心静脈内で血液温を直接コントロールすることにより、体温調節を行う

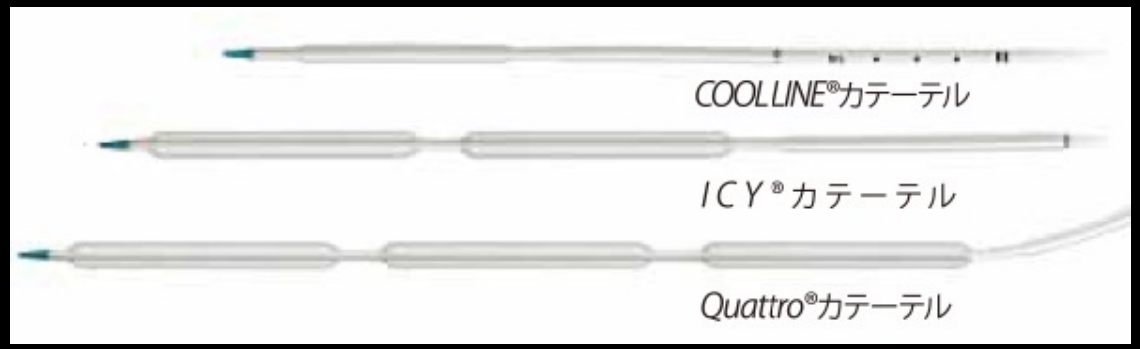
トリプルルーメン中心静脈カテーテル（CVC）としての機能を有する

自動制御

膀胱温などの体温データをフィードバックして自動制御

3種類のモードにより、制御を行う





導入済み　本格始動待ち

BSAS(Bedside shivering assessment scale)

Score	
0	咀嚼筋、頸部、胸部に触診上のシバリングがなく、心電図でも認めない
1	心電図でシバリングを認めるが、臨床的なシバリングなし
2	頸部 and/or 胸部に限局するシバリング
3	頸部や胸部に加え、上肢に肉眼的なシバリング
4	体幹、上下肢の肉眼的なシバリング

Badjatia et al. *Stroke*. 2008;39(12):3242-3247

➡ 2 点以下（できれば1点以下）を目指す

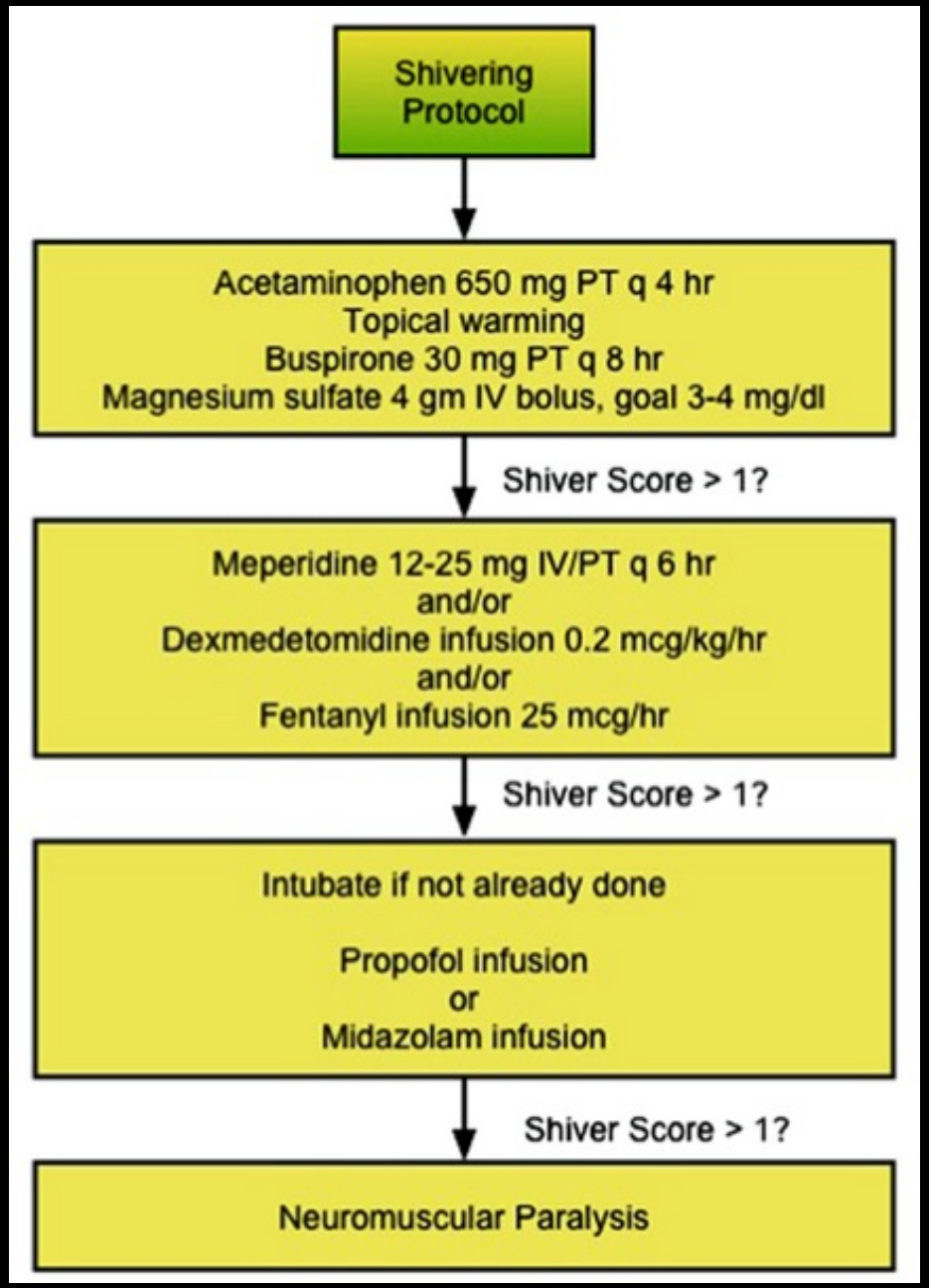
4h毎に採血　Mg 3-4 mg/dLに保つ

BSAS > 1のとき

1. カウンターウォーミング（四肢体幹の保温）
2. アセリオ1000mgを1時間で投与
3. ロキソニン30mg 内服
4. メペリジン12-25mg 静注

それでもBSAS > 1のとき

1. フェンタニル25μg/h or プレセデックス0.2μg/kg/h
2. プロポフォール、ミダゾラム
3. ロクロニウム



Brophy et al. *Neurocrit Care* 2015 23:S48–S68

カウンター
ウォーミング

Tier 1

- Maintain CPP 60–70 mmHg
- Increase analgesia to lower ICP
- Increase sedation to lower ICP
- Maintain P_aCO_2 at low end of normal (35–38 mmHg/4.7–5.1 kPa)
- Mannitol by intermittent bolus *(0.25–1.0 g/kg)*
- Hypertonic saline by intermittent bolus*
- CSF drainage if EVD *in situ*
- Consider placement of EVD to drain CSF if parenchymal probe used initially
- Consider anti-seizure prophylaxis for 1 week only (unless indication to continue)
- Consider EEG monitoring

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

抗てんかん薬は
イーケプラ
1週間のみ
（発作例は除く）

Level II A

- Prophylactic use of phenytoin or valproate is not recommended for preventing late PTS.
- Phenytoin is recommended to decrease the incidence of early PTS (within 7 days of injury), when the overall benefit is felt to outweigh the complications associated with such treatment. However, early PTS have not been associated with worse outcomes.

At the present time there is insufficient evidence to recommend levetiracetam over phenytoin regarding efficacy in preventing early post-traumatic seizures and toxicity.

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バルビツレート療法

Tier 3

- Pentobarbital or Thiopentone coma titrated to ICP control if efficacious‡
- Secondary decompressive craniectomy
- Mild hypothermia (35–36°C) using active cooling measures

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Level II B

- Administration of barbiturates to induce burst suppression measured by EEG as prophylaxis against the development of intracranial hypertension is not recommended.
- High-dose barbiturate administration is recommended to control elevated ICP refractory to maximum standard medical and surgical treatment. Hemodynamic stability is essential before and during barbiturate therapy.

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バルビツレート療法の位置づけ

- 基本的に奥の手
- ICPは低下させるが予後は改善しない (Majdan et al. *J Neurotrauma*. Jan 2013;30(1):23-29.)

- チオペンタール（ラボナール）をLoadingして持続
- 2-10 mg/kg → 1-6 mg/kg/h（4-6 mg/kg/hでBurst suppression)

- EEGモニタリングして使用
- Burst suppressionが出現したらそれ以上増量しない
- ICPを指標にし、血中濃度やEEGを指標にしない

脳波

Hawryluk et al. *Intensive Care Med* (2019) 45:1783–1794

Tier 1

- Maintain CPP 60–70 mmHg
- Increase analgesia to lower ICP
- Increase sedation to lower ICP
- Maintain P_aCO_2 at low end of normal (35–38 mmHg/4.7–5.1 kPa)
- Mannitol by intermittent bolus *(0.25–1.0 g/kg)*
- Hypertonic saline by intermittent bolus*
- CSF drainage if EVD *in situ*
- Consider placement of EVD to drain CSF if parenchymal probe used initially
- Consider anti-seizure prophylaxis for 1 week only (unless indication to continue)
- Consider EEG monitoring

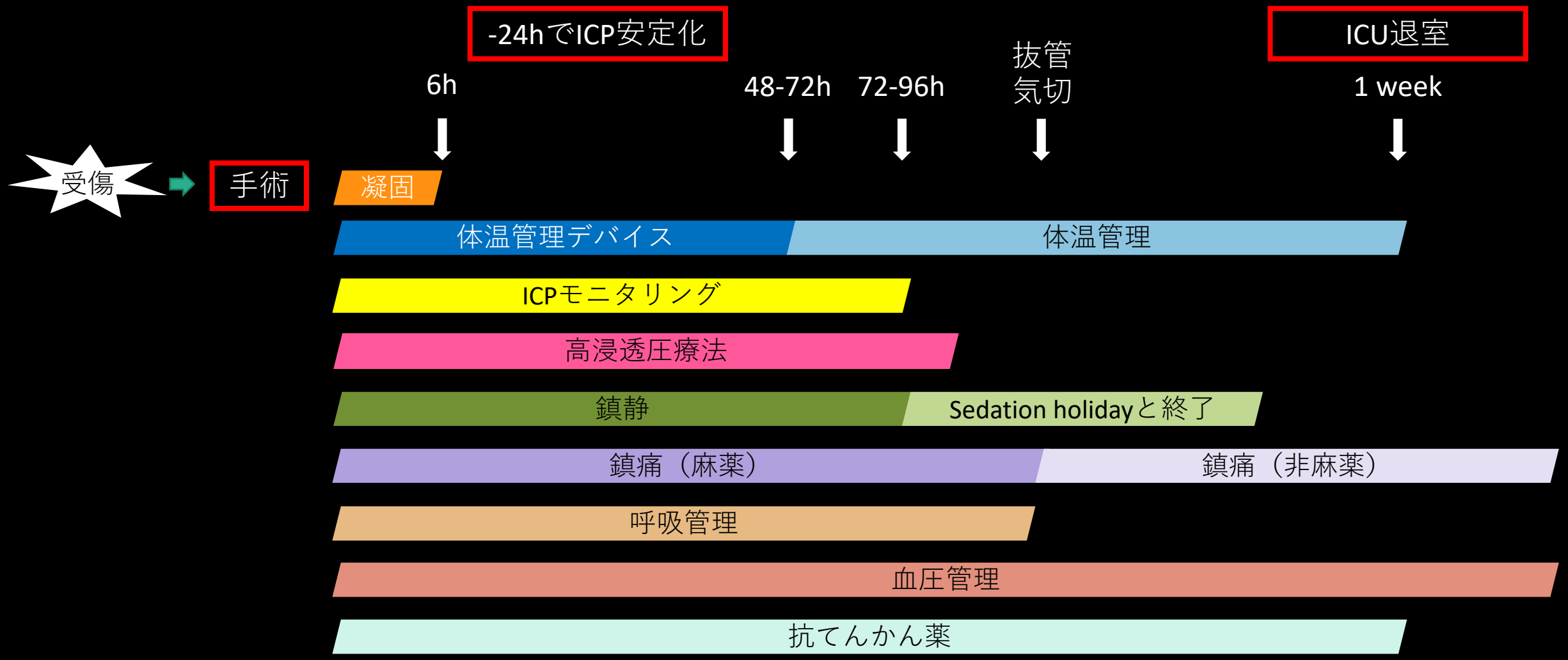
- ベッドサイドモニタリング脳波
- 通常脳波
- 24時間持続ビデオモニタリング脳波

ICPセンサー抜去

ICP安定してから72時間

MODERATE-SEVERE HYPERTENSION		GCS_M 6		GCS_M 5		GCS_M 4		GCS_M 1-3	
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for 24 hours	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for 48 hours	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for 72 hours	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								
		NP	AP	NP	AP	NP	AP	NP	AP
ICP "acceptable" for > 72 hours	DI 1-2								
	EML / DI 1-2								
	DI 3								
	EML / DI III								

タイムスケジュール


-24hでICP安定化
ICU退室
6h
48-72h
72-96h
抜管
気切
1 week
受傷
手術
凝固
体温管理デバイス
体温管理
ICPモニタリング
高浸透圧療法
鎮静
Sedation holidayと終了
鎮痛（麻薬）
鎮痛（非麻薬）
呼吸管理
血圧管理
抗てんかん薬

Take home message

- ICPコントロールとしての鎮静鎮痛を適切な期間
- ICPコントロールとしての血圧管理
- 適切なCO_2コントロール　長時間の過換気を避ける
- 高張食塩水の使用　高Na血症の許容
- 新たな体温管理デバイス　短期間の平温療法　シバリング対応
- 1週間のみの抗てんかん薬投与
- ICPセンサーの早期抜去と集中管理期間の短縮

救命のその先へ・・・