

# STATE OF THE ART

# SCHÄDELHINRTRAUMA

# STATE OF THE ART

# SCHWERES SCHÄDELHIRNTRAUMA

- Aktuelle Guidelines
- Evidenz zu aktuellen Therapieoptionen
- Praktische Aspekte

*A Joint Project of the*

**Brain Trauma Foundation**  
Improving the Outcome of Brain Trauma Patients Worldwide

*and*

*American Association of Neurological Surgeons (AANS)*

*Congress of Neurological Surgeons (CNS)*

*AANS/CNS Joint Section on Neurotrauma and Critical Care*

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# Guidelines for the Management of Severe Traumatic Brain Injury

## 3rd Edition

# SEVERE TRAUMATIC BRAIN INJURY MANAGEMENT AND CLINICAL OUTCOME USING THE LUND CONCEPT

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Intensive Care, Lund University, Sweden*

L.-O. D. Koskinen et al. / Neuroscience 283 (2014) 245–255

## Standard Basal Therapy (start soon after arrival)

ICP measurement

ICP < 20 mmHg

CPP > 50 mmHg

Normovolemia

(saline, albumin, blood;

Hb > 110 g/l, S-Alb 35-40 g/l)

Normotension

(metoprolol, clonidine, angiotensin

II antagonist for reduction

of blood pressure and catecholamine surge)

Normoventilation ( $P_a\text{CO}_2$  4.5-5.5 kPa,  $P_a\text{O}_2 \geq 12$  kPa)

Normonatremia (S-Sodium 135-145 mmol/l)

Normothermia (< 38°C)

Normoglycemia (5-10 mmol/l)

Sedation (midazolam)

Analgesia (fentanyl)

Early enteral nutrition (15-20 kcal/kg/24 h)

L.-O. D. Koskinen et al. / Neuroscience 283 (2014) 245–255

# THERAPIEOPTIONEN

- BLS, BICS, MMM
  - Oxygenation/Ventilation, Kreislaufsupport, Gerinnung, Thromboseprophylaxe, Ernährung, Monitoring, ...
- Sedation
- Entfernung von Raumforderungen, Liquordrainage
- Osmotherapie
- Hypothermie
- Kraniektomie

*The* **NEW ENGLAND JOURNAL of MEDICINE**

**REVIEW ARTICLE**

**CRITICAL CARE MEDICINE**

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., PH.D., *Editors*

# Traumatic Intracranial Hypertension

Nino Stocchetti, M.D., and Andrew I.R. Maas, M.D., Ph.D.

N Engl J Med 2014;370:2121-30

Therapy Steps	Levels of Evidence	Treatment	Risk
8	Not reported	Decompressive craniectomy	Infection or delayed hematoma Subdural effusion Hydrocephalus and syndrome of the trephined
7	Level II	Metabolic suppression (barbiturates)	Hypotension and increased number of infections
6	Level III	Hypothermia	Fluid and electrolyte disturbances and infection
5	Level III	Induced hypocapnia	Excessive vasoconstriction and ischemia
4	Level II	Hyperosmolar therapy Mannitol or hypertonic saline	Negative fluid balance Hypernatremia Kidney failure
3	Not reported	Ventricular CSF drainage	Infection
2	Level III	Increased sedation	Hypotension
1	Not reported	Intubation Normocarbic ventilation	Coughing, ventilator asynchrony, ventilator-associated pneumonia

# GUIDELINES ZUM MONITORING EVIDENZ ZU THERAPIEOPTIONEN

- Multimodales Monitoring
  - ICP
  - PtiO<sub>2</sub>
  - PRx, CPPopt
- Osmotherapie
- Therapeutischen Hypothermie
- Adjuvante Therapien
  - EPO, Progesteron, Steroide

Peter Le Roux  
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# **Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care**

**A statement for healthcare professionals from the  
Neurocritical Care Society and the European Society  
of Intensive Care Medicine**

Intensive Care Med (2014) 40:1189–1209

# MULTIMODALES MONITORING

- Multimodales Monitoring versucht das Zielorgan Hirn und dessen Zustand mit unterschiedlichen Techniken abzubilden
- „It must be recognized that no monitor in the end will change outcome. Instead it is how that information is interpreted and integrated into clinical decision-making and then how the patient is treated. That will influence outcome“

Intensive Care Med (2014) 40:1189–1209

# MULTIMODALES MONITORING

## ICP

- „ICP and CPP monitoring are recommended as a part of protocol-driven care in patients who are at risk of elevated intracranial pressure“
- „We recommend that ICP and CPP monitoring be used to guide medical and surgical interventions and to detect life-threatening imminent herniation; however, the threshold value of ICP is uncertain on the basis of the literature“
- „ICP per se does not provide a useful prognostic marker of functional outcome“

Intensive Care Med (2014) 40:1189–1209

*The* **NEW ENGLAND**  
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**A Trial of Intracranial-Pressure Monitoring  
in Traumatic Brain Injury**

Randall M. Chesnut, M.D., Nancy Temkin, Ph.D., Nancy Carney, Ph.D., Sureyya Dikmen, Ph.D., Carlos Rondina, M.D.,  
Walter Videtta, M.D., Gustavo Petroni, M.D., Silvia Lujan, M.D., Jim Pridgeon, M.H.A., Jason Barber, M.S.,  
Joan Machamer, M.A., Kelley Chaddock, B.A., Juanita M. Celix, M.D., Marianna Cherner, Ph.D., and Terence Hendrix, B.A.,  
for the Global Neurotrauma Research Group\*

N Engl J Med 2012;367:2471-81

- Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure (BEST TRIP)
- Multizenter
- 324 Patienten in Bolivien und Ecuador
- Pressure-monitoring group vs. Imaging–clinical examination group)
- „For patients with severe traumatic brain injury, care focused on maintaining intracranial pressure at 20mmHg or less was not shown to be superior to care based on imaging and clinical examination“

N Engl J Med 2012;367:2471-81

# A Consensus-Based Interpretation of the Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure Trial

Randall M. Chesnut,<sup>1</sup> Thomas P. Bleck,<sup>2</sup> Giuseppe Citerio,<sup>3</sup> Jan Classen,<sup>4</sup> D. James Cooper,<sup>5</sup>  
William M. Coplin,<sup>6</sup> Michael N. Diringer,<sup>7</sup> Per-Olof Grände,<sup>8</sup> J. Claude Hemphill III,<sup>9</sup> Peter J. Hutchinson,<sup>10</sup>  
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Claudia S. Robertson,<sup>16</sup> Juan Sahuquillo,<sup>17</sup> Nino Stocchetti,<sup>18</sup> Gene Sung,<sup>19</sup> Nancy Temkin,<sup>1,20</sup>  
Paul M. Vespa,<sup>21</sup> Walter Videtta,<sup>22</sup> and Howard Yonas<sup>23</sup>

JOURNAL OF NEUROTRAUMA 32 (2015):1722–1724

# CONSENSUS STATEMENTS

## BEST TRIP

- Statement 1 (100% Consensus)
  - The BEST-TRIP trial compared two management protocols for treatment of severe TBI: one involving ICP monitoring and the other involving serial CT imaging and neurologic examination
- Statement 2 (100% Consensus)
  - The BEST TRIP trial found no difference in outcome between patients treated according to BTF guidelines and patients treated according to a novel standardized protocol of sequential CT imaging and clinical examination

# CONSENSUS STATEMENTS

## BEST TRIP

- Statement 7 (83% Consensus)
  - The previously unstudied Imaging and Clinical Examination (ICE) protocol may lead to non-inferior clinical outcomes, compared with the BTF guidelines
- Statement 4 (94% Consensus)
  - The external validity of the BEST TRIP trial is low, primarily due to unquantified uncertainties surrounding the influence of the prehospital environment and rehabilitation

# CONSENSUS STATEMENTS

## BEST TRIP

- Statement 3 (100% Consensus)
  - Further investigation is necessary in the areas of selection of patients for ICP monitoring, determination of patient-specific ICP thresholds and development of treatment methods and paradigms
- Statement 6 (94% Consensus)
  - For those currently monitoring ICP, the results of the BEST TRIP trial should not change their practice

# MULTIMODALES MONITORING

## PbtO<sub>2</sub>, SjvO<sub>2</sub>, NIRS

- „We suggest the use of brain oxygen monitoring to assist titration of medical and surgical therapies to guide ICP/ CPP therapy“
- „Observational studies suggest a potential benefit when PbtO<sub>2</sub>-guided therapy is added to a severe TBI management protocol“
- „We recommend that brain oxygen monitors be used with clinical indicators and other monitoring modalities for accurate prognostication“

Intensive Care Med (2014) 40:1189–1209

# MULTIMODALES MONITORING AUTOREGULATION

- „Continuous bedside monitoring of autoregulation is now feasible, and we suggest that should be considered as a part of MMM“
- „We suggest that monitoring and assessment of autoregulation may be useful in broad targeting of cerebral perfusion management goals and prognostication in ABI“

Intensive Care Med (2014) 40:1189–1209

# PRx- Calculation principles

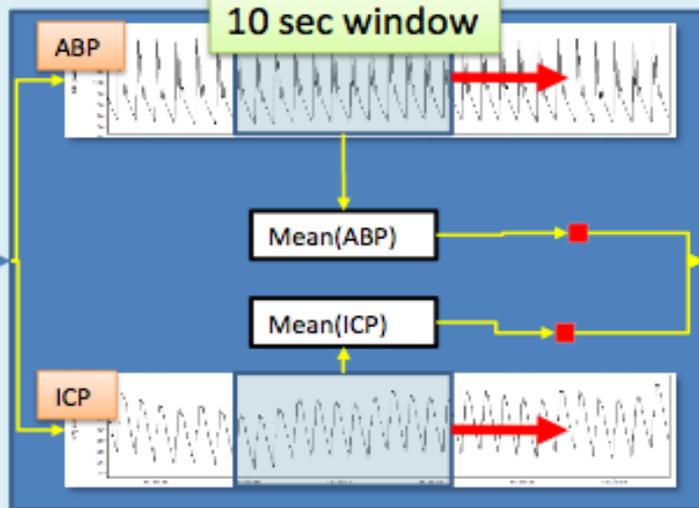
Input signals ICP, ABP



Output trend PRx

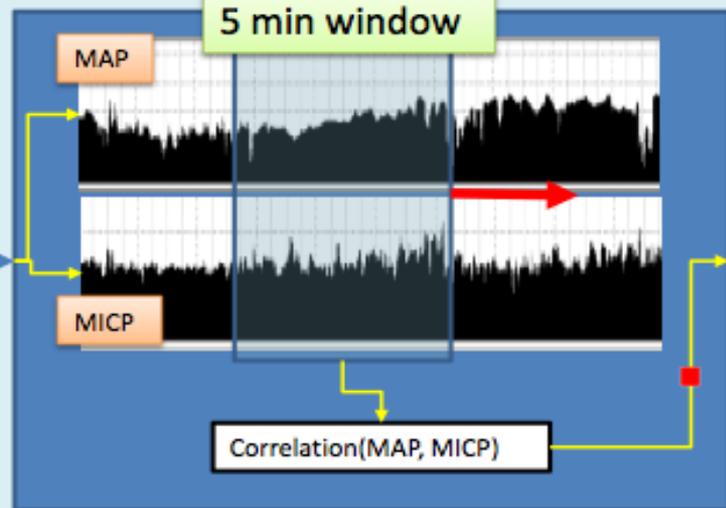


10 sec window



Primary analysis

5 min window

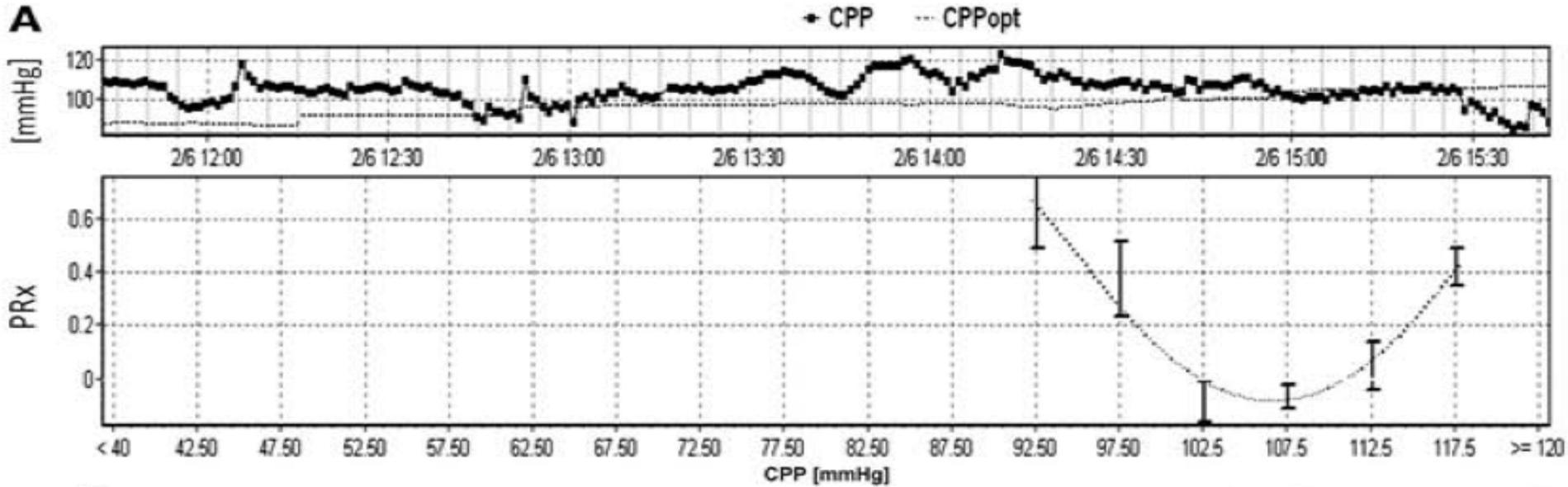


Final Analysis

# PRx

## CPPopt

- CPP vs PRx
- CPPopt = CPP mit dem tiefsten PRx



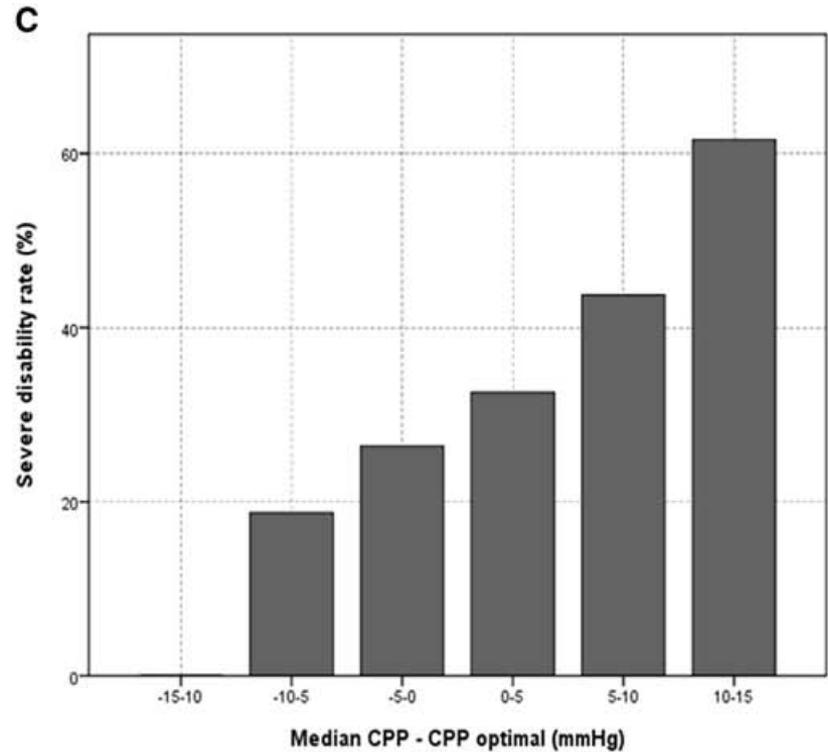
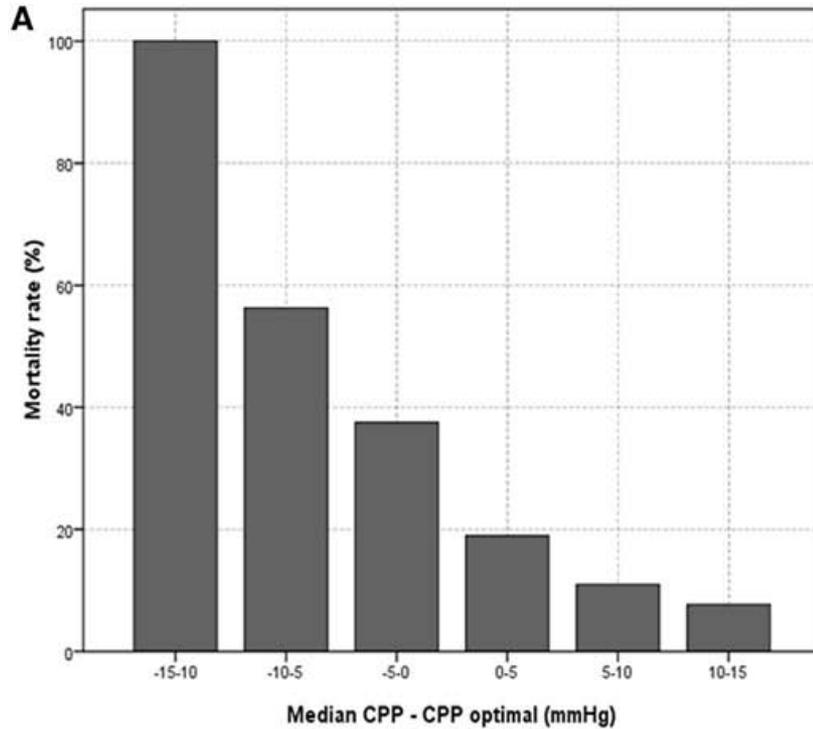
# Continuous determination of optimal cerebral perfusion pressure in traumatic brain injury\*

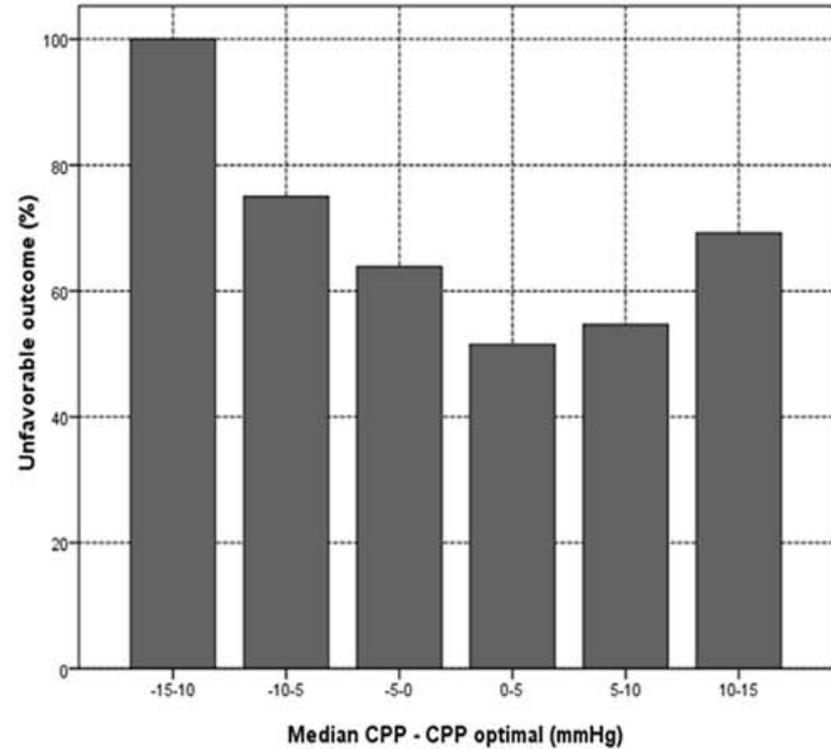
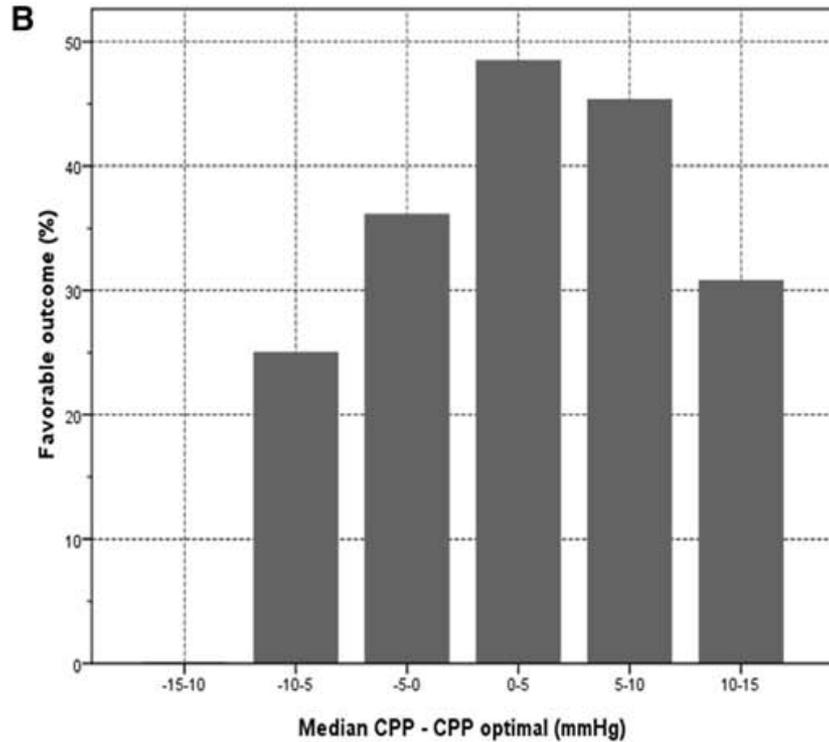
Marcel J. H. Aries, MD; Marek Czosnyka, PhD; Karol P. Budohoski, MD; Luzius A. Steiner, MD, PhD; Andrea Lavinio, MD; Angelos G. Koliass, MSc, MRCS; Peter J. Hutchinson, PhD, FRCS (SN); Ken M. Brady, MD; David K. Menon, PhD; John D. Pickard, FRCS (SN), FMedSci; Peter Smielewski, PhD

Crit Care Med 2012; 40: 2456–2463

# AUTOREGULATION

- Retrospective analysis of prospectively collected data
- Single Center (Addenbrookes NCCU, Cambridge)
- 327 traumatic head-injury patients with continuous monitoring of arterial blood pressure and intracranial pressure
- PRx
- CPPopt
- Outcome vs. CPPopt





# MULTIMODALES MONITORING CEREBRALE MIKRODIALYSE

- „We suggest the use of cerebral microdialysis to assist titration of medical therapies such as systemic glucose control, transfusion, therapeutic hypothermia, hypocapnia and hyperoxia“
- „We recommend that cerebral microdialysis only be used in combination with clinical indicators and other monitoring modalities for prognostication“

Intensive Care Med (2014) 40:1189–1209

**Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT**

# Effect of Erythropoietin and Transfusion Threshold on Neurological Recovery After Traumatic Brain Injury A Randomized Clinical Trial

Claudia S. Robertson, MD; H. Julia Hannay, PhD; José-Miguel Yamal, PhD; Shankar Gopinath, MD;  
J. Clay Goodman, MD; Barbara C. Tilley, PhD; and the Epo Severe TBI Trial Investigators

JAMA. 2014;312(1):36-47

# ERYTHROPOIETIN AND TRANSFUSION THRESHOLD

- Randomized clinical trial of 200 patients
- To compare the effects of erythropoietin and 2 hemoglobin transfusion thresholds (7 and 10 g/dL) on neurological recovery after traumatic brain injury
- „Neither the administration of erythropoietin nor maintaining hemoglobin concentration of greater than 10 g/dL resulted in improved neurological outcome at 6 months“
- „The transfusion threshold of 10 g/dL was associated with a higher incidence of adverse events“

# Erythropoietin in traumatic brain injury (EPO-TBI): a double-blind randomised controlled trial

*Alistair Nichol, Craig French, Lorraine Little, Samir Haddad, Jeffrey Presneill, Yaseen Arabi, Michael Bailey, D James Cooper, Jacques Duranteau, Olivier Huet, Anne Mak, Colin McArthur, Ville Pettilä, Markus Skrifvars, Shirley Vallance, Dinesh Varma, Judy Wills, Rinaldo Bellomo, for the EPO-TBI Investigators and the ANZICS Clinical Trials Group\**

Lancet 2015; 386: 2499–506

- Doppelblind, placebokontrolliert, Multicenter
- 606 Patienten, 40'000E sc Erythropoietin max. 3x
- „Following moderate or severe traumatic brain injury, erythropoietin did not reduce the number of patients with severe neurological dysfunction (GOS-E level 1–4) or increase the incidence of deep venous thrombosis of the lower limbs. The effect of erythropoietin on mortality remains uncertain“

Lancet 2015; 386: 2499–506

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**Very Early Administration of Progesterone for Acute  
Traumatic Brain Injury**

David W. Wright, M.D., Sharon D. Yeatts, Ph.D., Robert Silbergleit, M.D., Yuko Y. Palesch, Ph.D.,  
Vicki S. Hertzberg, Ph.D., Michael Frankel, M.D., Felicia C. Goldstein, Ph.D., Angela F. Caveney, Ph.D.,  
Harriet Howlett-Smith, R.N., Erin M. Bengelink, M.A., Geoffrey T. Manley, M.D., Ph.D., Lisa H. Merck, M.D., M.P.H.,  
L. Scott Janis, Ph.D., and William G. Barsan, M.D., for the NETT Investigators\*

N Engl J Med 2014;371:2457-66

# PROTECT III TRIAL

- Doppelblind, placebokontrolliert, Multizenter
- 882 Patienten (vorzeitig abgebrochen 1140 geplant)
- „This clinical trial did not show a benefit of progesterone over placebo in the improvement of outcomes in patients with acute TBI“

N Engl J Med 2014;371:2457-66

Review Article

# Mannitol or hypertonic saline in the setting of traumatic brain injury: What have we learned?

Myles Dustin Boone, Achikam Oren-Grinberg, Timothy Matthew Robinson<sup>1</sup>, Clark C. Chen<sup>2</sup>,  
Ekkehard M. Kasper<sup>1</sup>

Department of Anesthesiology, Beth Israel Deaconess Medical Center, <sup>1</sup>Department of Surgery, Division of Neurosurgery, Beth Israel Deaconess Medical Center, Boston, MA, <sup>2</sup>Division of Neurosurgery, UCSD Medical Center, San Diego, CA, USA

Surg Neurol Int. 2015; 6: 177

# HTS VS. MANNITOL

- Hämodynamik
  - Plasmaexpansion und zentrale Stimulation Cardiac Output
- Immunmodulation, Anti-Inflammation
  - TNFalpha vs. IL-ra, IL-10
- Neurochemie
  - Na<sup>+</sup>/Glutamat-Co-Transport reduziert Glutamat extrazellulär
- Mikrozirkulation
  - Verbesserung Mikrozirkulation und DO<sub>2</sub>

Surg Neurol Int. 2015; 6: 177

# HTS VS. MANNITOL

- Einfacheres Monitoring
- hyperosmolares Nierenversagen?
- Bisher keine pontine Myelinolyse beschrieben
  
- Mannitol ist altbewährt
- Chlorid-Belastung?

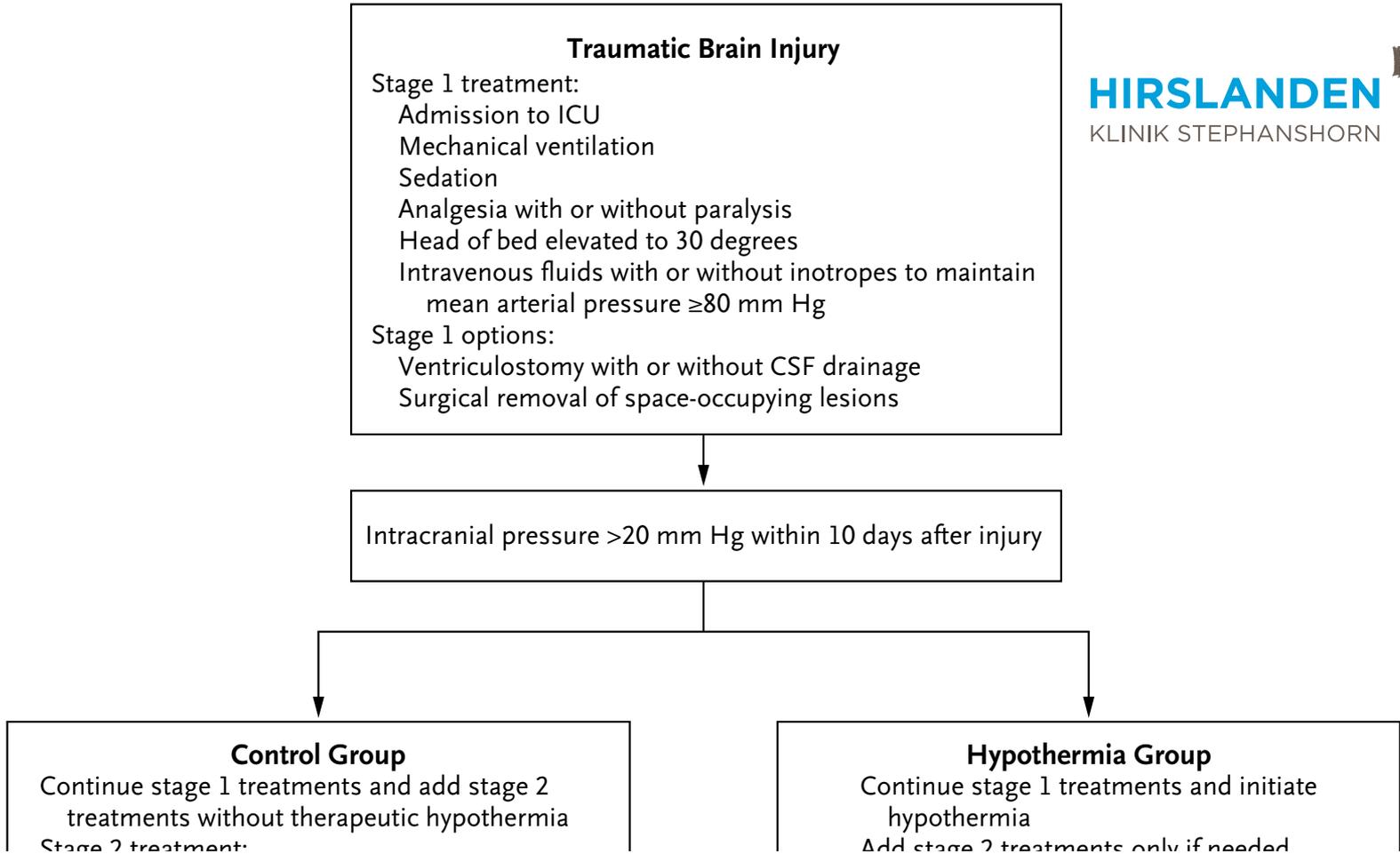
ORIGINAL ARTICLE

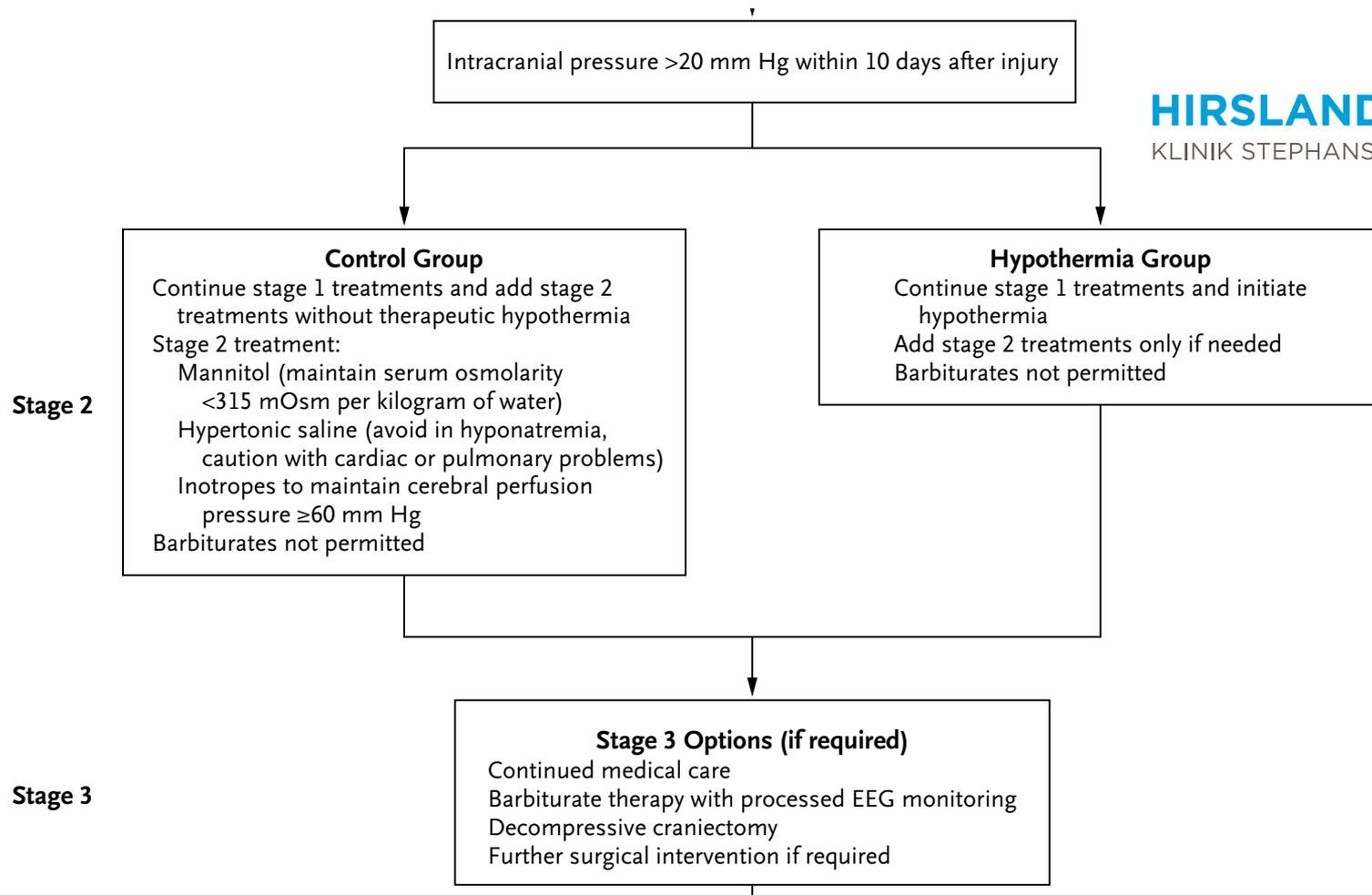
# Hypothermia for Intracranial Hypertension after Traumatic Brain Injury

Peter J.D. Andrews, M.D., M.B., Ch.B., H. Louise Sinclair, R.G.N., M.Sc.,  
Aryelly Rodriguez, M.Sc., Bridget A. Harris, R.G.N., Ph.D.,  
Claire G. Battison, R.G.N., B.A., Jonathan K.J. Rhodes, Ph.D., M.B., Ch.B.,  
and Gordon D. Murray, Ph.D., for the Eurotherm3235 Trial Collaborators\*

N Engl J Med 2015; 373:2403-2412

**Stage 1**





# EUROTHERM3235 TRIAL

- Multizenter
- 347 Patienten (600 geplant, abgebrochen for safety reasons)
- Standard care + Osmotherapie vs. Standard care + Hypothermie
- „In patients with an intracranial pressure of more than 20mmHg after traumatic brain injury, therapeutic hypothermia plus standard care to reduce intracranial pressure did not result in outcomes better than those with standard care alone“

# EUROTHERM3235 TRIAL

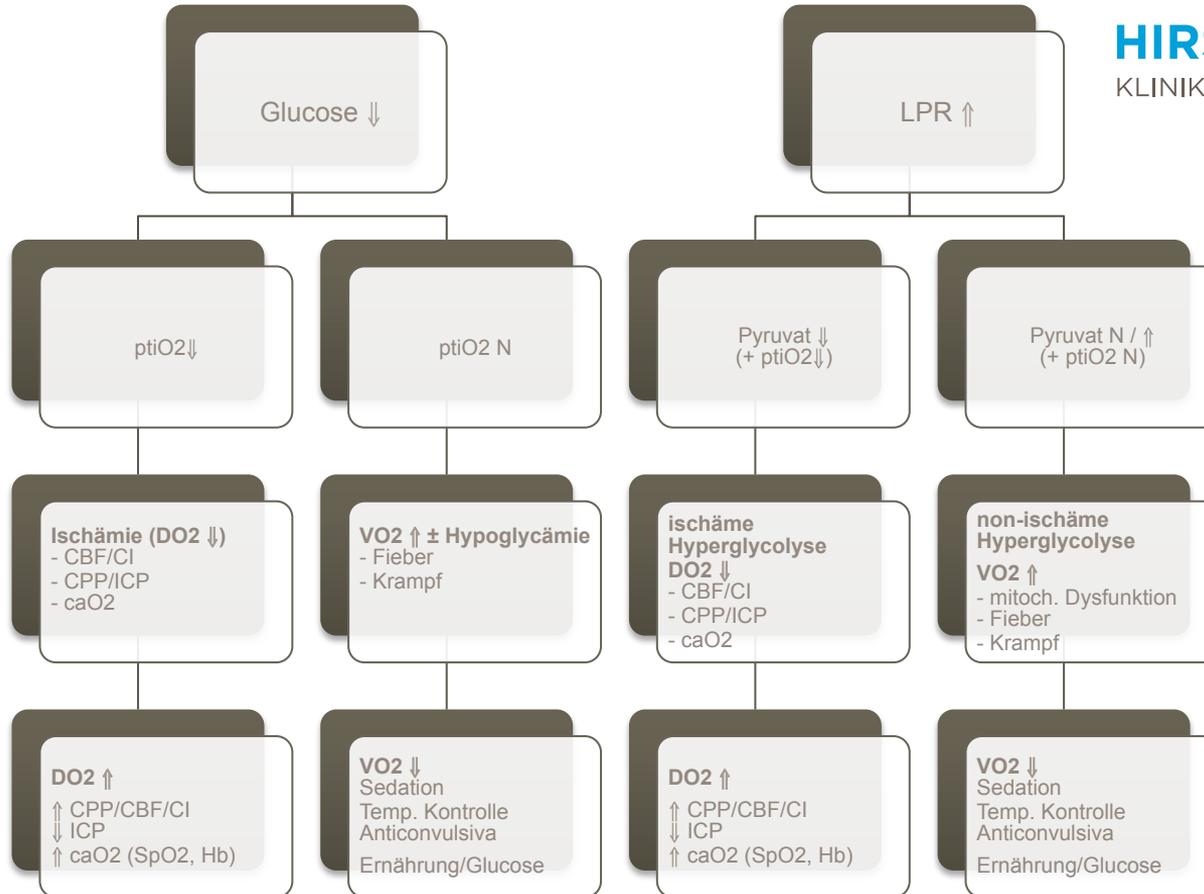
- Hypothermie senkt ICP, ändert nichts am Outcome
- Nicht als frühe Therapieoption
- Rescue Therapie vor Kraniektomie
- Ziel 35°C, kein Überschiessen beim Aufwärmen
- Aufwärmen? Wie?
- Fieberkontrolle ist wichtig!

# ZUSAMMENFASSEND PRAKTISCHE ASPEKTE

- BLS, BICS
- SHT-Protokoll mit festgelegten Therapiemodalitäten
  - Sedation
  - Liquordrainage, Entfernung Raumforderungen
  - Osmotherapie
  - Hypothermie
  - Kraniektomie

# ZUSAMMENFASSEND PRAKTISCHE ASPEKTE

- Multimodales Monitoring
  - Sondenlage? Läsion? Penumbra?
  - Messwerte plausibel? Fehlmessungen?
- Individualisierte Vital- und Zielparameter mit Hilfe des MMM
  - ICP, PbtO<sub>2</sub>, Mikrodialyse, PRx/CPPOpt



# HERZLICHEN DANK

MED. PRACT. THOMAS BRUNNER  
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