Brain under pressure
Managing ICP

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HIGH ICP

- Produces pressure gradients: herniation
- Reduces CBF
- Negative impact on outcome
The new "insufficient" evidence

Level I and II A

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

Level II B

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

Recommendation

• ICP and CPP monitoring are recommended as a part of protocol-driven care in patients who are at risk of elevated intracranial pressure based on clinical and/or imaging features. (Strong recommendation, moderate quality of evidence.)
ICP monitoring should be undertaken in patients with more severe SAH (WFNS ≥ 3), and that a ventricular catheter should be used as the ICP monitoring device because it offers the possibility of therapeutic draining of CSF to treat hydrocephalus.
International prospective observational Study on IntrAcranial PreSSurE in intensive care (ICU)
The SYNAPSE-ICU Study

ClinicalTrials.gov Identifier: NCT03257904
Primary Injury

Progressive damage

Biological Response

Secondary Insults

Secondary Damage

Age
Pre-injury health, Genetic factors

High ICP, low CPP, seizures, fever

Final Outcome
Primary Injury

Progressive damage

Biological Response

Age
Pre-injury health, Genetic factors

Counteracting secondary Insults

Reduce secondary damage

ICU monitoring

Final Outcome
Intro

Thresholds

Treating HICP

Conclusions
Historical thresholds (with Rx)

retrospective, n=100

treating @15 mmHg improves outcome

The outcome with aggressive treatment in severe head injuries

Part I: The significance of intracranial pressure monitoring

LAWRENCE F. MARSHALL, M.D., RANDALL W. SMITH, M.D.,
AND HARVEY M. SHAPIRO, M.D.

retrospective, n=207

treating @20 mmHg improves outcome

Intracranial pressure: to monitor or not to monitor?

A review of our experience with severe head injury

RAJ K. NARAYAN, M.D., PULLA R. S. KISHORE, M.D., DONALD P. BECKER, M.D.,
JOHN D. WARD, M.D., GREGORY G. ENAS, B.S., RICHARD P. GREENBERG, M.D., PH.D.,
A. DOMINGUES DA SILVA, M.D., MAURICE H. LIPPER, M.D., SUNG C. CHOI, PH.D.,
C. GLEN MATHALL, M.D., HARRY A. LUTZ III, PH.D., AND HAROLD F. YOUNG, M.D.

cohort, n=233

treating @15-25 mmHg improves outcome

Effect of intracranial pressure monitoring and aggressive treatment on mortality in severe head injury

THOMAS G. SAEI, M.D., AND THOMAS B. DUCKER, M.D.

Division of Neurological Surgery, University of Maryland School of Medicine, Baltimore, Maryland

prospective, n=70, barbiturates

failure to control ICP < 20mmHg = bad outcome

High-dose barbiturate control of elevated intracranial pressure in patients with severe head injury

HOWARD M. EISENBURG, M.D., RALPH F. FRANKOWSKI, PH.D., CHARLES F. CONTANT,
LAWRENCE F. MARSHALL, M.D., MICHAEL D. WALKER, M.D., AND THE COMPREHENSIVE CENTRAL NERVOUS SYSTEM TRAUMA CENTERS

Division of Neurosurgery, The University of Texas Medical Branch, Galveston, Texas
Why are we using 20mmHg?

| **Marmarou** | “Beyond age, admission motor score and pupils, the proportion of ICP measurements >20 mmHg is most indicative of outcome” |
| **TCDB** | |
| **Simplistic interpretation** | • 20 mmHg is the threshold for starting therapy |
| **BTF till the 3rd** | • Treatment should be initiated with ICP thresholds above 20mmHg (Level II) |

Lost in clinical translation...
Critical Thresholds for Cerebrovascular Reactivity After Traumatic Brain Injury. Neurocrit Care 2011;
“22” is the “new 20”

• Level II B

Treating ICP above 22 mm Hg is recommended because values above this level are associated with increased mortality.

Are these two patients really different?
Which is the sickest patient?
Kaplan–Meier survival curve of patients with aSAH stratified according to levels of PTDICP20
ICP time burden "Intensity*Time"


<table>
<thead>
<tr>
<th>ICP threshold</th>
<th>First line (65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;15 mmHg</td>
<td>N= 3 (5%)</td>
</tr>
<tr>
<td>&gt;20 mmHg</td>
<td>N= 54 (83%)</td>
</tr>
<tr>
<td>&gt;25 mmHg</td>
<td>N= 6 (9%)</td>
</tr>
<tr>
<td>&gt;30 mmHg</td>
<td>N= 0 (0%)</td>
</tr>
<tr>
<td>Individualized</td>
<td>N= 2 (3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Target CPP² (66)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50 mmHg</td>
<td>N= 7 (11%)</td>
</tr>
<tr>
<td>&gt; 60 mmHg</td>
<td>N= 39 (59%)</td>
</tr>
<tr>
<td>&gt; 70 mmHg</td>
<td>N= 14 (21%)</td>
</tr>
<tr>
<td>Individualized</td>
<td>N= 25 (38%)</td>
</tr>
</tbody>
</table>
Intro

Thresholds

Treating HICP

Conclusions
Continuous recording of the ventricular-fluid pressure in cases of severe traumatic injury of the head facilitates the evaluation of intracranial dynamics and offers a more rational basis for treatment than do conventional control measures.
The new "insufficient" evidence

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

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

Odds ratios of neurological outcomes at 1 year, comparing intracranial pressure (ICP) patterns

Glasgow Outcome Score: GR, Good Recovery; MD, Moderate Disability; SD, Severe Disability; V, Vegetative; D, Death

Sedation


<table>
<thead>
<tr>
<th>Sedatives and analgesics</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl (64)</td>
<td>37  (58%)</td>
</tr>
<tr>
<td>Midazolam (64)</td>
<td>48  (75%)</td>
</tr>
<tr>
<td>Morphine/ opioids (63)</td>
<td>32  (51%)</td>
</tr>
<tr>
<td>Propofol (65)</td>
<td>54  (83%)</td>
</tr>
<tr>
<td>Neuromuscular blocking agent (64)</td>
<td>16  (25%)</td>
</tr>
<tr>
<td>Alfa 2 agonist (64)</td>
<td>10  (16%)</td>
</tr>
<tr>
<td>Barbiturates (64)</td>
<td>12  (19%)</td>
</tr>
<tr>
<td>Other (66)</td>
<td>10  (15%)</td>
</tr>
</tbody>
</table>

CSF drainage \(^3\) (66) \(N=18\) (27%)
If ICP > 20-25 mmHg
- Continue sedation
  - Evaluate cEEG for titrating the dose

If ICP controlled > 24 hrs
- Re-evaluate the case/ICP therapy intensive level
  - Test withdrawal
    - if successful: stop sedation
    - if unsuccessful: restart sedation

Add therapy for HICP

### Hyperosmolar therapy

<table>
<thead>
<tr>
<th>Method</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mannitol (65)</td>
<td>43</td>
<td>66%</td>
</tr>
<tr>
<td>Hypertonic Saline (65)</td>
<td>44</td>
<td>68%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Administration</th>
<th>Mannitol (43)</th>
<th>HS (44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose titrated to ICP</td>
<td>18 (42%)</td>
<td>22 (50%)</td>
</tr>
<tr>
<td>Fixed bolus dosing</td>
<td>22 (51%)</td>
<td>18 (41%)</td>
</tr>
<tr>
<td>Continuous</td>
<td>3 (7%)</td>
<td>4 (9%)</td>
</tr>
</tbody>
</table>
Hyperosmolar fluids for the management of elevated ICP in neurocritical care patients

- Are available hyperosmolar fluids effective in reducing ICP?

Hyperosmolar fluids (MAN, HTS, HTL) are effective in reducing ICP.

GRADE: low quality evidence.

- Is there any evidence that hyperosmolar fluids have different efficacy (more or less effective) in reducing ICP?

Studies were too heterogeneous to be combined in an overall body of evidence.
## Mannitol

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>N</th>
<th>Weight</th>
<th>MD 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marshall, 1978</td>
<td>8</td>
<td>5.1</td>
<td>26.90 [16.11, 36.60]</td>
</tr>
<tr>
<td>Heimbach, 2011</td>
<td>11</td>
<td>7.3</td>
<td>7.10 [6.58, 7.62]</td>
</tr>
<tr>
<td>Mabulai, 1984</td>
<td>31</td>
<td>8.7</td>
<td>4.20 [1.16, 7.24]</td>
</tr>
<tr>
<td>Montaudo, 1980</td>
<td>41</td>
<td>8.4</td>
<td>4.70 [2.31, 7.07]</td>
</tr>
<tr>
<td>Rooner, 1987</td>
<td>16</td>
<td>8.3</td>
<td>15.00 [7.11, 22.80]</td>
</tr>
<tr>
<td>Miller, 1990</td>
<td>5</td>
<td>4.8</td>
<td>17.40 [6.92, 27.87]</td>
</tr>
<tr>
<td>Miller, 1992</td>
<td>3</td>
<td>5.2</td>
<td>11.00 [7.29, 14.71]</td>
</tr>
<tr>
<td>Miller, 1993</td>
<td>5</td>
<td>7.0</td>
<td>13.20 [7.53, 18.87]</td>
</tr>
<tr>
<td>Miller, 1993</td>
<td>4</td>
<td>1.1</td>
<td>14.50 [12.65, 16.35]</td>
</tr>
<tr>
<td>Larjava, 2014</td>
<td>13</td>
<td>7</td>
<td>14.70 [7.82, 21.58]</td>
</tr>
<tr>
<td>Oddo, 2009</td>
<td>10</td>
<td>8.9</td>
<td>9.10 [2.52, 15.69]</td>
</tr>
<tr>
<td>Waer, 2008</td>
<td>19</td>
<td>6</td>
<td>20.90 [12.50, 29.30]</td>
</tr>
<tr>
<td>Francione, 2008</td>
<td>10</td>
<td>8.4</td>
<td>14.00 [9.01, 18.99]</td>
</tr>
<tr>
<td>Scalfari, 2012</td>
<td>8</td>
<td>8.8</td>
<td>6.78 [4.93, 12.62]</td>
</tr>
<tr>
<td>Dringer, 2012</td>
<td>6</td>
<td>8.1</td>
<td>7.88 [2.43, 13.17]</td>
</tr>
</tbody>
</table>

### Total

<table>
<thead>
<tr>
<th>Weight</th>
<th>MD 95% CI</th>
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</thead>
<tbody>
<tr>
<td>11.44</td>
<td>8.39, 14.52</td>
</tr>
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</table>

### RE Model

- $p < 0.0001$
- $R^2 = 0.69$ (95% CI 0.38 - 0.88)

---

## HS

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>N</th>
<th>Weight</th>
<th>MD 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ware, 2005</td>
<td>13</td>
<td>2.7</td>
<td>16.00 [13.11, 18.89]</td>
</tr>
<tr>
<td>Francione, 2008</td>
<td>10</td>
<td>13.5</td>
<td>10.00 [7.51, 12.49]</td>
</tr>
<tr>
<td>Scalfari, 2012</td>
<td>8</td>
<td>8</td>
<td>6.70 [4.88, 12.52]</td>
</tr>
<tr>
<td>Hoeylty, 2011</td>
<td>50</td>
<td>12.4</td>
<td>10.00 [6.83, 13.17]</td>
</tr>
<tr>
<td>Bensin, 2006</td>
<td>22</td>
<td>10.3</td>
<td>3.30 [2.02, 4.58]</td>
</tr>
<tr>
<td>Al-Rawi, 2010</td>
<td>16</td>
<td>9.6</td>
<td>12.10 [7.38, 16.82]</td>
</tr>
<tr>
<td>Main, 2015</td>
<td>15</td>
<td>11</td>
<td>10.40 [6.48, 14.32]</td>
</tr>
<tr>
<td>Al-Rawi, 2005</td>
<td>14</td>
<td>5.5</td>
<td>14.90 [6.95, 22.85]</td>
</tr>
<tr>
<td>Lesoe, 2006</td>
<td>14</td>
<td>13.8</td>
<td>6.00 [3.68, 8.32]</td>
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</tbody>
</table>

### Total

<table>
<thead>
<tr>
<th>Weight</th>
<th>MD 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.63</td>
<td>6.50, 11.14</td>
</tr>
</tbody>
</table>

### RE Model

- $p < 0.0001$
- $R^2 = 0.69$ (95% CI 0.38 - 0.88)
Mannitol and HS for ICP treatment in TBI - Metaregression

\[
\text{Intercept} = -7.811 \\
\text{slope} = 0.659 \\
p = 1.496 \times 10^{-12} \\
Q = 19.414 \\
I^2 = 21 \\
95\% - CI: 0 - 81
\]

\[
\text{Intercept} = -3.998 \\
\text{slope} = 0.492 \\
p = 7.4 \times 10^{-9} \\
Q = 1.674 \\
I^2 = 0 \\
95\% - CI: 0 - 69
\]
<table>
<thead>
<tr>
<th>Procedure</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decompressive craniectomy</td>
<td>26</td>
<td>39%</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>16</td>
<td>25%</td>
</tr>
<tr>
<td>Deep hyperventilation</td>
<td>10</td>
<td>15%</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>21</td>
<td>32%</td>
</tr>
<tr>
<td>CSF drainage</td>
<td>22</td>
<td>33%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Target Temperature for Hypothermia (45)</th>
<th>N</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 35°C</td>
<td>5</td>
<td>11%</td>
</tr>
<tr>
<td>35°C</td>
<td>15</td>
<td>33%</td>
</tr>
<tr>
<td>33°C or 34°C</td>
<td>9</td>
<td>20%</td>
</tr>
<tr>
<td>32°C</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>Patient⁹</td>
<td>13</td>
<td>29%</td>
</tr>
<tr>
<td>Physician¹⁰</td>
<td>2</td>
<td>5%</td>
</tr>
</tbody>
</table>
STAGE 1
Mechanical ventilation
Sedation Analgesia with or without paralysis
Head of bed elevated to 30 degrees.
Intravenous fluids with or without inotropes for MAP > 80 mm Hg.
Opt: Ventriculostomy with or without CSF drainage.
Opt: Surgical removal of space-occupying lesions

Intracranial pressure >20 mmHg 5min within 10 days after injury

Control Group
Stage 2:
Add Mannitol, Hypertonic saline, Inotropes to maintain cerebral perfusion pressure >60 mmHg
Continued medical care.
Barbiturate therapy with processed EEG monitoring.
Decompressive craniectomy.
Further surgical intervention if required

Hypothermia Group
Add stage 2 treatments only if needed
Continued medical care.
Barbiturate therapy with processed EEG monitoring.
Decompressive craniectomy.
Further surgical intervention if required

• The adjusted common odds ratio for the GOS-E score was 1.53 (95% confidence interval, 1.02 to 2.30; P=0.04), indicating a worse outcome in the hypothermia group than in the control group.

• A favourable outcome (GOS-E score of 5 to 8, indicating moderate disability or good recovery) occurred in 26% of the patients in the hypothermia group and in 37% of the patients in the control group (P=0.03).

Implication for clinical practice

• NO HT in patients with intracranial hypertension that can be managed with stage 1 and 2 medical treatments.

• In patients with TBI who have severe intracranial hypertension, i.e., an ICP refractory to all stage 2 treatments before initiation of HT, the use of therapeutic HT when few alternatives remain, may be the single potential remaining indication for HT.
ICP > 20 mmHg, 15 minutes/1hr, despite optimized first-tier interventions.
Stage 1
Initial treatment measures
Ventilation
Sedation
Analgesia
± Paralysis
Nurse head up
Monitoring
CVP
Arterial line
ICP

Stage 2
OPTIONS:
Ventriculostomy
Inotropes
Mannitol
Hypertonic saline
Loop diuretics
Steroids
Hypothermia 34-36°C
BARBITURATES NOT PERMITTED

Stage 3
Randomise
ICP>25 mmHg
1-12 hours post start stage 2

Continued Medical treatment *
(stage 2 options) + barbiturates permitted

Decompressive craniectomy**
+ continued medical treatment (stage 2 options)

Medical

Surgical

4-6 h

For every 100 patients treated with DC rather than medical intent, 22 more survivors (CI 95% 13-31)

<table>
<thead>
<tr>
<th>State</th>
<th>Count</th>
<th>CI 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetative</td>
<td>6</td>
<td>6-10</td>
</tr>
<tr>
<td>Lower SD</td>
<td>4</td>
<td>2-8</td>
</tr>
<tr>
<td>Upper SD</td>
<td>7</td>
<td>4-11</td>
</tr>
<tr>
<td>Lower MD</td>
<td>2</td>
<td>1-5</td>
</tr>
<tr>
<td>Lower GR</td>
<td>3</td>
<td>1-6</td>
</tr>
</tbody>
</table>
International consensus meeting
on the role of Decompressive Cranectomy in
the management of Traumatic Brain Injury
Robinson College, University of Cambridge,
Cambridge, UK
28-29 September 2017
Intro

Thresholds

Treating HICP

Conclusions
Take home messages

High ICP is associated with negative outcome and has to be treated

Thresholds need to keep in consideration intensity and time of exposure

Therapies need to be order accordingly to their risk/benefit ratio

Extreme therapies need to be limited to sicker patients