UC Neuroscience Institute AT UNIVERSITY HOSPITAL
NEUROCRITICAL CARE
UNIVERSITY OF Cincinnati

Acute Management of TBI: Update on Guidelines

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Disclosures

- Grants / Research
  - NIH, DoD, UCB Pharma

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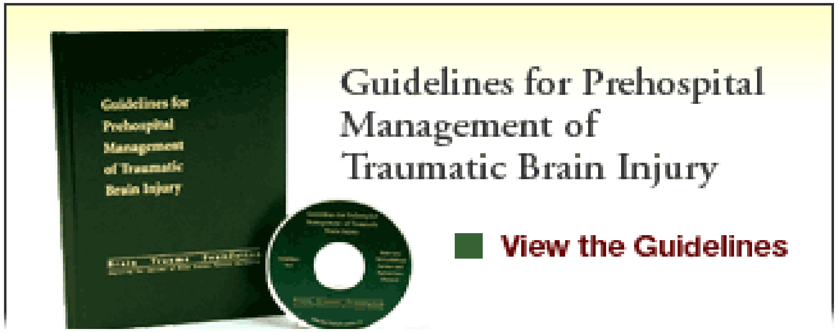
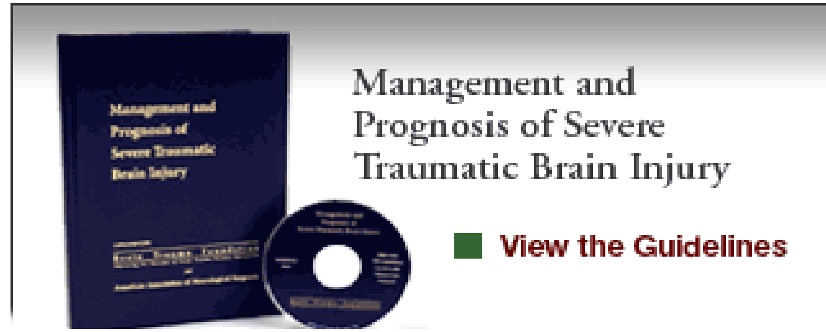
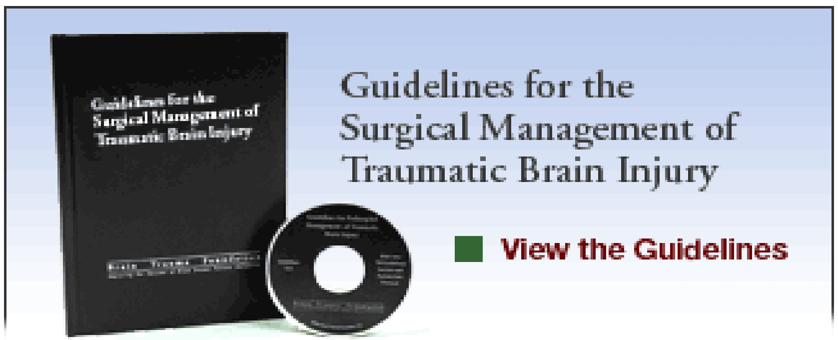
Objectives

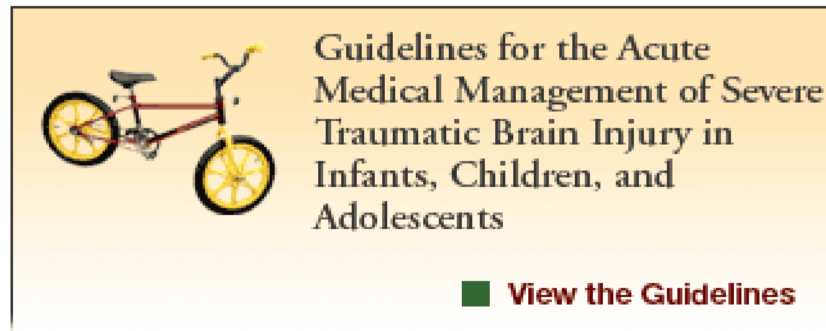
- Present guidelines for management of TBI
- Review evidence for guideline recommendations
- Discuss impact of guidelines on clinical care

TBI Guidelines









- Joint Projects of
  - The Brain Trauma Foundation
  - American Association of Neurological Surgeons (AANS)
  - Congress of Neurological Surgeons (CNS)
  - AANS/CNS Joint Section on Neurotrauma & Critical Care
  - **www.braintrauma.org**

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What is BTF?

- Non-profit organization, established in 1986
- Mission is to improve outcomes of traumatic brain injury (TBI) patients through:
  - Evidence based guideline development
  - AANS/CNS Neurotrauma Section partners
  - Medical education (*TBI-trac.edu*)
  - Clinical research (TBI-trac™)
  - Quality improvement programs (TBI-trac™)
  - Mild TBI (concussion) research

Topics

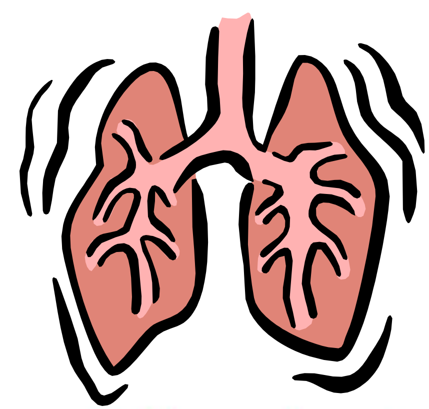
- Blood Pressure & Oxygenation
- ICP Monitoring Indications
- ICP Monitoring Technology
- ICP Thresholds
- CPP Thresholds
- Brain Oxygen Monitoring & Thresholds*
- Hyperosmolar Therapy*
- Anesthetics, Analgesics, and Sedatives*
- Hyperventilation
- Prophylactic Hypothermia*
- Steroids
- Antiseizure Prophylaxis
- Infection Prophylaxis*
- DVT Prophylaxis*
- Nutrition

*** New in 2007; 3rd edition**

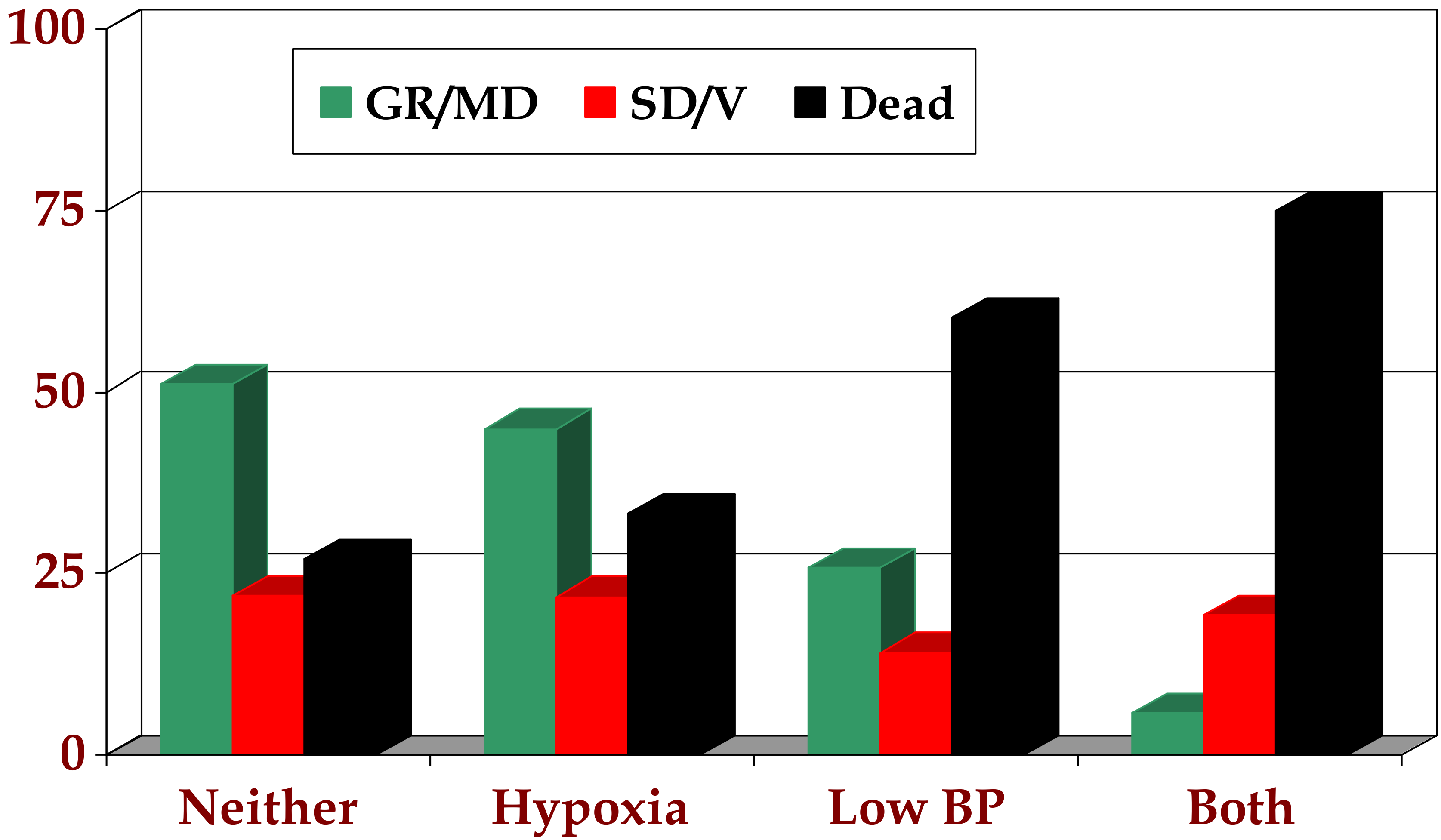
Journal of Neurotrauma Supplement May 2007

Early Medical Care Goals

- Avoid <u>hypoxia,</u> (any $SaO^2 < 90$ %)
  - Increases neuronal death / motor deficits & correlates with poor outcomes
  - Occurs at least once in 39%
- Avoid <u>hypotension,</u> (any SBP < 90 mmHg)
  - Mortality rates double; morbidity increases
  - Late hypotension seen in 32%; 66% become V/D (vs. 17%)
  - Do not treat ↑ BP (maintain cerebral perfusion)



Hypotension & Hypoxia



Chestnut RM, et al. J Trauma 1993;34:216-22

Blood Pressure and Oxygenation

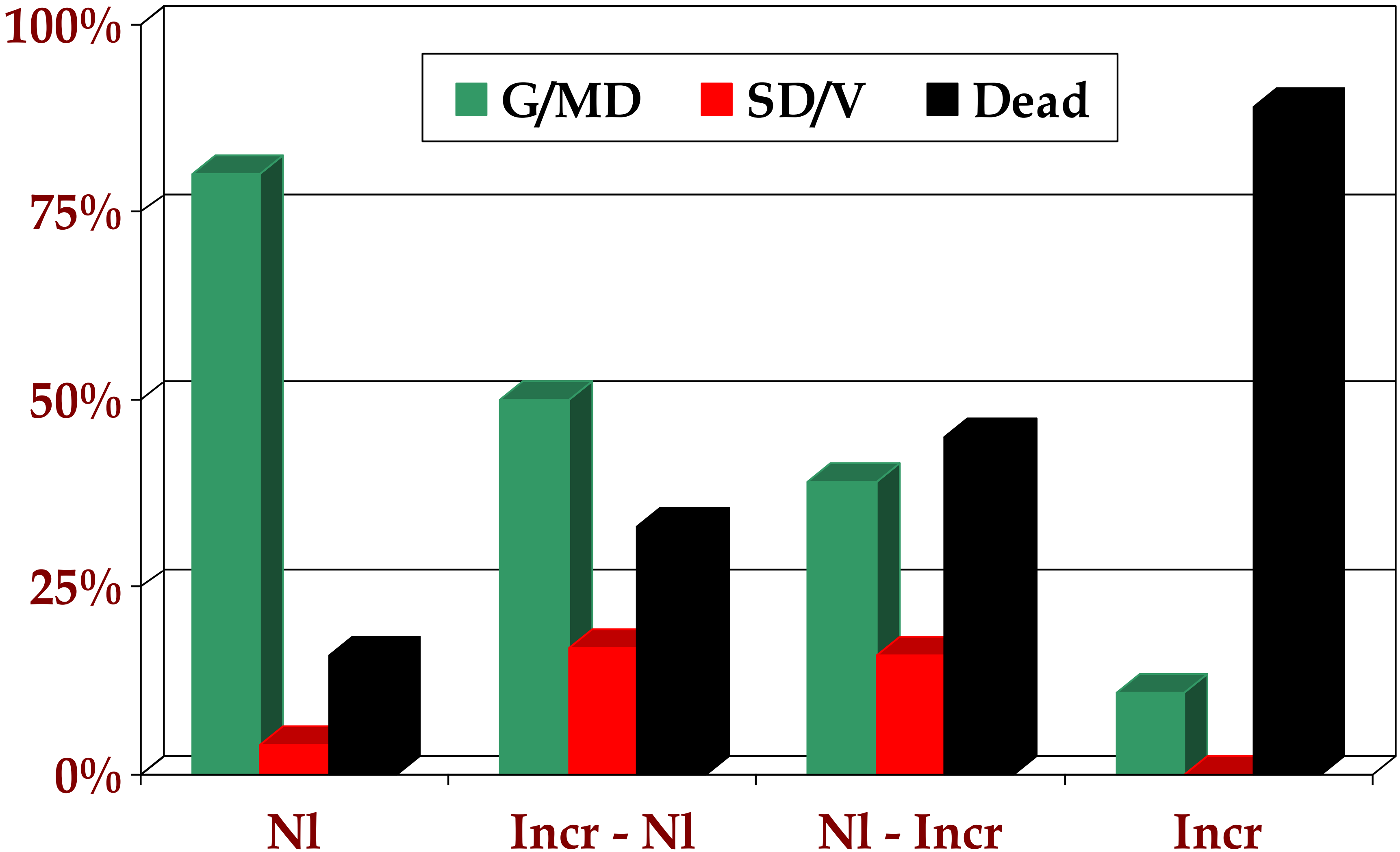
- Level II:

  Blood pressure should be monitored & hypotension (systolic blood pressure < 90 mm Hg) avoided.

- Level III:

  Oxygenation should be monitored & hypoxia (PaO^2 < 60 mm Hg or O^2 saturation < 90%) avoided.

Significance of ICP in TBI



Marmarou A, et al. J Neurosurg 1991;75:s59-66

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Indications for ICP Monitoring

- Level II:

  ICP should be monitored in all salvageable patients with a severe TBI (GCS 3 – 8 after resuscitation) and an abnormal CT scan (including signs of swelling, herniation, hematomas, contusions, or compressed basal cisterns).

- Level III:

  ICP monitoring is indicated in patients with severe TBI with a normal CT scan if two or more of the following on admission:

  1. age over 40 years
  2. unilateral or bilateral motor posturing
  3. systolic blood pressure (BP) < 90 mm

  Risk of increased ICP > 50 – 60% with above risk factors

ICP Monitoring Technology

- Conclusions

  In the current state of technology the **<u>ventricular catheter</u>** connected to an external strain gauge is the most accurate, low cost, and reliable method of monitoring ICP. It also can be recalibrated in situ. ICP transduction via fiberoptic or micro strain gauge devices placed in ventricular catheters provide similar benefits, but at a higher cost.

  Parenchymal ICP monitors cannot be recalibrated during monitoring. Parenchymal ICP monitors, using micro strain pressure transducers, have negligible drift. The measurement drift is independent of the duration of monitoring.

  Subarachnoid, subdural, and epidural monitors (fluid coupled or pneumatic) are less accurate.

ICP Treatment Threshold

- Level II:

  Initiate treatment with ICP thresholds > 20 mm Hg.

  Note: Although sustained episodes of ICP > 25 mm Hg are associated with ↑ mortality & poor outcome this should not be used alone, as prolonged (> 96 hours) elevations can still have favorable outcomes in up to 38%.

- Level III:

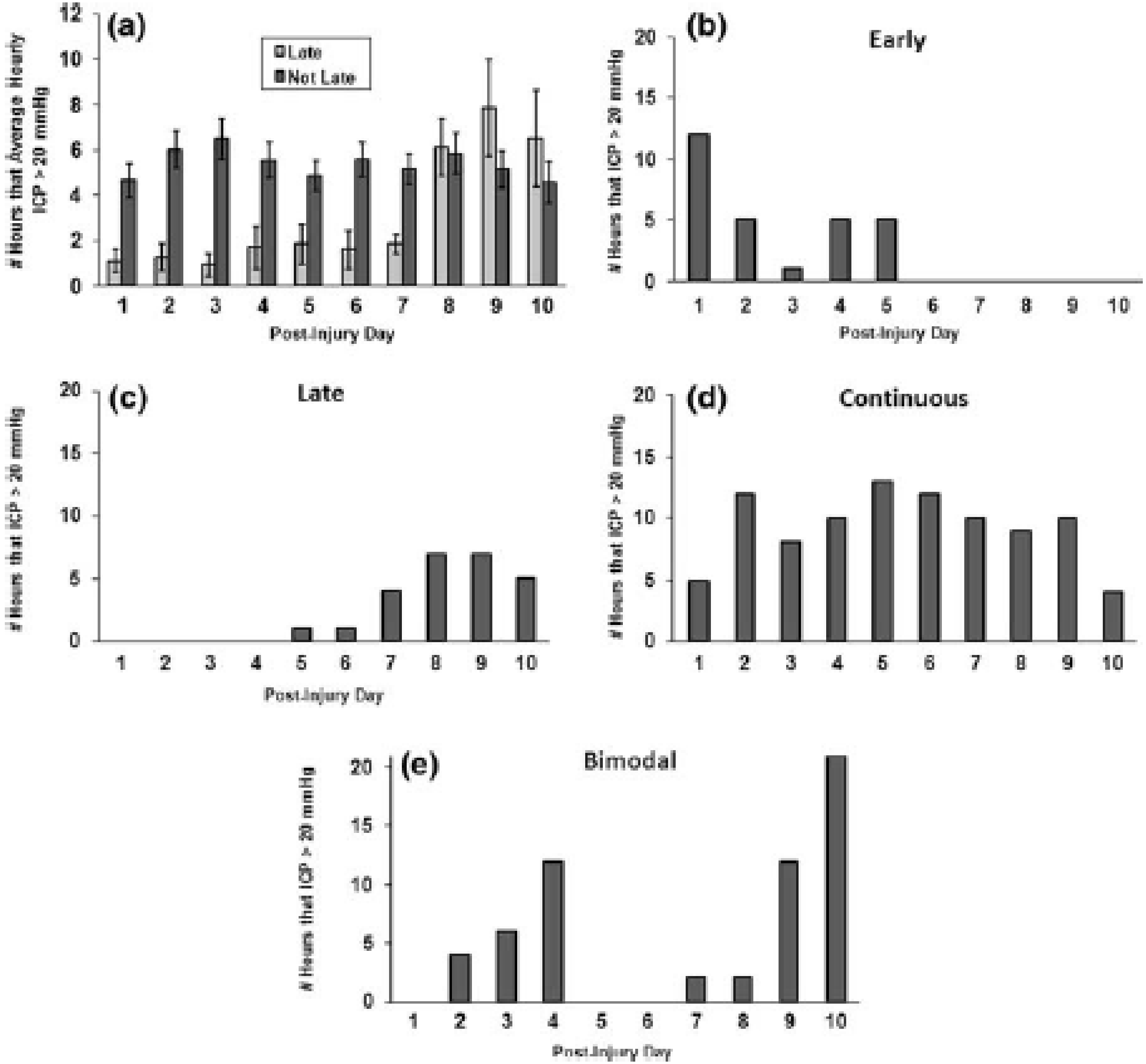
  A combination of ICP values, clinical & brain CT findings should be used to determine the need for treatment.

  Real life note: accept an ICP range of 20 – 25 mm Hg if other parameters (CPP, PbtO2, SjvO2) are acceptable

How Long to Monitor?

- Retrospective review, prospectively collected data looking at ICP patterns in 77 severe TBI patients
- Results
  - 4 patterns:
    1. early (in 72 hrs)
    2. late (after 72 hrs; 17%)
    3. bimodal (early increase, resolves, 2nd rise after 72 h)
    4. continuous
  - Peak swelling: day 7 for "late" group, all others on day 4
  - Contusion enlargement on 24 hr follow-up CT in 44%

O'Phelan KH, et al. Neurocrit Care 2009;10:280–6



O'Phelan KH, et al. Neurocrit Care 2009;10:280–6

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CPP Thresholds

- Level II:

  Aggressive attempts to maintain CPP > 70 mm Hg with fluids and pressors should be avoided (risk of ARDS).

- Level III:

  CPP < 50 mm Hg should be avoided.

  CPP value to target lies within the range of 50 – 70 mm Hg. Patients with intact pressure autoregulation tolerate higher CPP values.

  Ancillary monitoring of CBF, SjvO2, PbtO2, cerebral oxygen extraction or lactate production, and cerebral metabolism can facilitate CPP management.

Cerebral Perfusion Pressure

- CPP = MAP-ICP
  - low CPP → cerebral ischemia & secondary injury
  - CPP > 50 mm Hg helps cerebral oxygenation
- CPP driven therapy
  - CPP ≥ 70 mm Hg→ 29% mortality rate, & good outcomes in 35% (GCS 3) to 75% (GCS 7) ***(Rosner MJ, et al. J Neurosurg 1995;83:949-62)***
  - BUT, study was not randomized, controlled, or blinded
- Randomized, controlled study, ICP vs CBF (CPP ≥ 70) directed therapy ***(Robertson CS, et al. CCM 1999;27:2086-95)***
  - Less ischemia, BUT outcome was not better
  - Increased ARDS: 15 vs 3.3% (p=0.007, OR=5.06)
- New Guideline: keep CPP > 50-70

Brain Oxygen Monitoring & Thresholds*

- Level III:

Jugular venous saturation (< 50%) or brain tissue oxygen tension (< 15 mm Hg) are treatment thresholds

SjvO2 or PbtO2 measure cerebral oxygenation

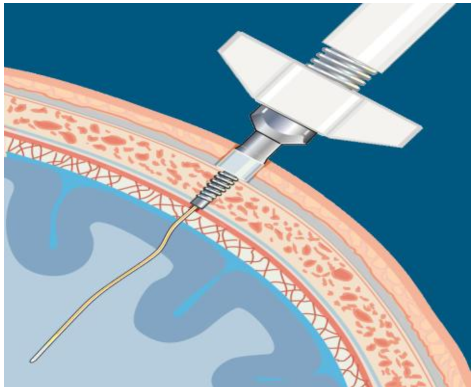
<u>Notes:</u>

1. Current evidence suggests that episodes of desaturation ($SjvO^2$ < 50-55%) are associated with worse outcomes & high extraction ($AJVO^2$) is associated with good outcome.
2. Low values of $PbtO^2$ (< 10-15 mm Hg) and the extent of their duration (greater than 30 minutes) are associated with high rates of mortality.

$PbtO^2$ Monitoring

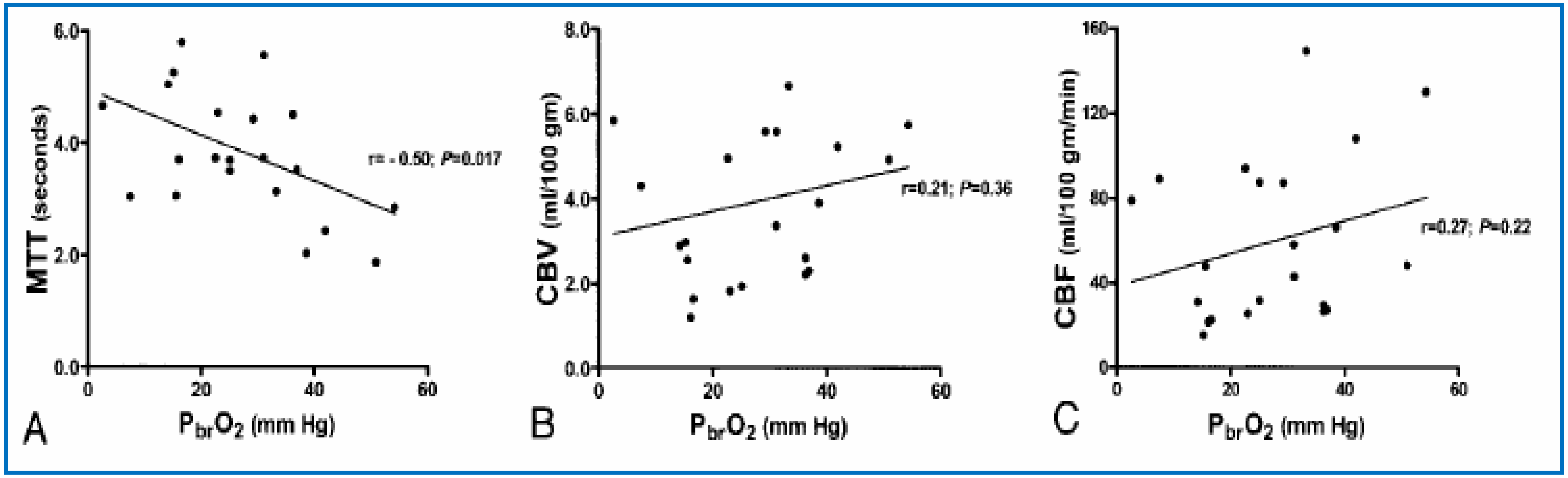
- Location
  - Placed in white matter (~35mm)
  - Normal tissue or pericontusional?
- Measures O^2 partial pressure (mmHg) in interstitial space
  - What does this represent?

    Thoughts: Total O^2 delivery; cerebral O^2 metabolism; O^2 diffusion; perfusion
- Values:
  - Normal > 20 mmHg
  - Ischemia: 8 - 12 mmHg
  - Critical: 5 - 8 mmHg



What does PbtO² represent?

- Observation study; n = 19 (15 TBI)
  - CTP studies = 22
  - Physiologic data: PbtO², MAP, CPP, ICP, FiO²
  - CTP data: MTT, CBF, CBV
- Results
  - Multivariant analysis: PbtO² independently associated w/ MTT (p=0.006)



Hemphill, et al. AJNR 2005;26:1095–1100

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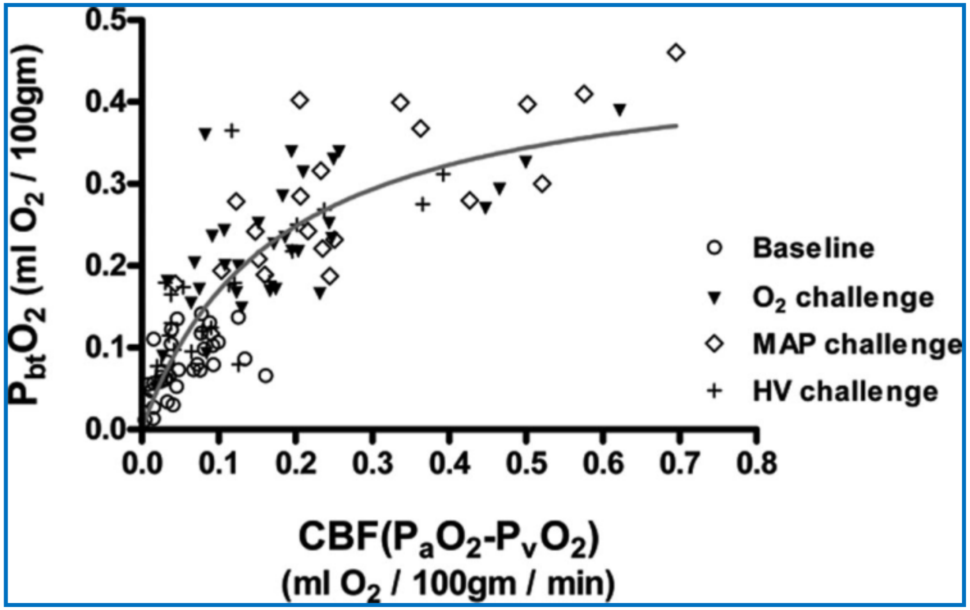
What does $PbtO^2$ represent?

- Prospective observation study; n = 14 sTBI
  - $PbtO^2$ & CBF monitoring with FiO^2, MAP, CO^2 challenges
  - Measured: PaO^2, CaO^2, PVO^2, CVO^2, $AVDO^2$, $locCMRO^2$
- Best association: CBF x (PaO^2-PvO^2)
  - Thus may represent the diffusion of dissolved plasma O^2 across the BBB and reflect O^2 accumulation in brain



Rosenthal, et al. CCM 2008;36:1917-24

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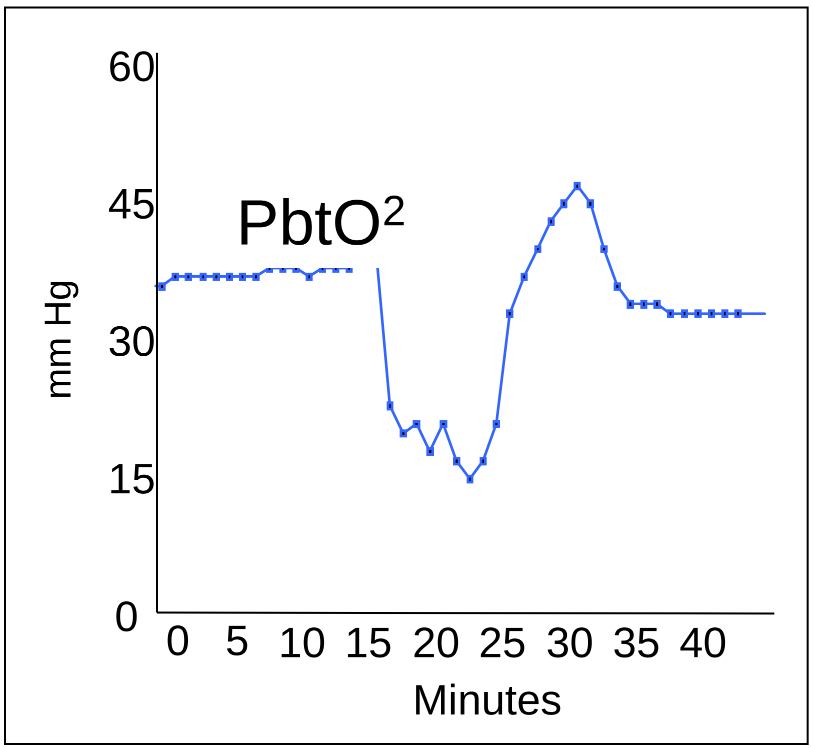
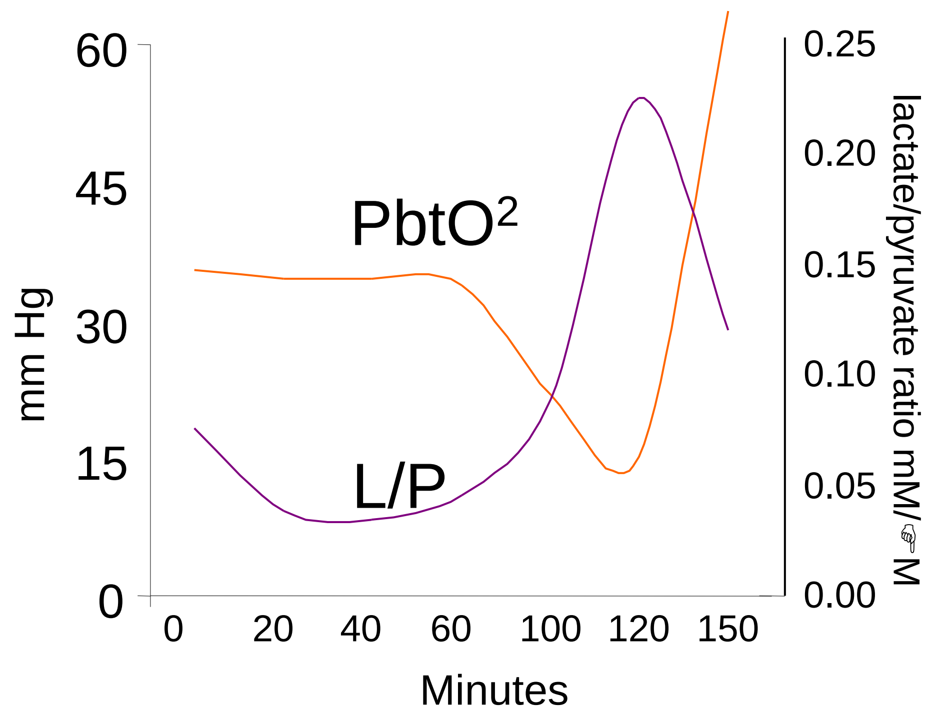
Effects of Hyperventilation on PbtO2

Swine



Human



Courtesy of Geoff Manley, MD; UCSF

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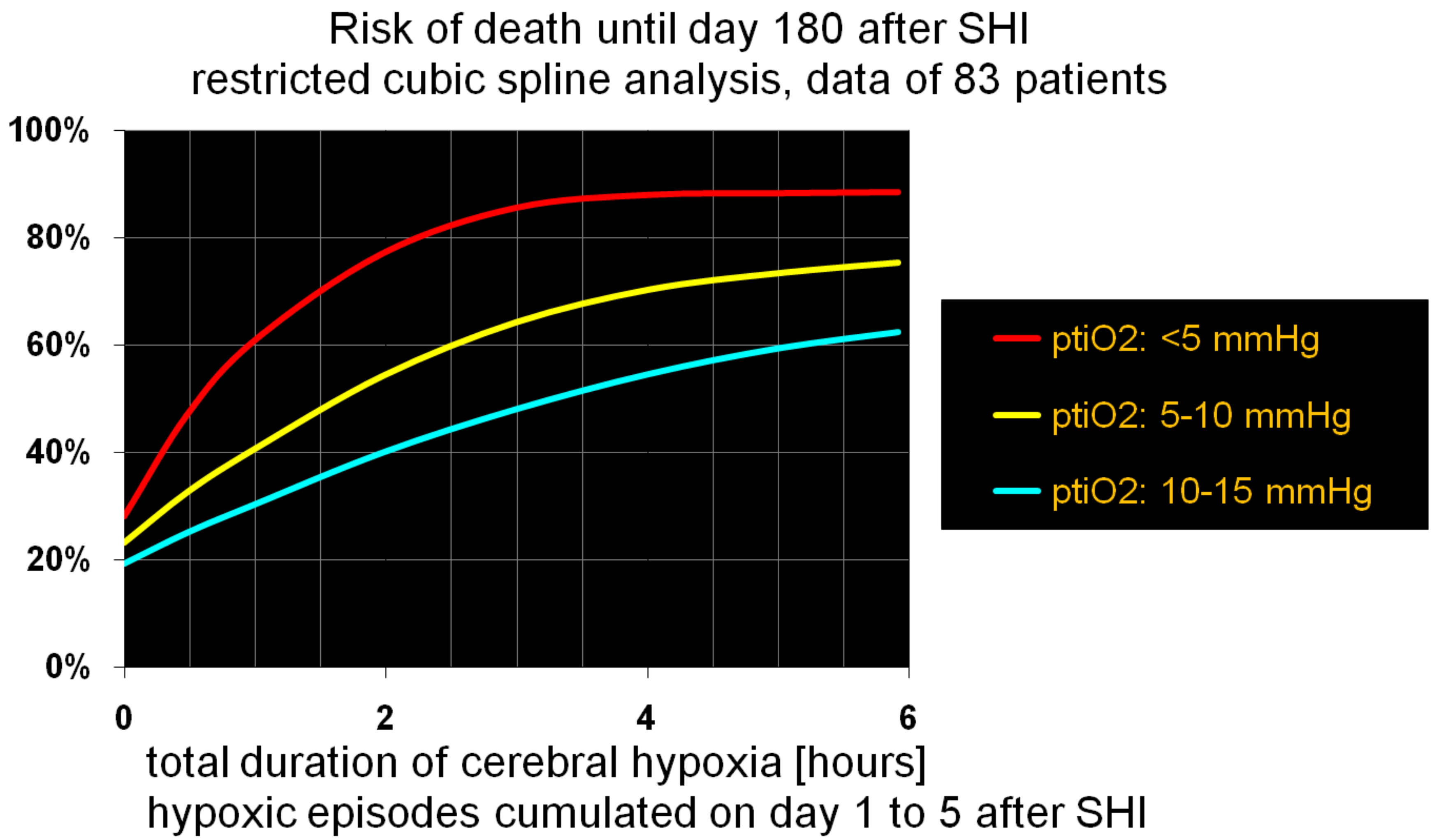
Rotterdam outcome study: Duration and severity of cerebral tissue hypoxia correlate with unfavorable outcome of TBI



Van den Brink WA, et al. Neurosurgery 2000;46:868-78

Is PbtO2 Important?

- Prospective observational cohort
- 82 patients with severe TBI (GCS <9)
- Simultaneous ICP, CPP, PbtO2 monitoring
- GCS clinical assessment
  - Pooled data with absolute & percentage abnormal values
- Univariate analysis (Student T test)
  - Logistic regression analysis:
  - GEE with logistic regression link function
  - Accounts for PbtO2 variations between subjects during time
  - 11,734 data points

Courtesy of Peter Le Roux, MD; UPenn

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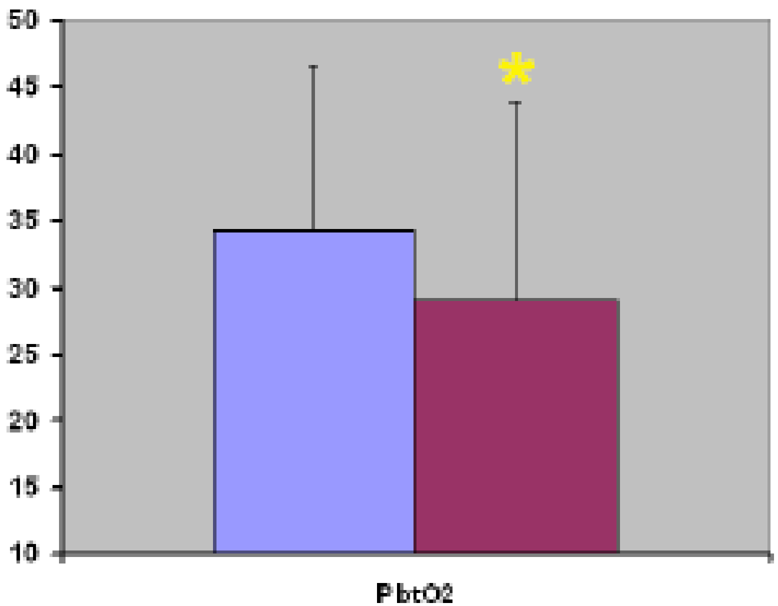
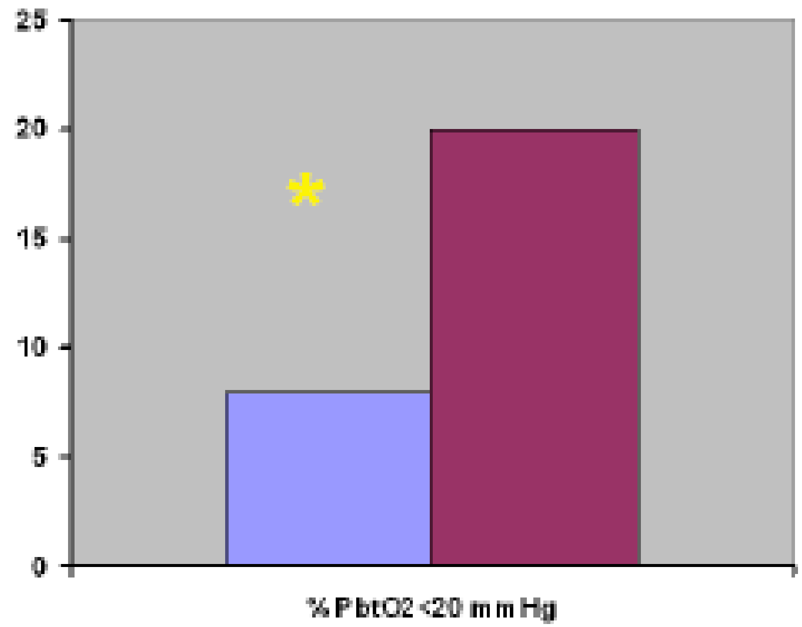
PbtO2 & Mortality





PbtO2 means (+ SD)

% PbtO2 < 20 mmHg

Survivors

Non-survivors

Courtesy of Peter Le Roux, MD; UPenn

PbtO[2] as a predictor of mortality

N=5222 data of simultaneous GCS, ICP, CPP and PbtO[2]

Variable	**OR**	**95% CI**	**P value**
PbtO[2] < 20 mmHg	0.46	0.28-0.77	**0.003**
CPP	1.00	0.98-1.03	0.74
ICP	1.02	0.99-1.05	0.30
GCS	0.92	0.83-1.01	0.08

Courtesy of Peter Le Roux, MD; UPenn

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ICP Treatments in the Guidelines

- Intubation ✓
- Sedation/Analgesia
  - Barbiturates
- Hyperosmotic therapy
- Hyperventilation
  - Mild (pCO^2 = 30 – 35)
  - Moderate (pCO^2 = 25 – 30)
- Hypothermia
- Steroids
- Decompression

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Anesthetics, Analgesics, & Sedatives**

- Level II:

  Prophylactic administration of barbiturates to induce burst suppression EEG 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.

  Propofol is recommended for the control of ICP, but not for improvement in mortality or 6 month outcome. High dose propofol can produce significant morbidity.

Barbiturates

- Mechanism of action
  - ↓ cerebral metabolic requirements → ↓ CBF demand → ↓ cerebral blood volume & ICP
- Do not use prophylactically
  - hypotension, hypoxia & secondary ischemia
  - no benefit on GOS at 1 year
- Refractory ICP elevations
  - Lower mortality rates, better outcome if respond
  - Pentobarbital used most often:
    - loading dose = 10 mg/kg over 30 minutes
    - maintenance = 1 mg/kg/hr infusion
  - Need an EEG to monitor (issues in brain death)
  - Contraindicated in hypotensive patients

Hyperosmolar Therapy

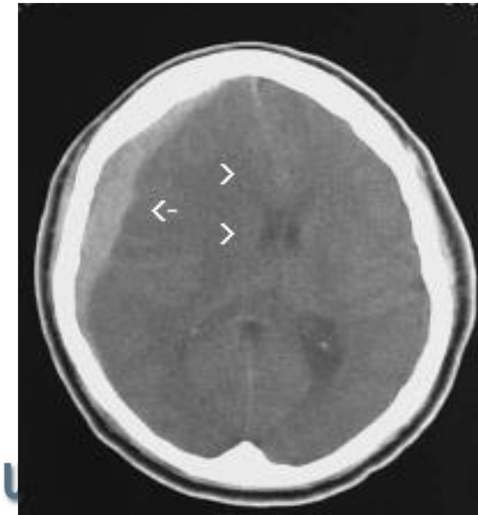
- Level II:

  Mannitol is effective for control of raised intracranial pressure (ICP) at doses of 0.25g/kg to 1g/kg body weight. However, arterial hypotension should be avoided.

- Level III:

  Restrict mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurological deterioration not attributable to extracranial causes.

Note: Data on hypertonic saline still limited



Mannitol for ICP

Effects:

- Plasma expander - ↓ hematocrit, ↑ blood flow, ↑ cerebral oxygen delivery
- Osmotic effect delayed for 15 to 30 minutes while gradients established between plasma and cells
  - "opening of BBB" → mannitol accumulation → reversed osmotic shift → ↑ brain osmolality → exacerbates ICP by ↑ brain edema = **Rebound ICP**
- **Never** subjected to randomized, placebo-controlled trial in TBI
- **Never** had a dose – response curve established

Mannitol Dose Response

- Retrospective; n = 28; continuous ICP collection
  - 20 patients got a total of 85 doses of 50 gm; 18 patients got a total of 50 doses of 100 gm
  - Average ICP when treated: 22 +/- 10.6 mm Hg
- Results
  - 0 – 30 min: fell immediately & continued to fall to 15.7 =/- 8.1 mm Hg for both doses
  - 100 min: 50 gm = 18.6 +/- 7.6 vs 100 gm = 14.2 +/- 6.7 (p=0.001)
- Conclusion
  - Dose dependent changes
  - Higher dose effects are more durable

Sorani MD, et al. J Neurotrauma 2008;25:291-8

Hypertonic Saline

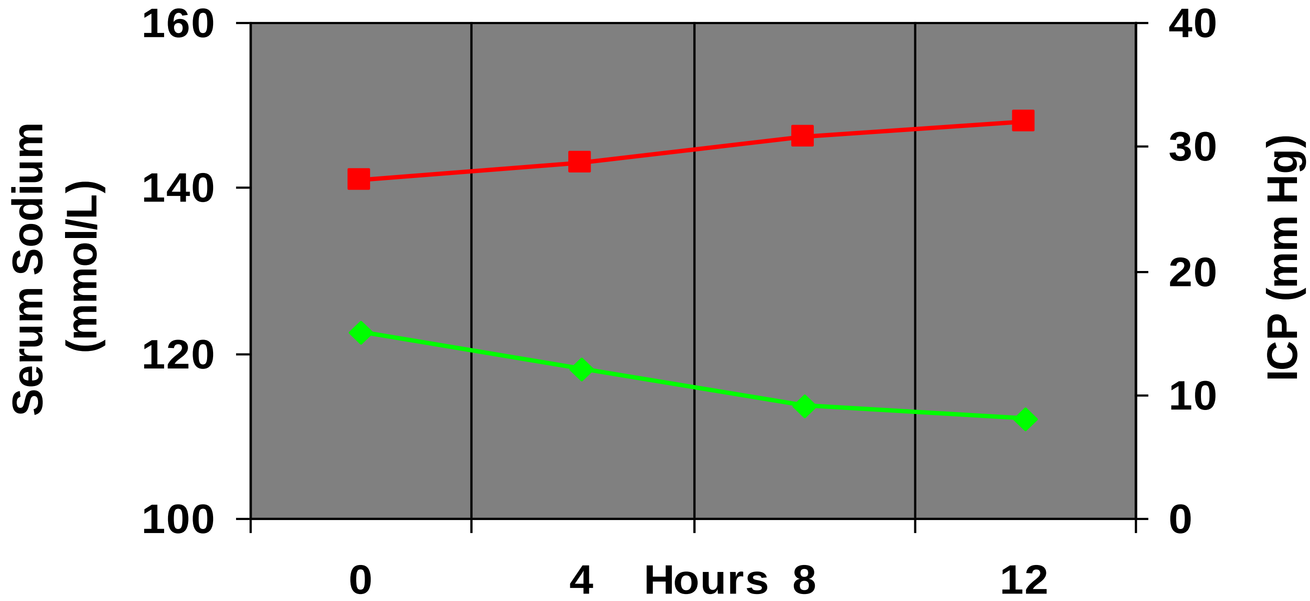
- Establishes osmotic gradient
- Volume expander w/ minimal renal effects, thus maintains MAP
- Less tendency to cross BBB than mannitol, thus less rebound cerebral edema
- Vascular endothelial effects may reverse vasospasm & related hypoperfusion
- Modulation of inflammatory response
  - ↓ WBC adherence, migration & prostaglandin production
- NMDA receptor effects

HTS in TBI

- Limited studies to date with small numbers
  - Resuscitation vs ICP control
- Resuscitation fluid
  - 7.5% HTS with or without dextran
  - Increased survival in TBI patients
- ICP control
  - Rescue therapy
  - Variable concentrations (1.7% - 29.2%)
  - Bolus therapy vs continuous infusions
  - Most report Na^+ levels of 145 – 160
  - Results generally show a ↓ in ICP as Na^+ rises

Osmolality: 3% vs Mannitol

- Osmolality ↑ is comparable to mannitol.
- Elevated osmolality is maintained longer.
- ICP reductions are ≥ than mannitol (5 – 20 mmHg)
- CPP maintained (improved hemodynamic stability



Qureshi, et al. Critical Care Med 1998; 26:440-6; Neurosurgery 1999; 44:1055-63
Vialet, et al. Crit Care Med 2003;31:1683-7

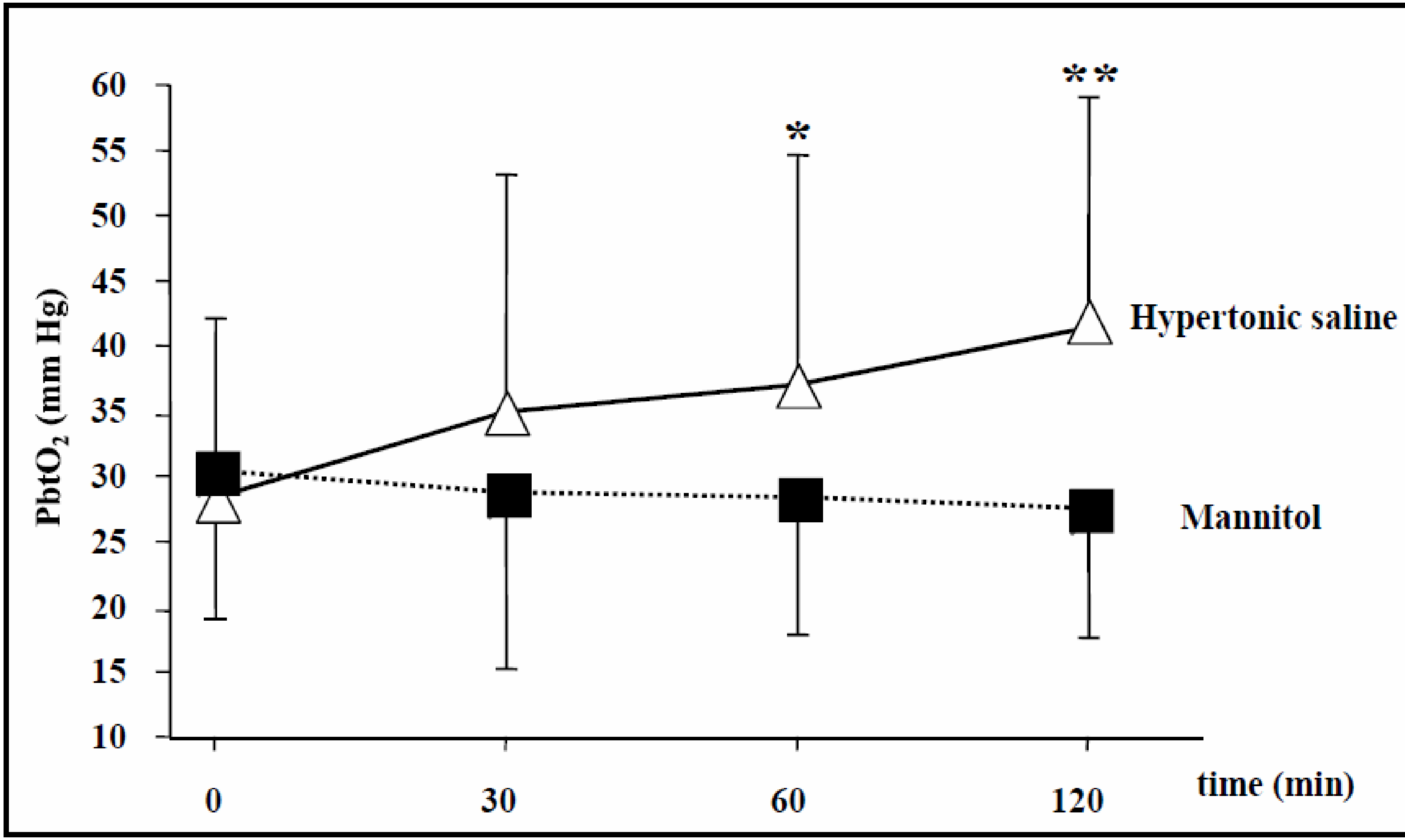
Mannitol vs HTS (7.5%)

- N=12; severe TBI with refractory ICP treated with
  - Mannitol (25%, 0.75 g/kg) or HTS (7.5%, 250 ml)
- Results: 42 episodes treated: mannitol (n=28); HTS (n=14)

ICP (mm Hg)	Mannitol	HTS	P value
Baseline	29 ± 8	27 ± 8	0.40
30 min	21 ± 8	17 ± 7	0.15
60 min	23 ± 12	15 ± 6	**<0.001**
120 min	24 ± 9	15 ± 5	**<0.001**
CPP (mm Hg)			
Baseline	60 ± 17	63 ± 15	0.56
30 min	71 ± 16	78 ± 18	0.32
60 min	67 ± 20	76 ± 16	**0.05**
120 min	65 ± 19	76 ± 17	**0.02**

Oddo, et al. JNNP 2009; Mar 16 epub

Mannitol vs HTS effect on PbtO^2



Oddo, et al. JNNP 2009; Mar 16 epub

Mannitol vs HTS (23.4%)

- Retrospective; severe TBI w/ mean ISS 28 $\pm$ 11
  - n = 22; 210 doses of mannitol (n=102) or HTS (n = 210)
- Data assessed for 60 minutes after infusion
  - ICP; ICP reduction after treatment; CPP
  - Serum sodium, osmolality, & dose response
- Results
  - HTS patients had significantly higher ICP at start of therapy (31 vs. 28 mm Hg). CPP similar.
  - Mean ICP reduction was greater with HTS (9.3 vs. 6.4 mm Hg; p = 0.0028)
  - More responded to HTS (93% vs. 74%; p = 0.0002).
  - No difference in the duration of ICP reduction
  - No adverse events identified with either

Kerwin AJ, et al. J Trauma 2009;67:277-82

Hyperventilation

- Level II:

  Prophylactic hyperventilation ($PaCO^2 \leq 25$ mm Hg) is not recommended. **(Muizelaar JP, et al. J Neurosurg 1991;75:731-739)**

- Level III:

  Hyperventilation is recommended as a temporizing measure for the reduction of elevated intracranial pressure (ICP).

  Hyperventilation should be avoided during the first 24 hours after injury when cerebral blood flow (CBF) is often critically reduced.

  If hyperventilation is used, $SjvO^2$ or $PbtO^2$ measurements are recommended to monitor oxygen delivery.

Hyperventilation

- Start out w/ normocapnia (pCO^2 35 – 40).
  - Hypocapnia induces vasoconstriction, thus ↓ CBF
  - CBF already compromised (esp in 1st 24º after injury), thus can worsen ischemia early
- Therapeutic hyperventilation (pCO^2 30 – 35 mm Hg) may be beneficial for acute ICP elevations
  - Use with CBF monitoring ($SjvO^2$, $PbtO^2$)
  - After 10 – 20 hours, arterioles re-dilate causing a rebound increased CBF/CBV & ICP

Prophylactic Hypothermia**

- Level III

Pooled data indicate that prophylactic hypothermia is not significantly associated with decreased mortality when compared with normothermic controls. However, preliminary findings suggest that a greater decrease in mortality risk is observed when target temperatures are maintained for more than 48 hours.

Prophylactic hypothermia is associated with significantly higher Glasgow Outcome Scale (GOS) scores when compared to scores for normothermic controls.

"for experts only"

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Induced Normothermia

- **Comparative cohort study; n = 42**
  - Normothermia (36 – 36.5ºC) by endovascular device
  - Historical sTBI controls w/ fever & conventional therapy
  - End points: Fever (rectal temperature > 38ºC) and ICP in first 72 hours

	Treatment Group	**Historical controls**	***p* value**
Fever burden (%)	1.6	10.6	0.03
Mean ICP (mm Hg)	12.74	16.37	0.027
% time ICP > 25	2.3	9.4	0.03

Puccio AM, et al. Neurocrit Care 2009;11:82-87

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Steroids

- **Level I**

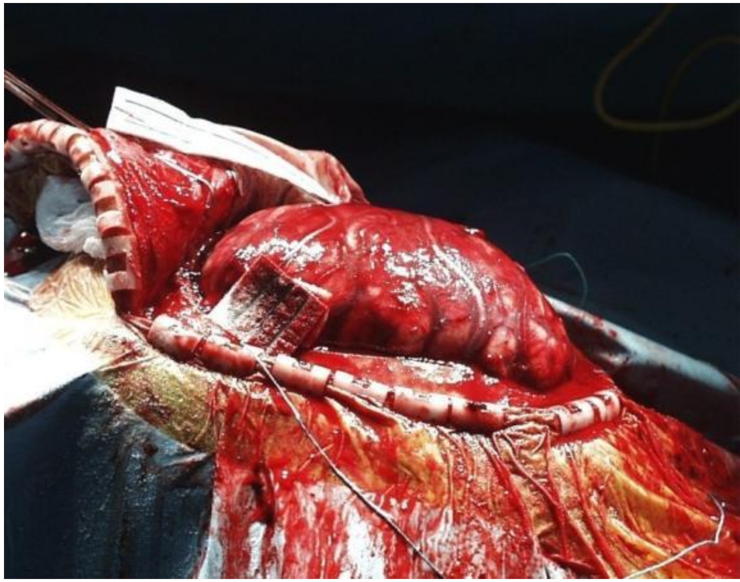
  The use of steroids is not recommended for improving outcome or reducing ICP. In patients with moderate or severe TBI, high dose methylprednisolone is associated with increased mortality and is contraindicated.

  Notes:

  1. CRASH trial (10k pts) showed increased mortality.
     (Lancet 2004; 364:1321-28)
  2. Detrimental systemic effects: shown to cause hyperglycemia, ↑ infections, other complications

Decompressive Craniectomy

- Let the brain swell
  - Intuitively appealing
- No good studies
  - May be an epiphenomenon
- Problems
  - Too often, too early, too small
  - Craniectomy / duraplasty / +/-lobectomy
- Thoughts
  - Younger patients may better candidates
  - May not be useful when irreversible brainstem damage has occurred



Decompressive Hemicraniectomy

- Retrospective (trauma registry)
  - N = 137; severe TBI with AIS 4 – 5
  - treated with DC for increased ICP
  - Compared dichotomized GOSE at 1 to 6 years later
- Results
  - Overall mortality = 32% (head-related = 22%)
  - 117 survivors, follow-up was obtained in all but 6 (95%)
  - Good outcome in 96 (56% overall, 82% of survivors)
- Characteristics of good outcome
  - Younger (26 years vs. 43 years, $p = 0.0028$)
  - Greater ICP change pre- to post-decompression (Reduced by 23 vs. 10 mm Hg, $p < 0.0001$)

Williams RF, et al. J Trauma 2009;66:1570-74

Decompression Studies

- DECRA (Australia)
  - Purpose: Assess early decompressive craniectomy (within 6 hours of randomization) in sTBI with refractory ICP (>20 mm Hg x >15 min)
  - Outcome: GOSE at 6 mos
    - Secondary: ICP 36 hrs post randomization; Mortality; GOSE at 12 months; ICU LOS; Microdialysis
- Rescue-ICP (Cambridge)
  - Purpose: Assess decompressive craniectomy vs medical management in sTBI with refractory ICP (>25 mm Hg x 1-12 hrs)
  - Outcome: GOS at d/c & GOSE @ 6 mos
    - Secondary: SF-36, ICP control, LOS in ICU & on NS unit, health-economic assessment

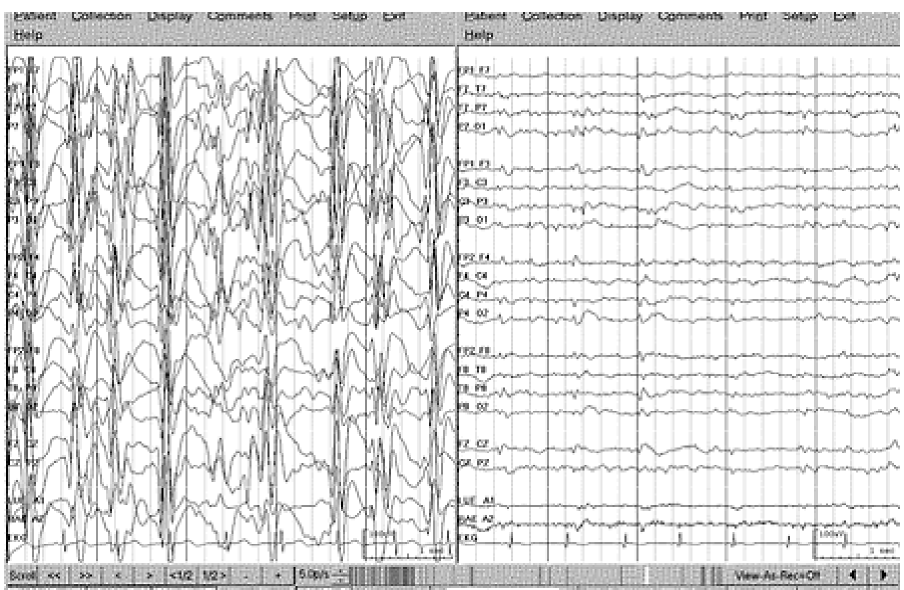
Antiseizure Prophylaxis

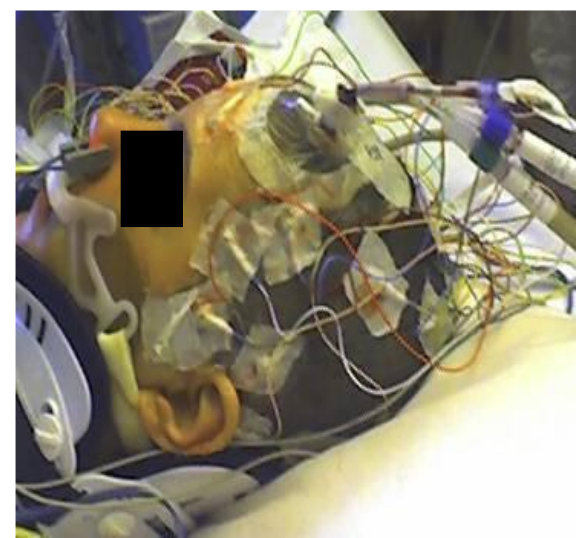
- Level II:

  Prophylactic use of phenytoin or valproate is not recommended for preventing late posttraumatic seizures.

  Anticonvulsants are indicated to decrease the incidence of early PTS (within 7 days of first drug administration).

  However, early PTS is not associated with worse outcomes.





Incidence of EPTSz

- Peak incidence in initial 48 – 72 hrs
  - high risk period up to 1 week
- Incidence using continuous EEG in TBI patients (all with therapeutic anticonvulsant levels)
  1. 94 patients with GCS $\leq$ 12; 21 (24%) had seizures.
     - Non-convulsive in 57%
  2. 51 TBI patients; 9 (18%) had seizures.
     - All were non-convulsive.
  3. 46 severe TBI patients; 8 (17%) had seizures.
     - All were non-convulsive

1. Vespa PM, et al. J Neurosurg 1999;91:750-60

2. Claassen J, et al. Neurology 2004; 62:1743-1748

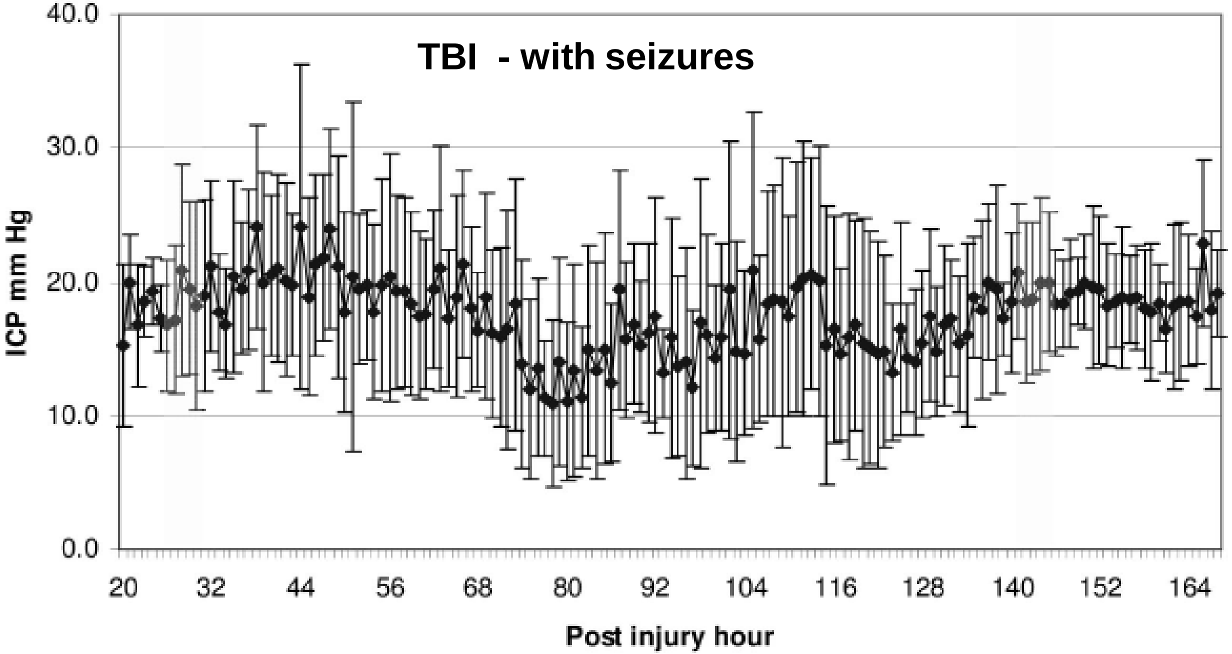
3. Szaflarski J, et al. Neurocrit Care 2010;12:165-72

Do Seizures Matter?

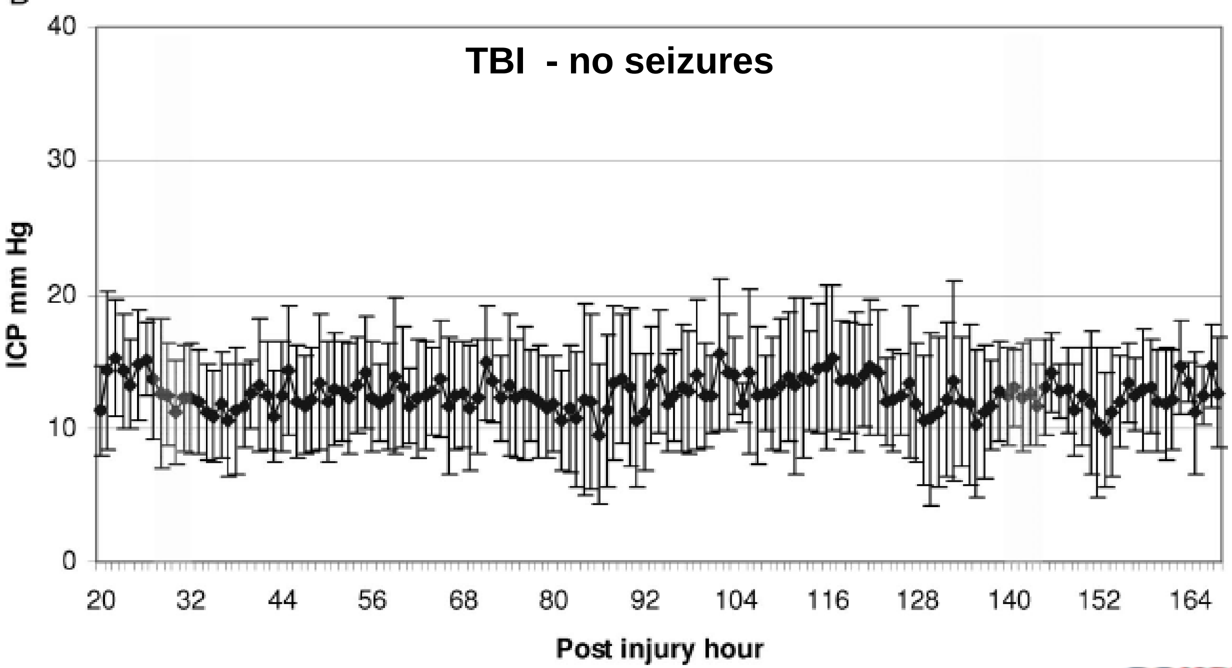
- Prospective monitoring; retrospective data analysis.
  - 20 mod - severe TBI (GCS = 3–13)
  - Continuous EEG & microdialysis for 7 days after injury.
  - Seizures occurred in 10 (SE in 7)
  - Patients were compared with a matched cohort of TBI patients without seizures.
- Results: Patients with PTSz had:
  - Episodic increases in ICP (22 vsv 13 mm Hg; $p < .001$) and L/P ratio (49 vs. 24; $p < .001$)
  - Higher mean ICP (18 vs. 12 mm Hg; $p < .001$) and L/P ratios (39 vs. 27; $p < .001$)
  - ICP & L/P ratio elevations for > 5 days ($p < 0\ .02$)

Vespa PM, et al. CCM 2007;35:2830-2836.

A


TBI - with seizures
40.0
30.0
20.0
10.0
0.0
ICP mm Hg
20
32
44
56
68
80
92
104
116
128
140
152
164
Post injury hour

B

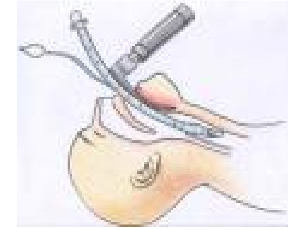

TBI - no seizures
40
30
20
10
0
ICP mm Hg
20
32
44
56
68
80
92
104
116
128
140
152
164
Post injury hour

Do Seizures Matter?

- Prospective monitoring; retrospective data analysis.
  - 10 mod - severe TBI (GCS = 3–13)
  - Continuous EEG & MD for 7 days after injury.
  - Seizures occurred in 5 (SE in 7)
  - MRI on day 7 & at 6 months
- Results in pts with PTSz:
  - ICP elevations & MD markers of cellular distress
  - 1st ADC & GRE images: no primary hippocampal injury
  - MRI @ 6 months:
    - global atrophy = 7.8 $\pm$ 4.4%
    - hippocampal atrophy = 32% vs 10% (p<0.001)

Vespa PM, et al. Abstract, 5th NCS Meeting, 2007

Infection Prophylaxis**



- Level II:

  <u>Peri-procedural antibiotics</u> for intubation should be used to reduce the incidence of pneumonia. However, it does not change length of stay or mortality.

  <u>Early tracheostomy</u> should be done to reduce mechanical ventilation days. However, it does not alter mortality or the rate of nosocomial pneumonia.

- Level III:

  Routine ventricular catheter exchange or prophylactic antibiotic use for ventricular catheter placement is not recommended to reduce infection.

  Early extubation in qualified patients can be done without increased risk of pneumonia.

DVT Prophylaxis**

- Level III:

  Graduated compression stockings or intermittent pneumatic compression (IPC) stockings are recommended, unless lower extremity injuries prevent their use. Use should be continued until patients are ambulatory.

  LMWH or low dose unfractionated heparin should be used in combination with mechanical prophylaxis unless the patient has CT evidence of ICH.

  There is insufficient evidence to support recommendations regarding the preferred agent, dose, or timing of pharmacologic prophylaxis for DVT.

DVT Prophylaxis after TBI

- Retrospective study, 64 patients w/ severe TBI
  - Two groups:
    - Early: within 72 hours of admission (n=47)
    - Late: after 3rd day of hospitalization (n=17)
  - CTs to assess for intracranial bleeding
  - Results:
    - No ↑ in intracranial bleeding; Same VTE rates
- Prospective, observational study, 150 patients w/ hemorrhagic TBI lesions treated w/ enoxaparin @ 24 hrs
  - CTs at admission, 24 hours later and prn
  - Results:
    - 23% had worsening on CT; 19% worsened before, 4% worsened after enoxaparin (no deaths)
    - DVT identified in 2 of 106 patients.

Kim et al. J Trauma. 2002;53:38-42;
Norwood et al. Arch Surg. 2002;137:696-701

Nutrition

- Level II

  Patients should be fed to attain full caloric replacement by 7th day post-injury.

  Notes:

  1. Fluids: Start with NS (no dextrose), aggressively treat low Na. Avoid hypovolemia (has been associated w/ worse outcomes)
  2. Glucose control: Early hyperglycemia has been associated with poor outcomes.

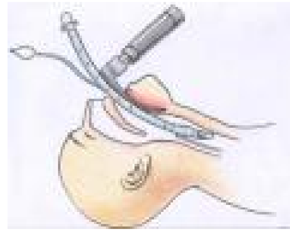
Nutrition in TBI

- Retrospective review; prospectively collected multi-center data (n = 797)
  - Assessed calories fed per day. Controlled for age, GCS, hypotension, pupillary status, CT scan findings
  - Delayed nutrition increased mortality.
    - Not fed within 5 days = 2-fold & 7 days = 4-fold increase.
  - Amount of nutrition in first 5 days was related to death
    - Every 10 kcal/kg decrease in caloric intake associated with a 30 – 40% increase in mortality

Hartl R, et al. J Neurosurg 2008;109:50-6

TO DO LIST

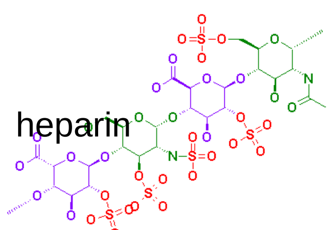
Develop Protocols !!!



Mannitol .25-1.0 g/Kg

treat ICP> 20

PbtO2



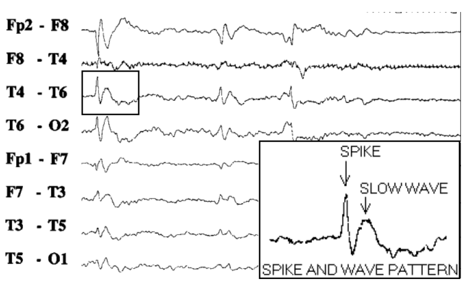
DON'T LIST

Hypotension

CRASH

Steroids

Prophylactic Hyperventilation



Long Term Seizure Prophylaxis

Improvement In Adherence To TBI Guidelines In US Trauma Centers

Methods: Survey; 413 trauma centers that admit severe TBI. Good adherence was defined as adherence to the median number of guidelines (median=6, interquartile range 5-7).

Results: Good adherence was predicted by Level I trauma center designation & presence of treatment protocols.

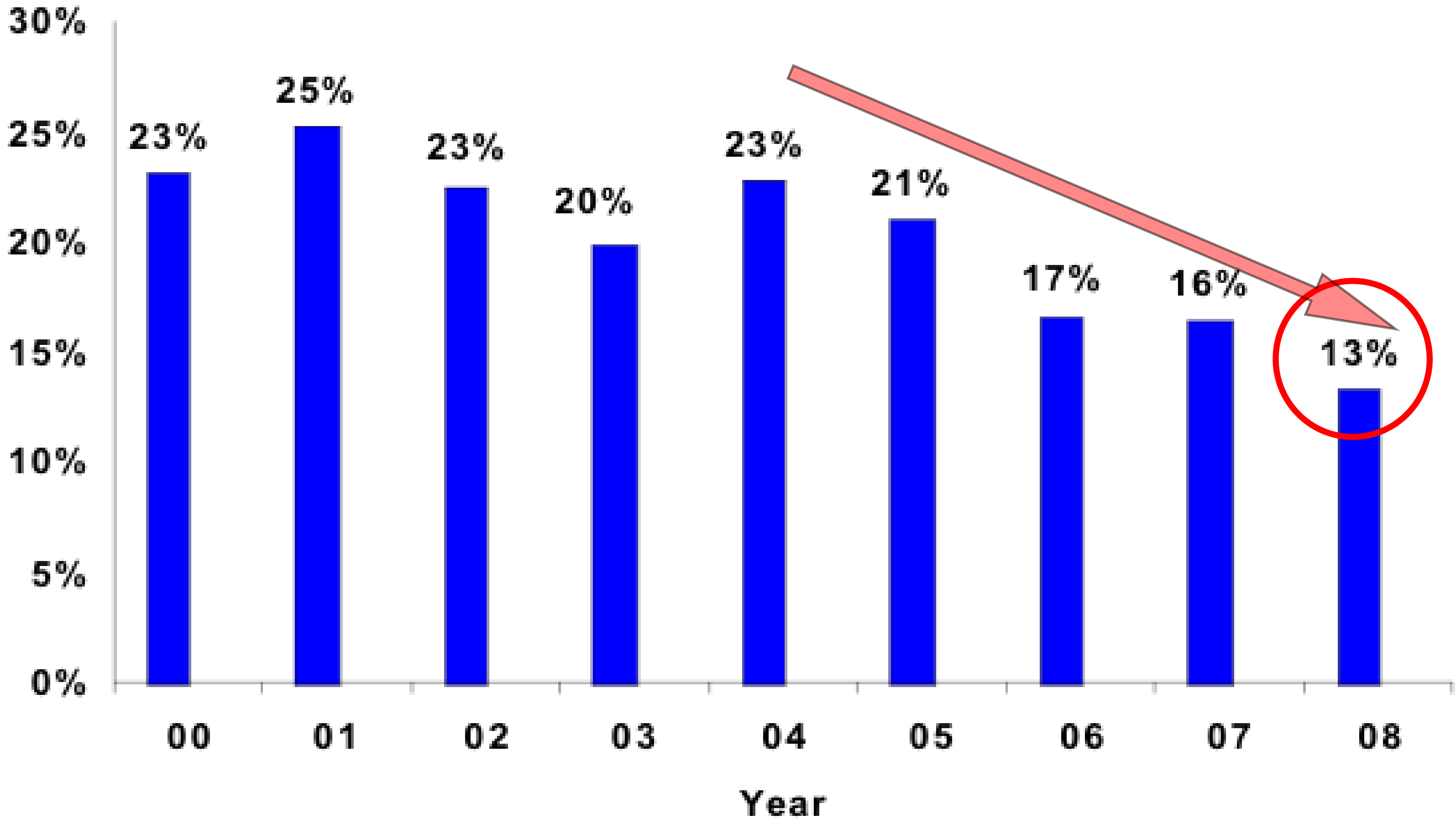
Conclusions: Adherence to evidence based guidelines for severe TBI has improved since 1991. Directing patients with severe TBI to Level I and Level II trauma centers with treatment protocols will improve outcome for these patients.

Hesdorffer & Ghajar. J Trauma. 2006;60:1250-6

Improvement In Adherence To TBI Guidelines In US Trauma Centers

	1991	2000	2006	*p* value
Routine ICP monitor	32%	51%	77%	$p<0.0001$
No steroids	48%	52%	86%	$p<0.0001$
Failure to follow guidelines	67%		35%	

NYS TBI Mortality by Year (2000-2008)



20+ Level 1 Trauma Centers

Courtesy of Roger Härtl, Weill-Cornell Medical College

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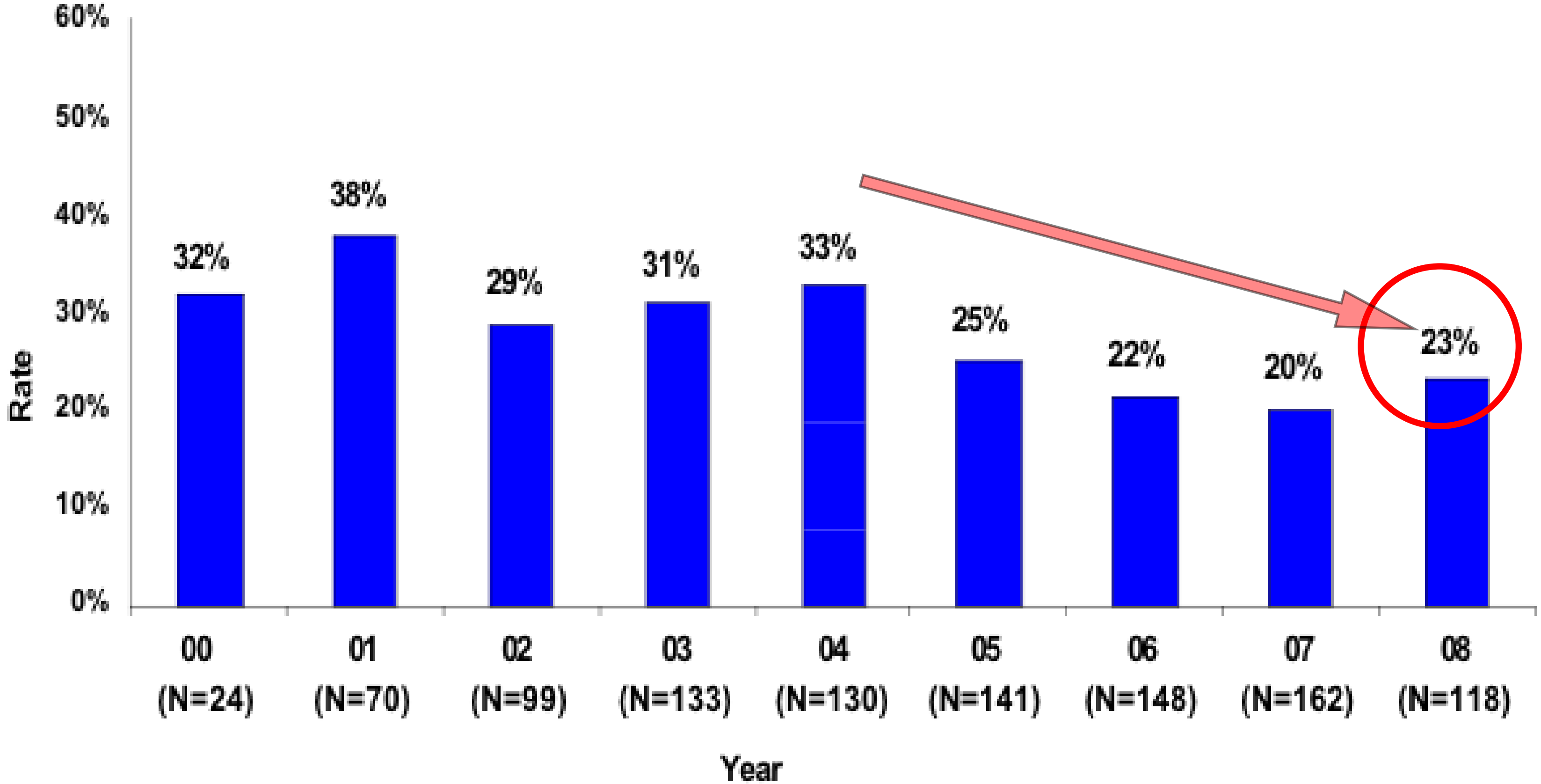
NY In-Hospital ICP >25 mm Hg Rate in Qualified Patients



Courtesy of Roger Härtl, Weill-Cornell Medical College

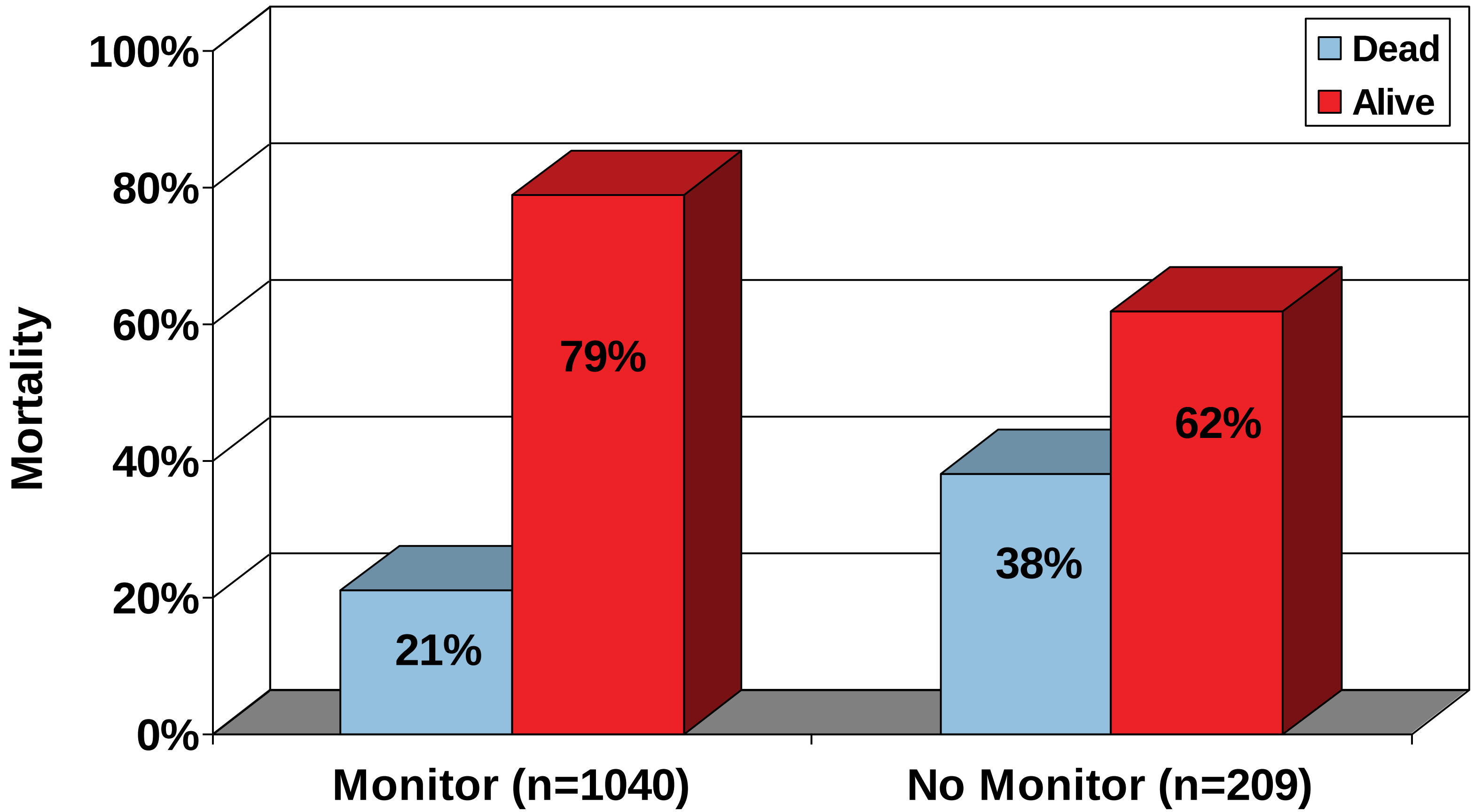
Mortality in TBI patients & Response to ICP Therapy

- NY State Database review
  - ICP monitoring on 1052 patients on day 1, 2 or 3.
  - Assessed response to ICP therapy
- Results:
  - 43% had ICP > 25 mm Hg for at least one hour on any of those days.
  - Mortality for ICP treatment responders was 14% vs. non-responders 31%.
  - After adjusting for known outcome predictors, the odds of 2 week mortality for "responders" were 57% lower than odds for non-responders (p=0.01).

Froelich M, et al. Submitted

Courtesy of Roger Härtl, Weill-Cornell Medical College

ICP Monitoring & Adjusted Mortality



Patients without ICP monitoring have a significant increase in mortality (in submission)

Courtesy of Roger Härtl, Weill-Cornell Medical College

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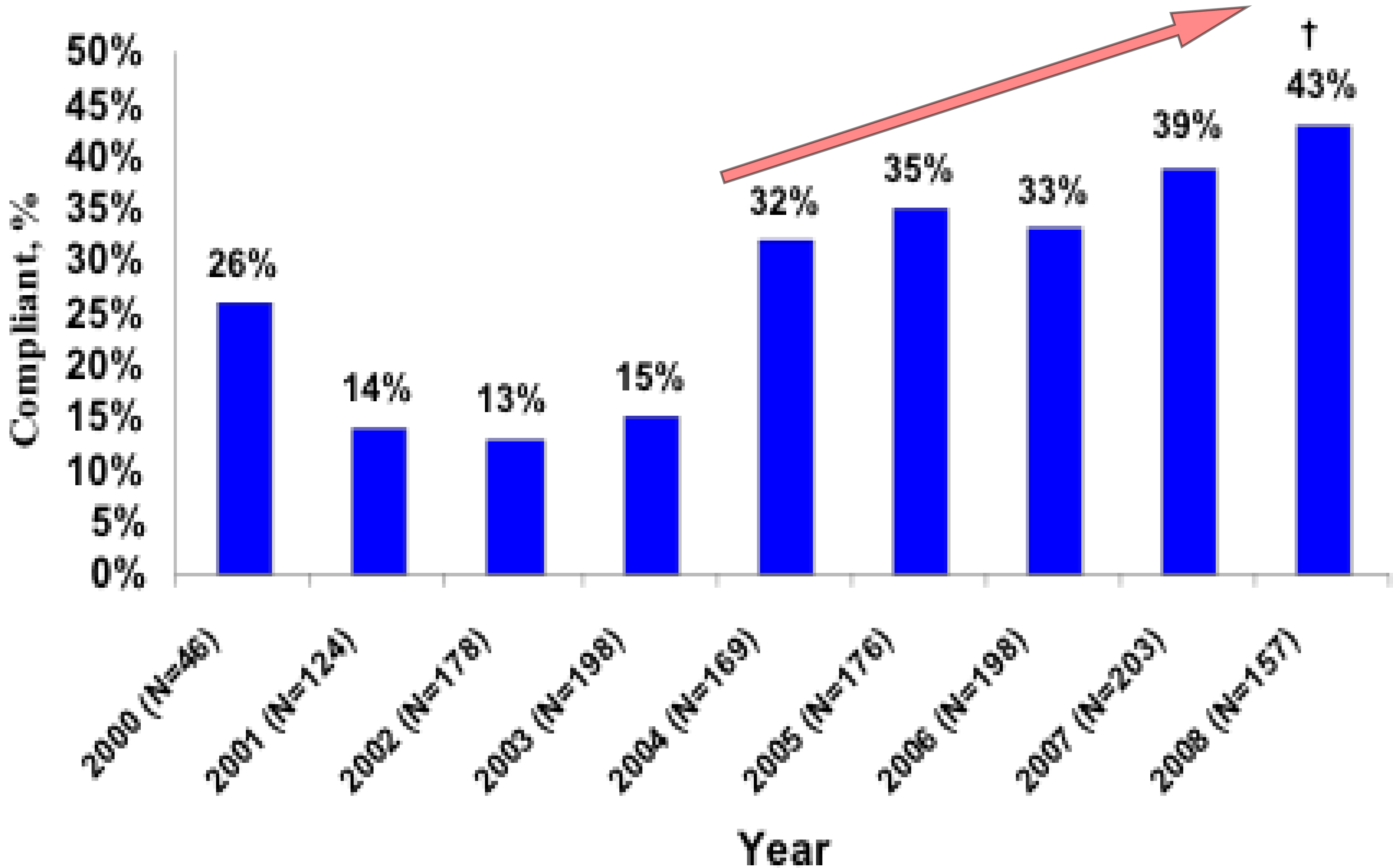
Compliance with CPP Component



Courtesy of Roger Härtl, Weill-Cornell Medical College

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Do the “Guidelines” make a difference in patient outcome?

	Palmer et al.	Vitaz et al.	Fakhry et al.	Bulger et al.
Ref.	J Trauma 2001	J Trauma 2001	J Trauma 2004	Crit Care Med 2002
N	37/56	43/119	219/188	106/74
Institutions	1	1	1	33
Class study	III	III	III	III
Description	Rapid resusc, CPP > 70, ICP < 20, CVP 5-10, PCWP 5-10, SjVo2 55-75%, pCo2 35 mmHg, early nutrition	Multidisciplinary pathway focussing on organisational aspect of patient management	Rapid resusc, CPP > 70, ICP < 20, CVP 7-13, PCWP 10-18, CI > 2.8, pCo2 30-35 mmHg	Comparision of "aggressive" (36%) vs. "non-aggressive" centers
Mortality (%)	At 6 months	At discharge	At discharge	At discharge
No Guidelines protocol	43%	39	18	45
Guidelines protocol	16% *	47 n.s.	11 *	27*
	ICU days	ICU days	ICU days	Hospital LOS
No Guidelines protocol	21	21	10	
With Guidelines protocol	22 n.s.	17 *	7 *	reduced by 6 days *

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Effects of Guidelines

- Community hospital setting
  - Developed guideline based standardized TBI protocol
  - Two groups, pre-guideline = 37; post guideline = 56
- Results / Conclusions
  - Implementation of protocol resulted in a 9.13 times higher odds ratio of a good outcome
  - Hospital charges increased
  - Dedicated neurotrauma team and comprehensive treatment algorithms are critical elements

Group	GOS 1	GOS 2&3	GOS 4&5
Pre-TBI Guidelines	16 (43%)	11 (30%)	10 (27%)
Post-TBI Guidelines	9 (16%)	8 (14%)	39 (70%)

Palmer S, et al. J Trauma 2001;50:657-64

Effect of Guidelines

- Protocol developed & education provided
  - Compared mortality, ICU days, total hospital days & charges, & outcome to historical controls
- Results:
  - Compliance initially 50%, by year 3 was 88%
    - Pre-protocol (n=219), low (n=188) and high (n=423) compliance
  - ICU stay decreased by 1.8 days ($p = 0.021$)
  - Hospital stay decreased by 5.4 days ($p < 0.001$).
  - LOS charge reduction per patient: $6,577 in low vs $8,266 in high compliance ($p = 0.002$)
  - Overall mortality rate: pre-protocol & high compliance (17.8% vs. 13.8%, ns)
  - GOS GR/MD change: 43% to 50% to 62% ($p < 0.001$).
  - Rancho Los Amigos Scores appropriate responses: 44% to 44% to 57% ($p = 0.004$)

Fakhry SM, et al. J Trauma 2004;56:492-9

International

Journal of Critical Care (2009) xx, xxx–xxx

ELSEVIER

Journal of Critical Care

Mortality reduction after implementing a clinical practice guidelines–based management protocol for severe traumatic brain injury

Yaseen M. Arabi MD, FCCP, FCCM[a,b,*], Samir Haddad MD, CES[a], Hani M. Tamim PhD[b], Abdulaziz Al-Dawood MD, FCCP, FRCP(C)[a,b], Saad Al-Qahtani MD, FCCP, FRCP(C)[a,b], Ahmad Ferayan MD, MBBS[c], Ibrahim Al-Abdulmughni MD[a], Jalal Al-Oweis MD[a], Asia Rugaan MD[a]

[a]*Intensive Care Department, King Abdulaziz Medical City, Riyadh, Saudi Arabia 11426*
[b]*King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia 11426*
[c]*Division of Neurosurgery, Department of Surgery, King Abdualziz Medical City, Riyadh, Saudi Arabia 11426*

Variable	Control group (n = 72)	Protocol group (n = 362)			
Categorical outcomes			Adjusted OR	95% CI	*P*
Hospital mortality, n (%)	20 (27.8)	68 (18.8)	0.45	0.24 to 0.86	.02
ICU mortality, n (%)	15 (20.8)	50 (13.8)	0.47	0.23 to 0.96	.04
Tracheostomies, n (%)[a]	28/52 (53.9)	123/294 (41.8)	0.66	0.34 to 1.28	.22
Continuous outcomes			Coefficient	95% CI	*P*
Mechanical ventilation duration, mean ± SD[a] (d)	10.4 ± 6.9	11.2 ± 7.4	1.56	−0.58 to 3.71	.2
ICU LOS, mean ± SD[a] (d)	11.5 ± 7.3	11.9 ± 7.9	1.28	−0.96 to 3.52	.3
Hospital LOS, mean ± SD[a] (d)	82.3 ± 78.9	71.4 ± 79.1	−2.98	−27.59 to 21.62	.8

[a] Among survivors.

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Impact of Guidelines on Costs

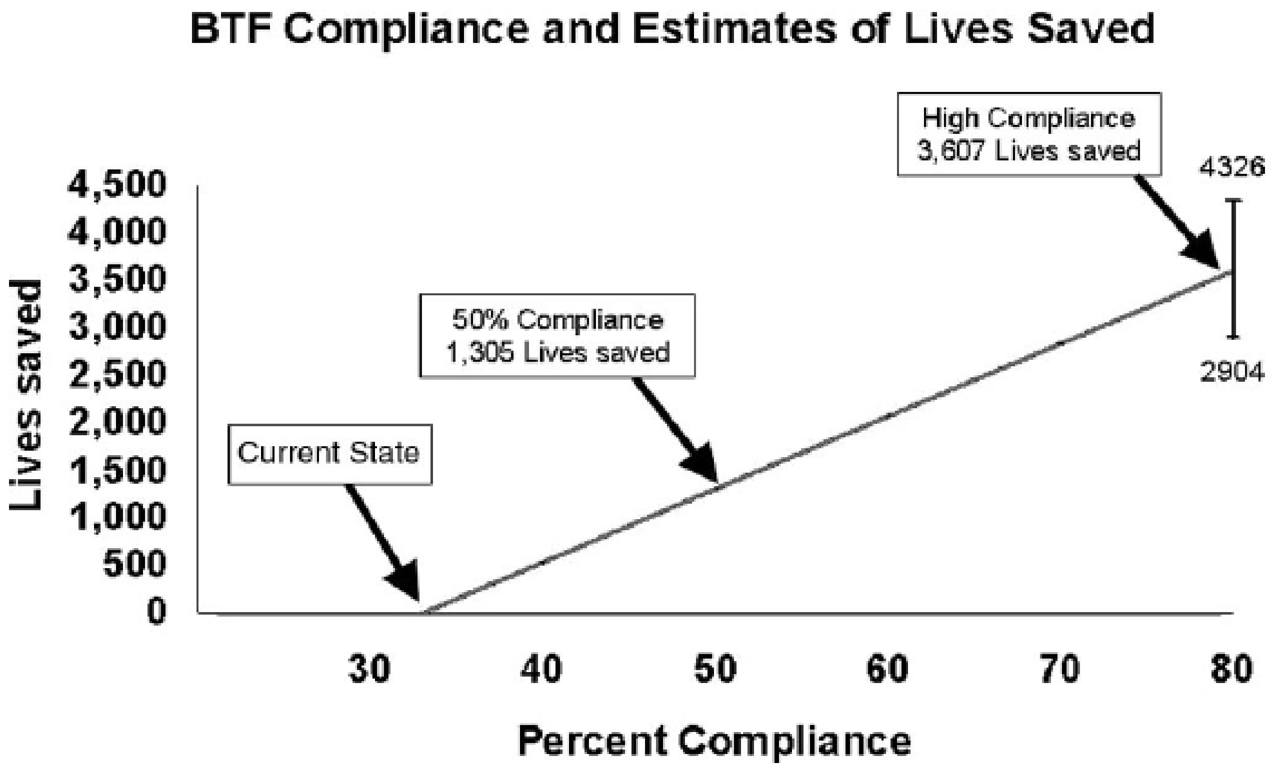

Table 3 Overall Cost Savings and Lives Saved Resulting From Adoption of BTF Guidelines—Costs per Person

	Deaths	Direct Medical Costs	Rehabilitation Costs	Societal Costs	Implementation Costs	Total Costs
BTF adoption	3,466	$ 49,607	$ 2,751	$ 165,876	$ 2,618	$ 220,853
Current state	7,073	$ 60,887	$ 4,618	$ 330,827	$ 0	$ 396,331
Difference	3,606	$ 11,280	$ 1,866	$ 164,951	($ 2,618)	$ 175,479

Calculated medical costs probabilities are subject to rounding errors.

Faul M, et al. J Trauma 2007;63:1271-8

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The Journal of TRAUMA® Injury, Infection, and Critical Care

Using a Cost-Benefit Analysis to Estimate Outcomes of a Clinical Treatment Guideline: Testing the Brain Trauma Foundation Guidelines for the Treatment of Severe Traumatic Brain Injury

Mark Faul, PhD, Marlena M. Wald, MLS, MPH, Wesley Rutland-Brown, MPH, Ernest E. Sullivent, MD, and Richard W. Sattin, MD

- Center for Disease Control; Journal of Trauma (Dec 2007)
- Patients are 2x as likely to survive if TBI guidelines are followed
- Proportion of patients with "good" outcomes rose from 35% to 66%
- Proportion of patients with "poor" outcomes fell from 34% to 19%
- Potential savings of $3.8 Billion

Direct Transport in an Organized State Trauma System

- Effect of prehospital care on early mortality
  - N = 1123 patients, severe TBI; 22 trauma centers.
  - Collected time of arrival to trauma center, mode & direct or indirect transport, BP & O2 sat, GCS, pupillary assessment, and airway management procedures.
- Results
  - Direct transport resulted in > 50% lower mortality.
  - Transport mode, time to admission, and prehospital intubation were not related to 2-week mortality.
- Conclusion
  - Patients with severe TBI should be transported directly to a Level I or Level II trauma center, even if this center may not be the closest hospital

Hartl R, et al. J Trauma 2006;60:1250-6

BTF TBI Program

Goal of the Program

- Improve outcome for patients with TBI by implementing scientific evidence-based guidelines

Continuous QI in TBI Care

Final Thoughts

- Guidelines are just that – guidelines
  - Explain / document your reasons to vary
- Standardized care does improve outcomes
  - Day to day management is very important
- Algorithm for care
- Role of advanced monitoring
  - Indications & duration
  - Options: PbtO2, CBF, cEEG, ECog
- When do mild / moderate injuries need to be transferred to higher level of care?
- Pros & cons of multi-center randomized trials

Clinical Pathway for ICP Control

↑ ICP

Position
Sedation / Analgesia
Ventricular Drainage

↑ ICP

Consider Repeat CT Scan

Hyperosmotic Rx

↑ ICP

Hyperventilation
$PaCO^2$ 30 – 35 mm Hg

↑ ICP

Final Tier Therapies:
1) Decompressive Hemicraniectomy
2) High Dose Barbiturates (BS cEEG)
3) HV to $PaCO^2$ < 30 mm Hg w/ monitoring ($SjvO^2$, $PbtO^2$, $AVDO^2$, or CBF)
4) Hypothermia

- Not in edition 3
- Too ‘cookbook’
- Assumes every patient the same

Final Thoughts

- Guidelines are just that – guidelines
  - Explain / document your reasons to vary
- Standardized care does improve outcomes
  - Day to day management is very important
- Algorithm for care
- Role of advanced monitoring
  - Indications & duration
  - Options: $PbtO_2$, CBF, cEEG, ECog
- When do mild / moderate injuries need to be transferred to higher level of care?
- Pros & cons of multi-center randomized trials

Questions?