TBI - Neurocritical care and medical management

김 태 정
서울의대

Kim Tae Jung
Department of Neurology, Seoul National University Hospital

Contents

- Introduction
- Managements of TBI
  - IICP control
  - Medical managements in NICU
- Conclusion

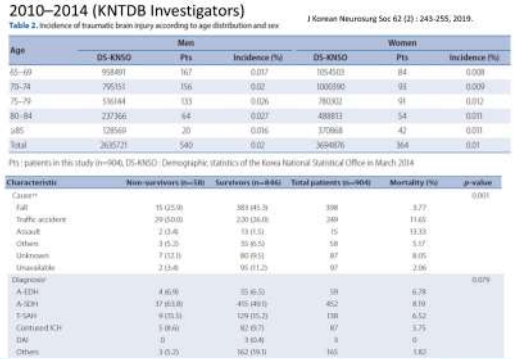
Epidemiology of TBI

Epidemiology of TBI

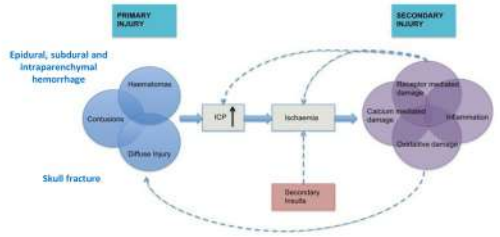
- Trauma is the leading cause of death in young ages
- Traumatic brain injury (TBI)
  - 1.6 million TBIs each year
  - over 50,000 deaths per year in the United States
  - overall mortality rates of 20–30% and associated with disability
  - The economic impact is over $80 billion in the US alone.
  - in high-income countries: the number of elderly people with TBI is increasing, mainly due to falls
  - low-middle income countries: the burden of TBI from road traffic incidents is increasing.

TBI in Korea

- A Multicenter Analysis Using Korean Neuro-Trauma Data Bank System 2010–2014 (KNTDB Investigators)



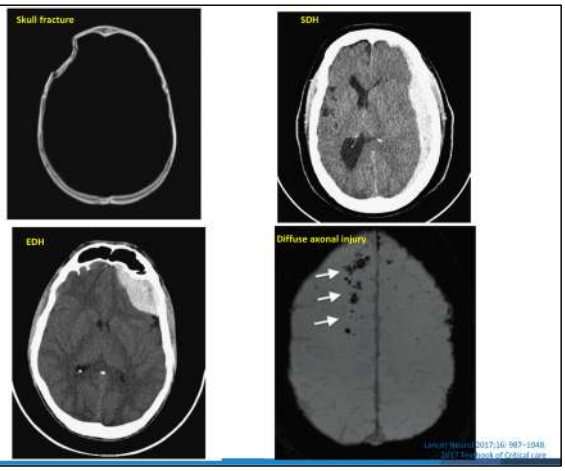
Traumatic brain injury



Subdural hematoma in 67% patients with cerebral contusion.

Coma in 20-25% patients in subdural hematoma.

Front Neurol. 2014; 5: 121.



Pathophysiology of TBI

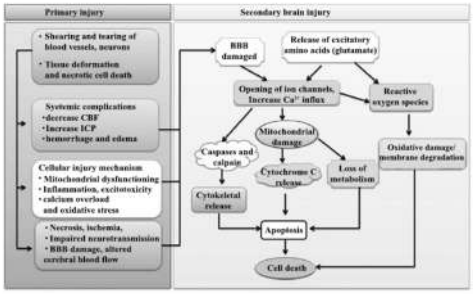


Fig. (1). Primary and Secondary events during Traumatic brain injury (TBI).

Curr Neuropharmacol. 2019 Jul; 17(7): 614–629.

Severity and Outcome

- Classification of clinical severity in TBI
- Mild TBI: GCS 13–15 (~80%) are with
- Moderate TBI: GCS 9-12 (~10%)
- Severe TBI: GCS 3–8 (~10%)
- Moderate to severe TBI patients: ~70% patients have disability and death

- Computed Tomographic Classification of TBI

TABLE 56-3 Relationship of Computed Tomographic Classification to Outcome at Discharge

CATEGORY	DEFINITION	UNFAVORABLE OUTCOME* (%)	FAVORABLE OUTCOME† (%)
Diffuse injury I	No visible intracranial pathology	38	62
Diffuse injury II	Cisterns present, with midline shift 0 to 5 mm; no high-density lesion >25 mL	85	26
Diffuse injury III (swelling)	Cisterns compressed or absent, with midline shift 0 to 5 mm; no high-density lesion >25 mL	84	16
Diffuse injury IV (shift)	Midline shift >5 mm; no high-density lesion >25 mL	94	6
Evacuated mass lesion	Any lesion surgically evacuated	77	23
Nonevacuated mass lesion	High-density lesion >25 mL, not surgically evacuated	89	11

Data from Marshall LF, Marshall SB, Klauber MR, Clark M. A new classification of head injury based on computerized tomography. J Neurosurg 1991;75:S14–S20.

2017 Textbook of Critical care

Management for IICP of TBI

Brain Trauma Foundation

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

Treatments

1. Decompressive Craniectomy
2. Prophylactic Hypothermia
3. Hyperosmolar Therapy
4. Cerebrospinal Fluid Drainage
5. Ventilation Therapies
6. Anesthetics, Analgesics, and Sedatives
7. Steroids
8. Nutrition
9. Infection Prophylaxis
10. Deep Vein Thrombosis Prophylaxis
11. Seizure Prophylaxis

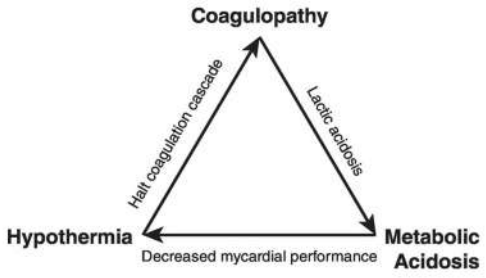
Monitoring

12. Intracranial Pressure
13. Cerebral Perfusion Pressure
14. Advanced Cerebral Monitoring

Thresholds

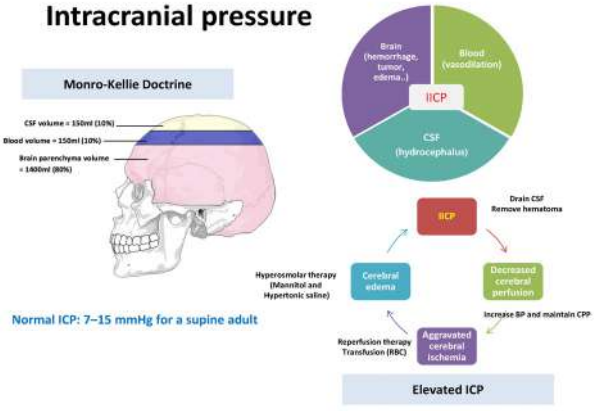
15. Blood Pressure
16. Intracranial Pressure
17. Cerebral Perfusion Pressure
18. Advanced Cerebral Monitoring

Lethal triad of trauma

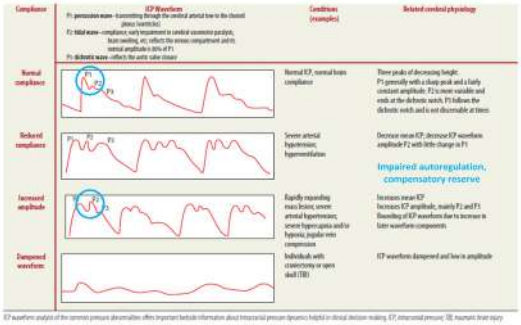


The Emergency Medicine Trauma Handbook

Intracranial pressure



ICP waveform analysis



Source: Jesse B. Hall, Gregory A. Schmidt, John P. Kress: *Principles of Critical Care*, 4th Edition: www.accessmedicine.com
Copyright © McGraw-Hill Education. All rights reserved.

Head position and Ventilation therapy

- **Position:** 30° head elevation

TABLE 2

*Effects of head elevation on cerebral and systemic physiological parameters in 23 patients**

Parameter	30° Head Elevation	0° Head Elevation	Mean Difference	P Value
mean cerebral pressure (mm Hg)	14.3 ± 4.5	15.5 ± 4.6	−1.2 ± 0.1	0.0067
intracranial pressure (mm Hg)	14.1 ± 5.1	15.2 ± 5.3	−1.2 ± 0.2	0.0051
cerebral perfusion pressure (CPP) (mm Hg)	70.2 ± 18.1	69.7 ± 18.7	0.45 ± 0.6	0.8
cerebral blood flow (CBF) (ml/100 gm/min)	47.8 ± 16.9	48.9 ± 20.4	−1.03 ± 10.8	0.057
cerebrovascular resistance (CPP/CBF)	1.72 ± 0.8	1.72 ± 0.9	−0.0014 ± 0.316	0.9846
cerebral metabolic rate of oxygen (μmol/100 gm/min)	1.35 ± 0.59	1.28 ± 0.53	0.073 ± 0.23	0.14
arteriovenous oxygen difference (μmol/ml)	1.81 ± 0.63	1.72 ± 0.73	0.093 ± 0.37	0.23
$PaCO_2$ (mm Hg)	32.54 ± 5.09	32.46 ± 6.4	+0.1 ± 1.9	0.77
arteriovenous difference of lactate (μmol/ml)	−0.05 ± 0.65	−0.05 ± 0.86	−0.0002 ± 0.06	0.48
oxygen saturation in jugular bulb (%)	69.4 ± 9	70.5 ± 10.2	−0.0045 ± 0.042	0.61

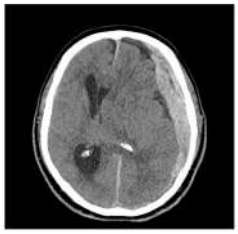
* Values represent mean ± standard deviation.

J Neurosurg. 1992 Feb;76(2):207-11

- **Ventilation therapy (hyperventilation)**
  - Hyperventilation → Decrease PaCO2 → Vasoconstriction → decrease CBV → decrease ICP
  - Prolonged prophylactic hyperventilation: hypoxia and aggravate ischemic damage – a few hours (~4-6 h) with PbO2 monitoring
  - Partial pressure of carbon dioxide in arterial blood (PaCO2): 25 -30 mm Hg

Decompressive Craniectomy

- **Decompressive craniectomy**: relieving elevated intracranial pressure with outcome improvement in severe TBI with aggravating neurological symptom
- **Bifrontal decompressive craniectomy to control ICP**
  - In Severe TBI patients with ICP > 20 mmHg
  - Bifrontal decompressive craniectomy (DC) is better than standard ICU management for good outcome ?



Severe TBI with herniation

Bifrontal decompressive craniectomy

DECRA Trial: RCT of bifrontal craniectomy within 72 hours after admission vs. ICU management for ICP > 20 after TBI (GCS 3-8). Clearly lower ICP with craniectomy.

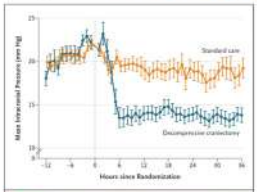


Figure 1. Intracranial Pressure before and after Randomization.
Shown are the mean measurements of intracranial pressure in the two study groups during the 12 hours before and the 36 hours after randomization. The I bars indicate standard errors.

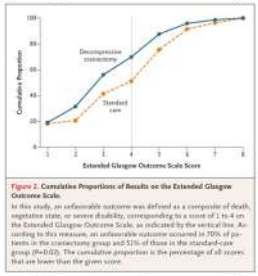


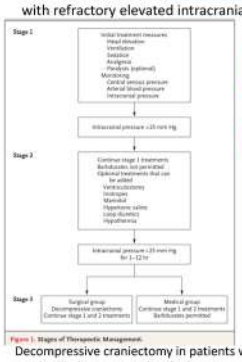
Figure 2. Cumulative Proportions of Results on the Extended Glasgow Outcome Scale.
In this study, an unfavorable outcome was defined as a composite of death, vegetative state, or severe disability, corresponding to a score of 1 to 4 on the Extended Glasgow Outcome Scale, as indicated by the vertical line. According to this measure, an unfavorable outcome occurred in 70% of patients in the craniectomy group and 51% of those in the standard-care group ($P=0.02$). The cumulative proportion is the percentage of all scores that are lower than the given score.

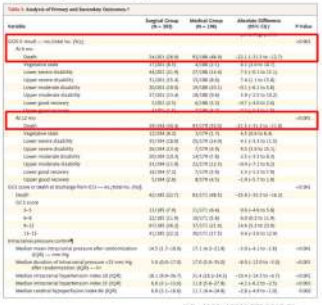
DC group have greater risk of an unfavorable outcome (odds ratio, 2.21; 95% CI, 1.14 to 4.26). Rates of death at 6 months were similar in the craniectomy group (19%) and the standard-care group (18%).

N Engl J Med 2011;364:1493-502

Bifrontal decompressive craniectomy

RESCUEicp Trial: RCT of DC (unilateral or bilateral) vs. standard care in TBI patients with refractory elevated intracranial pressure (>25 mm Hg).





N Engl J Med 2016;375:1119-30.

Decompressive craniectomy in patients with refractory intracranial hypertension after TBI resulted in lower mortality, higher rates of vegetative state, and lower severe disability,. But, rates of moderate disability and good recovery were similar in two groups.

Bifrontal decompressive craniectomy

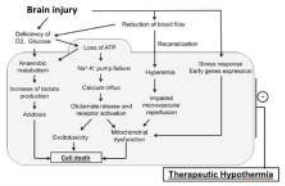
- Bifrontal DC is not recommended to improve outcomes in severe TBI patients with diffuse injury (without mass lesions), and with ICP elevation (ICP > 20mmHg).
- The treatment of DC target goal ICP ≤ 20 mm Hg is wrong goal.

- Monitoring for IICP control
  - Cerebral perfusion pressure (CPP): pressure gradient across the cerebral vascular bed, between blood inflow and outflow (CPP = MAP- ICP)
  - Cerebral autoregulation: maintenance of cerebral blood flow (CBF) over a wide range of CPPs : Pressure reactivity index (PRx) and RAP index
  - Brain tissue oxygenation

Journal of Stroke 2013;15(2):99-108.

Targeted temperature management (Hypothermia)

- **Mechanism of TTM for treatment**
- Reduction in cerebral metabolism (CMRO2) by approximately 6% per 1°C: Less oxygen and glucose consumption
- Promotion of cerebral vasoconstriction: Decreased ICP and brain edema
- Protection of neuro-vascular injury: Decreased ischemic cascade, especially inflammation response, decreased vascular permeability

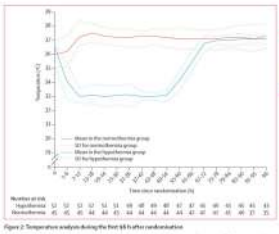


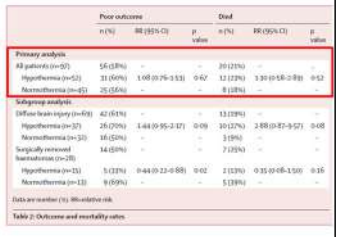
Neuropharmacology. 2018 May 15;134(Pt B):302-309.

Targeted temperature management (Hypothermia)

Very early hypothermia induction in patients with severe brain injury (the National Acute Brain Injury Study: Hypothermia II): a randomised trial Lancet Neurol 2011; 10: 131–39.

- RCT of hypothermia (33°C) vs. normothermia within 2.5 hours after severe TBI and Maintained for 48 h

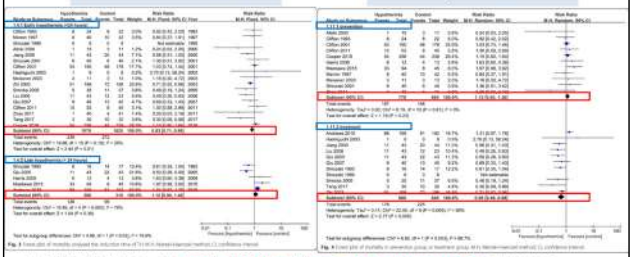




This study did not show the utility of hypothermia as a primary neuroprotective strategy in patients with severe traumatic brain injury.

Targeted temperature management in TBI

Induction time of TTM | **Purpose of TTM**



- Early, short-term, and prophylactic hypothermia is not recommended to improve outcomes in patients with diffuse injury.
- However, traumatic brain injury patients with elevated intracranial hypertension could benefit from hypothermia in therapeutic management instead of prophylaxis when initiated within 24 h.

Crit Care. 2019 Dec 5;23(1):396.

Hyperosmolar therapy

- **Osmotic agents: control brain edema and IICP**
- Pulls free water across the semipermeable membrane of the blood-brain barrier (BBB).
- Osmotic agent: mostly stays in serum and raises serum osmolality compared to the osmolality in brain.

- **Mannitol (peripheral line and central line)**
- Osmotic diuretics: sugar or sugar alcohol
- Duration: 6-8 hours
- Action time: 15 min after injection
- Osmotic diuresis and AKI

- **Hypertonic saline (central line)**
- Generally comes in 3%, 7%, and 23.4%
- Number of osmoles similar: 1,000 mL 0.9% ≈ 250 mL 3% ≈ 30 mL 23.4%
- May be given as a bolus (23.4% or 11.7% in Korea)
- Not an osmotic diuretic (mannitol)

Mannitol & Hypertonic saline

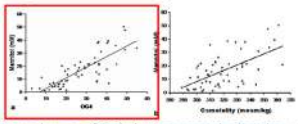
Sodium Chloride Concentration (%)	Osmolarity (mOsm/L)	Sodium Concentration (mEq/L)
0.9	308	154
1.7	582	291
3.0	1026	513
7.5	2566	1283
10.0	3424	1712
23.4	8008	4004

For comparison, the osmolarity of 20% mannitol is 1098 mOsm/L.

- Mannitol dose: 0.5g/Kg – 1.5g/Kg (1g/Kg)
  - <0.5g/Kg dose: less effect of controlling ICP (20%)
- In Korea : 11.7% NaCl: 40mEq/20cc - 60cc IV shooting [NACL4IP]

Forsyth LL, et al. Pharmacotherapy. 2008 Apr;28:469-84

Monitoring and Complications



- Monitoring Osmolar gap (OG) during mannitolization: estimating mannitol concentration
  - **Actual serum osmolarity – Calculated serum osmolarity (<55 mOsm)**
  - Calculated serum osmolarity: 2Na + BUN/2.8 + glucose/18
  - **Not stopping based on serum osmolarity**

Table 3. Avoiding Adverse Effects of Osmotic Agents

Complication	Mannitol	Hypertonic Saline
Renal Failure Rebound	Avoid continuous infusion, repeat high dosing Allow clearance prior to repeat dosing	Avoid prolonged hypernatremia >160 mEq/L Allow clearance prior to repeat dosing
Metabolic Acidosis	n/a	Reduce chloride in admixture
Hypokalemia	n/a	Add potassium to fluids
Hypovolemia	Concurrent volume resuscitation	n/a

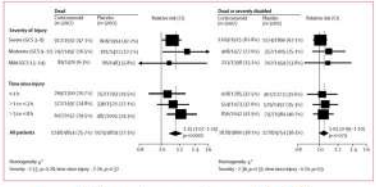
Garcia-Morales EJ, et al. Crit Care Med. 2004;32(4):986-991
Hinson HE, et al. J Intensive Care Med. 2013 28(1):3-11

Steroid in TBI

Final results of MRC CRASH, a randomised placebo-controlled trial of intravenous corticosteroid in adults with head injury—outcomes at 6 months

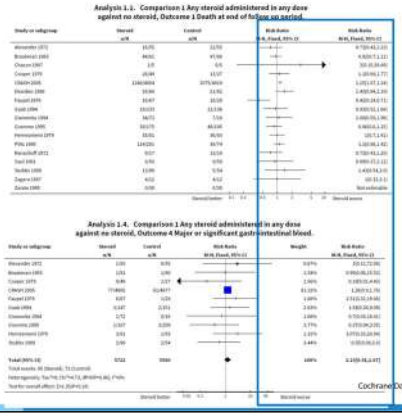
Lancet 2005; 365: 1957–59

- Randomly allocated 10 008 adults with head injury and a Glasgow Coma Scale score of 14 or less within 8 h of injury
- 48-h infusion of corticosteroid (methylprednisolone, 2g loading over 1 and 0.4g maintenance dose/h) vs. placebo.



Steroids increased mortality and poor outcome after TBI.

Steroid in TBI



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

Cochrane Database Syst Rev. 2005 Jan 25;(1):CD000196.

Sedation and Analgesic

- Analgesics, and sedatives: prophylaxis or control of elevated ICP
- Proper sedation
  - Light and reversible sedation is recommended to allow repeated neurological evaluation.
  - Minimizing hypotension and decreased cardiac output which may lead to hypoxia and low CPP
- Sedative drugs
  - Dexmedetomidine: Selective α2 receptor agonist (light sedation and pain control), Potentially significant hypotension and bradycardia or hypertension, 0.3 – 1.5 mcg/Kg/h
  - Remifentanil: ultra-short acting opioid, prompt reversal of analgesia and sedation, chest wall rigidity with higher dose, 0.03-0.25 mcg/kg/min
  - Midazolam and propofol: deep sedation, side effect and context sensitive half-life
  - High-dose barbiturate is recommended to control refractory elevated ICP condition.

	Propofol	Midazolam	Lorazepam	Fentanyl	Remifentanil
Rapid onset	+++	+++	+	+++	+++
Fast recovery	+++	++	+	++	+++
Easily titrated	+++	++	+	++	+++
ICP reduction	↓↓	↓	↓	↓/↔	↓/↔
CBF reduction	↓↓	↓↓	↓	↔	↔
$CMRO_2$ reduction	↓↓	↓	↓	↓	↓
MAP	↓↓	↓	↓	↓	↓↓

Textbook of Neurointensive Care..

Target blood pressure in TBI

- Maintaining SBP at ≥100 mm Hg for patients 50 to 69 years old or at ≥110 mm Hg or above for patients 15 to 49 or over 70 years old may be considered to decrease mortality and improve outcomes.
- Target MAP ≥ 65 mmHg

Optimal SBP and mortality in isolated moderate to severe TBI patients.

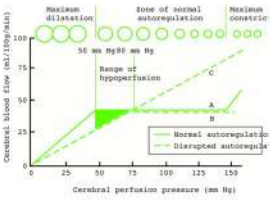
Age group	Optimal SBP	Mortality	AOR	95% CI	p-Value
15–49 years (n = 10284)	<110 mm Hg	21%	1.98	1.65–2.39	<0.0001
50–69 years (n = 3093)	<100 mm Hg	29%	2.20	1.46–3.31	0.0002
50–69 years (n = 3093)	≤110 mm Hg	20%	1.60	1.13–2.28	0.009
≥70 years (n = 2356)	<110 mm Hg	38%	1.92	1.35–2.74	0.0003

Adjusted odds ratio (AOR): Optimal SBP is compared to SBP reference groups, adjusting for age, gender, ISS ≥ 16, and GCS ≤ 8: reference groups for age 15–49 (≥110 mm Hg); for age 50–69 (≥100 mm Hg), for age ≥ 70 (≥130 mm Hg)

Injury. 2012 Nov;43(11):1833-7..

Cerebral perfusion pressure (CPP) in TBI

- CPP is the blood pressure metric to which brain autoregulatory mechanisms respond.



- Target CPP value for survival and favorable outcomes: 60 and 70 mm Hg (at least above 50 mmHg).
- Avoiding aggressive attempts to maintain CPP above 70 mm Hg with fluids and pressors related to respiratory failure in older patients.

CPP (Cerebral perfusion pressure) = MAP (mean arterial pressure) – ICP (Intracranial pressure)

J Neurol Neurosurg Psychiatry 2002;73(Suppl I):i23–i27

Medical managements in TBI

Arterial partial pressure of oxygen (PaO2)

- Arterial partial pressure of oxygen (PaO2) level between 60 and 100 mmHg during interventions for life-threatening hemorrhage or emergency neurosurgery.
- SpO2 < 90% (corresponding near to a PaO2 of 60 mmHg) and hyperoxia (defined as a PaO2 > 200 mmHg) are associated with poor outcomes in TBI.
- Avoid hypoxia (PaO2 < 60 mmHg) and hyperoxia (PaO2 >200 mmHg)

Table 3. Effect of Hypoxia Compared With Normoxia on Outcome Measures*

	OR (95% CI)	P Value
<100 vs 100-200 mm Hg		
Mortality	2.20 (1.33-3.63)	.002[b]
Discharge GCS score 3-8	1.66 (1.01-2.75)	.05[b]
HLOS	0.38 (0.25-0.58)	<.001[b]
ICULOS	0.40 (0.25-0.66)	<.001[b]

Table 4. Effect of Hyperoxia Compared With Normoxia on Outcome Measures*

	OR (95% CI)	P Value
>200 vs 100-200 mm Hg		
Mortality	1.50 (1.15-1.97)	.003[b]
Discharge GCS score 3-8	1.32 (1.18-1.96)	.001[b]
HLOS	0.75 (0.60-0.94)	.01[b]
ICULOS	0.92 (0.74-1.15)	.46

Arch Surg. 2012;147(11):1042-1046.

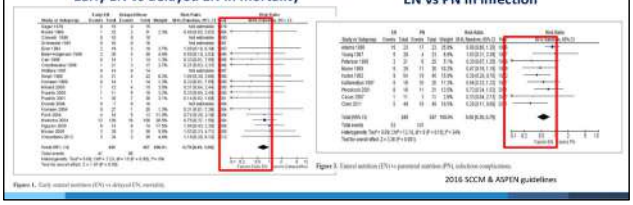
Nutrition

- Feeding patients to attain basal caloric replacement at least by the fifth day and at most by the seventh day post-injury is recommended to decrease mortality.
- **EN supports the functional integrity of the gut**
  - Food in gut: activated pathogenic microorganism in the gut and maintaining tight junctions between the intraepithelial cells stimulating blood flow

Early EN start and EN > PN

Early EN vs delayed EN in mortality

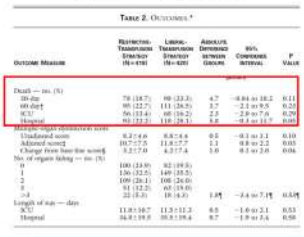
EN vs PN in infection



2016 SCCM & ASPEN guidelines

Transfusion

- There are no current recommendations regarding appropriate hemoglobin or hematocrit concentrations in patients with severe TBI.
- The Transfusion Requirements in Critical Care (TRICC) study
  - trigger for transfusion Hb > 10 g/dl group and the trigger for transfusion Hb > 7 g/dl group
  - Mortality at 30 days and 60 days



- There is no benefit of a liberal transfusion strategy (goal, 10 g/dL) compared to a restrictive strategy (goal, 7 g/dL) could be demonstrated.
- Hb threshold of 7 g/dl is recommended value of Hb in TBI polytrauma patients.

N Engl J Med. 1999 Feb 11;340(6):409-17.

Prophylaxis

- **Infection**
  - Prophylactic antibiotics is not recommended for preventing infection.
  - Antimicrobial-impregnated catheters may be considered to prevent catheter-related infections during EVD.
  - Early tracheostomy (<10 days) is recommended to reduce mechanical ventilation in severe TBI.
- **Deep vein thrombosis (DVT)**
  - 54% incidence of deep venous thrombosis without prophylactic treatment and a 25% incidence in patients with isolated TBI treated with sequential compression devices.
  - Low molecular weight heparin (LMWH) or low-dose unfractioned heparin may be used in combination with mechanical prophylaxis (after 48-72 h).
  - Consider stocking and ICP in patients with increased risk for expansion of intracranial hemorrhage.

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

Prophylaxis

- Seizure
  - clinical post traumatic seizure (PTS): ~ 12%,
  - subclinical seizures: 20% to 25% in EEG
  - early PTS occur within 7 days of injury and late PTS occur after 7 days following injury
  - Early PTS have not been associated with worse outcomes
  - Early PTS: AED for a few weeks/ late PTS: AED for several years
- Prophylactic use of AED
  - Prophylactic use of phenytoin or valproate is not recommended for preventing late PTS.
  - There is insufficient evidence to recommend levetiracetam compared with phenytoin regarding efficacy in preventing early post-traumatic seizures and toxicity.

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

Neuropharmacologic therapies for recovery

- Amantadine: act as an N-methyl-D-aspartate antagonist and indirect dopamine agonist.
- Amantadine for TBI: Diffuse axonal injury after TBI → Damage and death of neurons → Associated with a reduction in dopamine release → amantadine increase dopamine
- RCT of amantadine therapy (100 mg bid for 14 days - 150 mg vid for 7 days – 200mg bid for 7 days vs. placebo for 4 weeks in a vegetative or minimally conscious state 4 to 16 weeks after traumatic brain injury

N Engl J Med 2012;366:819-26.

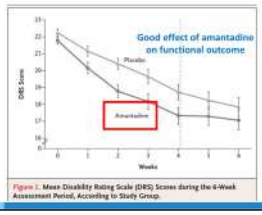


Figure 1. Mean Disability Rating Scale (DRS) Scores during the 6-Week Assessment Period, According to Study Group.

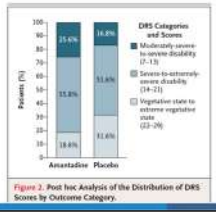


Figure 2. Post hoc Analysis of the Distribution of DRS Scores by Outcome Category.

Neuropharmacologic therapies for recovery

The effects of amantadine on traumatic brain injury outcome: a double-blind, randomized, controlled, clinical trial

BRAIN INJURY 2018, VOL. 32, NO. 8, 1050–1055.

- TBI patients who scored nine or lower on the Glasgow Coma Scale (GCS)
- The protocol included administration of the drug (placebo or amantadine) for 6 week → **no beneficial effect on outcome**

Table 3. The results of this study.

	Amantadine (N = 19)	Placebo (N = 21)	P-value
Male sex	19(100%)	18(85.7%)	0.09
Age(years old)			
Mean ±SD	32.16 ± 13.87	40.95 ± 20.86	0.13
Age group number			
16–35 y/o	14(73.7%)	11(52.4%)	-
36–55 y/o	4(21%)	5(23.8%)	
56–75 y/o	1(5.3%)	3(14.3%)	
76–80 y/o	0	2(9.5%)	
Trauma mechanism			
Motor vehicle accident	6(31.6%)	7(33.3%)	
Pedestrians	4(21%)	5(23.8%)	
Fallings	5(26.3%)	7(33.3%)	
Direct trauma	1(5.3%)	1(4.8%)	
Unknown	3(15.8%)	1(4.8%)	
Mechanical ventilation at the start of study	15(78.9%)	20(95.2%)	0.11
Mean GCS			
Beginning day	7.1 ± 1.56	6.95 ± 1.74	0.77
Third day	8.58 ± 2.63	7.74 ± 2.65	0.35
Seventh day	11.16 ± 3.28	9.33 ± 3.29	0.1
Mean GCS Motor			
Beginning day	4.36 ± 1.01	4.28 ± 1.27	0.82
Third day	6.77 ± 0.94	4.36 ± 1.42	0.31
Seventh day	5.22 ± 1.00	4.77 ± 1.35	0.27
Mean GCS Eye			
Beginning day	1.52 ± 0.89	1.52 ± 0.60	0.99
Third day	2.00 ± 0.76	1.84 ± 0.76	0.53
Seventh day	2.88 ± 0.96	2.44 ± 0.78	0.13
Mean GCS Verbal			
Beginning day	1.21 ± 0.41	1.14 ± 0.35	0.28
Third day	1.94 ± 1.25	1.52 ± 1.07	0.28
Seventh day	3.11 ± 1.52	2.11 ± 1.52	0.58
Mean FOUR score			
Beginning day	8.81 ± 2.23	7.52 ± 2.68	0.46
Third day	9.79 ± 2.93	8.26 ± 3.41	0.15
Seventh day	12.33 ± 3.32	10.11 ± 4.01	0.07
ΔGCS?-GCS1*	4	2.34	0.044
ΔFOURscore7-FOURscore1†	4.17	2.67	0.089
Mortality			
In hospital	4	5	0.9
From discharge to 6 months follow-up	2	0	
Mean hospital stay (days)	24.94 ± 16.53	21.13 ± 13.97	0.49
Mean time from trauma to start study (days)	3.21 ± 2.32	3.42 ± 2.87	0.78
After 6 months			
MMSE	23.1 ± 4.22	20.3 ± 5.2	0.2
GOS	4.09 ± 0.99	4.5 ± 0.7	0.28
DRS	4.45 ± 4.86	2.6 ± 3.53	0.34
KPS	68.45 ± 28.57	81 ± 17.91	0.25
Presence of drug-usage limitation factors	2	6	0.11

Conclusions

- Not recommended prophylactic DC and hypothermia after TBI
- DC and hypothermia for IICP control
- Optimal hyperosmolar therapy with monitoring
- Proper sedation for controlling ICP and pain
- Maintaining MAP and CPP for cerebral autoregulation
- Optimal transfusion (Hb < 7g/dl)
- Not recommended prophylactic AED and antibiotics