ACS tqip TRAUMA QUALITY IMPROVEMENT PROGRAM

TRAUMATIC BRAIN INJURY GUIDELINES: A REVIEW OF THE AVAILABLE LITERATURE

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GENERAL TBI STATISTICS

- 1,000,000 patients treated in ED and released with diagnosis of TBI
- 250,000 patients admitted to the hospital for TBI
- 80,000 patients leave hospital with some TBI related morbidity
- 50,000 patients suffer mortality related to TBI
- Annual cost of non-fatal TBI- ~$40 billion

WHAT IS THE EVIDENCE AVAILABLE FOR TREATING THESE PATIENTS?

WHERE DO I FIND IT?

ACS tqip®

TRAUMA QUALITY IMPROVEMENT PROGRAM

BRAIN TRAUMA FOUNDATION GUIDELINES

- 4th Edition
- Published in September 2016
- 189 publications used for evidence
  - 5 Class 1
  - 46 Class 2
  - 136 Class 3
  - 2 Meta-Analysis

LEVEL OF EVIDENCE DETERMINATION

- Two reviewers independently evaluated each study and assigned an evidence grade
  - If differences were noted, reconciliation occurred either via consensus or addition of a third reviewer
- Levels of Evidence
  - Class 1- Good quality RCT
  - Class 2- Moderate quality RCT OR Good quality cohort/case-control studies
  - Class 3- Low quality RCT OR Low quality cohort/case-control studies OR case series

ACS TQIP BEST PRACTICES IN THE MANAGEMENT OF TBI

- Produced in collaboration with the committee on trauma
- Use the best available evidence (or expert opinion) to guide the treatment of TBI patients
- Do not discuss their grading system in the available guidelines

BLOOD PRESSURE

BLOOD PRESSURE

- BTF Guidelines
  - Level III: SBP > 100 in 50-69 year olds, SBP > 110 in 15-49 or > 70 year olds
  - Based on retrospective study by Berry et al (2012) who looked for hypotensive thresholds associated with mortality in TBI patients
  - Additional Class 3 studies available to suggest the previous goal of SBP > 90 should be reexamined
- ACS TQIP
  - SBP > 100
- Neither guideline suggest goal for hypertension

INTRACRANIAL PRESSURE

INTRACRANIAL PRESSURE

- BTF Guidelines
  - Level IIB: Treating ICP > 22 mmHg is associated with decreased mortality
  - Level III: A combination of ICP values, clinical and radiographic findings can be used to make decisions
- ACS TQIP
  - ICP should be treated when it reaches 20-25 mmHg

INTRACRANIAL PRESSURE

- Sorrentino et al, 2012 (Class 2)
  - 459 patients identified using a database in UK
  - Sequential chi-square tests were used in which were dichotomized into survivors v. non-survivors and GOS 1-3 v 4-5
  - ICP threshold of 22 mmHg was identified as the threshold for both survival and favorable outcome

CEREBRAL PERFUSION PRESSURE

CEREBRAL PERFUSION PRESSURE

- BTF Guidelines
  - Level IIB: Target CPP 60-70 mmHg for survival and favorable outcomes, however autoregulatory status must be taken into account
  - Level III: Avoid aggressive measures (i.e. fluids, pressors) to maintain CPP > 70 mmHg secondary to risk of ARDS
- ACS TQIP
  - CPP > 60 mmHg

CEREBRAL PERFUSION PRESSURE

- Allen et al, 2014 (Class 2)
  - Higher survival rates noted in those with CPP > 60 versus those < 50
  - No difference between > 60 and 50-60 was noted
- Sorrentino et al, 2012 (Class 2)
  - 70 mmHg was noted as optimal CPP threshold for survival and favorable outcome
  - A subgroup analysis showed that in those > 55 y.o., 75 mmHg led to better outcomes
  - If autoregulation is intact (PRx < 0.05), no difference was noted with regards to CPP goals; however, with impaired autoregulation, CPP < 70 led to worse outcomes
- Robertson et al, 1999 (Class 3)
  - Compared CBF protocol (CPP > 70, CO2 ~ 35) to ICP protocol (CPP > 50, CO2 25-30)
  - No difference in neurologic outcome noted
  - Increased systemic complications in CBF groups: **5x increased risk of ARDS**

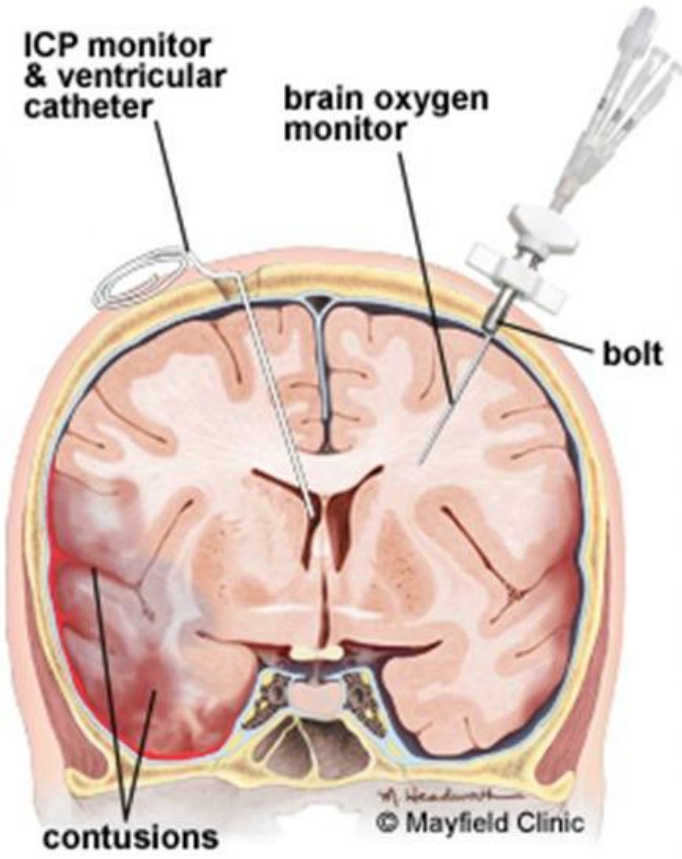
ADVANCED CEREBRAL MONITORING VALUES

ADVANCED CEREBRAL MONITORING

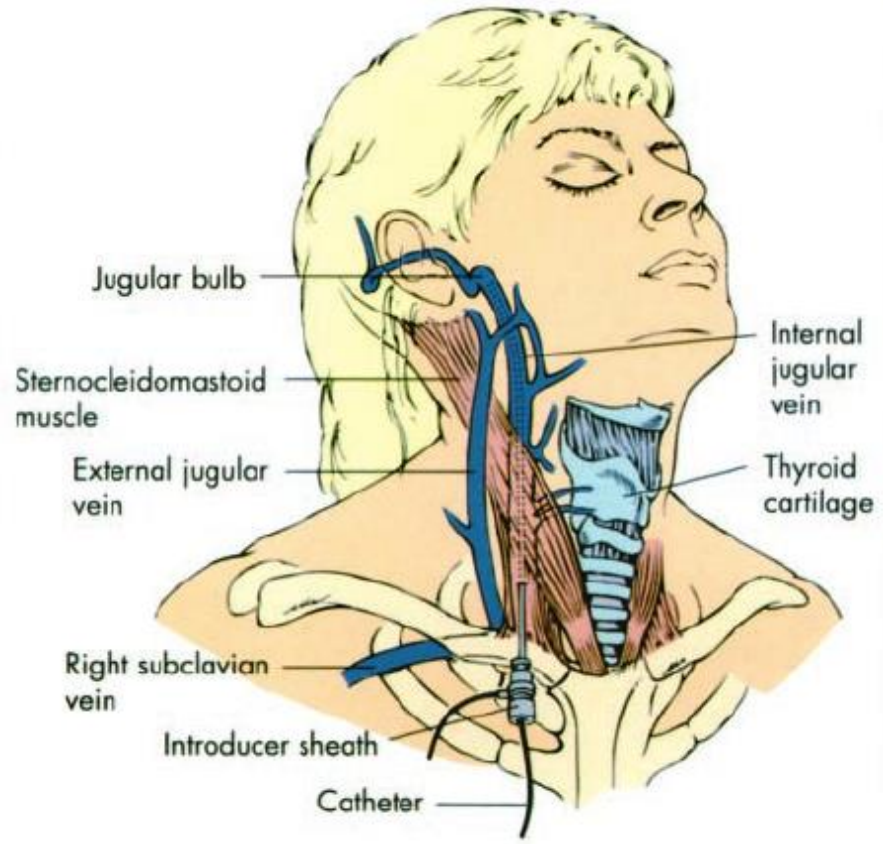
- BTF Guidelines
  - Level III: Jugular venous saturation of < 50% may reduce mortality and improve outcomes
- ACS TQIP
  - PbtO2 > 15 mmHg

BRAIN OXYGENATION

- PbtO2



- $AVDO_2/SjvO_2$



OTHER VITAL SIGNS

OTHER VITAL SIGNS

- BTF Guidelines
  - No Recommendation
- ACS TQIP
  - Temperature 36-38 degrees Celsius
  - Pulse Oximetry > 95%

LABORATORY VALUES

LABORATORY VALUES

- BTF Guidelines
  - No Recommendation
- ACS TQIP
  - ABG
    - pH: 7.35-7.45
    - PaCO2: 35-45
    - PaO2: > 100
  - Glucose: 140-180
  - Sodium: 135-145
  - INR: < 1.4
  - Platelets: > 75
  - Hgb: >7

TRANSFUSION

- Robertson et al, 2014
  - RCT comparing two transfusion threshold (7 and 10) after TBI
  - No difference in neurologic outcome noted
  - Higher transfusion threshold was noted to have increased adverse events

ICP MONITORING

ICP MONITORING

- BTF Guidelines
  - Level IIB: Use of ICP monitors is recommended to reduce in-hospital mortality and 2-week post injury mortality in severe TBI
- ACS TQIP
  - ICP monitoring is important, but it does not replace clinical and radiographic examination
  - ICP monitoring is indicated in GCS < 8 and structural injury on CT
  - ICP monitoring is NOT indicated in GCS < 8 with no structural injury or signs of elevated ICP (i.e. compressed cisterns) on CT
  - ICP monitoring should be considered in patients with GCS > 8 and structural brain injury with high risk of progression (i.e. contusions, coagulopathy)
  - ICP monitoring should be considered in the following situations regardless of GCS:
    - Urgent surgery for extracranial injuries
    - Mechanical ventilation due to extracranial injuries
    - Progression of pathology on CT
    - Clinical Deterioration
  - Preferred method for ICP monitoring is EVD (Diagnostic and Therapeutic)

ICP MONITORING

- Alali et al, 2013 (Class 2)
  - Retrospective cohort of 1,874 patients with ICP monitors in the ACS TQIP database
  - Significantly lower odds of mortality (OR 0.44) with ICP monitoring
  - More pronounced difference in those under 65
- Chestnut et al, 2012 (**Class 1**)
  - Randomized controlled trial
  - 324 patient in Bolivia and Ecuador, Randomized to ICP monitoring v. clinical/radiographic examination
  - No difference in 6-month mortality (39 v. 41%)
  - No difference in GOS-E at 6 months (Unfavorable 17 v. 17%, Favorable 44 v. 39%)
  - Reduced treatment time noted in the ICP monitoring group

ICP MONITORING

- Gerber et al, 2013 (Class 2)
  - Retrospective cohort study which compared trends in mortality over time with trends in adherence to guideline recommendations
  - As an increase with compliance to guideline recommendations for ICP monitoring was noted, a decrease in mortality was also noted
- Farahvar et al, 2012 (Class 2)
  - Retrospective cohort of 20 NY Level I and II Trauma Centers
  - 223/1307 patients with ICP monitors
  - OR 0.64 for 2 week mortality for adults

ADVANCED NEUROMONITORING

ADVANCED NEUROMONITORING

- BTF Guidelines
  - Level IIB: Using CPP monitoring with guideline based recommendations for management of severe TBI patients may decrease 2-week mortality
  - Level III: Jugular bulb monitoring may be considered to reduce mortality and improve outcomes at 3 and 6 months post-injury
- ACS TQIP
  - Advanced neuromonitoring and assessment of autoregulation may be helpful in individualizing treatment
  - Impaired oxygenation can occur with normal ICP and CPP
  - Cerebrovascular reactivity (PRx) and CBF can help assess autoregulation status

PBTO2

- Eriksson et al, 2012 (Class 2)
  - Retrospective cohort of 32 patients
  - Compared survivors v. non-survivors
  - PbtO2 was significantly higher in those who survived with a threshold of 29 mmHg
  - ICP and CPP not significantly different
- Okonkwo, 2017 (BOOST-2)
  - 119 patients, randomized to ICP + PbtO2 v. ICP alone
  - Brain tissue oxygen monitoring was performed in the ICP group, however was blinded
  - Decreased brain tissue hypoxia time with ICP + PbtO2
  - ICP similar in both groups
  - Trend towards decreased mortality and more favorable outcomes noted
  - BOOST-3 enrolling now

ADVANCED NEUROMONITORING

- Martini et al, 2009 (Class 2)
  - Retrospective cohort of 629 patients (123 PbtO2/ICP and 506 ICP alone)
  - Group with both monitors had more severe injuries and were treated more intensively
  - Mortality not significantly different between groups (29.3 v. 22.5%) but was overall higher in the PbtO2 group

Table 13-2. Summary of Evidence – Class 2 Study (Cerebral Perfusion Pressure Monitoring)

Table 13-3. Summary of Evidence – Class 3 Studies (Cerebral Perfusion Pressure Monitoring)

Table 14-2. Summary of Evidence: Class 2 Study (Advanced Cerebral Monitoring)

Reference Study Topic	Study Description	Data Class	Results Conclusion
Brain Tissue Oxygen Monitoring			
Stiefel 2005[9]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
McCarthy 2009*[6] Assessed cerebral oxygen monitoring-guided management	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Meixensberger 2003*[16] Assessed PbrO2 guided treatment	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Narotam 2009*[7] Assessed brain tissue oxygen monitoring-directed therapy	Prospective Cohort vs Historical Data Prospective for subgroup analysis of severe TBI=96 Historical controls from Traumatic Coma Data Bank=25 Single University Medical Center in the United States Compared outcomes for patients managed based on information from PbrO2 monitoring with those from a ICP/CPP-managed historical controls Mortality, and GOS at discharge and 6 months post-injury	Class 3	Patients showing Pattern 1 had a lower mortality rate (17.1 vs. 39.6%) and a better 6-month functional outcome among survivors (41.2 vs. 20.7%).
Jugular Bulb Monitoring			
Cruz, 1998[10]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Le Roux 1997[11]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Robertson 1993[12]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Howells 2005[8]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Robertson 1999[3]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Rosner 1990[9]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Robertson 1995[13]	Prospective Cohort	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Spiotta 2010*[8] Assessed brain tissue oxygen-based therapy vs. ICP/CPP-based therapy	Prospective Cohort Dichotomized GOS at post-injury	Class 3	PbrO2 with ICP and CPP vs. no PbrO2
Cerebral Autoregulation			
Budohoski 2012*[14] Assessed cerebral autoregulation using transcranial Doppler systolic, mean, and diastolic flow velocity	Prospective Cohort Mortality and GOS at 6 months post-injury	Class 3	Patients showing Pattern 1 had a lower mortality rate (17.1 vs. 39.6%) and a better 6-month functional outcome among survivors (41.2 vs. 20.7%).
Microdialysis Monitoring			
Chamoun 2010*[15] Assessed extracellular glutamate measured by cerebral microdialysis	Prospective Cohort Mortality and GOS at 6 months post-injury	Class 3	Patients showing Pattern 1 had a lower mortality rate (17.1 vs. 39.6%) and a better 6-month functional outcome among survivors (41.2 vs. 20.7%).

Table 14-3. Summary of Evidence – Class 3 Studies (Advanced Cerebral Monitoring)

Reference Study Topic	Study Description	Data Class	Results Conclusion
New Studies			
Brain Tissue Oxygen Monitoring			
Green 2013*[4] Assessed goal-directed $PbrO_2$ monitoring vs. ICP/CPP monitoring	Retrospective Cohort N=74 Single Level I Trauma Center in the United States Mortality, discharge GCS, GOS, and FIMS	Class 3	No significant difference in mortality, GCS, GOS, or FIMS. $PbrO_2$ group had significantly lower ISS (26 [25–30] vs. 30 [26–36], p=0.03) and AIS Chest (0 [0–0] vs. 2 [0–3], p=0.02).
Lee 2010*[5] Assessed $PbrO_2$ monitoring-guided management	RCT N=45 Single University Hospital in Taichung, Taiwan Compared outcomes for Group A (ICP/CPP management) N=16, Group B (ICP/CPP management with hypothermia) N=15, and Group C (brain tissue oxygen monitoring $P_{ti}O_2$ and CPP management with hypothermia) N=14 Mortality and GOS at 6 months post-injury	Class 3	Mortality 12.5% in Group A, 6.7% in Group B 8.5% in Group C (no significant difference). Favorable neurologic outcome 50% in Group A, 60% in Group B, 71.4% in Group C (p=0.0426). Mean GOS Group A 3.3 ± 1.3 Group B 3.5 ± 1.2 Group C 3.9 ± 1.2.

MANAGEMENT OF INTRACRANIAL HYPERTENSION

ACS TQIP

MANAGEMENT OF INTRACRANIAL HYPERTENSION

- Recommend a three-tiered approach
- Failure to control ICP/CPP should prompt rapid progression to the next tier's treatment options
- Repeat CT imaging and neurological examination should be considered to rule out development of surgical lesion and guide management

TIER 1

- Head of bed elevated at 30 degrees (reverse Trendelenburg) to improve cerebral venous outflow
- Sedation and analgesia using recommended short-acting agents (for example, propofol, fentanyl, midazolam) in intubated patients
- Ventricular drainage performed intermittently. Continuous drainage is not recommended unless an additional ICP monitor is placed, as when the drain is open, it does not accurately reflect the true ICP
- Repeat CT imaging and neurological examination should be considered to rule out the development of a surgical mass lesion and guide treatment

If ICP remains ≥ 20 - 25 mmHg proceed to Tier 2

TIER 2

- In patients with a parenchymal ICP monitor an EVD should be considered to allow for intermittent CSF drainage
- Hyperosmolar therapy should be given intermittently as needed for ICP elevation and not on a routine schedule
  - Mannitol should be administered in intermittent boluses (0.25 - 1 gm/kg body weight). Caution should be taken in the hypovolemic patient when osmotic diuresis is instituted with mannitol. The serum sodium and osmolality must be assessed frequently (every 6 hours) and additional doses should be held if serum osmolality exceeds 320 mOsm/L. Mannitol may also be held if there is evidence of hypovolemia
  - Hypertonic saline may be administered in intermittent boluses of 3% sodium chloride solution (250 ml over ½ hour) or other concentrations (e.g., 30cc of 23.4%). Serum sodium and osmolality must be assessed frequently (every 6 hours) and additional doses should be held if serum sodium exceeds 160 mEq/L
- Cerebral autoregulation should be assessed (see Advanced Neuromonitoring section). If the patient is not autoregulating, the CPP goal should be lowered to reduce ICP (to no less than 50 mm Hg). Additional neuromonitoring (e.g., PbtO2, SjvO2, CBF) may help determine optimal CPP
- PaCO2 goal of 30 - 35 mmHg should be maintained, as long as brain hypoxia is not encountered. Additional neuromonitoring (e.g., PbtO2, SjvO2, CBF) may help determine optimal PaCO2
- Repeat CT imaging and neurological examination should be considered to rule out development of a surgical mass lesion and guide treatment
- Neuromuscular paralysis achieved with a bolus “test dose” of a neuromuscular blocking agent should be considered if the above measures fail to adequately lower ICP and restore CPP. If there is a positive response, continuous infusion of a neuromuscular blocking agent should be employed (Tier 3)

If ICP remains ≥ 20 - 25 mmHg proceed to Tier 3

TIER 3

(includes potential salvage therapies)

- Decompressive hemi-craniectomy or bilateral craniectomy should only be performed if treatments in Tiers 1 and 2 are not sufficient or are limited by development of side effects of medical treatment
- Neuromuscular paralysis via continuous infusion of a neuromuscular blocking agent can be employed if there is a positive response to a bolus dose. The infusion should be titrated to maintain at least two twitches (out of a train of four) using a peripheral nerve stimulator. Adequate sedation must be utilized
- Barbiturate or propofol (anesthesia dosage) coma may be induced for those patients who have failed to respond to aggressive measures to control malignant intracranial hypertension, however it should only be instituted if a test dose of barbituate or propofol results in a decrease in ICP, thereby identifying the patient as a "responder." Hypotension is a frequent side effect of high dose therapy with these agents. Meticulous volume resuscitation should be ensured and infusion of vasopressor/inotropes may be required. Prolonged use or high dose of propofol can lead to propofol infusion syndrome. Continuous EEG may be used to ensure targeting of the infusion to burst suppression
- Hypothermia (<36 °C) is not currently recommended as an initial TBI treatment. Hypothermia should be reserved for "rescue" or salvage therapy after reasonable attempts at ICP control via the previous Tier 3 treatments have failed

BTF GUIDELINES

HYPEROSMOLAR THERAPY

- Insufficient evidence to support a recommendation
- Note that these treatments may lower intracranial pressure
- Previous recommendations:
  - Mannitol is effective to control elevated ICP at dose 0.25-1.0 g/kg; avoid hypotension
  - Restrict use of mannitol in those without ICP monitoring to those with herniation signs

HYPEROSMOLAR THERAPY

- Mangat et al, 2014 (Class 2)
  - Retrospective cohort study using NY trauma database
  - 73 patients matched in either 1:1 or 2:1 fashion (Mannitol v. HTS)
  - No difference in two week mortality
  - HTS was more effective in lowering ICP burden
- Cottenceau et al, 2011 (Class 3)
  - RCT, 47 patients, HTS v. Mannitol
  - No difference in ICP burden or 6 month GOS
- Ichai et al, 2009 (Class 3)
  - RCT, 34 patients, Sodium Lactate v. Mannitol
  - ICP significantly lower in sodium lactate group
  - Better 1-year GOS score but not powered to answer this question

CSF DRAINAGE

- Level III
  - An EVD system zeroed at midbrain with continuous drainage may lower ICP burden more than intermittent drainage
  - Use of CSF drainage to lower ICP in those with an initial GCS < 6 during first 12 hours may be considered

CSF DRAINAGE

- Nwachuka et al, 2013 (Class 3)
  - Retrospective cohort study, continuous v. intermittent drainage
  - No difference in 6 month survival or GOS
  - However, significantly lower ICP burden in continuous drainage group
- Griesdale et al, 2010 (Class 3)
  - Retrospective cohort study, EVD v. No EVD with focus on mortality
  - In hospital mortality increased in those with GCS > 6 and EVD placement
  - Small benefit in hospital mortality may be seen with EVD placement in those with GCS < 6 (OR 0.76, CI 0.18-3.2) as well as in 28 day mortality (OR 0.47, CI 0.11-2.1)

VENTILATION THERAPIES

- Level IIB: Prolonged prophylactic hyperventilation with $PaCO_2$ of <25 is not recommended
- Previous recommendations
  - Hyperventilation as a temporizing measure is recommended
  - Avoid hyperventilation during first 24h due to decrease in CBF
  - If hyperventilation is used, $SjvO_2$ or $PbtO_2$ should also be used to monitor oxygen delivery

VENTILATION THERAPIES

- Muizelaar et al, 1991 (Class 2)
  - RCT, 113 patients randomized to control ($PaCO_2$ ~35) v. hyperventilation ($PaCO_2$ ~25)
  - Worse outcomes noted at 3 and 6 months via GOS score in hyperventilation group
  - No difference noted in GOS score at 12 months

ANESTHETICS, ANALGESICS AND SEDATIVES

- Level IIB
  - Barbiturates to induce burst suppression as prophylaxis for intracranial hypertension is not recommended
  - High-dose barbiturate therapy to control ICP refractory to maximal medical and surgical management is recommended
    - Hemodynamic stability is paramount
  - Propofol is recommended for ICP control, but not for improvement in mortality or 6-month outcomes
    - High-dose propofol can cause significant morbidity

PROPHYLACTIC HYPOTHERMIA

- Level IIB
  - Early, short term prophylactic hypothermia is not recommended to improve outcomes in patients with diffuse injury

PROPHYLACTIC HYPOTHERMIA

- Clifton et al
  - 1993: RCT, 46 patients comparing hypothermia (33 C) and normothermia (Class 2)
    - 35 v. 36% mortality which was not significant
    - In addition, no significant difference in 3 month GOS (52.2 v. 36.4%)
    - No significant difference in complications between the groups
  - 2001: RCT, 392 patients comparing 2 days of hypothermia (33 C) v. normothermia (**Class 1**)
    - No difference in mortality (28 v. 27%)
    - No difference in 6 month GOS (57% in both groups)
    - Concern was that hypothermia was not induced early enough
  - 2011: RCT, 97 patients comparing 2 days of early hypothermia (33 C) v. normothermia (Class 2)
    - No difference in mortality (RR 1.30, CI 0.58-2.52)
    - No difference in outcomes (RR 1.08, CI 0.76-1.53)
    - No difference noted in complications
    - Also broke down groups by injury type with regards to poor outcomes
      - Diffuse injury- no difference (70 v. 50%)
      - Surgically evacuated hematoma- fewer poor outcomes (33 v 69%)

SURGICAL MANAGEMENT

SURGICAL MANAGEMENT

- BTF Guidelines
  - Bifrontal decompressive craniectomy is not recommended to improve outcomes in diffuse injury with ICPs > 20 refractory to first line therapy
    - Does reduce ICP and minimize days in the ICU
  - Large craniectomy (12x15 cm) is recommended over small craniectomy to reduce mortality and improve neurologic outcome in severe TBI patients
- ACS TQIP
  - Large traumatic hematomas should be evacuated before neurologic deterioration, regardless of GCS
  - If the patient is comatose on admission and found to have a large hematoma as the cause, emergent surgery is indicated for evacuation
  - Decompressive craniectomy is effective in controlling ICP, but its ability to improve outcomes is uncertain

STEROIDS

STEROIDS

- BTF Guidelines
  - Level 1: Not recommended for improving outcomes or reducing ICP. High-dose methylprednisolone is associated with increased mortality in severe TBI and is contraindicated
- ACS TQIP
  - No recommendation

STEROIDS

- Roberts et al, 2004 (CRASH Trial, **Class 1**)
  - RCT, 10,008 patients with TBI (GCS 14 or less and hospital admission within 8 hours) randomized to either high dose methylprednisolone (2g load followed by 0.4g/hr for 48 hours) or placebo
  - Study stopped early based on 2-week mortality results at a planned interim analysis
    - Severe TBI: 39.8 v. 34.8%, RR 1.14 (CI 1.05-1.23)
    - All patients: 21.1 v. 17.9%, RR 1.18 (CI 1.09-1.27)
- Edwards et al, 2005 (CRASH Trial, **Class I**)
  - 6 month results of CRASH trial, 9,673 patients (96.7% of original enrollment)
  - Mortality at 6 months:
    - Severe TBI: 47.1 v. 42.2%, RR 1.12 (CI 1.04-1.20)
    - All patients: 25.7 v. 22.3%, RR 1.15 (CI 1.07-1.24)
  - Unfavorable outcomes at 6 months:
    - Severe TBI: 62.8 v. 62.1%, No difference
    - All patients: 38.1 v. 36.3%, No difference

STEROIDS ARE BAD FOR TBI

OR ARE THEY?

STEROIDS

- Methylprednisolone to Decadron conversion
  - 4 mg methylprednisolone = 0.75 mg decadron
  - 2000 mg methylprednisolone = 375 mg decadron
  - 400 mg methylprednisolone = 75 mg decadron
  - 75 mg x 48 hours = 3,600 mg decadron
  - Total dose of methylprednisolone in CRASH trial = 21.2g
  - Equivalent decadron dose = 3,975 mg

SEIZURE PROPHYLAXIS

SEIZURE PROPHYLAXIS

- BTF Guidelines
  - Level IIA
    - Prophylactic use of phenytoin or VPA is not recommended to prevent late seizures
    - Phenytoin is recommended to decrease incidence of early post-traumatic seizures (but these have not been shown to have worse outcomes)
- ACS TQIP
  - No Recommendation

SEIZURE PROPHYLAXIS

- Temkin et al, 1990 (Class 2)
  - RCT, 404 patients received either 1 year of phenytoin v. placebo after TBI
  - Significant reduction in early PTS: RR 0.27 (CI 0.12-0.62)
  - No difference in late PTS (21.5 v. 15.7%)
- Temkin et al, 1999 (Class 2)
  - RCT, 379 patients with three groups: 1 week of Phenytoin, 1 month of VPA or 6 months of VPA
  - No difference in early PTS with Phenytoin or VPA (1.5 v. 4.5%)
  - No difference in late PTS with any of the groups (15 v. 16 v. 24%)
  - Non-significant trend toward higher mortality in VPA groups

WAIT A MINUTE! WHY NOT KEPPRA?

LEVETIRACETAM V. PHENYTOIN

- Inaba et al, 2013 (Class 2)
  - Prospective observational study, 813 patients with levetiracetam v. phenytoin
  - No difference in seizure rate (1.5% in both), adverse drug reactions (7.9 v. 10.3%) or mortality (5.4 v. 3.7%)
  - Single center study

NUTRITION

NUTRITION

- BTF Guidelines
  - Level IIA: Feeding to attain basic caloric requirements by day 5 (at most day 7) is recommended
  - Level IIB: Post-pyloric feeding is recommended due to decreased VAP risk
- ACS TQIP
  - Nutrition should begin early (24-48 h; when hemodynamically stable)
  - Enteral nutrition is preferred over parenteral nutrition
  - Post-pyloric feeding is preferred as this is associated with lower pneumonia rates
  - Full nutrition supplementation should be achieved by 7 days

NUTRITION

- Chourdakis et al, 2012 (Class 2)
  - RCT, 59 patients early (24-48h) v. late (48h-5d) enteral feeding
  - No difference in pneumonia, CNS infection or hyperglycemia rates
- Hartl et al, 2008 (Class 2)
  - Retrospective cohort which looked at the day nutrition goal was reached and 2-week mortality
  - In those not fed within 7 days, OR 4.10 with regards to 2 week mortality
  - In those not fed within 5 days, OR 2.06 with regards to 2 week mortality
    - If fed, but max nutrition not reached in 5 days, OR 1.30 with regards to 2 week mortality
- Lepelletier et al, 2010 (Class 2)
  - Retrospective cohort to determine effect of early feeding on VAP
  - Protective effect on early VAP when controlling for other factors, OR 0.33 (CI 0.21-0.85)
- Acosta-Escribano et al, 2010 (Class 2)
  - RCT, 104 patients post-pyloric v. gastric feeding
  - Post-pyloric feeding had a lower incidence of all pneumonias, OR 0.3 (CI 0.1-0.7)
  - No difference noted in early pneumonia, but significant decrease in the incidence of late pneumonia was seen

GLYCEMIC CONTROL

- Bilotta et al, 2008 (Class 2)
  - RCT, 97 patients randomized to intense (80-120) versus conventional (<220) insulin therapy
  - Significantly increased number of hypoglycemic events in the intense group
  - ICU stay was longer in the conventional group
  - Hypoglycemic events had no effect on outcome
- Coester et al, 2010 (Class 2)
  - RCT, 88 patients randomized to intense (80-110) versus conventional (<180) insulin therapy
  - Once again, more hypoglycemic episodes in the intensive therapy group but no difference in outcome or mortality
- Yang et al, 2009 (Class 2)
  - RCT, 240 patients randomized to intense (80-100) versus conventional (<200) insulin therapy
  - No difference in mortality noted but decreased infection, decreased days in ICU and better neurologic outcome was noted

TIMING OF VTE PROPHYLAXIS

TIMING OF VTE PROPHYLAXIS

- BTF Guidelines
  - Level III: Low molecular weight heparin or low-dose unfractionated heparin may be used in combination with mechanical prophylaxis, however there is a risk for expansion of hemorrhage
- ACS TQIP
  - TBI patients are high risk for VTE (20-30%)
  - VTE prophylaxis should be considered within 72h of TBI and early (<72h) initiation appears safe in patients with low risk of expansion of hemorrhage
  - Placement of IVC filter should be considered in those high risk patients

Low risk	Moderate risk	High risk
No moderate or high risk criteria	Subdural or epidural hematoma > 8 mm Contusion or intraventricular hemorrhage > 2 cm Multiple contusions per lobe Subarachnoid hemorrhage with abnormal CT angiogram Evidence of progression at 24 hrs	ICP monitor placement Craniotomy Evidence of progression at 72 hrs
Initiate pharmacologic prophylaxis if CT stable at 24 hrs	Initiate pharmacologic prophylaxis if CT stable at 72 hrs	Consider placement of an IVC filter*

**Consider alternate strategies as described in text*

SUMMARY

- Two major sets of guidelines available for treatment of patients with severe TBI
- Paucity of level I recommendations available
- Paucity of level I studies available to contribute to the recommendations
- Research in the area of multimodality neuromonitoring and how this can be used to guide our treatment protocols is very likely the way of the future

QUESTIONS?

THANK YOU!