Prognostication in Traumatic Brain Injury

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I have no relevant financial disclosures

TBI

Objectives

- Classification and prognosis
- Mechanisms and types of injury
- Primary and secondary injury
- Sequelae of TBI
- **Neuro-prognostication in TBI**

Predictive Factors

- GCS (**motor**)
- **Age** (physiologic), comorbidities, frailty
- **Pupillary response**
- **CT findings**
- Location of primary injury
- Mechanism and type of injury
- PHE
- Secondary injury
- Hypotension, shock, hypoxia
- MRI findings

Guidelines for the management and prognosis of severe traumatic brain injury part II: early indicators of prognosis in severe traumatic brain injury

RM Chesnut, J Ghajar, AR Maas - J Neurotrauma, 2000

- Hippocratic aphorism: “No head injury is so serious that it should be despaired of nor so trivial that it can be ignored.” Today, physicians’ estimates of prognosis are still often unduly optimistic, unnecessarily pessimistic, or inappropriately ambiguous.
- It still remains impossible to say with certainty what will be the future course of events in an individual patient, but intensive research in the last two decades has made it possible to be much more confident about what is likely to happen, and to consider prognosis in terms of probabilities rather than prophecies.

TBI Classification Based on Severity, Imaging and Cause

- GCS score of 13 to 15 is considered mild injury, 9 to 12 is considered moderate injury, and 8 or less is considered severe TBI
- Classification scales based on imaging: The Marshall scale and The The Rotterdam scale
- Classification based on cause: Blunt injury, blast injury, penetrating injury

GCS

- Narayan et al. found a positive predictive value of 77% for a poor outcome (dead, vegetative, or severely disabled) was measured for patients with a GCS score of 3-5 and 26% poor predictive value for a GCS score 6-8

- When attempts were made to predict more precisely into one of the five categories of the Glasgow Outcome Scale (GOS), the predictive accuracy of the initial GCS score was poor

Guidelines for the management and prognosis of severe traumatic brain injury part II: early indicators of prognosis in severe traumatic brain injury

RM Chesnut, J Ghajar, AR Maas - J Neurotrauma, 2000

Colohan,[9] 1989

Description of Study: Prospective comparison of outcomes for 551 patients from New Delhi and 822 patients from Charlottesville with severe TBI; all ages.

Classification: Class II Study

Conclusions:

New Delhi

	GOS
GCS Motor	1
1	81.3%
2-4	40.9
5	4.8
6	0.2

Charlottesville

	GOS
GCS Motor	1
1	88.9%
2-4	56.2
5	12.5
6	0.4

Miller,[26] 1981

Description of Study: Prospective study of 225 patients with severe TBI to analyze factors related to outcome; all ages.

Classification: Class II Study

Conclusions:

	GOS	
GCS Motor	1	4, 5
3-4	71%	16%
5-7	30	59
8-15	13	79

Young,[35] 1981

Description of Study: Prospective study of outcomes at one year following severe TBI in 94 patients; all ages.

Classification: Class II Study

Conclusions:

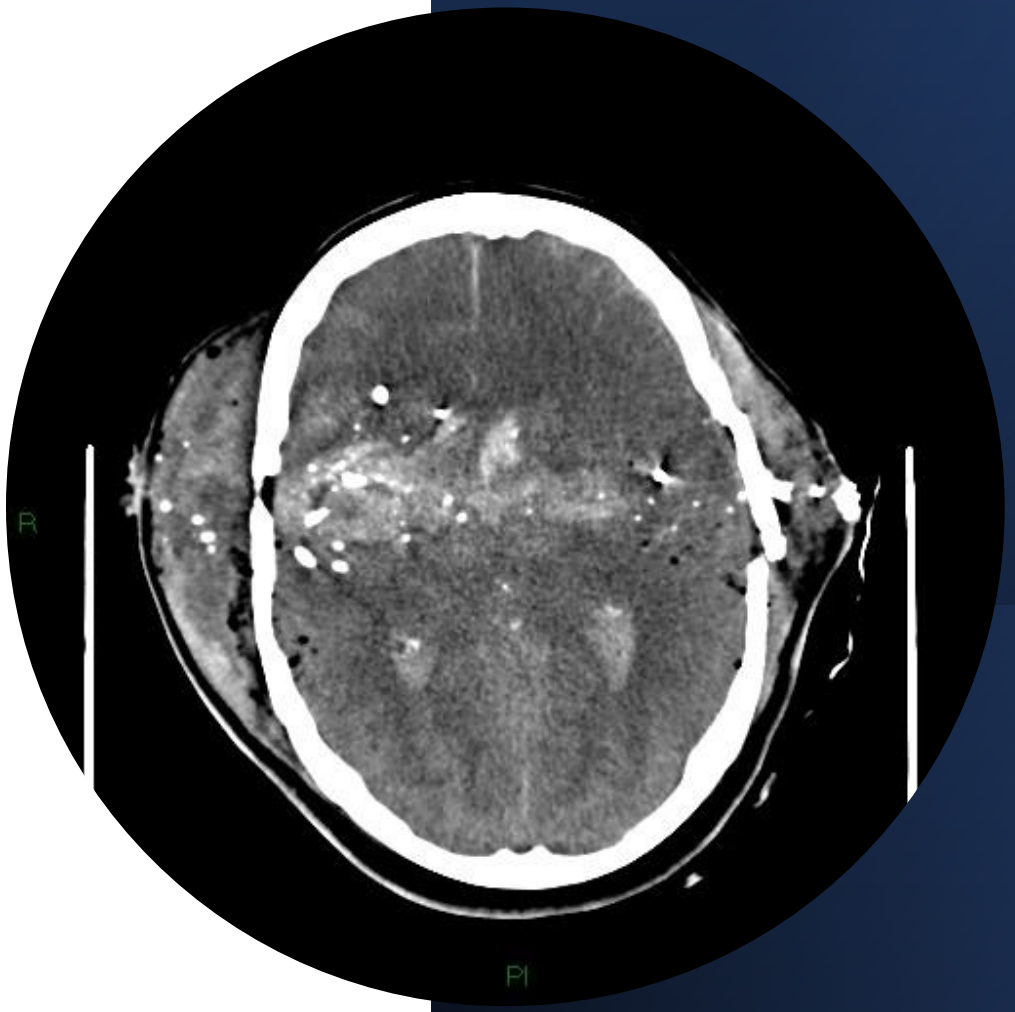
	GOS	
GCS Motor	1	4, 5
3-4	90%	5%
5-7	33	49

Rotterdam CT Score and 6-month Mortality

- 1: 0%
- 2: 7%
- 3: 16%
- 4: 26%
- 5: 53%
- 6: 61%

Basal cisterns	
Normal	0
Compressed	1
Absent	2
Midline shift	
No shift or shift ≤5 mm	0
Shift >5 mm	1
Epidural mass lesion	
Absent	0
Present	1
Intraventricular blood or subarachnoid hemorrhage	
Absent	0
Present	1
Sum score	**Total + 1**

Penetrating Brain Injury



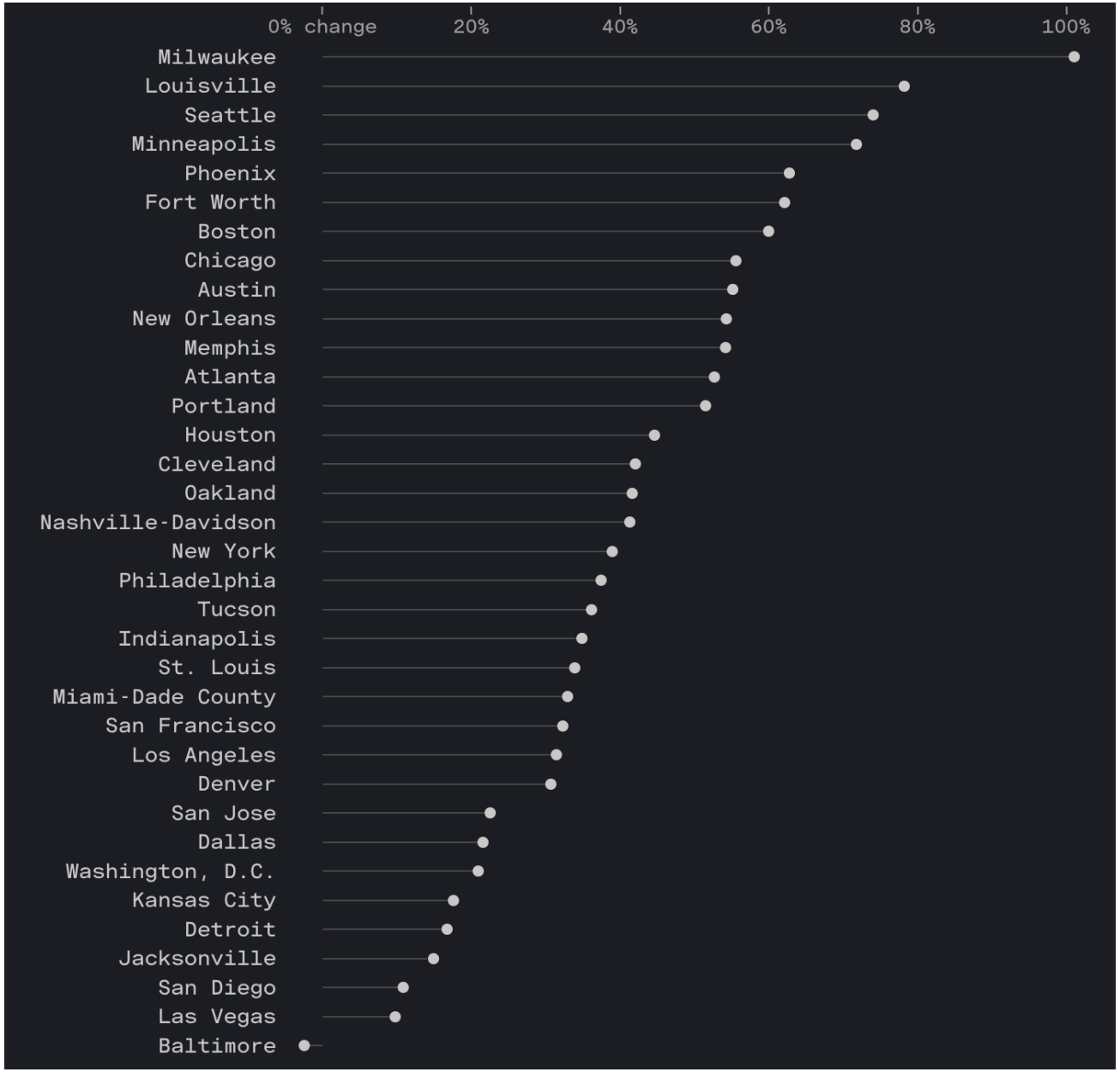
Penetrating/Perforating

TBI/PBI/GSWH

- In the US over 30 000 GSWH occur annually
- 90% of civilian PBI are due to GSWH
- 12% of all TBI are due to PBI
- Survival rate is 10-20% overall. Around 60% die before getting to the hospital.

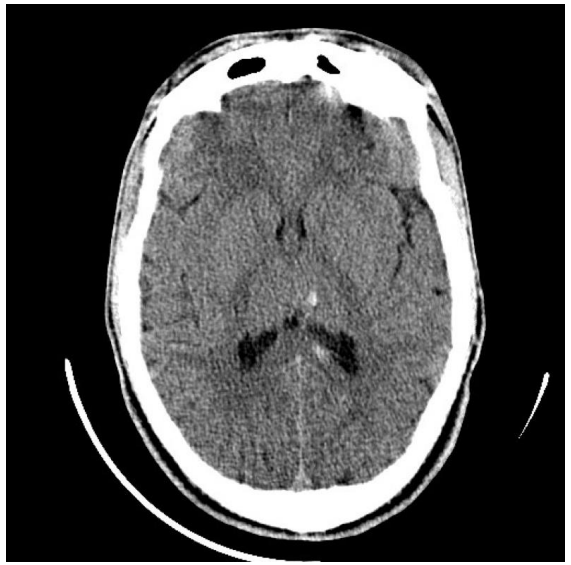
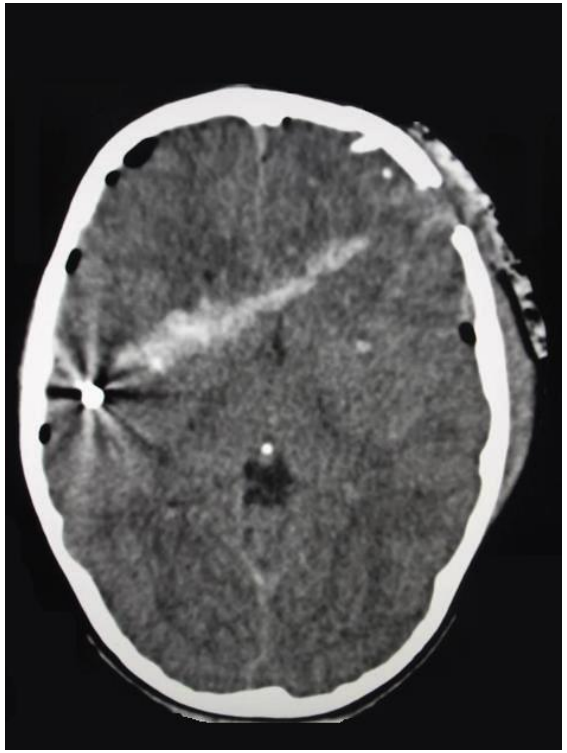
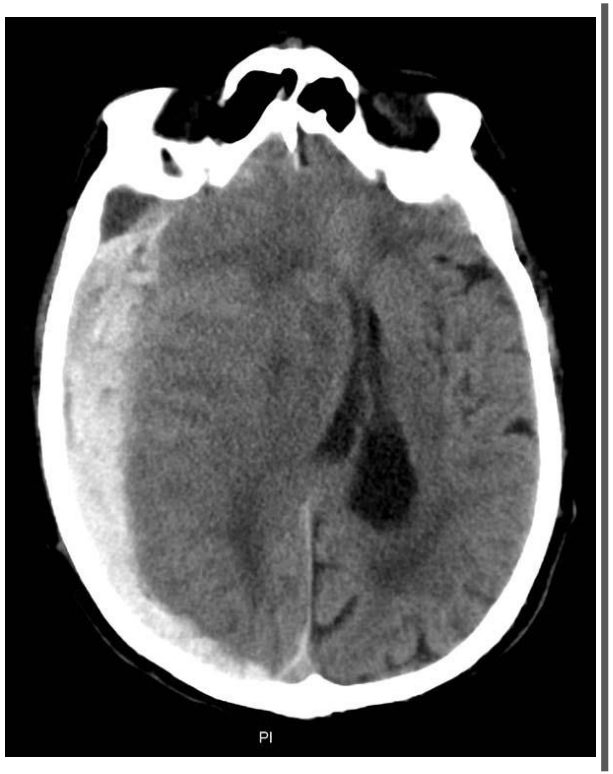
2019-2020

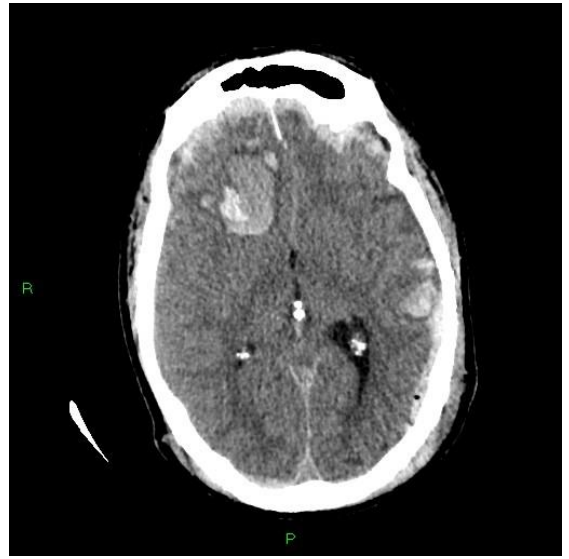
Over 100% increase in gun homicides



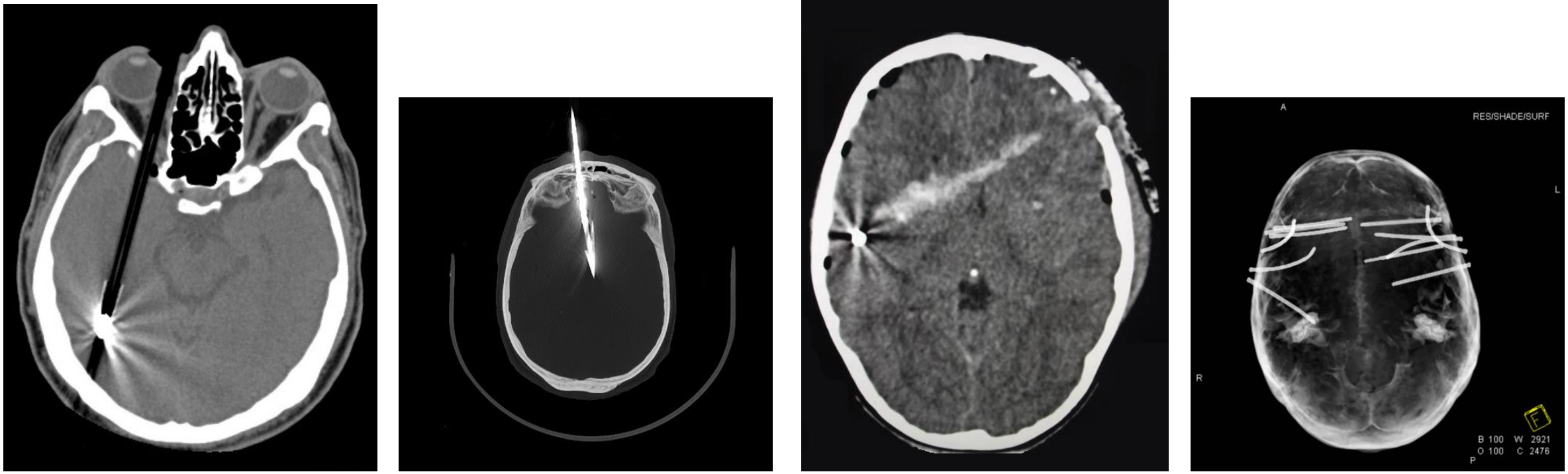
Adjusting the Focus

- Acute TBI and TBI as a chronic condition
- Primary and Secondary Injury
- All-cause TBI
- TBI severity



Severe TBI



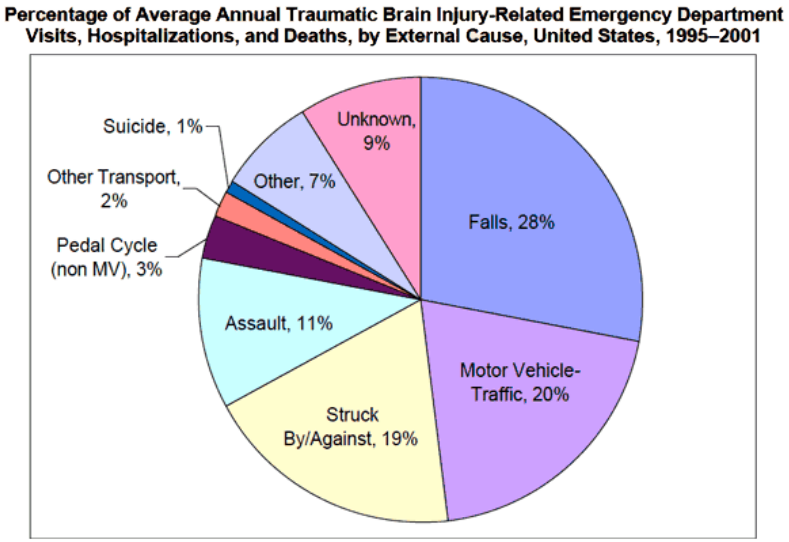
Penetrating Brain Injury

Traumatic Brain Injury

- Head injuries account for most morbidity and mortality from trauma, and are responsible for > 50% of all trauma-related deaths.
- There are approximately 1.5 million new traumatic brain injuries per year in the USA.
- The direct cost is around $4 billion annually in the USA, indirect cost is closer to $40 billion annually.

TBI

- Most common causes
  - Motor vehicle crashes
  - Falls (most common in elderly)



Types of Injury

- Scalp laceration
- Skull fracture
- Focal brain injury
- Diffuse brain injury

Focal Injury

- Contusion
- Subdural hematoma
- Epidural hematoma
- Intracerebral hematoma

Contusion

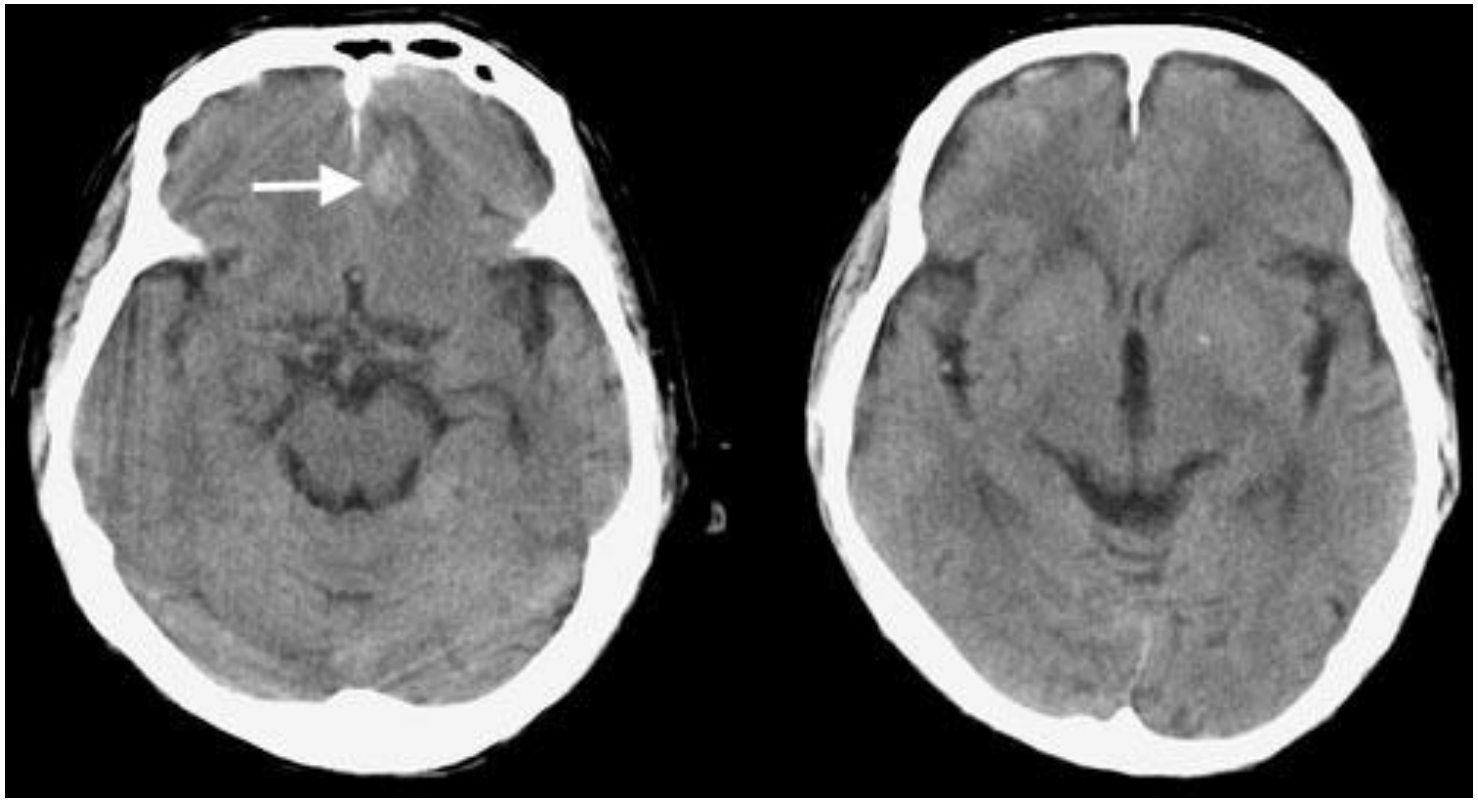
- Usually from deceleration

and brain impacting bony

prominences of skull

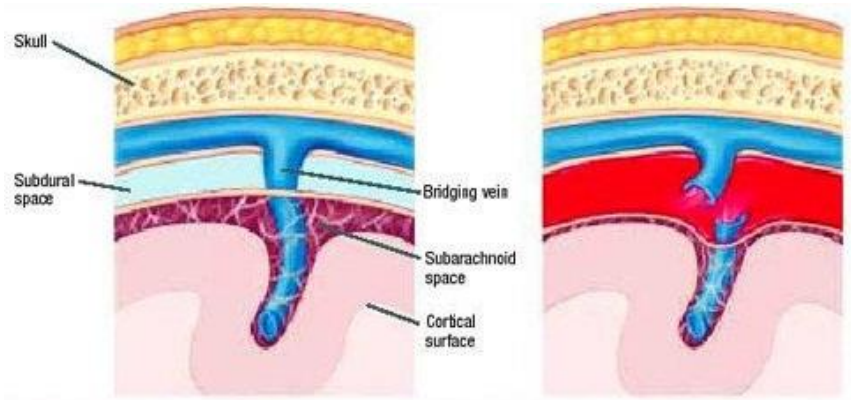
- Focal deficits correlate to location of contusion
- Continued bleeding and edema can lead to increased ICP

Contusion



Subdural hematoma

- Pathogenesis is usually tearing of bridging veins between cerebral cortex and dural venous sinuses
- More frequent in falls and assault than in MVA



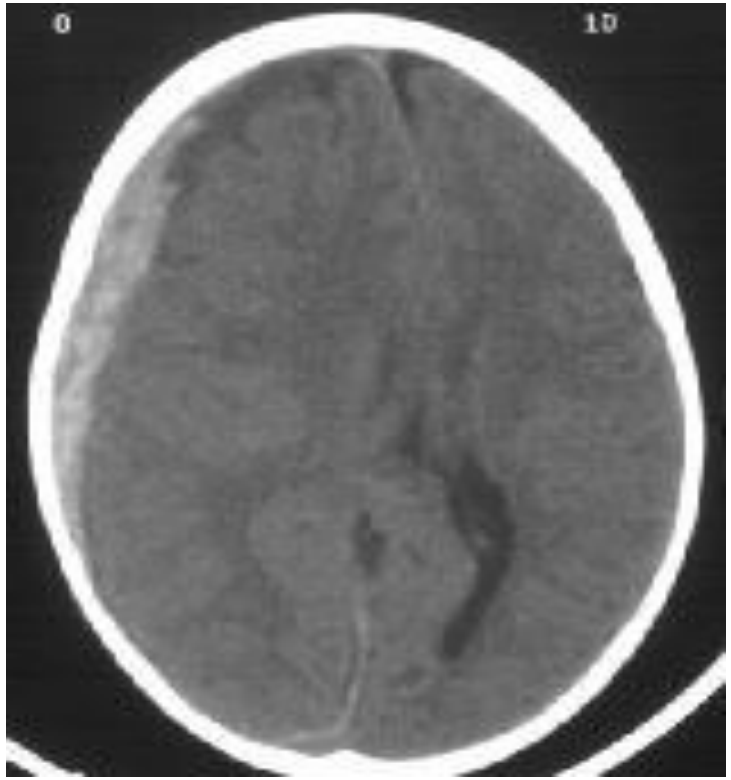
Shearing of the bridging vein (right) causes the subdural space to fill quickly with blood.

Subdural hematoma

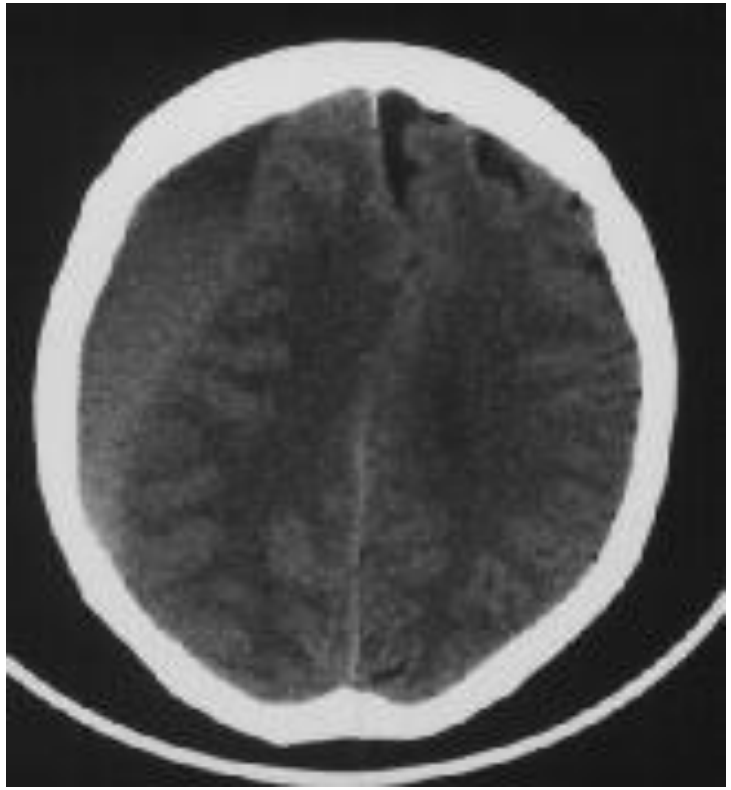
- In some cases, subacute or chronic SDH can be managed conservatively

- In acute setting, symptomatic SDH usually require surgical evacuation

Subdural Hematomas
CT SCAN APPEARANCE



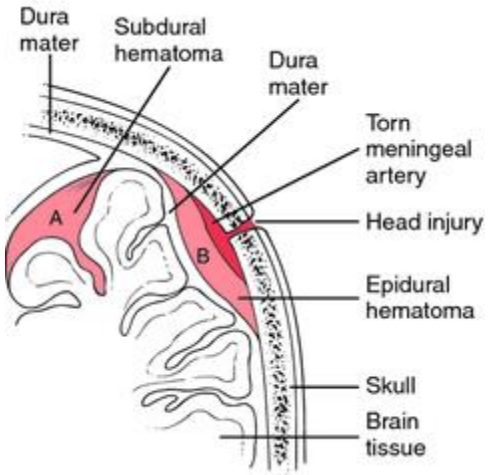
Acute



Subacute

Epidural hematoma

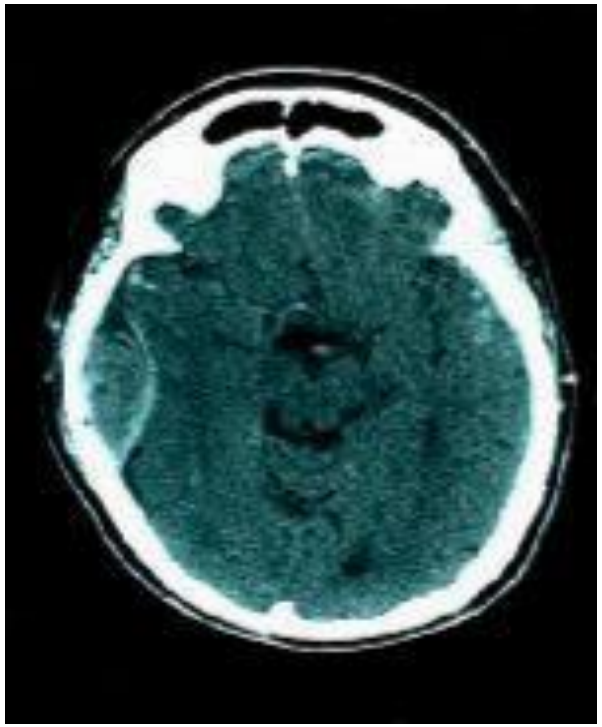
- Most commonly caused by torn artery after a skull fracture (middle meningeal artery)
- Classically associated with momentary loss of consciousness, followed by a lucid interval, then neurologic deterioration

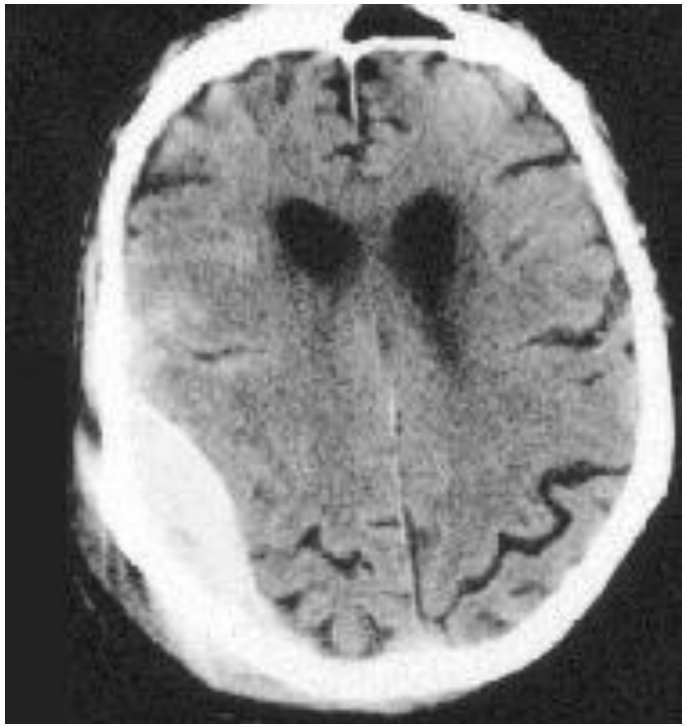


Epidural Hematoma

- Immediate surgical evacuation is the treatment of choice.
- Mortality from 5-55%

Epidural Hematomas
CT SCAN APPEARANCE

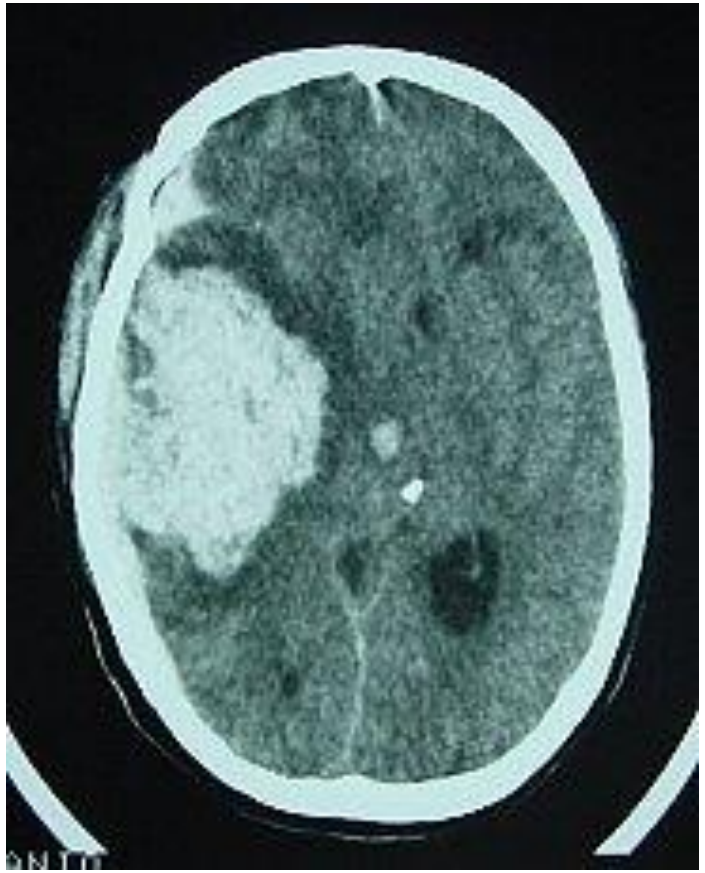




Intracerebral hematoma

- Mechanism is similar to contusion, with brain impacting bony prominence of skull
- Usually in temporal and frontal lobes
- Some will require surgical evacuation if mass effect becomes significant

Intracerebral hematoma



Types of Injury

Diffuse injury

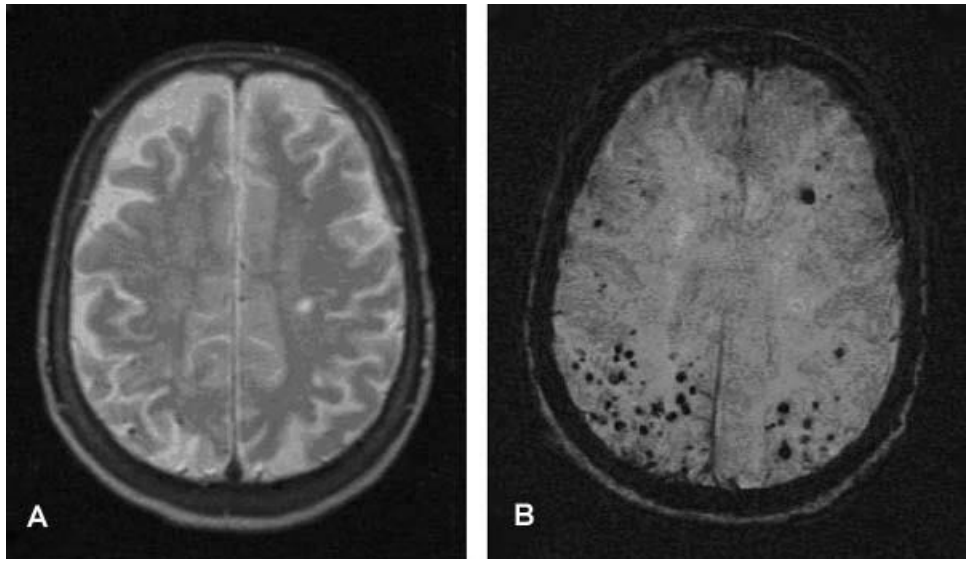
- Concussion
- Diffuse axonal injury

Concussion

- A clinically defined entity (no imaging findings).
- Transient alteration in consciousness with confusion and amnesia.
- Does NOT require loss of consciousness

Diffuse Axonal Injury

- Disruption of axons due to angular acceleration and shear forces at gray-white border



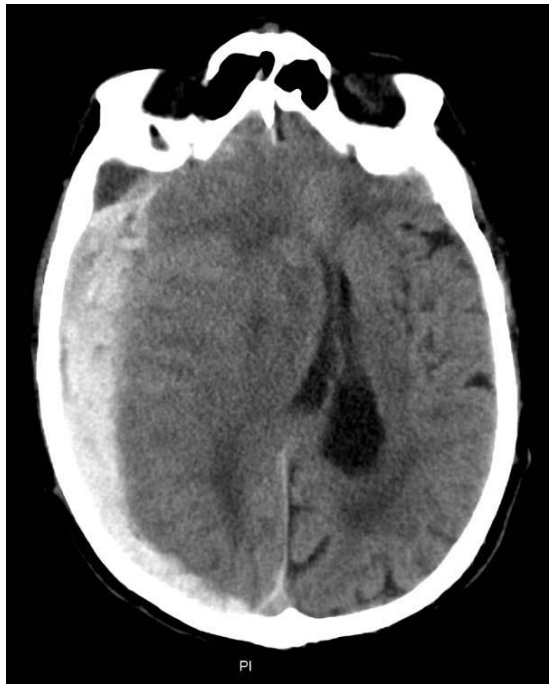
Diffuse Axonal Injury

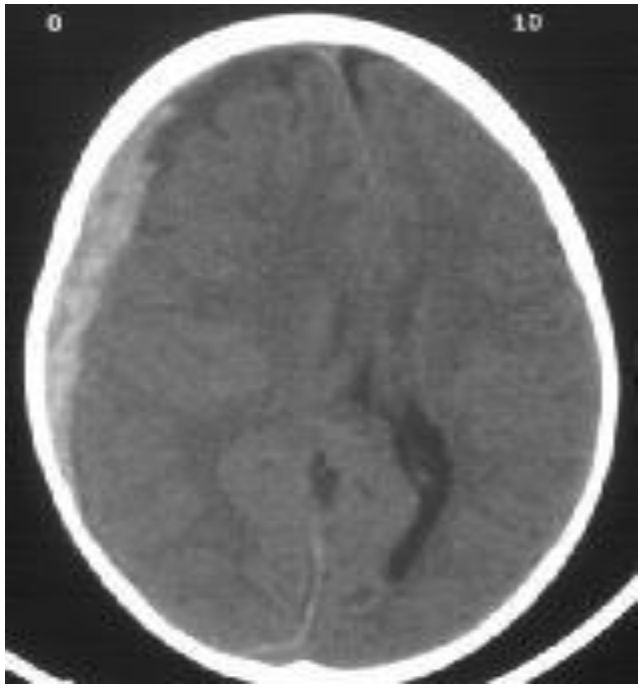
- May see microhemorrhages in white matter
- Axonal retraction bulbs develop hours after the injury suggesting there may be a window of opportunity for brain-saving measures
- Treatment presently is supportive with control of ICP

Poor Prognosis

- Low GCS (<5)
- Hemodynamic instability / Progressive Hemorrhage / Coagulopathy
- Hypoxia
- Disruption of ventricular system
- Brainstem involvement
- Bihemispheric involvement

No two are exactly alike





Gun, Projectile and Tract

- Cross midline: mortality rate ~ 85%
- Multilobar involvement that does not cross midline: Mortality rate ~ 35%

GSW in the NICU

- Manage Primary Injury and complications
- Prevent and Manage Secondary Injury

Complications:

- Intracranial infections
- Cerebrospinal fluid leaks
- Traumatic intracranial aneurysms/vascular injury
- Intraventricular hemorrhage/Hydrocephalus
- Dural venous sinus thrombus

Primary Injury

- Direct tissue/vascular damage
- Cavitation

Both are dependent on the bullet range, bullet type and bullet speed

Low velocity: <300m/s

Medium Velocity: 300–600m/s

High velocity: >600 m/s

Secondary Injury

Post-traumatic ischemia

- Vessel Injury
- Autoregulatory failure
- Decreased nitric oxide or cholinergic neurotransmitters
- Prostaglandin-induced vasoconstriction

Secondary Injury

Cerebral Hyperperfusion

- Loss of coupling between CBF and cerebral metabolism
- Initial hypermetabolism of Glucose

Cerebral Vasospasm

- Depolarization of vascular smooth muscle due to reduced potassium channel activity
- Release of endothelin
- Reduced availability of nitric oxide
- Cyclic GMP depletion of vascular smooth muscle
- Prostaglandin-induced vasoconstriction
- Free radical formation

Secondary Injury

Cerebral Metabolic Dysfunction

- Reduced ATP-production: reduced nicotinic co-enzyme and increased intramitochondrial Ca^{2+}

Decreased Oxygenation

- Inability to maintain adequate CPP
- Loss of autoregulation
- Normal CPP, reduced Pbt02

Secondary Injury

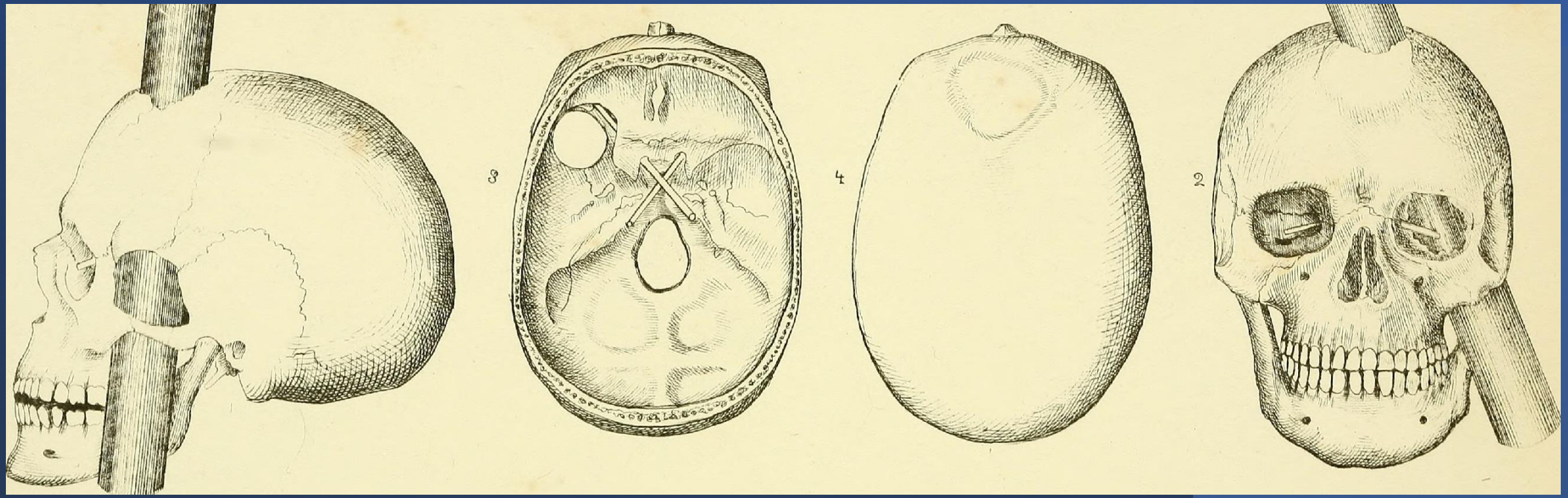
Excitotoxicity and oxidative stress

- Release of extracellular Glutamate, resulting in efflux of Calcium
- Increased Na/K ATPase activity resulting in further metabolic uncoupling
- Saturation of endogenous antioxidant system (superoxide dismutase, glutathione peroxidase)
- Oxygen free radicals result in protein breakdown, damage to DNA and further inhibition of mitochondrial electron transport chain

Secondary Injury

Edema and Inflammation

- Vasogenic and Cytotoxic
- Proinflammatory enzymes (TNF, IL-1, IL-6) are upregulated within hours of the injury and this continues as secondary damage progresses
- Inflammation further disrupts the integrity of the blood-brain barrier
- Necrosis followed by apoptosis


3
4
2

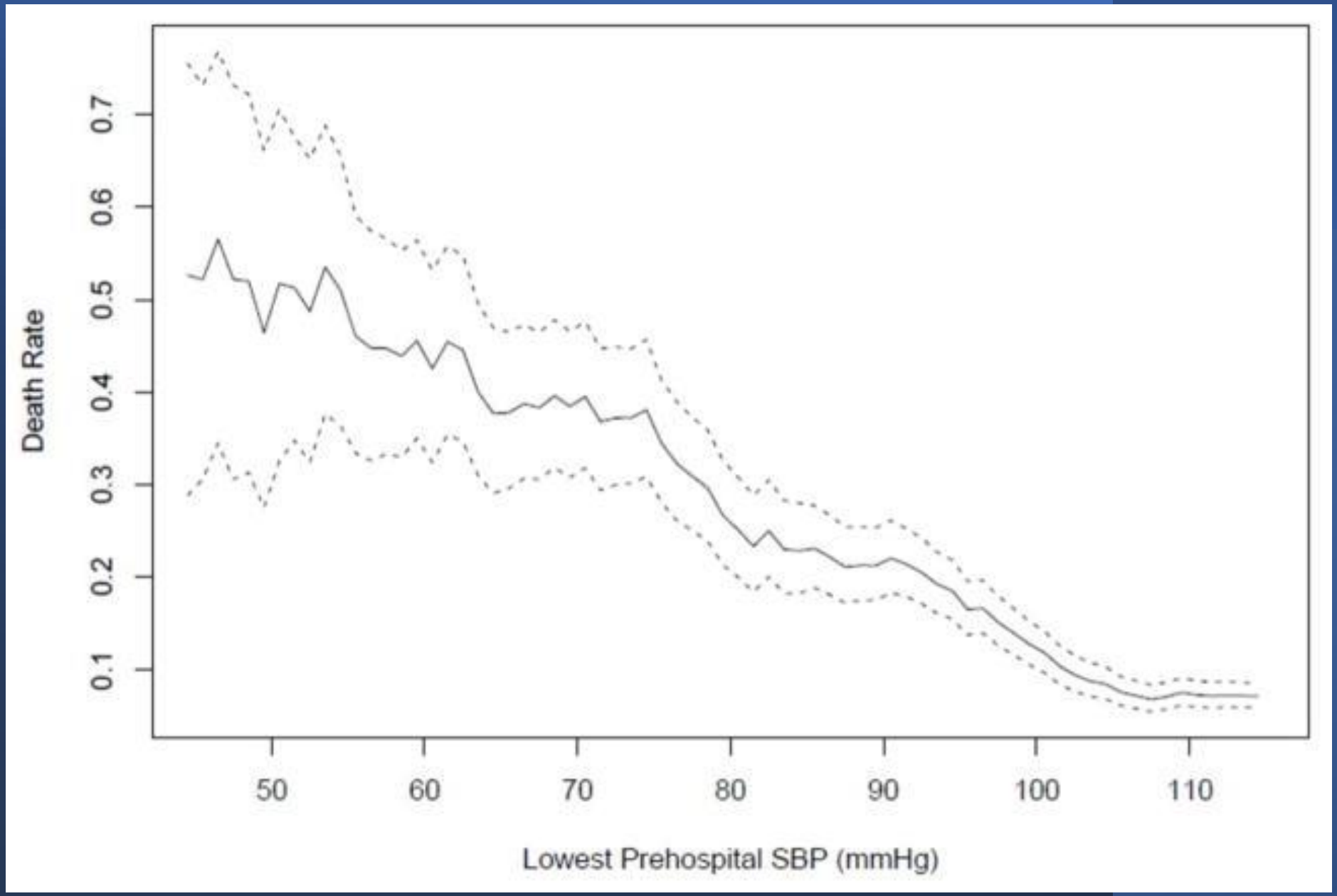
Primary Hemorrhagic Expansion

- Progressive hemorrhage defined as area of new hemorrhage or expansion of previous hemorrhage
- Worsening both primary and secondary injury

Hemorrhagic Shock

- Hemodynamic instability due to hypovolemia
- Worsening both primary and secondary injury
- Postpone surgical intervention

Hemostasis


Death Rate
0.1
0.2
0.3
0.4
0.5
0.6
0.7
50
60
70
80
90
100
110
Lowest Prehospital SBP (mmHg)

Trauma Induced Coagulopathy (ATC)

4X increase in mortality

25-35% of Trauma patients with an injury severity >8 presented with coagulopathy

Likelihood of coagulopathy increases with increasing injury severity

Secondary Coagulopathy: Vicious Triad

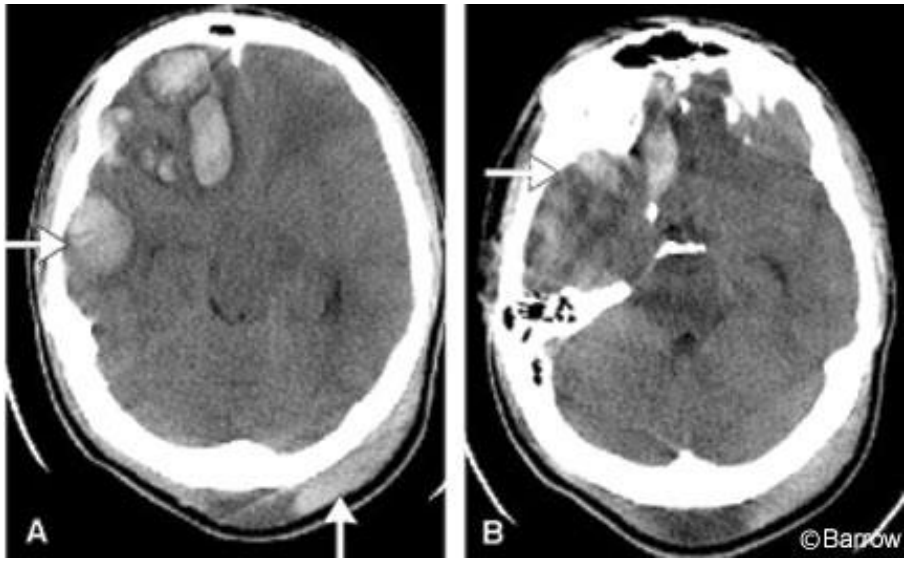
- Acidosis
- Hypothermia
- Hemodilution

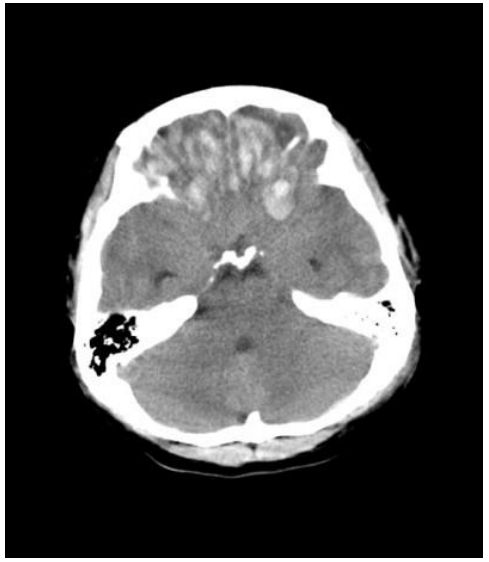
ATC

Often immediate, unlike secondary coagulopathy

Worsens with hypotension, higher injury severity score, and head injury

- Avoid Hypoxia
- Avoid Hypotension
- Avoid Progressive hemorrhagic injury

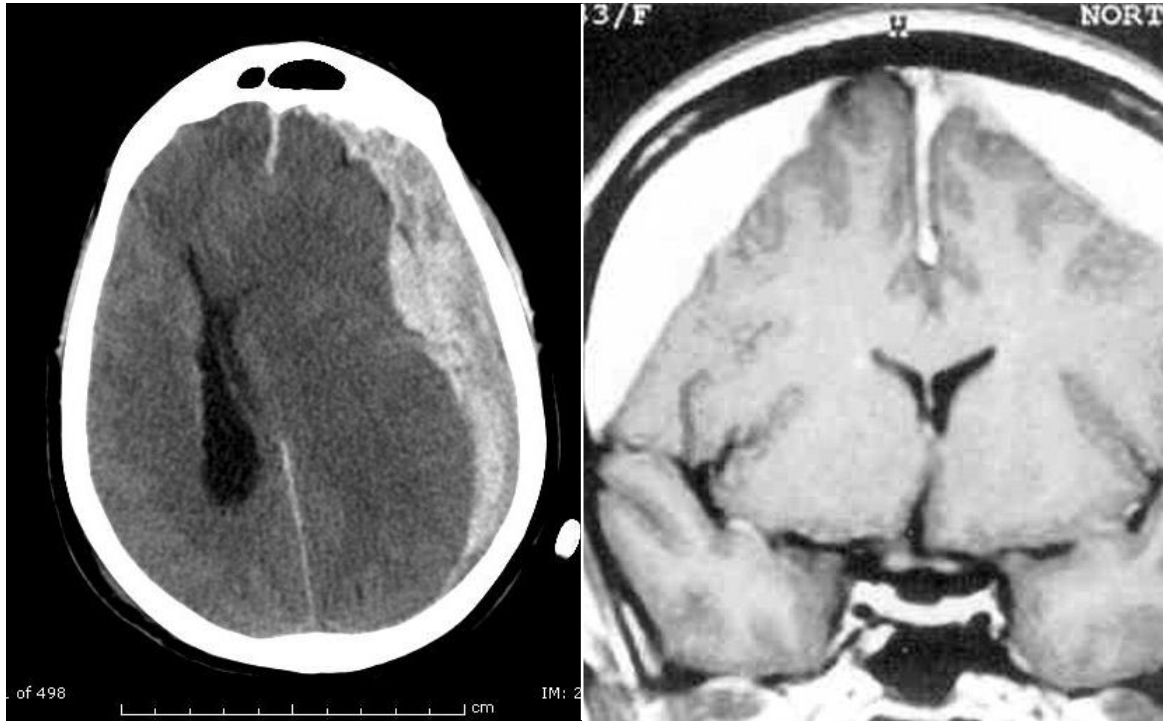




Neurologic Damage

- Deficits similar to stroke patients
- Dependent upon location of injury
- Improvement based upon age and extent of injury – highly variable

Sequelae of Severe TBI



Sequelae of Severe TBI

- DAI tends to have long term sequelae
  - Particularly if there are microhemorrhages in the brainstem or corpus callosum
- Contusions are in between
  - Frontal hematomas have neuropsych issues
  - Temporal lesions tend to develop epilepsy

Long term sequelae

- Secondary cognitive decline
  - Double the risk of dementia/Alzheimer's in post TBI population (different from CTE)
- Epilepsy
  - 5% of all epilepsy pts
  - Can develop at any time
  - More common after penetrating injury or contusion/ICH
  - "preventive" AEDs are ineffective

Particular Issues

- Neuropsych issues
  - Depression – up to 25% of pts (likely higher)
  - Attention and Executive function issues (frontal lobe)
  - Behavioral disorders (frontal and temporal lobe)
    - Explosive, antisocial, anxious and agitated

Mild TBI

- War and football
  - Injury of the Iraq/Afghanistan wars
    - (overlap with PTSD)
- Post concussion syndrome
  - Dizziness, blurry vision, headaches, cognitive slowing (particularly short term memory), depression, irritability

Postconcussion syndrome

- Irritability
- Anxiety/depression
- Restlessness
- Aggression/anger
- Mood swings/emotional lability
- Impulsiveness/disinhibition
- Flat affect

Mild TBI

- 90% improve in 6-12 weeks, how many have complete resolution of symptoms?
- 10% have permanent issues with postconcussion syndrome symptoms
  - Diffusion tensor has shown decreased white matter connectivity
  - SPECT and PET have shown alterations in metabolism and brain blood flow

Prognosis in TBI

- Outcome prediction models: IMPACT and CRASH
- Longitudinal data: TRACK-TBI
- Avoiding self-fulfilling prophecies
- Defining poor outcome
- Overestimating poor outcome

Predictive Factors

- GCS (**motor**)
- **Age** (physiologic), comorbidities, frailty
- **Pupillary response**
- **CT findings**
- Location of primary injury
- Mechanism and type of injury
- PHE
- Secondary injury
- Hypotension, shock, hypoxia
- MRI findings

CRASH Model

Head injury prognosis

CRASH

These prognostic models may be used as an aid to estimate mortality at 14 days and death and severe disability at six months in patients with traumatic brain injury (TBI). The predictions are based on the average outcome in adult patients with Glasgow coma score (GCS) of 14 or less, within 8 hours of injury, and can only support - not replace - clinical judgment. Although individual names of countries can be selected in the models, the estimates are based on two alternative sets of models (high income countries or low & middle income countries).

Country	Canada
Age, years	50
Glasgow coma score	7
Pupils react to light	Both
Major extra-cranial injury?	No
CT scan available?	☑

Presence of petechial haemorrhages	No
Obliteration of the third ventricle or basal cisterns	No
Subarachnoid bleeding	Yes
Midline shift	Yes
Non-evacuated haematoma	Yes

Prediction

Risk of 14 day mortality (95% CI)	**30.7% (21.4 - 41.9)**
Risk of unfavourable outcome at 6 months	**70.4% (60.2 - 78.8)**

IMPACT Model

Prediction models for 6 month outcome after TBI

Admission Characteristics	Value
Core	
Age (14-99 years)	50
Motor Score	Extension
Pupils	Both reacting
Core+CT	
Hypoxia	No
Hypotension	No
CT Classification	Diffuse Injury II
tSAH on CT	Yes
Epidural mass on CT	No
Core+CT+Lab	
Glucose (54-360 mg/dL)	100 mg/dL
Hb (6-17 g/dL)	13 g/dL

Calculate Reset

This model predicts outcome in the following patients:

Adults with head injury, Glasgow Coma Scale 12 or less.

Prognostic Results:

Predicted probability of 6 month mortality: *Core model: 50%*
Predicted probability of 6 month unfavourable outcome: *Core model: 79%*

Predicted probability of 6 month mortality: *Core+CT model: 41%*
Predicted probability of 6 month unfavourable outcome: *Core+CT model: 74%*

Predicted probability of 6 month mortality: *Core+CT+Lab model: 29%*
Predicted probability of 6 month unfavourable outcome: *Core+CT+Lab model: 67%*

Validation

- CRASH CT model, the predicted 14 day mortality of 46.6% approximated the observed outcome, whereas the predicted 6 month unfavorable outcome was an overestimate at 74.8%

Characteristics	Measure or Category	IMPACT Database ($n = 8,509$)	CRASH Trial[a] ($n = 6,681$)
Age, years	Median (25 −75 percentile)	30 (21–45)	32 (23–47)
Motor score	None (1)	1,395 (16%)	785 (12%)
	Extension (2)	1,042 (12%)	515 (8%)
	Abnormal flexion (3)	1,085 (13%)	658 (10%)
	Normal flexion (4)	1,940 (23%)	1,156 (17%)
	Localizes/obeys (5/6)	2,591 (30%)	3,567 (53%)
	Untestable/missing (9)	456 (5%)	0
Pupillary reactivity	Total	7,126	6,272
	Both pupils reacted	4,486 (63%)	4,956 (74%)
	One pupil reacted	886 (12%)	530 (8%)
	No pupil reacted	1,754 (25%)	786 (12%)
Hypoxia	Total	5,452	NA
	Yes or suspected	1,116 (20%)	NA
Hypotension	Total	6,420	NA
	Yes or suspected	1,171 (18%)	NA
CT classification[b]	Total	5,192	5,654
	I	360 (7%)	954 (17%)
	II	1,838 (35%)	1,517 (27%)
	III	863 (17%)	604 (11%)
	IV	187 (4%)	133 (2%)
	V	1,435 (28%)	815 (14%)
	VI	509 (10%)	1,631 (29%)
Traumatic subarachnoid hemorrhage	Total	7,393	5,653
	Yes	3,313 (45%)	2,045 (36%)
Epidural hematoma	Total	7,409	NA
	Yes	999 (13%)	NA
Glucose (mmol/l)	Total	4,830	NA
	Median (25–75 percentile)	8.2 (6.7–10.4)	NA
Hb (g/dl)	Total	4,376	NA
	Median (25–75 percentile)	12.7 (10.8–14.3)	NA
Six-month outcome	Dead	2,396 (28%)	2,146 (32%)
	Vegetative	351 (4%)	993 (15%)[c]
	Severe disability	1,335 (16%)	—
	Moderate disability	1,666 (20%)	1,224 (18%)
	Good recovery	2,761 (32%)	2,318 (35%)

Characteristics	Coding	6 Month Outcome Number (%)		Odds Ratios (95% CI)			
		Dead (n = 2,396)	Unfavorable (n = 4,082)	Univariate	Core Model (n = 8,509)	Extended Model[a] (n = 6,999)	Lab Model[b] (n = 3,554)
Age, years	45 versus 21 years	—	—	2.2 (2.0–2.3)	2.4 (2.2–2.5)	2.2 (2.0–2.3)	1.9 (1.7–2.1)
Motor score	None (1)	625 (45%)	894 (64%)	4.9 (4.3–5.5)	3.9 (3.4–4.5)	3.4 (2.9–4.0)	2.8 (2.1–3.7)
	Extension (2)	496 (48%)	807 (77%)	7.2 (6.3–8.3)	5.7 (4.9–6.6)	4.6 (3.9–5.4)	4.3 (3.5–5.4)
	Abnormal flexion (3)	326 (30%)	619 (57%)	3.5 (3.1–4)	3.0 (2.6–3.5)	2.8 (2.4–3.2)	2.7 (2.2–3.3)
	Normal flexion (4)	411 (21%)	800 (41%)	1.8 (1.6–2)	1.7 (1.5–1.9)	1.6 (1.4–1.8)	1.5 (1.3–1.8)
	Localizes/obeys (5/6)	383 (15%)	699 (27%)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	Untestable/missing (9)	155 (34%)	263 (58%)	2.2 (1.8–2.7)	2.1 (1.7–2.6)	2.0 (1.7–2.5)	1.3 (0.6–2.6)
Pupillary reactivity	Both pupils reacted	790 (18%)	1,578 (35%)	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
	One pupil reacted	295 (33%)	521 (59%)	2.7 (2.4–3.1)	1.8 (1.6–2.1)	1.6 (1.4–1.8)	1.4 (1.1–1.7)
	No pupil reacted	946 (54%)	1,351 (77%)	5.9 (5.3–6.6)	3.3 (3.0–3.7)	2.7 (2.4–3.1)	2.1 (1.6–2.6)
Hypoxia	Yes or suspected	481 (43%)	713 (64%)	2.1 (1.9–2.4)	—	1.3 (1.1–1.5)	1.4 (1.2–1.7)
	No	1,158 (27%)	1,928 (44%)	1.0 (ref)	—	1.0 (ref)	1.0 (ref)
Hypotension	Yes or suspected	578 (49%)	794 (68%)	2.7 (2.4–3.1)	—	1.8 (1.6–2.1)	1.5 (1.2–1.8)
	No	1,315 (25%)	2,263 (43%)	1.0 (ref)	—	1.0 (ref)	1.0 (ref)
CT classification[c]	I	24 (7%)	50 (14%)	0.41 (0.33–0.52)	—	0.64 (0.51–0.82)	0.65 (0.47–0.89)
	II	256 (14%)	582 (32%)	1.0 (ref)	—	1.0 (ref)	1.0 (ref)
	III	287 (33%)	456 (53%)	2.6 (2.3–3)	—	1.7 (1.5–2.0)	1.7 (1.4–2.0)
	IV	86 (46%)	107 (57%)	—			
	V	422 (29%)	709 (49%)	2.3 (2–2.6)	—	1.6 (1.4–1.9)	1.8 (1.5–2.2)
	VI	217 (43%)	293 (58%)	—			
Traumatic subarachnoid	Yes	1,193 (36%)	1,925 (58%)	2.6 (2.4–2.9)	—	1.7 (1.5–1.8)	1.8 (1.6–2.1)
Hemorrhage	No	724 (18%)	1,462 (36%)	1.0 (ref)	—	1.0 (ref)	1.0 (ref)
Epidural hematoma	Yes	207 (21%)	358 (36%)	0.64 (0.56–0.72)	—	0.61 (0.53–0.70)	0.56 (0.46–0.69)
	No	1,794 (28%)	3,101 (48%)	1.0 (ref)	—	1.0 (ref)	1.0 (ref)
Glucose	10.4 versus 6.7.mmol/l	—	—	1.7 (1.6–1.8)	—	—	1.3 (1.2–1.4)
Hb	14.3 versus 10.8 g/dl	—	—	0.66 (0.61–0.72)	—	—	0.78 (0.70 – 0.87)

NEUROLOGIC CRITICAL CARE

Delayed neurological recovery after decompressive craniectomy for severe nonpenetrating traumatic brain injury*

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14 days, 3 months, 6 months, 12 months, 18 months

- 176 patients who required decompressive craniectomy between 2004 and 2010, 104 (59%) had moderate to severe disability 6 months after surgery
- Fifty of these patients (48%, 95% CI: 39–58) had ≥1 grade of improvement in Glasgow Outcome Scale score between 6 and 18 months after surgery
- Of the 59 patients who had an unfavorable outcome (severe disability or vegetative state) 6 months after surgery, 15 patients (25%, 95% CI: 16–38) improved and had attained a favorable outcome (moderate disability or near normal neurologic function) by the 18-month follow-up

Interpretation

- Delayed neurologic recovery after decompressive craniectomy for severe nonpenetrating traumatic brain injury was common
- Evacuated intracerebral hematoma and a high admission Glasgow Coma Scale were associated with a higher chance of delayed neurologic recovery after decompressive craniectomy

DAI

- Microhemorrhages at gray-white junction (Grade I), the corpus callosum (Grade II), and the dorsolateral, rostral brainstem (Grade III)

DAI

Severity of TBI	Outcome		Total	*P*-value
	Satisfactory	Unsatisfactory		
Moderate	47	39	86	0.041
Severe	17	30	47	
Total	64	69	133	

Grade of DAI	Outcome		Total	*P*-value
	Satisfactory	Unsatisfactory		
Grade I	32	23	55	0.020
Grade II	24	24	48	
Grade III	8	22	30	
Total	64	69	133	

DAI

- In a study of 50 patients, the average time to regain consciousness was 1–2 weeks for Grade I DAI patients, 3–4 weeks for Grade II patients, and 3–4 months for Grade III patients

Grade of DAI	Outcome		Total	*P*-value
	Satisfactory	Unsatisfactory		
Grade I	32	23	55	0.020
Grade II	24	24	48	
Grade III	8	22	30	
Total	64	69	133	

Best prognostic information

- Motor exam
- Age
- Pupillary reactivity

JAMA Neurology | Original Investigation

Functional Outcomes Over the First Year After Moderate to Severe Traumatic Brain Injury in the Prospective, Longitudinal TRACK-TBI Study

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Prospective, longitudinal outcome collected throughout different phases of recovery in acute/chronic moderate and severe TBI

TRACK-TBI

- 18 level 1 trauma centers in the US from February 2014 to August 2018
- Prospectively assessed longitudinal outcomes
- Assessments were completed at 2 weeks and 3, 6, and 12 months postinjury
- Primary outcome: GOSE
- Dichotomized as a favorable outcome (GOSE scores 4-8) or an unfavorable outcome (GOSE scores 1-3)
- Function at home without supervision for more than 8 hours per day

GOS-E

GOS 5-point scale	GOSE 8-point scale	Domain	Criteria
Dead	1. Dead		
Vegetative State	2. Vegetative State	Consciousness	
Severe Disability (SD) Conscious but dependent	3. Lower SD	Function in Home	Unable to look after themselves for 8 h
	4. Upper SD	Function in Home	Unable to look after themselves for 24 h OR
		Function Outside the Home	Unable to shop OR
			Unable to travel
Moderate Disability (MD) Independent but with limitations in one or more activities	5. Lower MD	Work/Study	Unable to work/study OR
		Social and Leisure Activities	Unable to participate OR
		Family and Friendships	Constant problems
	6. Upper MD	Work	Reduced work capacity OR
		Social and Leisure Activities	Participate much less OR
		Family and Friendships	Frequent problems
Good Recovery (GR) Return to normal life	7. Lower GR	Social and Leisure Activities	Participate a bit less OR
		Family and Friendships	Occasional problems OR
		Symptoms	Some symptoms affecting daily life
	8. Upper GR		No problems

TRACK-TBI

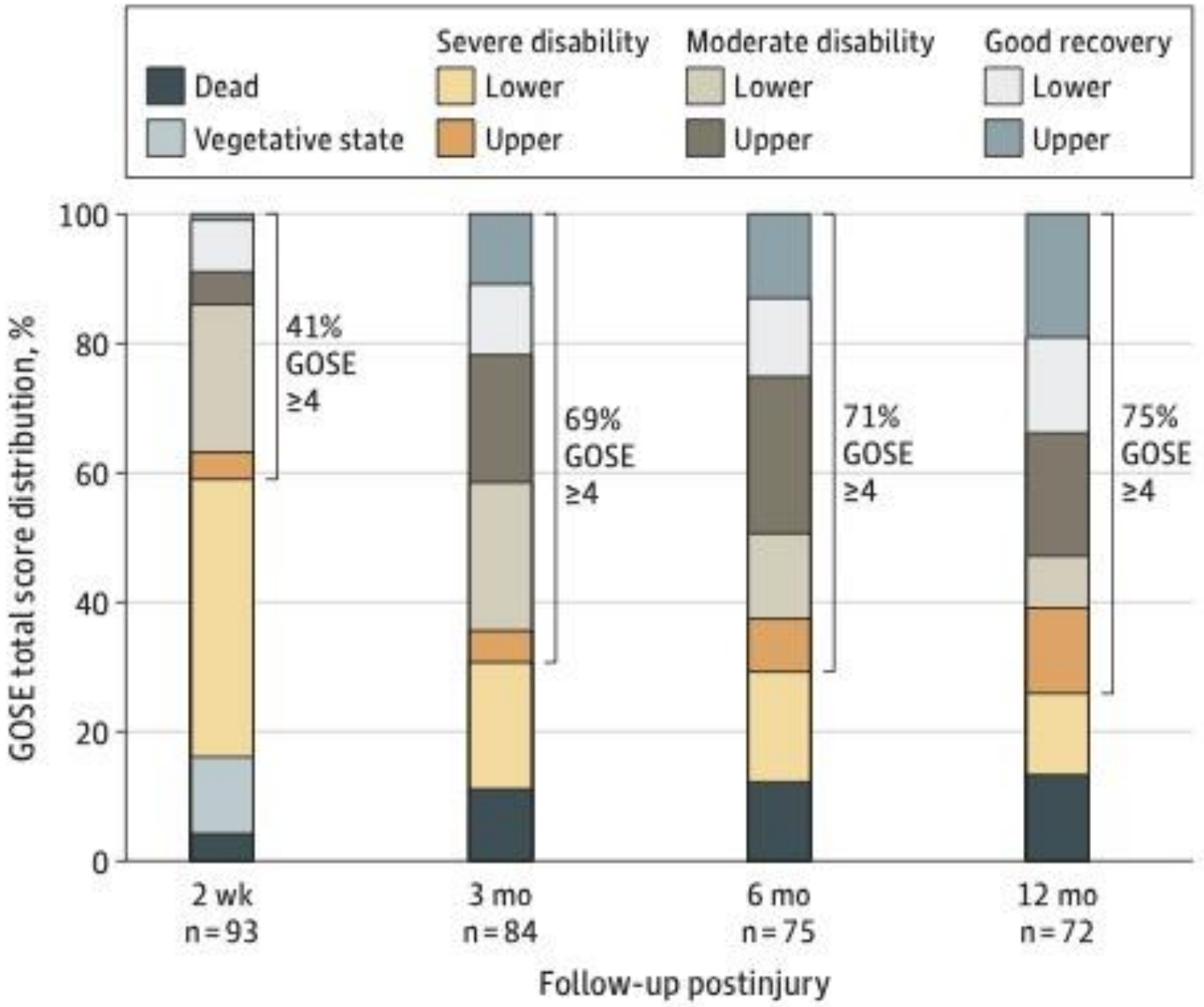
- Secondary outcome: DRS
- Enrolled 2697 patients
- 484 had moderate (n=122) or severe (n=362) TBI and were included in this analysis
- The mean GCS score was 4.3 in the severe TBI group and 10.4 in the moderate TBI group
- Mean hospital stay severe TBI: 29.5 days, moderate TBI :15.6

Eye Opening		0 = *spontaneous* 1 = *to speech* 2 = *to pain* 3 = *none*
Communication Ability		0 = *oriented* 1 = *confused* 2 = *inappropriate* 3 = *incomprehensible* 4 = *none*
Motor Response		0 = *obeying* 1 = *localizing* 2 = *withdrawing* 3 = *flexing* 4 = *extending* 5 = *none*
Cognitive Ability for Self Care Activities	Feeding	0 = *complete* 1 = *partial* 2 = *minimal* 3 = *none*
	Toileting	0 = *complete* 1 = *partial* 2 = *minimal* 3 = *none*
	Grooming	0 = *complete* 1 = *partial* 2 = *minimal* 3 = *none*
Dependence on Others	Level of Functioning	0 = *completely independent* 1 = *independent in special environment* 2 = *mildly dependent* 3 = *moderately dependent* 4 = *markedly dependent* 5 = *totally dependent*
Psychosocial Adaptability	Employability	0 = *not restricted* 1 = *selected jobs* 2 = *sheltered workshop (non-competitive)* 3 = *not employable*

Outcomes Moderate TBI

- 38 of 93 (41%) had a favorable outcome (GOSE scores ≥4) by 2 weeks postinjury, which increased to 69% at 3 months, 71% at 6 months, and 75% by 12 months
- 35% participants with moderate TBI had achieved a good recovery (GOSE scores 7-8), including 19% who had a complete recovery (GOSE score 8)

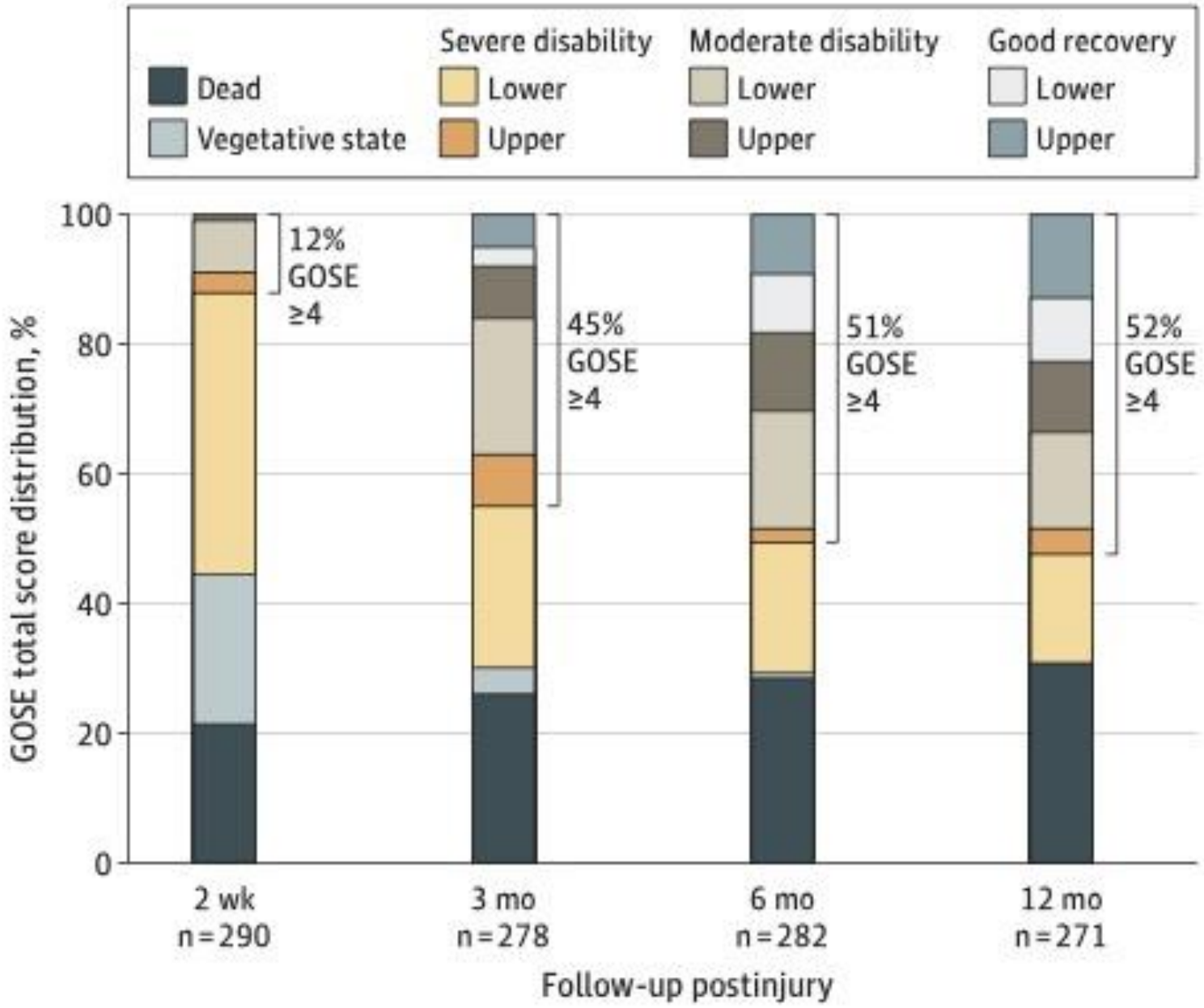
GOS-E for moderate TBI



Outcomes Severe TBI

- At 2 weeks postinjury, 36 of 290 (12.4%) in the severe TBI group had achieved a favorable outcome (GOSE scores 4-8) and only 2 of 290 (0.7%) made a good recovery (defined as a GOSE score of 7 or 8)
- The percentage of participants with severe TBI and GOSE scores of 4 or more nearly quadrupled from 2 weeks (12.4%) to 3 months (45.0%) and reached 52.4% by 12 months postinjury
- Good recovery (GOSE scores 7-8) increased to 8.3% at 3 months, 18.4% at 6months, and22.9% at 12 months

GOS-E for severe TBI



Secondary Outcome: DRS

- At 2 weeks postinjury, 94% of the severe TBI group and 79% of the moderate TBI group had moderate to severe disability or worse (DRS scores ≥4) and approximately 80% required assistance in basic aspects of everyday function
- By 12 months 50% the severe TBI group and 75% of the moderate TBI group were able to function independently at home for at least 8 hours per day
- In severe TBI group 19% had no disability (DRS score 0) and 14% had only mild disability (DRS scores 1-3) at 12 months postinjury

Secondary Outcome: VS

- Of participants who were in a VS at 2 weeks and survived, all recovered consciousness and more than 25% regained orientation by 12 months
- All but 1 of the 79 participants in VS at 2 weeks postinjury who survived up to 1 year recovered at least basic communication ability and 25% were fully oriented
- Traumatic VS is a dynamic condition that evolves over the first year

Withdrawal of life support

- Withdrawal of life-sustaining treatment based on early prognostication of poor outcome accounts for most deaths in patients hospitalized for severe TBI
- One-third of deaths here occurred within the first 72 hours after injury, half within the first week, and nearly three-quarters by 2 weeks

Concerns

- Clinicians should be cautious about suggesting a high likelihood of permanent severe disability within the first 2 weeks postinjury
- AAN strongly recommended that clinicians avoid statements suggesting that patients with disorders of consciousness who are within 28 days of injury have a universally poor prognosis

- Baseline prognostic scores are often obtained within the first 24 hours, although the optimal timing has not been thoroughly studied

Concerns

- The role of severity scores in adjustment for hospital and system-level quality measures of TBI care is unclear and requires further study
- The use of baseline severity scores in stratification for care decisions or placement in clinical trial strata requires further investigation
- The concept of patient frailty, increasingly studied as a predictor of disease outcome for elderly individuals, has not yet been incorporated into prediction of TBI outcome

Biomarkers

- ubiquitin carboxyl-terminal hydrolase isozyme L1 [UCH-L1]
- neuron-specific enolase [NSE]
- total tau
- neurofilament protein-light [NFL]
- glial fibrillary acid protein [GFAP]
- S100 calcium-binding protein B [S100B]

CENTER-TBI & TRACK-TBI

CENTER-TBI

- When compared with the IMPACT and CRASH models alone, the addition of the blood biomarkers significantly enhanced prediction of mortality and unfavorable outcome, with most value contributed by UCH-L1

February 2023

BRAIN
ORIGINAL ARTICLE

Acute thalamic connectivity precedes chronic post-concussive symptoms in mild traumatic brain injury

Rebecca E. Woodrow,[1,2] Stefan Winzeck,[1,3] Andrea I. Luppi,[1,2,4] Isaac R. Kelleher-Unger,[1,2] Lennart R. B. Spindler,[1,2] J. T. Lindsay Wilson,[5] Virginia F. J. Newcombe,[1] Jonathan P. Coles,[1] CENTER-TBI MRI Substudy Participants and Investigators, David K. Menon[1,6,†] and Emmanuel A. Stamatakis[1,†]

Mild TBI

- Recovery from mild TBI is functionally and/or symptomatically incomplete in almost half of mild TBI participants at 6 months post-injury
- Mild injury is associated with widespread increases in acute connectivity of thalamic nuclei; to cortical, subcortical, and other thalamic regions
- These changes are uniquely associated with the presence of persistent post-concussive symptoms

Prognostication in TBI

- 2-way conversation that is timed appropriately
- Patient AND the Injury
- Use any and all clear prognostic indicators
- Speak in terms of probabilities and provide a spectrum of possible outcomes
- Provide clarity in length of recovery
- Likelihood of regaining independence

Thank you

- Cascade of injury in TBI
- Artificial intelligence in prognostication
- Biomarkers in TBI
- Neuroleptics in TBI
- Epilepsy in TBI
- Coagulopathy in TBI
- Electrolyte disorders in TBI
- Vasospasm and stroke in TBI
- Levels of consciousness in TBI
- Long term outcomes in TBI
- Intracranial pressure monitoring in TBI
- PbtO2 in TBI
- Brain death / Organ donation in TBI

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