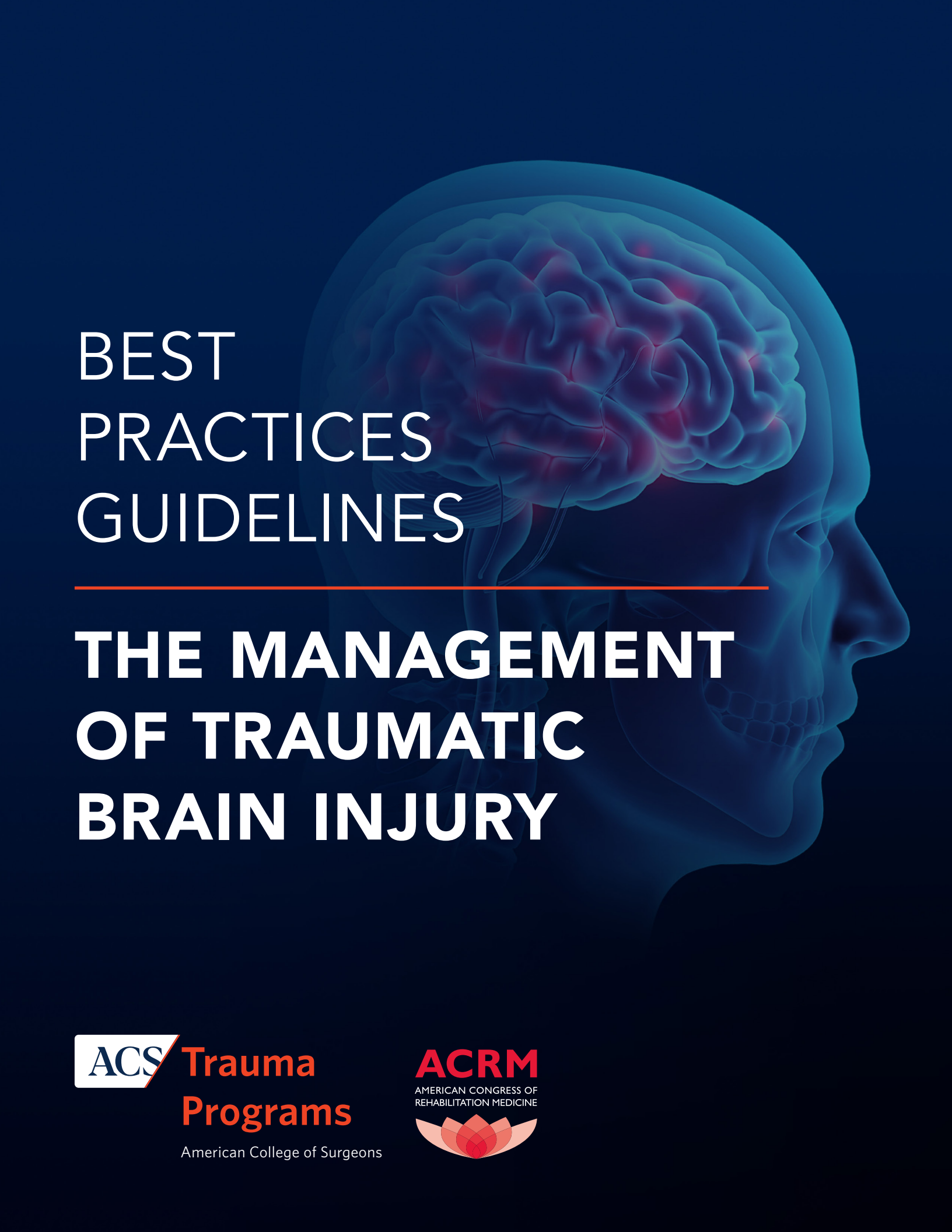

BEST PRACTICES GUIDELINES

THE MANAGEMENT OF TRAUMATIC BRAIN INJURY

ACS Trauma Programs
American College of Surgeons

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ACS Trauma Programs
American College of Surgeons

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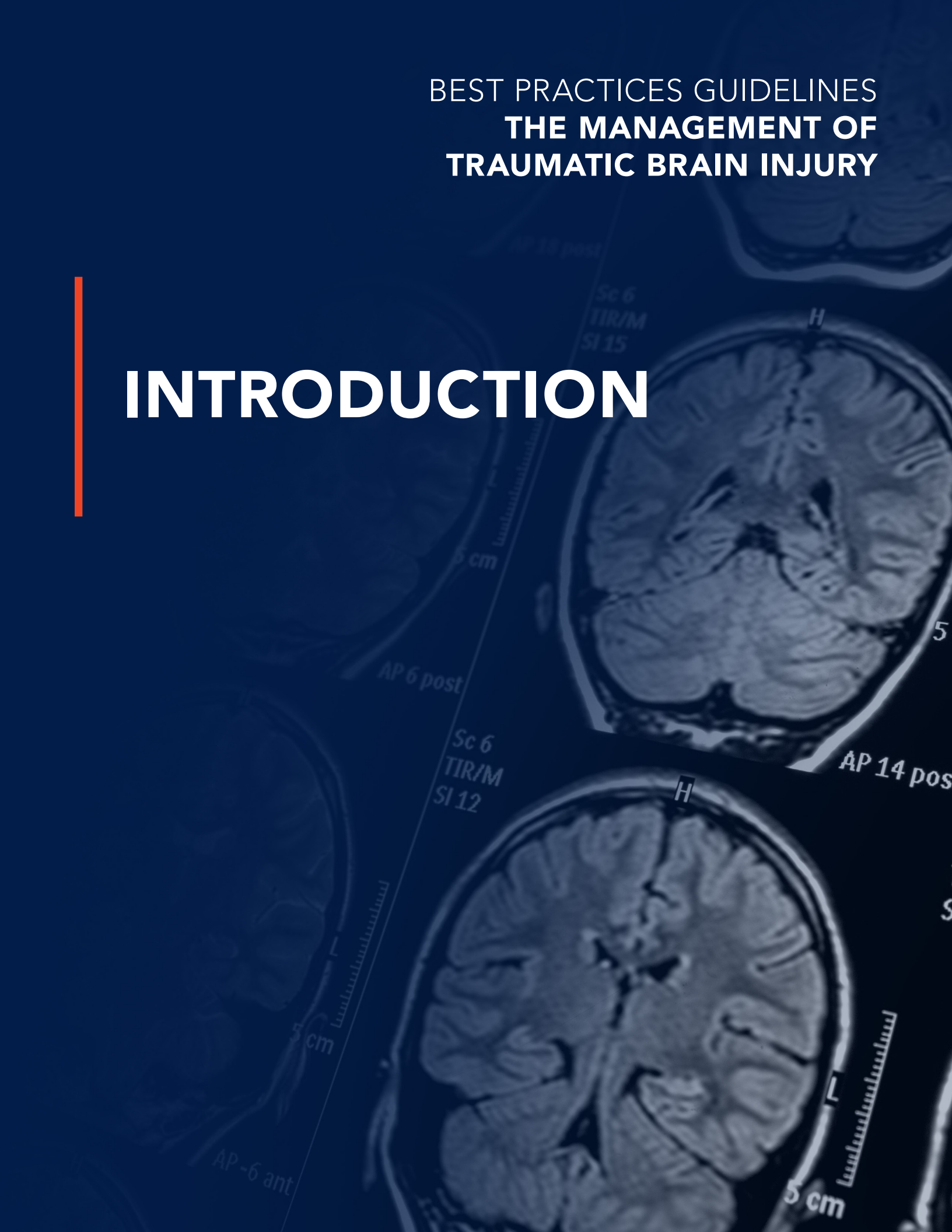

INTRODUCTION

Traumatic brain injury (TBI) is a disease process that carries major public health and socioeconomic consequences. It has the highest incidence and prevalence of all neurological disorders.[1] Annually in the United States (US), TBI is associated with an estimated 4.8 million emergency department (ED) visits, 214,000 hospitalizations, and 69,000 individuals die from TBI each year.[2,3] Moreover, a considerable proportion of TBI survivors incur temporary or permanent disability. Globally, it is estimated that 50 to 60 million people experience a TBI each year, costing the global economy the equivalent of 400 billion US dollars.[2] TBI is increasingly viewed as both an acute condition and a chronic disease with long-term consequences that require ongoing follow-up and management.[4]

Evidence-based guidelines for TBI management are compiled, but a paucity of high-quality studies limits the strength and scope of their counsel. The American College of Surgeons (ACS) Trauma Quality Improvement Program (TQIP) published the first *Best Practices in the Management of Traumatic Brain Injury* in 2015. It presented recommendations regarding care of patients with TBI, based on the best available evidence at that time, as well as expert panel consensus opinion when evidence was lacking.[5]

The introduction and dissemination of the 2015 *ACS TQIP Best Practices in the Management of Traumatic Brain Injury* resulted in treatment improvement for some areas of TBI care. For example, prophylaxis for deep vein thrombosis at trauma centers participating in the ACS TQIP increased from 48% in 2014 to 71% in 2022 for TBI patients.[6] However, many other aspects of TBI management still need improvement. The care of the neurotrauma patient is an important and demanding task that requires a dedicated and coordinated multidisciplinary team from the time of injury, during acute care, and throughout postacute care and recovery.

The revised *ACS Trauma Quality Programs (TQP) Best Practices Guidelines for the Management of Traumatic Brain Injury* includes new evidence and novel insights. An international multidisciplinary panel composed of widely recognized experts in all aspects of TBI care was assembled. Revisions include renaming and expansion of some sections, as well as the addition of the following new sections: imaging, blood-based biomarkers, pharmacologic management, rehabilitation, and systems of postacute care. The aim is to present a comprehensive but practical guide for the management of patients with TBI. Best practices can improve standards of care as well as patient outcomes.

IMPORTANT NOTE

The intent of the ACS TQP Best Practices Guidelines (BPGs) is to provide healthcare professionals with evidence-based information regarding care of the trauma patient. The BPGs do not include all potential options for prevention, diagnosis, and treatment, and they are not intended as a substitute for the provider's clinical judgment and experience. Responsible providers must make all treatment decisions based upon their independent judgment and the patient's individual clinical presentation. Although these BPGs have been reviewed with significant care, they are provided as is and without liability. The ACS and any entities endorsing the guidelines shall not be liable for any direct, indirect, special, incidental, or consequential damages related to the use or misuse of the information contained herein. The ACS may modify the TQP BPGs at any time without notice.

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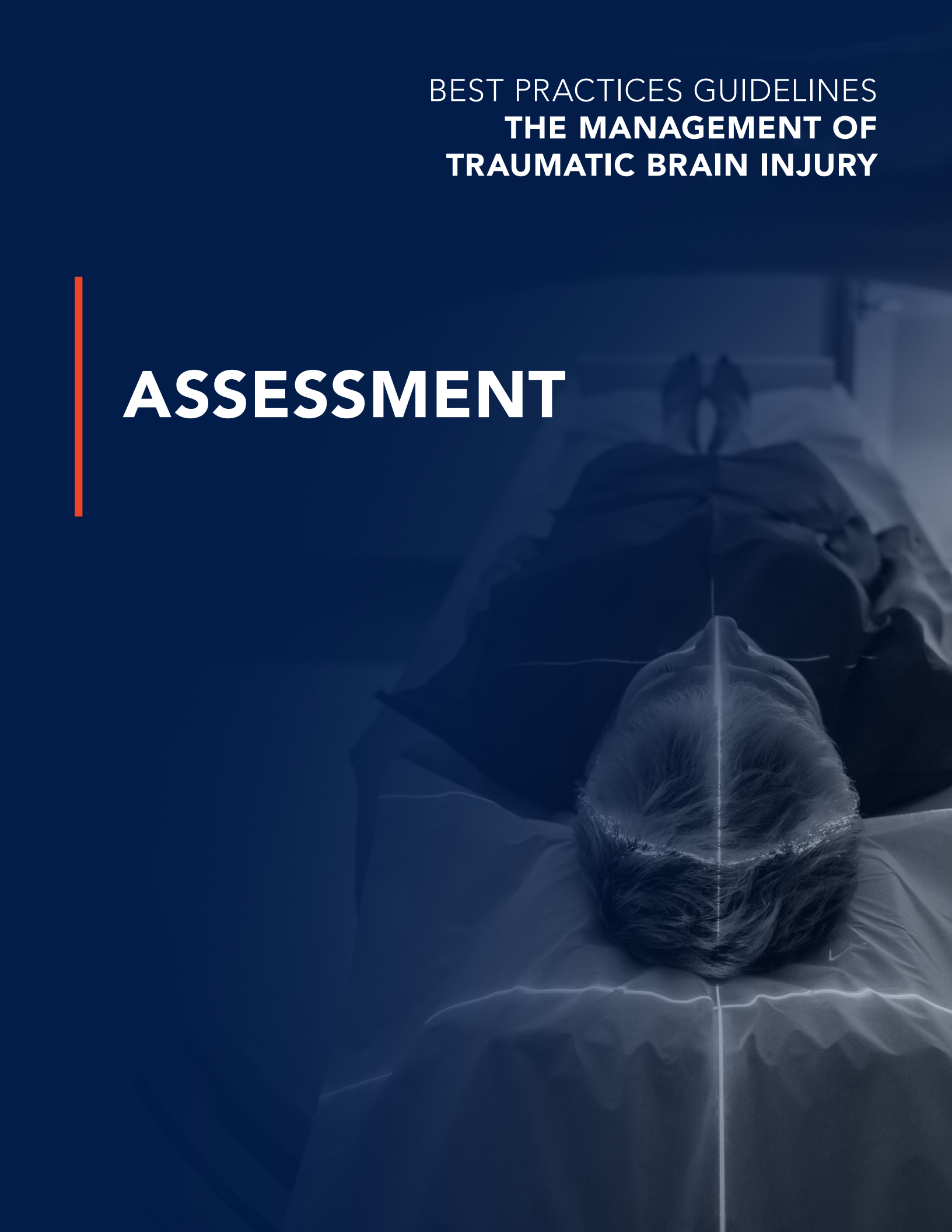
BEST PRACTICES GUIDELINES
THE MANAGEMENT OF TRAUMATIC BRAIN INJURY

ASSESSMENT



TRIAGE AND TRANSPORT

KEY POINTS

- Rapidly transport adult and pediatric patients with suspected TBI who meet any high-risk criteria from the scene to the highest-level trauma center available.
- During transport, monitor patients with suspected TBI for hypotension, hypoxia, hypercarbia, and hypothermia, and begin corrective actions.

Proper field triage is critical for adult and pediatric patients with suspected TBI. Trauma patients with TBI can require rapid resuscitation, surgical intervention, and critical care management to prevent secondary brain injury. Refer to the ACS National Guideline for the Field Triage of Injured Patients.[1] Emergency medical services clinicians are directed to transport all patients to the highest-level trauma center when TBI is suspected and any of the following high-risk criteria are present:

- Glasgow Coma Scale (GCS) motor score < 6
- GCS total score < 13
- Skull deformity or suspected skull fracture
- Signs of basilar skull fracture
- Penetrating head injury
- Caregiver report of baseline behavior change in an infant/child following injury

Within the geographic constraints of the regional trauma system, trauma centers provide the expertise, personnel, and facilities to rapidly deliver definitive care for patients with TBI. Suspect TBI for all trauma patients with an altered mental state, who are "found down," or with any neurologic signs and symptoms following a high-energy impact mechanism of injury or any reported head impact. Have a high index of suspicion for TBI in young children (age < 5 years) or older adults (age > 65 years) with significant head impact following a low-level fall or concern for nonaccidental trauma. Preferentially triage children to pediatric-capable centers.

Closely monitor patients in the prehospital setting with appropriate equipment to assess blood pressure, pulse oximetry, end-tidal CO_2, and temperature. Perform frequent serial assessments of the GCS, and note changes. It is important to document and communicate the individual components of the GCS, especially the motor score.

Providing initial resuscitative care in hospitals without neurosurgical care may occasionally be rationalized in rural settings with long transport times. However, these hospitals need predefined air/ground transfer protocols and agreements in place to provide for the immediate transfer of patients to a center that has the continuous availability of resources and expertise to care for all aspects of TBI. This is critical for patients with an abnormal neurological exam, displaced skull fracture, or significant intracranial injury such as a large subdural hematoma (SDH), epidural hematoma (EDH), intraparenchymal hemorrhage (IPH), or intraventricular hemorrhage (IVH).

Older Adult Considerations

The Centers for Disease Control and Prevention (CDC) recommends that injured older adults be triaged to trauma centers when possible. Factors that can affect prehospital triage accuracy with older adults include the following: major trauma resulting from low-energy impact mechanisms (low-level falls) not captured by the current triage tools, polypharmacy, age-related physiological responses to injuries, frailty, and anticoagulant and antiplatelet medication use. Comorbidities that may also be factors in prehospital triage accuracy include dementia, cerebral atrophy permitting accumulation of (initially) asymptomatic traumatic hemorrhage, co-occurring stroke or syncope (which may have preceded head trauma), and presence of other chronic organ insufficiencies.[2,3]

Pediatric Considerations

Pediatric patients with presumed clinically important injuries are, ideally, transported to a pediatric trauma center or other trauma center with pediatric capabilities. Transfer to pediatric trauma centers may be unnecessary for a subset of pediatric patients with the following low-risk injuries:

- Low-energy blunt trauma
- No concern for nonaccidental mechanism
- Low risk based on pediatric minor head injury computed tomography (CT) guidelines published by the Pediatric Emergency Care Applied Research Network (PECARN)[4]
- Negative imaging
- Imaging with isolated, nondisplaced skull fractures without other intracranial injuries

Note: The development of pediatric-specific guidelines is a vital component of pediatric care. For additional guidance on pediatric prehospital and interfacility tool kits, visit the website of the United States Health Resources and Services Administration (HRSA) Emergency Medical Services for Children program: https://emscimprovement.center/education-and-resources/toolkits/.

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BASIC ASSESSMENT

KEY POINTS

- The GCS provides for the reliable assessment of level of consciousness. It requires a standardized assessment and reporting approach to assure reliability, accurate patient status communication between healthcare providers, and recording of changes over time.
- Assess and report each of the three GCS components (eye, verbal, and motor) for individual patients. Use GCS sum scores (e.g., 3–15) for patient group-level comparisons and injury classification.
- The pupillary light response provides diagnostic and prognostic information in patients with TBI.
- Quantitative pupillometry is a useful tool that provides more reliable and reproducible measurements than standard clinical assessment of pupillary reactivity.

Basic assessment of a patient with TBI in the ED and hospital is essential to prioritize diagnostic and therapeutic interventions and to allow appropriate detection of changes in the patient's clinical condition. This assessment may prompt repeat CT, therapeutic interventions, and other strategies to lessen secondary brain injury.

In the ED, initial assessment follows the principles of the Advanced Trauma Life Support® (ATLS®) program and includes a brief evaluation of level of consciousness (via GCS), pupillary reactivity, and signs of lateralization.[1] Dependent on treatment priorities, a more extensive neurologic examination follows, with an additional focus on the presence of scalp lacerations, signs of penetrating injury, and clinical signs of basilar or depressed skull fractures. Throughout the subsequent clinical course, the level of consciousness is monitored, with the GCS and pupillary reactivity as the main pillars of basic clinical neuromonitoring. Clinical neuromonitoring with repeat CT scanning is the main component of the Consensus-Revised Imaging and Clinical Examination (CREVICE) protocol, which is advocated for in settings in which more advanced neuromonitoring—including intracranial pressure (ICP) monitoring—is not available.[2] The vulnerability of the injured brain to physiological insults makes continued assessment and optimization of blood pressure and gas exchange critical, in addition to neurological monitoring.

Assessing the Level of Consciousness: GCS and Other Tools

The GCS is an internationally recognized tool with demonstrated reliability to assess the level of consciousness across all brain injury severity levels.[1,3,4] The GCS scores patient responses in three domains: eye, verbal, and motor. For preverbal children (0–2 years), the pediatric GCS demonstrates greater reliability.[3,5,6] See Table 1 for GCS tools. In older adults, the verbal component of the GCS may be confounded by preexisting conditions such as delirium, dementia, and aphasia. The component that is most associated with long-term outcomes is the motor score.

The GCS can be used during all phases of patient care. Adopt a standardized approach for both assessment and reporting to ensure reliable patient assessment over time and for accurate communication between healthcare professionals. Complete a baseline assessment as soon as possible, after imminent threats to life are managed.

When used in individual patients, assess and document each of the GCS component scores (e.g., Eye 4, Verbal 4, Motor 6). Each GCS component score provides complementary information with differential relevance across injury severities.[7] The eye and verbal component scores are more discriminating in patients with less severe brain injuries. For the assessment of more severe brain injuries, the motor score is more relevant. Use this sequence when assessing the GCS:

- Observe and record spontaneous patient activities and responses prior to the application of any stimulus.
- Provide verbal stimuli while observing for eye opening, verbal, or upper extremity motor responses. **Note:** Document only the reactions of the best arm, not the legs.
- Use another stimulus to elicit a response (e.g., fingertip pressure, supra-orbital pressure, trapezius pinch) if the patient has no response to verbal stimuli. Document the type of stimulus applied (i.e., central or peripheral), and then use this stimulus as a standard for future assessments.

The individual component scores of the GCS may be summed to provide a useful measure for overall injury classification, prognosis estimation (in conjunction with other factors), and patient group-level comparisons.

Table 1. Glasgow Coma Scale (GCS): Standard and Pediatric Versions

Standard Version		Pediatric Version (pGCS)	
Best Eye Response (E)		**Best Eye Response (E)**	
None	1	No eye opening	1
To pressure	2	Eye opening to pain	2
To sound	3	Eye opening to speech	3
Spontaneous	4	Eye opening spontaneously	4
Untestable	Reason:	Untestable	Reason:
Best Verbal Response (V)		**Best Verbal Response (V)**	
None	1	No verbal response	1
Sounds	2	Inconsolable, agitated	2
Words	3	Inconsistently inconsolable, moaning	3
Confused	4	Cries but consolable, inappropriate interactions	4
Oriented	5	Smiles, oriented to sounds, follows objects, interacts	5
Untestable	Reason:	Untestable	Reason:
Best Motor Response (M)		**Best Motor Response (M)**	
None	1	No motor response	1
Extension	2	Extension to pain (decerebrate response)	2
Abnormal flexion	3	Abnormal flexion to pain for an infant (decorticate response)	3
Normal flexion (withdrawal)	4	Infant withdraws from pain	4
Localizing	5	Infant withdraws from touch	5
Obeys commands	6	Infant moves spontaneously or purposefully	6
Untestable	Reason:	Untestable	Reason:

Data from: Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet*. 1974 Jul 13;2(7872):81–84. doi: 10.1016/s0140-6736(74)91639-0; Teasdale G, Maas A, Lecky F, Manley G, Stocchetti N, Murray G. The Glasgow Coma Scale at 40 years: Standing the test of time. *Lancet Neurol*. 2014 Aug;13(8):844–854. doi: 10.1016/S1474-4422(14)70120-6; Holmes JF, Palchak MJ, MacFarlane T, Kuppermann N. Performance of the pediatric Glasgow Coma Scale in children with blunt head trauma. *Acad Emerg Med*. 2005 Sep;12(9):814–819. doi: 10.1197/j.aem.2005.04.019; Borgialli DA, Mahajan P, Hoyle JD Jr, et al. Performance of the pediatric Glasgow Coma Scale score in the evaluation of children with blunt head trauma. *Acad Emerg Med*. 2016 Aug;23(8):878–884. doi: 10.1111/acem.13014.

The GCS sum score is often used to stratify degrees of brain injury: a sum score ≥ 13 correlates with mild injury, a sum score 9–12 is consistent with moderate injury, and a sum score ≤ 8 is indicative of severe brain injury. **Caution:** Recognize that injury severity classification using only the GCS sum score represents an overly simplistic and unidimensional approximation of injury load.

Posttraumatic Amnesia: Posttraumatic amnesia (PTA) is widely used as an indicator of injury severity, but it can be difficult to assess in many patients early after injury. It is a more relevant assessment for rehabilitation settings. The Full Outline of UnResponsiveness (FOUR) score[8] was developed primarily for use in patients with impaired consciousness in the intensive care unit (ICU) setting.

It includes the eye and motor components of the GCS, as well as brainstem reflexes and respiration. The verbal component of the GCS was omitted because intubation and ventilation make it untestable. Among pediatric patients, the FOUR score displays good inter-rater reliability among physicians and nurses.[8] The FOUR score provides greater neurologic detail than the GCS in patients with more severe impairments of consciousness, and it is applicable in patients with locked-in syndrome.[8] The GCS is applicable across patients of all injury severities and remains the preferred tool for general use to assess and monitor level of consciousness in the ICU.

Pupillary Reactivity and Pupillometry

The pupillary light response is an important element of the neurologic exam because it provides useful diagnostic and prognostic information. Some degree of pupillary asymmetry may be normal, but the development of new pupillary asymmetry can indicate compression of the brainstem with impending uncal herniation, triggering the need for further evaluation and intervention. In uncal herniation, the parasympathetic fibers on the surface of the third cranial nerve are compressed, leading to a slowly reactive—or eventually unreactive—pupil. A unilateral unreactive pupil is consistent with an ipsilateral mass lesion, while bilaterally fixed and dilated pupils portend a poor overall prognosis for functional recovery.

Older Adults: In older adults, evaluation of the pupillary response may be confounded by preexisting chronic ophthalmic diseases (e.g., glaucoma or cataract disease). Quantitative pupillometry may be of limited value in patients with postsurgical pupils (i.e., after cataract surgery), however, this does not influence pupillary light reflex parameters measured by automated pupillometry.[9,10] In these patients, a medical history is essential to correctly interpret physical examination findings such as an abnormal pupillary light reflex, anisocoria, or oculomotor palsy.

Quantitative Pupillometry: Both the inter-rater and intra-rater reliability of the standard clinical determination of pupillary size and reactivity are relatively poor. Quantitative pupillometers provide increased reliability and consistency of pupillary measurements.[11–13] The quantitative pupillometer is a small handheld device that uses both visible and infrared light to measure a pupil, capture its response to a light stimulus, and quantify the pupil's characteristics. It has six items measured (see Box 1). In pediatric patients, however, developmental changes in myelination during infancy can alter the normal latency observed, potentially limiting the application of a priori thresholds.[14,15]

Box 1. Output from Quantitative Pupillometer

- Starting diameter (mm)
- Ending diameter (mm)
- % Change
- Latency (s)
- Average constriction velocity (mm/s)
- Average dilation velocity (mm/s)

Clinical experience shows that quantitative pupillometry can facilitate a more accurate clinical assessment by providing an objective and reliable assessment of pupillary reactivity. Pupillary changes may be detected before a provider's clinical assessment of pupillary size and reactivity, thus providing an early warning sign. Quantitative pupillometry can assess reactivity even when opioids and other drugs result in small pupils, which make clinical assessment difficult. Moreover, the pupillometry output can be directly entered into the patient's electronic medical record.

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IMAGING

KEY POINTS

- A head CT scan is needed for adult trauma patients with an external-force injury mechanism to the head, who present with altered mental status, loss of consciousness (LOC), PTA, or focal neurologic deficit.
- Determine indications for head CT in children using a validated decision rule such as the PECARN decision guide.
- A negative head CT does not rule out a TBI.
- Magnetic resonance imaging (MRI) is more sensitive than CT for identification of traumatic intracranial injury.
- Traumatic intracranial findings on CT and MRI inform prognosis.

Initial Imaging

Head CT is the cornerstone of acute imaging in TBI because of its high sensitivity and specificity for identification of acute intracranial injury, as well as craniofacial and cervical spine fractures. A head CT can be acquired much more quickly than an MRI, with total image acquisition time < 5 seconds using modern multi-slice CT scanners, a major advantage for agitated patients, polytrauma patients, and young children.[1] Head CT without contrast also has no contraindications, unlike MRI (e.g., metallic foreign body or implant), which requires a time-consuming screening process. For head CT, axial, coronal, and sagittal images of the brain with 2.0 mm to 3.75 mm slice thickness are recommended, in addition to 0.5 mm to 1.25 mm "bone-algorithm" images to improve the visibility of craniofacial fractures.

Guidelines for Imaging

A number of guidelines and clinical decision rules provide indications for head CT in patients with suspected TBI.[2–5] The CDC/American College of Emergency Physicians (ACEP) clinical policy strikes a balance between sensitivity and specificity and recommends a non-contrast head CT in patients 16 years of age and older with LOC or PTA, if any of the following are *also* present:[2]

- GCS less than 15
- Age greater than 60 years
- Physical evidence of trauma above the clavicle
- Coagulopathy (supra-therapeutic international normalized ratio [INR] or thrombocytopenia)
- Headache
- Vomiting
- Drug or alcohol intoxication
- Short-term memory deficit
- Posttraumatic seizure
- Focal neurologic deficit

In addition, consider a head CT for patients with no LOC or PTA in the following cases: GCS less than 15, age 65 years and older, coagulopathy, focal neurologic deficit, severe headache, vomiting, physical signs of basilar skull fracture, or dangerous mechanism of injury (e.g., ejection from motor vehicle, pedestrian struck by motor vehicle, fall down five stairs or 3 feet or more).[2] Comparable guidelines are published in the sports concussion literature and contain very similar criteria.[6–8]

Older Adult Considerations

Guidance for imaging in older adult patients with suspicion of TBI is similar to that used in younger adults. The use of anticoagulants in many older patients may complicate the recommended indications for imaging. In patients who are anticoagulated, the incidence of intracranial hemorrhage (ICH) is higher; therefore, a more liberal use of early CT scanning may be appropriate.[9] Given that current guidelines also recommend imaging based on older age, blood-based biomarkers may be helpful in identifying older patients with GCS 13–15 who do not need CT imaging (refer to the Blood-Based Biomarkers section on page 15).

Pediatric Considerations

For children with acute TBI requiring emergent imaging, CT is often the first choice because it is rapid, widely available, and might not require sedation. However, use CT judiciously, due to the greater vulnerability of children to radiation-induced malignancy.[10,11] In order to mitigate the risks of radiation to the developing brain, some trauma centers are performing rapid MRI as first-line imaging in nonsedated infants and young children.[11–13] Regardless

of which imaging methodology is used, indications for emergent head imaging in children need to follow a validated pediatric decision rule such as the PECARN decision guide. For select pediatric patients with GCS 15, no palpable skull fracture, and no findings concerning for basilar skull fracture, a brief period of observation (4 to 6 hours) may obviate the need for neuroimaging, even in the presence of 1 or 2 PECARN predictors of clinically important TBI.[14] *See also* https://www.cdc.gov/traumatic-brain-injury/hcp/clinical-guidance/?CDC_AAref_Val=https://www.cdc.gov/traumaticbraininjury/PediatricmTBIGuideline.html.

CT and the Incidence and Prognostic Implications of Intracranial Injury

The incidence of intracranial injury found on initial head CT increases as GCS score decreases. More than 80% of patients with GCS 3–12 have evidence of intracranial injury.[15] The Rotterdam CT score uses traumatic intracranial CT imaging features (basal cistern effacement, midline shift, EDH, IVH, and subarachnoid hemorrhage) to determine a score (1 to 6) that is predictive of 6-month mortality related to TBI in patients with GCS 3–12. While the incidence of CT abnormalities in patients with GCS 13–15 is lower, certain features such as subarachnoid hemorrhage, contusion, and SDH are associated with incomplete recovery, and IVH and/or petechial hemorrhage are associated with more severe impairment.[16]

Clinical Role of MRI

MRI has superior sensitivity relative to CT for most acute intracranial findings, including small brain contusions, small extra-axial hematomas,[17,18] and microhemorrhages and small white-matter lesions that represent acute traumatic axonal and/or microvascular injury. Several studies reported that more than 25% of patients with TBI presenting to Level 1 trauma centers with a negative initial head CT are determined to have intracranial injuries upon brain MRI.[17] Thus, a negative initial head CT does not rule out a TBI. The injuries identified on MRI predict disability in TBI.[17,18] In current clinical practice, brain MRI is used mainly for investigation of persistent concerns (e.g., unexplained alteration in consciousness in acute TBI, management of subacute TBI with persistent symptoms or deficits, and identification of intracranial injuries not detected by CT).

Include the following in the brain MRI protocol: T1, T2, T2 fluid-attenuated inversion recovery, diffusion-weighted imaging/apparent diffusion coefficient, susceptibility-weighted imaging (SWI) or, if unavailable, conventional T2*-weighted gradient echo. SWI and T2*-weighted gradient echo sequences are very sensitive to blood products and greatly enhance the visibility of microhemorrhages that are often occult on CT.

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BLOOD-BASED BIOMARKERS

KEY POINTS

- Brain injury biomarkers such as glial fibrillary acidic protein (GFAP), ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), and S100 calcium-binding protein (S100B) can be used to rule out the need for brain CT imaging for patients with suspected TBI who meet the following criteria:
  - GCS of 13–15
  - Clinical criteria for brain CT imaging based on brain CT imaging decision rules
  - The clinician assesses a low but nonzero risk for traumatic ICH
- The extent of GFAP, UCH-L1, and S100B elevation on the day of injury provides clinicians with an estimate of the underlying structural brain injury severity. These blood levels are also useful as adjuncts for predicting functional recovery at 6 months postinjury in patients with GCS 3–12 associated with TBI.

Characterizing and quantifying the severity of structural brain injury in acute TBI is critically important to inform treatment strategies and guide discussions about the patient's expected prognosis. Until recently, the primary diagnostic resource for characterizing the severity of structural brain injury in acute TBI was the non-contrast brain CT scan. Brain CT is excellent for visualizing vascular structure injury, brain tissue edema, and the effect of injury on brain tissue deformation. Thus, the acute brain CT scan is key to identifying TBI patients requiring surgical management. However, the brain CT is limited in its ability to quantify injury to neurons and glial cells. As a result, a significant proportion of patients with a negative brain CT have persistent and debilitating neurologic and psychiatric symptoms that may persist for prolonged periods. Additionally, the diagnostic yield of brain CT scans is low. In the US, approximately 90% of the brain CTs performed each year during the acute evaluation for TBI are negative.[1] These patients are exposed to avoidable ionizing radiation, and the healthcare system absorbs increased cost and prolonged ED length of stay (LOS).

Biomarkers and Imaging Decisions

Two blood-based protein biomarkers, GFAP and UCH-L1, can be measured in patients (18 years or older) with a potential TBI to help rule out the need for a brain CT scan.[2] Recently, the US Food and Drug Administration (FDA) authorized devices for the rapid measurement of GFAP and UCH-L1 for routine clinical use.[3,4] These include a point-of-care device that can analyze blood samples collected by venipuncture and deliver test results in as little as 15 minutes, as well as a lab-based test that offers results in 18 minutes. Other devices with FDA clearance are expected in the near future.

S100B: S100B is a calcium-binding protein primarily found in glial cells. It is the most extensively studied brain injury biomarker for aiding in decision-making regarding brain CT imaging in patients evaluated for TBI. Similar to GFAP it is released into circulation following glial cell injury. It has excellent diagnostic sensitivity for identifying patients likely to have a positive CT, however, given its short half-life, it is recommended to use this biomarker only when blood sampling can be performed within 6 hours of injury.[5] S100B is not FDA-cleared for routine clinical use in the US; however, it was incorporated into the Scandinavian guidelines for brain CT imaging in 2013.

The Scandinavian guidelines recommend using S100B analysis in adult patients with mild head injury meeting the following criteria[6]:

- Less than 6 hours have elapsed following trauma, and
- **EITHER** GCS 14 and no risk factors (such as anticoagulant therapy or coagulation disorders, posttraumatic seizures, clinical signs of depressed or basal skull fracture, and focal neurological deficits)
- **OR** GCS 15 with LOC or repeated vomiting (≥ 2) and no other risk factors.

If S100B is less than 0.10 mcg/L, the patient may be discharged without a brain CT.[6]

GFAP and UCH-L1: GFAP is an intermediate filament protein found predominantly in astrocytes, and UCH-L1 is an enzyme that neurons express in high abundance. These proteins are released into circulation when astrocytes and neurons are injured. UCH-L1 is detectable in blood within 30 minutes of injury, peaks within 8 hours postinjury, and then decreases steadily. GFAP is released within 1 hour of

injury, peaks at about 20 hours postinjury, and decreases subsequently. Prospective observational data from at least three large, multicenter studies (representing > 6,000 patients in the US and Europe) demonstrated that the combination of day-of-injury GFAP and UCH-L1 values have an excellent negative predictive value for ruling out traumatic ICH (see Table 2).[7-10]

Table 2. Summary of Observational Data from Prospective Studies

1st Author	Assay	Cutoff	AUC	N (%pos)	Sensitivity	Specificity	PPV	NPV
Bazarian[7]	Banyan	GFAP = 22 pg/mL UCH-L1 = 327 pg/mL	Not available	1977 (66%)	97.6%	36.4%	9.5%	99.6%
Bazarian[8]	iSTAT	GFAP = 30 pg/mL UCH-L1 = 360 pg/mL	Not available	1936 (62%)	95.8%	40.4%	9.8%	99.3%
Okonkwo[9]	iSTAT	GFAP = 37.8 pg/mL	0.85 (0.83–0.87)	1359 (78%)	96.4%	30.3%	38.9%	94.9%
Czeiter[10]	SIMOA	Not available	0.89 (0.87–0.90)	2867	No cutoffs examined.			

Key: AUC =area under to ROC curve; PPV = positive predictive value; NPV = negative predictive value.

For the FDA-approved iSTAT assay, GFAP values less than 30 pg/mL and UCH-L1 values less than 360 pg/mL are considered not elevated, ruling out the need for a brain CT. If either biomarker exceeds its cutoff value (i.e., an elevated test), a brain CT is indicated. However, an elevated test does not definitively indicate a brain CT will be positive. A brain CT may be negative even in cases where structural brain injury is present, as some injuries might only be detectable on a brain MRI.[11] Current FDA clearance requires measurement of these biomarkers on whole blood within 24 hours of injury. GFAP levels also add incremental diagnostic information to existing head CT decision rules that leverage clinical data.[10]

Biomarkers and Functional Recovery

Biomarker blood levels can inform the prediction of a patient's functional recovery.[12-14] Higher biomarker levels are associated with worse structural brain injury and portend a worse prognosis. One study compared patients with day-of-injury iSTAT GFAP values < 1200 pg/mL to those with values > 12,000 pg/mL; patients with values > 12,000 pg/mL had a 6.98 times higher risk of mortality within 6 months.[12] Similarly, patients with day-of-injury iSTAT UCH-L1 values > 2000 pg/mL were reported to have a 22.38 times higher risk of mortality within 6 months, compared to patients with day-of-injury iSTAT UCH-L1 values < 360 pg/mL.[12] The majority of these patient deaths occurred during the first month postinjury. Among patients with GCS 3–12 TBI, these biomarkers also have a high discriminative ability for distinguishing between patients more likely to function independently outside the home (Glasgow Outcome Scale-Extended [GOS-E] > 4) versus those who are not (C-statistic 0.89; 95% confidence interval [CI] 0.86–0.91).[12]

Note: These biomarkers alone do not predict functional recovery in GCS 13–15 TBI with sufficient accuracy. However, GCS 15 patients with significantly elevated GFAP and/or UCH-L1 levels are at risk for protracted recovery and warrant referral to a brain injury/concussion clinic for further management. Patients with nonelevated GFAP and UCH-L1 values may also be at risk for protracted recovery, though their risk is much lower than patients with elevated GFAP and/or UCH-L1. Therefore, counsel these patients with recommendations to seek care if they have persistent symptoms.

Older Adult Considerations

Increasing age and age-related neurodegenerative disease (e.g., Alzheimer's disease and related dementias) are associated with higher baseline levels of brain injury biomarkers, including GFAP and UCH-L1.[15-17] This results in a smaller range within which acute brain injury may be discriminated. It raises the possibility that age- and/or comorbidity-specific cutoff values may be useful for reducing unnecessary head CTs in older adults, as demonstrated for S100B (measured within 3 hours of injury).[17] Several large cohort studies investigated sensitivity and specificity of plasma GFAP and UCH-L1 assays, and/or S100B assays, in older adult TBI.[17-19] Studies pertaining to FDA-approved GFAP and UCH-L1 assays are summarized in Table 3.[17,19]

Pediatric Considerations

Current research suggests that blood biomarkers are associated with intracranial injury in children. However, insufficient data exist regarding the utility of GFAP, UCH-L1, or S100B measurements in pediatric patients with suspected TBI. At this time, clinical decision rules guiding the use of CT neuroimaging, such as the PECARN rule, are the best tools available to aid in the evaluation of TBI in children following head injury.[20-22]

Table 3. Diagnostic Accuracy of Blood GFAP and UCH-L1 Assays among Older Adults (> 65 Years Old) for Discriminating CT-positive from CT-negative TBI on the Day of Injury

1st Author	Assay	Cutoff	AUC	N (%pos)	Sensitivity	Specificity	PPV	NPV
Ward[19]	Banyan Brain Trauma Indicator (< 12 h postinjury)	GFAP 22 pg/mL UCH-L1 327 pg/mL	Not available	504 (9%)	100% (< 12 h)	13% (< 12 h)	10% (< 12 h)	100% (< 12 h)
Gardner [17]	iSTAT GFAP (< 24 h postinjury)	30 pg/mL	0.84 (0.78–0.89)	240 (71%)	100% (< 24 h)	10% (< 24 h)	73% (< 24 h)	100% (< 24 h)
Gardner [17]	iSTAT UCH-L1 (< 24 h postinjury)	360 pg/mL	0.56 (< 24 h) Subgroups: 0.68 (< 6 h) 0.60 (7–12 h)	240 (71%) Subgroups: N(%) not available	37% (< 24 h) Subgroups: 63% (< 6 h) 43% (7–12 h)	71% (< 24 h) Subgroups: 58% (< 6 h) 69% (7–12 h)	76% (< 24 h) Subgroups: 39% (< 6 h) 75% (7–12 h)	31% (< 24 h) Subgroups: 79% (< 6 h) 36% (7–12 h)

Key: AUC =area under to ROC curve; PPV = positive predictive value; NPV = negative predictive value.

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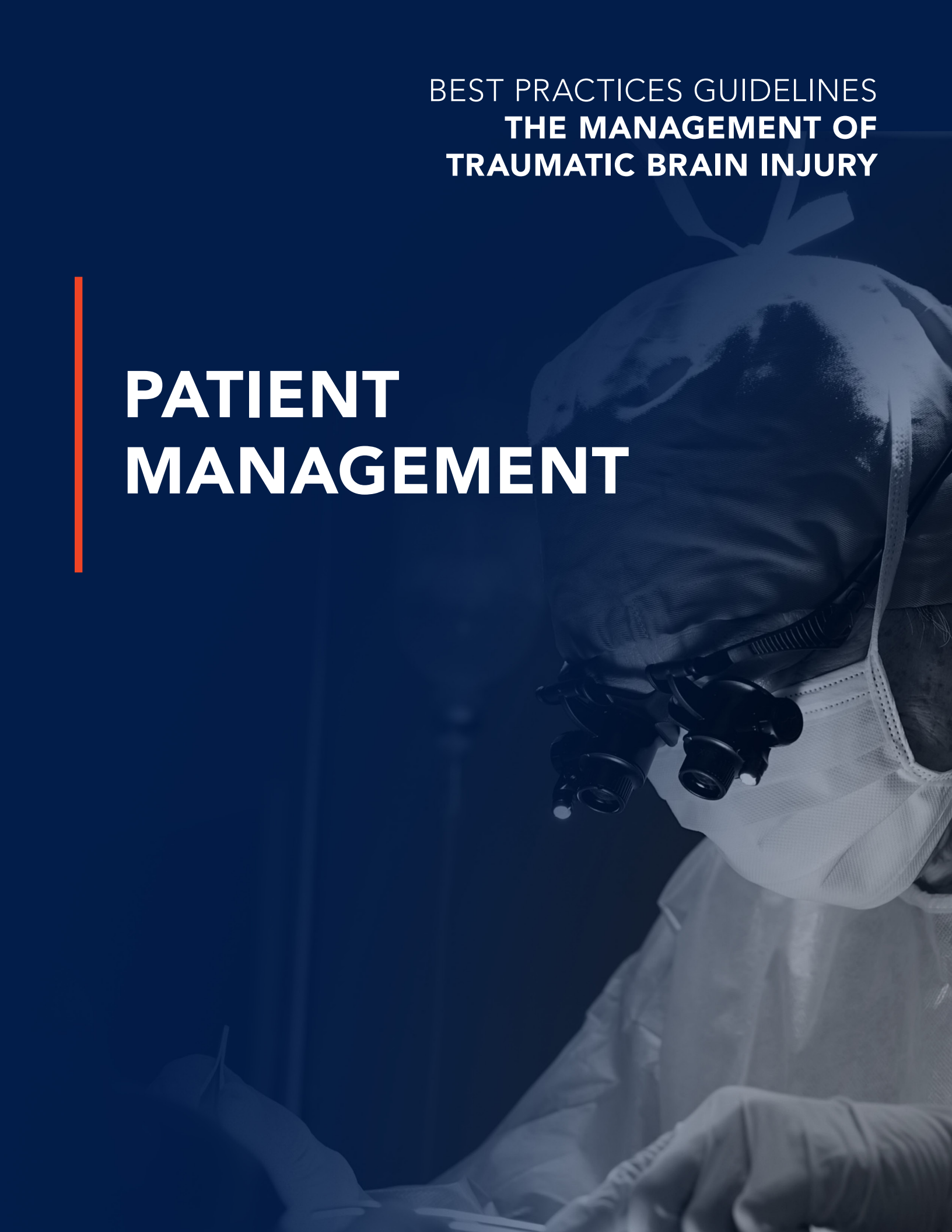
BEST PRACTICES GUIDELINES
THE MANAGEMENT OF TRAUMATIC BRAIN INJURY

PATIENT MANAGEMENT



GOALS OF DIRECTED CARE

KEY POINT

- Ideally, it is recommended to keep clinical parameters within normal physiologic ranges for patients with TBI, after considering potential risks and benefits of intervention.

A cornerstone of effective goal-directed treatment for TBI is aiming to maintain clinical parameters within normal physiological ranges. Some of these parameters are more relevant for patients in the ICU setting—such as cerebral perfusion pressure (CPP), ICP, and partial brain tissue oxygenation ($PbtO_2$)—while others, such as oxygen saturation (SpO_2), are applicable to all patients. Interventions to achieve desired parameters are best provided within the overall context of the patient's condition. When achieving clinical parameter goals require intensive therapy, carefully consider the potential risks and benefits of each intervention. The recommended parameters for goal-directed treatment in Table 4 represent ideal ranges rather than mandatory, at-all-costs goals for all scenarios.

Table 4. Goals of Treatment Recommended Parameters

Parameter	Goal Range
Pulse oximetry	≥ 94%
PaO_2	80–100 mm Hg
$PaCO_2$	35–45 mm Hg
Systolic blood pressure	≥ 110 mm Hg
ICP	< 22 mm Hg
$PbtO_2$	≥ 15 mm Hg
CPP*	60–70 mm Hg
Serum sodium	135–145 mEq/L
Serum osmolality	≤ 320 mOsm
INR	≤ 1.4
Temperature	36.0–37.9°C
Platelets	≥ $75 \times 10^3/mm^3$
pH	7.35–7.45
Glucose	100–180 mg/dL
Hemoglobin	≥ 7 g/dL

*Depending on status of cerebral autoregulation
Key: PaO_2: partial pressure of oxygen; $PaCO_2$: partial pressure of carbon dioxide; ICP: intracranial pressure; $PbtO_2$: partial brain tissue oxygenation; CPP: cerebral perfusion pressure; INR: international normalized ratio.

An ICP of 22 mm Hg is a useful initial threshold for treatment. However, when the risk/benefit of advancing treatment becomes a concern, such as for therapy with significant hazards (e.g., decompressive craniectomy), consider a treatment range of 20–25 mm Hg. A CPP of ≥ 60 mm Hg is a practical target, adjusted as needed, based on cerebral autoregulation status. A $PbtO_2$ value of ≥ 15 mm Hg is recommended, if monitored.

Initial oxygenation targets include SpO_2 ≥ 94% and PaO_2 of 80–100 mm Hg. Given concerns about the hazards of hyperoxia, avoid PaO_2 > 100 mm Hg, unless guided by brain oximetry. $PaCO_2$ of 35–45 mm Hg and pH of 7.35–7.45 are recommended initial targets in the absence of intracranial hypertension. Patients with significant pulmonary issues (e.g., acute respiratory distress syndrome) may require lung-specific targets, such as permissive hypercapnia, based on their clinical condition while controlling ICP elevation using other interventions.

Vital Signs

Closely monitor systolic blood pressure (SBP) and mean arterial pressure (MAP) to avoid hypotension. Providing treatment targeting SBP ≥ 110 mm Hg/MAP > 80 mm Hg will allow adequate cerebral perfusion in most cases when ICP is not being monitored.[1] While no clear cutoff exists for blood pressure, the probability of mortality increases linearly with every 10-point drop of SBP below 119 mm Hg in patients with TBI, suggesting that higher targets may be indicated than previously recognized.[2]

The target for temperature management is maintenance of normothermia (36–37.9°C). Treat fever aggressively.

Electrolyte Management

Electrolyte management is essential, with specific emphasis on maintaining sodium levels within the range of 135–145 mEq/L. Preventing hyponatremia is critical to avoid exacerbation of cerebral edema. Frequent monitoring of serum sodium levels may be necessary, because TBI patients can develop conditions such as diabetes insipidus or the syndrome of inappropriate antidiuretic hormone / cerebral salt wasting syndrome. Measure osmolality when mannitol is used as an osmotic agent.

Hyperglycemia and hypoglycemia may each have detrimental effects on patient outcomes. Closely monitor serum glucose levels, with a target range of 100–180 mg/dL. More frequent monitoring may be appropriate upon initiation of nutritional support, particularly in patients with confirmed or suspected diabetes mellitus.

Hematology Monitoring

Hematology monitoring is essential in patients with TBI. Although recommendations for hemoglobin transfusion thresholds vary somewhat, the current literature and expert consensus suggest a transfusion threshold of ≥ 7 g/dL.[3,4]

Early evaluation for coagulopathy is important for patients with TBI. Assessment of direct and indirect coagulation cascades using INR is essential (a target INR ≤ 1.4 is appropriate in most cases). Utilization of thromboelastography (TEG), rotational thromboelastometry (ROTEM), and platelet function assays may provide additional information regarding the need for targeted therapy to reverse coagulopathy.

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INTRACRANIAL PRESSURE MONITORING

KEY POINTS

- ICP monitoring is important, but it does not replace careful serial neurological and radiographic examination of the patient with TBI.
- ICP monitoring is recommended in comatose patients (GCS ≤ 8) when evidence of structural brain damage is seen on initial CT imaging.
- The gold standard for ICP measurement is an external ventricular drain (EVD) attached to an external strain-gauge transducer, as this has both diagnostic and therapeutic value. An intraparenchymal transducer can also be used to monitor ICP.
- For pediatric patients, ICP monitoring by an EVD or an intraparenchymal transducer may result in similar clinical outcomes. Technical reasons to choose an intraparenchymal transducer may exist in specific cases, although an EVD may facilitate a lower ICP.
- For pediatric patients, the ICP target (the normal range of ICP, as a contributor to CPP) is lower than in adults. An upper limit of 20 mm Hg is recommended for children based on retrospective evidence, as outcomes were not improved by other limits.

Persistently elevated ICP is predictive of poor outcome. ICP monitoring is important because CPP, an important marker of cerebral blood flow (CBF), is derived from ICP (MAP – ICP = CPP). Augmenting the CPP can help restore cerebral perfusion and oxygen delivery. ICP monitoring can also provide warning of impending structural brain derangements (e.g., contusion/hematoma progression, increased cerebral edema, and postoperative complications).

ICP monitoring is recommended in comatose patients (GCS ≤ 8) if evidence of structural brain damage is seen on initial CT imaging. ICP monitoring should be carefully considered for other patients:

- Patients with a GCS > 8 who have structural brain damage and high risk for progression (e.g., large/multiple contusions)
- Patients with a GCS > 8 when knowing the ICP might facilitate management of other issues (e.g., allowing earlier surgery for orthopaedic injuries or application of treatments that can potentially increase ICP like prone positioning for acute respiratory failure)
- Patients with evidence of pathology progression on CT imaging or clinical deterioration
- Patients who require urgent surgery for extracranial injuries or sedation to facilitate mechanical ventilation because of airway compromise or respiratory failure.

ICP monitoring is generally not indicated in comatose patients without evidence of structural brain damage or of elevated ICP on initial CT imaging (e.g., compressed or absent basal cisterns). These patients may continue to be observed without ICP monitoring by neurological exams and serial CT imaging.

ICP Monitoring Role in Patient Management

Identification of elevated ICP can prompt further imaging, pharmacologic intervention, and definitive operative management. Knowing that ICP elevation is absent can also allow for de-escalation of care (e.g., early surgery for extracranial injuries, decreasing sedation, extubation, etc.). When instituted, it is important to continue ICP monitoring for patients transported out of the ICU for extracranial surgery, imaging, or special procedures.

ICP monitoring remains a critical component in the management of severe TBI. However, studies highlight the need to better define how ICP monitoring is used in the treatment of TBI. In the largest study of ICP monitoring to date, observational data from hospitals participating in the ACS TQIP demonstrated that use of ICP monitoring was associated with lower in-hospital mortality.[1] Worldwide, the use of ICP monitoring and management varies greatly across hospitals and countries. A large, international, prospective observational cohort study of ICP monitoring (SYNAPSE-ICU) demonstrated that ICP monitoring is associated with a more intensive therapeutic approach and with lower 6-month mortality in more severe cases.[2] Intracranial hypertension treatment guided by monitoring might be considered in severe TBI due to the potential associated improvement in long-term clinical results.

A South American randomized controlled trial (RCT) compared patient treatment using ICP monitoring to maintain ICP ≤ 20 mm Hg to patient treatment based upon imaging and neurological examination.[3] Although no difference in outcomes was found between the study groups, the result did not support discontinuation of ICP monitoring in the treatment of TBI. Rather, it demonstrated the importance of aggressive treatment using ICP monitoring or, alternatively, frequent clinical and radiographic examination to identify intracranial hypertension.[4] The findings of this study also challenge the currently accepted rigid ICP alert threshold used for all patients. The currently accepted alert threshold is an ICP of 22 mm Hg, with a reasonable range of 20–25 mm Hg for more than 5 minutes, as a trigger for treatment of intracranial hypertension; however, ongoing research suggests that this threshold is dependent upon individual patient factors such as injury type and severity. The ICP "dose," reflecting both the magnitude and time of exposure to intracranial hypertension, might be more important than a fixed ICP treatment threshold. Higher ICP dose is associated with worse outcomes over the entire Glasgow Outcome Scale (GOS) range, not only mortality.[5]

Escalation of treatment for intracranial hypertension needs to be based on both the level and duration of ICP elevation. For example, the threshold for proceeding to higher-tier therapies such as decompressive craniectomy needs to be at a higher ICP threshold, or "dose," as demonstrated by the RESCUE-ICP trial.[6] A trend over time is more relevant than a momentary ICP value. Differentiate a gradual rise of ICP from short-term elevations due to events such as ventilator dyssynchrony or plateau waves. Interpret measured values of ICP in relation to arterial blood pressure, CPP, and autoregulatory responses (see the Neuromonitoring section on page 29). A clinical approach based on injury type and augmented by advanced neuromonitoring may lead to individualized treatment pathways.

The gold standard for ICP measurement is an EVD attached to an external strain-gauge transducer. The monitor, centrally placed within the cerebral ventricles, can measure global ICP, and it offers the therapeutic advantage of draining cerebrospinal fluid (CSF) to reduce intracranial volume. Intraparenchymal ICP monitoring is also a reliable method, but it does not allow for CSF drainage. Subdural and epidural monitors have been used, but these are not recommended due to lower accuracy.

Older Adult Considerations

Despite recommendations for ICP monitoring in patients with severe TBI, the above recommendations may not always be applicable to older adults. Older adult patients have cerebral atrophy and may generally be at lower risk of intracranial hypertension. A few studies have specifically investigated the use of ICP monitoring in older adult patients with TBI. ICP monitoring rates in older adult patients range from 5% to 44%, depending on the population studied.[7,8] Some observational studies on severe TBI reported lower mortality in patients older than 65 years who received ICP monitoring, while other studies concluded that ICP monitoring was associated with an unfavorable outcome (severe disability, vegetative, or death) in older adult patients.[9-13] In a recent large observational study, the overall utilization of ICP monitoring in older adults meeting the Brain Trauma Foundation (BTF) criteria remained low across high-volume trauma centers. A mortality or functional benefit to ICP monitoring in older adults remains to be elucidated.[14]

Pediatric Considerations

Pediatric consensus guidelines based on aggregate retrospective data suggest utility in monitoring ICP in children with severe TBI. Although limited pediatric studies report no improvement in functional survival or even showed increased morbidity and mortality, these studies were unable to control for critical differences between the groups with and without ICP monitoring. Recent retrospective data suggest that, compared to an EVD, an intraparenchymal pressure transducer may achieve similar long-term outcome measures. However, the therapeutic benefit of an EVD may contribute to slightly lower ICP during acute management.[15] These data suggest that the choice of ICP monitoring technique should include consideration of the different risks and relative advantages of the two techniques relevant to the clinical scenario, such as age and other factors.

Normal CBF has age-dependent variability related to metabolic changes during different stages of brain development. Depending on the child's age, this variability affects the relationship between cerebrovascular autoregulation, ICP, SBP, and CPP. Age-appropriate MAP, and therefore CPP, is lower in children than in adults. A

narrower window of appropriate CPP and ICP may exist in children as compared to adults. CPP goals above 50 mm Hg for patients aged 6 to 17 years, and above 40 mm Hg in children aged 0 to 5 years, seem to be appropriate targets for treatment-based studies.[16] Studies in ICP targets among children may be limited by the use of 20 mm Hg as a priori target for treatments. Current literature does not report improved outcomes among children with specific ICP targets lower than 20 mm Hg, and further research is needed.

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TIERED MANAGEMENT OF INTRACRANIAL PRESSURE

KEY POINTS

- ICP elevation is a key measurable secondary insult that providers must treat to prevent secondary brain damage following severe TBI.
- Rigorous, consensus-based algorithms, such as those from the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC), augment evidence-based guidelines by addressing gaps between the available evidence and necessities of patient care.
- The SIBICC algorithms employ a three-tiered approach to therapy in which interventions with more favorable risk-benefit ratios generally are used before interventions with less favorable ratios. The tiered approach retains medical decision-making within tiers and supports targeting interventions at specific physiological disruptions, where suspected.
- Although derived through a rigorous, consensus-based process, view the SIBICC algorithms as recommendations that offer the benefits inherent to care standardization. Do not consider the SIBICC algorithms as standards of practice. Optimally, these algorithms are reviewed by all relevant disciplines at a trauma center and approved or adapted for the local environment.

Without treatment, ICP elevation may rapidly become fatal, either because of transtentorial brain herniation and brainstem compression or due to critical CPP reduction leading to brain ischemia. In extreme situations, brain death ensues when elevated ICP prevents brain perfusion. Because of their accuracy, invasive monitors are currently preferred for the management of intracranial hypertension.

- ICP measurement can detect an expanding intracranial lesion and facilitate targeted treatment of intracranial hypertension.
- It allows computation of CPP and calculation of cerebrovascular autoregulatory status.
- The morphology of the ICP waveform can also provide input into cerebral compliance and compensatory reserve.

Although implementation of evidence-based TBI guidelines is associated with marked improvement in outcome, these guidelines are restricted to what is available in the scientific literature. The Delphi-based consensus process is valuable to bridge gaps in evidence upon which treatment algorithms are based until formal evidence is generated. SIBICC used this rigorous consensus process to tap into the collective wisdom of experts and produce the first severe TBI management algorithms published in a generation.[1,2]

The SIBICC algorithms are a suggestion for care, not a standard of care. They aim to be comprehensive, providing a consensus-based approach with the goals of standardizing care and minimizing treatment variability. The full SIBICC documents provide three-tiered algorithms and address the following:

- Management of ICP and ICP + low $PbtO_2$
- Interventions to be discouraged
- A definition of clinical neurologic worsening and its management
- Recommendations for weaning therapy

Tiered Treatments

The SIBICC algorithms are organized into tiers, with treatments placed into individual tiers based on their relative risk-benefit ratios. Tier Zero represents interventions either expected or recommended for all patients with TBI admitted to the ICU, regardless of their ICP (e.g., basic ICU care). Tiers One, Two, and Three are directed at management of intracranial hypertension.

Guidance for using tiered treatments is based on three principles:

- No ranked ordering of treatments exists within an individual tier
- It is not necessary to use all modalities in a lower tier before moving to the next tier
- If considered advantageous, tiers can be skipped when advancing treatment (e.g., early decompressive craniectomy)

The tiered approach provides structure while retaining medical decision-making within tiers. The variety of treatments within each tier also supports targeting interventions at specific physiological disruptions (targeted therapy). See Box 2 for Tier Zero treatment algorithms. See Box 3 for the ICP treatment algorithms for Tiers One, Two, and Three. Full descriptions of the SIBICC I protocol (ICP monitoring)[2] and SIBICC II protocol (ICP plus $PbtO_2$ monitoring)[1] are open access.

Box 2. Tier Zero—Basic ICU Care Interventions—SIBICC I Algorithm

Expected Interventions:

- Admission to ICU
- Endotracheal intubation and mechanical ventilation
- Serial evaluations of neurological status and pupillary reactivity
- Elevate head of bed 30–45°
- Analgesia to manage signs of pain (not ICP directed)
- Sedation to prevent agitation, ventilator asynchrony, etc. (not ICP directed)
- Temperature management to prevent fever
- Measure core temperature
- Treat core temperature above 38.0°C
- Consider prophylactic anti-seizure medications for 1 week only (in the absence of indication to continue)
- Maintain CPP initially ≥ 60 mm Hg
- Maintain hemoglobin > 7 g/dL
- Avoid hyponatremia
- Optimize venous return from head (e.g., keep head midline, ensure cervical collars are not too tight)
- Arterial line for continuous blood pressure monitoring
- Maintain SpO_2 ≥ 94%

Recommended Interventions:

- Insertion of a central line
- End-tidal CO_2 monitoring

From: Hawryluk GW, Aguilera S, Buki A, et al. A management algorithm for patients with intracranial pressure monitoring: The Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med.* 2019 Dec;45(12):1783–1794. doi: 10.1007/s00134-019-05805-9. Used with permission

Box 3. SIBICC I Tiers for ICP Treatment of Intracranial Hypertension for Patients with ICP Monitoring

Tier One

- Maintain CPP 60–70 mm Hg
- Increase analgesia to lower ICP
- Increase sedation to lower ICP
- Maintain $PaCO_2$ at low end of normal (35–38 mm Hg/4.7–5.1 kPa)
- Administer mannitol by intermittent bolus (0.25–1.0 g/kg)*
- Administer hypertonic saline by intermittent bolus*
- Drain CSF if EVD is in situ
- Consider placement of EVD to drain CSF if parenchymal probe used initially
- Consider anti-seizure prophylaxis for 1 week only (in the absence of indication to continue)
- Consider electroencephalography (EEG) monitoring

Tier Two

- Maintain mild hypocapnia (32–35 mm Hg/4.3–4.6 kPa)
- Use neuromuscular paralysis in adequately sedated patients, if efficacious in lowering ICP**
- Perform a MAP Challenge† to assess cerebral autoregulation and guide MAP and CPP goals in individual patients (see page 29 in Neuromonitoring)
- Adjust the target MAP back to baseline (disrupted autoregulation) or to a new, elevated target to lower ICP (intact autoregulation)

Tier Three

- Administer pentobarbital or sodium thiopentone. The barbiturate coma is titrated to ICP control if it is efficacious on testing††
- Perform secondary decompressive craniectomy
- Maintain mild hypothermia (35–36°C) using active cooling measures

* Limits for sodium (155 mEq/L) and osmolality (320 mEq/L) are recommended for administration of either hypertonic saline or mannitol.
** It is recommended to begin with a trial dose of neuromuscular paralysis and only proceed to continuous infusion if efficacy is demonstrated.
† See MAP challenge protocol described in the open access papers, references 1 and 2.
†† Barbiturate administration is continued only when a beneficial effect on ICP is demonstrated. Titrate barbiturate to achieve ICP control, but do not exceed the dose that achieves burst suppression. **Avoid** hypotension when barbiturates are administered.
From: Hawryluk GW, Aguilera S, Buki A, et al. A management algorithm for patients with intracranial pressure monitoring: The Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med.* 2019 Dec;45(12):1783–1794. doi: 10.1007/s00134-019-05805-9. Used with permission.

Treatments Not Recommended for Intracranial Hypertension in Severe TBI

The SIBICC working group lists treatments to be discouraged for management of patients with severe TBI. The group's decision-making included both evidence against treatments (e.g., steroids, CPP > 70 mm Hg) and lack of sufficient supporting evidence (e.g., lumbar CSF drainage, scheduled infusion of hyperosmolar therapy). Inclusion in this list does not proscribe consideration in some individual cases. See Box 4.

Box 4. Treatments Not Recommended for Use in the Management of Intracranial Hypertension in Patients with Severe TBI

- Mannitol by non-bolus, continuous intravenous infusion
- Scheduled infusion of hyperosmolar therapy (e.g., every 4 to 6 hours)
- Lumbar CSF drainage
- Furosemide
- Routine use of steroids
- Routine therapeutic hypothermia to temperatures below 35°C due to systemic complications
- High dose propofol to attempt burst suppression
- Routinely decreasing $PaCO_2$ below 30 mm Hg/4.0 kPa
- Routinely raising CPP above 90 mm Hg

From: Hawryluk GW, Aguilera S, Buki A, et al. A management algorithm for patients with intracranial pressure monitoring: The Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med.* 2019 Dec;45(12):1783–1794. doi: 10.1007/s00134-019-05805-9. Used with permission.

Inter-Tier Recommendations

An ancillary value of the tiered structure is that the tiers act as a proxy for treatment resistance (i.e., disease severity). The SIBICC working group formulated inter-tier recommendations to be considered when advancing between tiers (see Figure 1). These recommendations are directed at ensuring that the baseline management parameters remain acceptable, that judgment calls (e.g., operability of cerebral contusions) do not need reassessment, and that treatable outside influences of ICP are not involved (e.g., intrathoracic or intra-abdominal pressures). This is also a good time to consider consultation or transfer, if such resources are available.

Older Adult Considerations

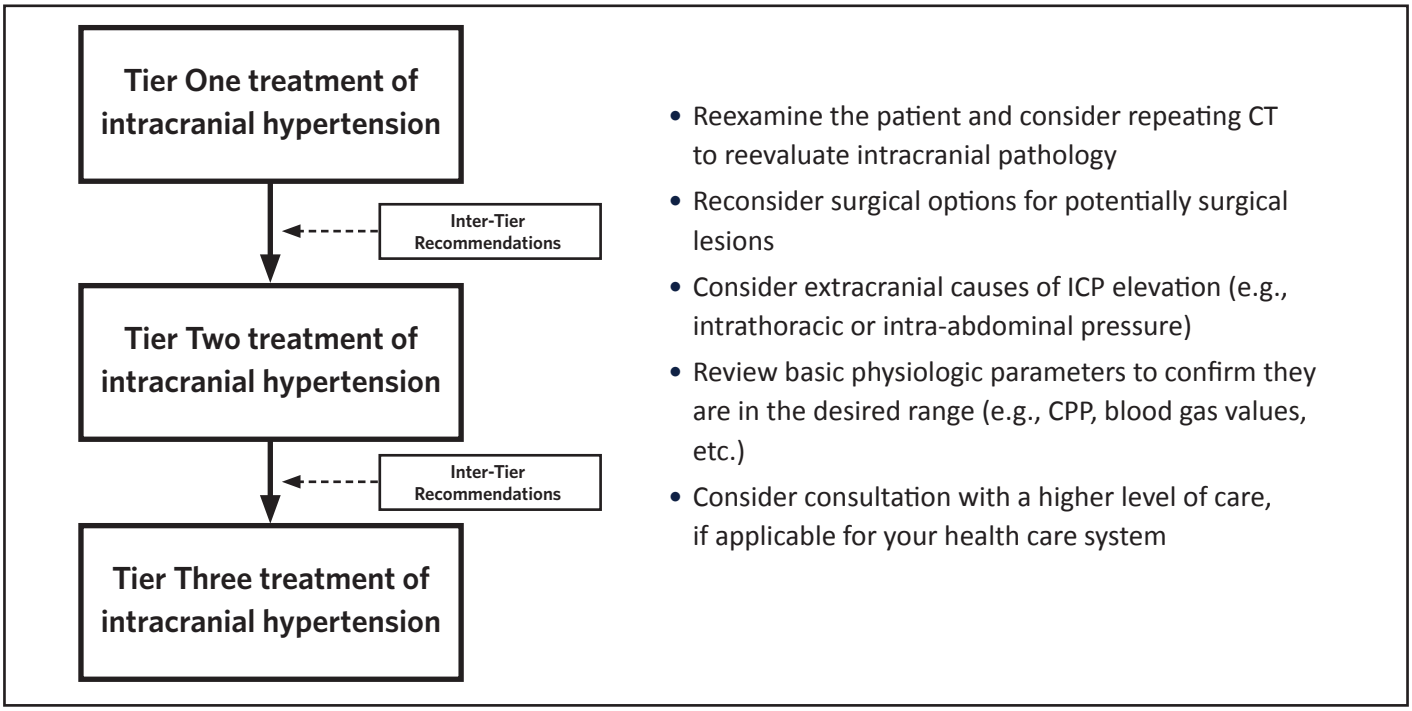
For ICP management in older adults, evaluate pharmacotherapeutic strategies for dosage adjustments to prevent toxicity and prolonged duration of action. Increased concentrations of active drugs may result from older adults' physiologic responses, including decreases in volume distribution, protein binding with hypoalbuminemia, hepatic metabolism, and renal function. Comorbidities and preexisting conditions, such as dementia or stroke, as well as adverse effects of medication make the diagnosis and treatment goals more challenging as well. Older adult patients may also have slower recovery trajectories and worse outcomes, which can be mitigated through aggressive treatment and good preinjury health status.[3–5]

Pediatric Considerations

In 2019, the consensus guideline to manage severe TBI injury for children was updated by an interdisciplinary team.[6] An accompanying algorithm of tiered therapy was included, similar to that of SIBICC, although condensed into two tiers.[7] Minor variations in the tier classifications do not indicate evidence-based discrepancies. Note: These guidelines predate results from the Approaches and Decisions in Acute Pediatric TBI Trial (ADAPT).[8]

In a few instances, available evidence supports different approaches to the care of children with severe TBI. For example, evidence supports the use of hypertonic 3% saline boluses, either 2 to 5 mL/kg over 10 to 20 min or at a constant rate of 0.1–1 mL/kg/hour, or a 23.4%

Figure 1. Inter-Tier Recommendations



From: Hawryluk GW, Aguilera S, Buki A, et al. A management algorithm for patients with intracranial pressure monitoring: The Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med.* 2019 Dec;45(12):1783–1794. doi: 10.1007/s00134-019-05805-9. Used with permission.

concentration at 0.5 mL/kg (up to 30 mL) over 10 to 20 minutes. Less evidence supports the use of mannitol.[7] Additionally, a lower hypoventilation target of 28 to 34 mm Hg is recommended in the Tier Two interventions.[7] Moderate prophylactic hypothermia (32–33°C) is not recommended over normothermia to improve overall outcomes, but it is suggested for ICP control.[6,7]

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NEUROMONITORING

KEY POINTS

- Serial clinical assessment of neurological status in regular intervals provides the foundation of neuromonitoring in TBI patients.
- Neuromonitoring, beyond monitoring of ICP in isolation, can help establish individualized patient care goals and therapy.
- Assessment of cerebral autoregulation can help establish CPP goals in individual patients. Consider performing neuromonitoring in patients who do not respond to initial (Tier One) therapies to decrease ICP.
- Impaired cerebral oxygenation can occur with both normal or increased ICP. Consider treatment of brain tissue hypoxia based on the underlying pathophysiology and a tiered approach of escalating therapies.
- Continuous electroencephalography (EEG) assists in seizure detection and management, especially for nonconvulsive seizures.

Repeated clinical assessment of neurological status provides the foundation of neuromonitoring in TBI. It can be supplemented by noninvasive methods, such as the use of quantitative pupillometry at set intervals to quantify the pupillary light reflex (see the Basic Assessment section on page 10). While ICP monitoring is most commonly used to supplement clinical assessment, other techniques can supplement clinical assessment as well (see Intracranial Pressure Monitoring on page 22).

TBI is a complex disease with substantial heterogeneity. ICP monitoring alone cannot detect all potential insults to the brain, nor does it allow for patient-specific individualized care based on factors such as the presence or absence of autoregulation. Cerebral pressure autoregulation is the brain's intrinsic ability to maintain constant CBF over a range of systemic blood pressures. This mechanism protects the brain from cerebral ischemia due to hypotension and from excessive blood flow that can lead to elevated ICP. The SIBICC algorithm recommends assessment of autoregulation status in patients who do not respond to initial therapy to reduce elevated ICP (see Tier One in Box 3 on page 26).[1]

Assessment of Cerebral Autoregulation

Mean arterial pressure challenge: Cerebral autoregulation can be assessed at the bedside in the ICU by performing a MAP challenge while monitoring ICP in the closed cranium. This challenge is performed by initiating or increasing a vasopressor infusion in euvolemic patients to increase the MAP by 10–15 mm Hg for no more than 20 minutes. Perform a MAP challenge under the direct supervision of a bedside provider experienced in performing the challenge so that patient response and safety are assured. Perform no other therapeutic adjustments during the MAP challenge.

Record key physiological parameters (MAP, ICP, CPP, $PbtO_2$) before and after the MAP challenge. Patients with a closed cranium in whom ICP increases with a MAP challenge are considered to have impaired autoregulation, and they may benefit from a lower CPP goal. Conversely, patients with a closed cranium in whom ICP decreases or does not change significantly with a MAP challenge are considered to have intact autoregulation, and these patients—particularly those with decreasing ICP in response to the MAP challenge—may benefit from a higher CPP goal.

Cerebrovascular pressure reactivity index: Another ICP-based method used to continuously assess cerebral autoregulation status is to follow the cerebrovascular pressure reactivity index (PRx). The PRx is defined as the slope of the regression line relating MAP and ICP, and it can be used to establish patient-specific CPP thresholds. For patients with impaired cerebral autoregulation (PRx slope > 0.13), a lower CPP (50–60 mm Hg) may be considered as an option for treatment. Patients with intact autoregulation (PRx slope < 0.13) may benefit from a higher CPP (60–70 mm Hg). Of note, assessment of the PRx requires specialized technical expertise and additional hardware and software, which are commercially available.

Brain tissue oxygen tension: Autoregulation status may also be assessed by following $PbtO_2$, as long as systemic oxygenation (PaO_2) is maintained at a constant level. Verify this by checking the arterial blood gas before and after the MAP challenge.

Monitoring cerebral blood flow: Directly monitoring CBF can also be used to assess autoregulation status with a MAP challenge.[2] In patients with intact autoregulation, CBF will change minimally in response to an increase in MAP. Conversely, CBF will rise with increasing MAP in patients with impaired autoregulation. Once determined, autoregulation status can be used to set CPP goals as described above. Similarly, transcranial doppler ultrasonography and hemodynamic challenge can also be used to assess autoregulation in TBI patients.

Research findings: Multiple studies demonstrated an association between low $PbtO_2$ (≤ 15 mm Hg) and episodes of jugular venous oxygen desaturation (≤ 50%) with poor patient outcomes.[3–7] It is important to note that brain tissue hypoxia can occur even when ICP and CPP are normal. A Phase II prospective RCT (BOOST II) investigating $PbtO_2$-based management of severe TBI compared treatment guided by ICP alone to treatment guided by both ICP and $PbtO_2$. This study demonstrated that the ICP + $PbtO_2$ management group had statistically significant decreased duration and severity of brain hypoxia, as well as a trend towards reduced mortality and improved neurologic outcome at 6 months.[8] However, this trial was not powered to show significant differences in outcome. Several appropriately powered Phase III trials (BOOST III and BONANZA) are underway to compare outcomes between therapy guided by ICP alone versus therapy guided by ICP + $PbtO_2$. The recently concluded Oxy-TC trial did not find a difference in functional outcome between nonpenetrating TBI patients treated with ICP + $PbtO_2$-based monitoring versus those treated with ICP-based monitoring alone.[9]

Brain tissue oxygen management: Accepted thresholds for treatment of brain tissue hypoxia are between 15–20 mm Hg.[8,10,11] Interventions that may be used to improve brain tissue oxygenation are detailed in the tiered SIBICC II algorithm and include the following[1]:

- Increase fraction of inspired oxygen (FiO_2) to 60% (Tier One) or increase PaO_2 to as high as 150 mm Hg (Tier Two)
- Attempt increased sedation or neuromuscular paralysis to improve $PbtO_2$ (Tier Two)
- Increase CPP in patients with intact autoregulation per MAP challenge (Tier Two)
- Increase PaO_2 above 150 mm Hg (Tier Three)
- Transfuse 1 unit of packed red blood cells if $PbtO_2$ remains less than 20 mm Hg despite CPP optimization (Tier Three)

Knowledge of cerebral autoregulation status as described above may also facilitate the use of $PbtO_2$ to individualize CPP goals. Keep the potential harmful effects of hyperoxia in mind, especially when proceeding to Tier Three therapies.

Electroencephalography

Use of EEG allows continuous monitoring of brain function at the bedside, assisting in seizure detection and management. It has a significant role in the detection of nonconvulsive seizures as the potential cause for a diminished level of consciousness that would otherwise go undetected.[12] Nonconvulsive seizures were reported to occur in an estimated 25% of patients with moderate to severe TBI, and they were reported to be associated with worse outcomes and long-term hippocampal atrophy.[13–14]

Surface EEG requires a trained, on-site technician and a physician trained to interpret the waveforms. Emerging techniques, including quantitative EEG, may decrease the need for a physician trained to interpret waveforms, but this is not available at all trauma centers. The role of EEG is expanding beyond the detection of seizures. While still considered experimental, the detection of secondary brain ischemia and covert consciousness is possible using depth and surface EEG.

Multimodal Neuromonitoring

Trauma centers treating larger numbers of patients with severe TBI, and those centers with expertise in neurocritical care, may attempt to undertake multimodality neuromonitoring, incorporating at least one element of neuromonitoring beyond ICP monitoring in isolation. Trauma centers treating lower volumes of patients with TBI may not have the resources to implement a full regimen of neuromonitoring beyond ICP monitoring.

Older Adult Considerations

Little literature exists specifically addressing the use of multimodality monitoring in older adult patients. Thus, potential impacts must be extrapolated. Differences in the aging physiology may influence both the utility and interpretation of data derived from these modalities.

Studies published suggest a decreased use of invasive ICP monitoring for older adult patients and/or worse outcomes with use.[15,16] These observations may reflect a difference in aggressiveness of care or decreased suspicion about a raised ICP due to cerebral volume loss. Other studies reported a negative correlation between age and invasively measured ICP in patients with TBI. It follows that "normal" ICP is believed to decrease with advancing age.[17]

Aging vessels may react to brain injury insults differently or unpredictably. Increasing arterial stiffness translates into a reduction in CBF and increased blood flow pulsatility—the net effect is impaired CBF regulation.[18] Orthostatic episodes and syncope may expose the brain to periods of hypoperfusion. However, the capacity for autoregulation is believed to be preserved with aging.[19] Chronic hypertension shifts the autoregulatory curve to the right, protecting the brain from higher blood pressures but potentially increasing the risk of hypoperfusion with periods of relative hypotension. Interpretation of pupillometry data may be confounded by natural changes that occur with aging (see the Basic Assessment section on page 10 for more information about pupillometry).

Baseline EEG abnormalities—most often diffuse or focal slowing, but sometimes epileptiform activity—are common in older adult patients with a range of medical comorbidities.[20] While this likely reflects a certain prevalence of cerebral dysfunction among older adult patients, it may confound interpretation of an EEG performed in the setting of an acute change in clinical status.

Pediatric Considerations

Clinical examination may be more difficult to follow in children, and age-appropriate adaptations to maximize the sensitivity of a clinical exam need to be applied. Fewer data exist on the application of cerebral tissue oxygenation in children than in adults, and age-dependent variability is recognized. In the absence of validated normative thresholds, it is not known how to use data such as $PbtO_2$ or measures of autoregulation in pediatric patients.

Although continuous EEG is not routinely used in children at this time, a subset of children, particularly infants, may be at particularly high risk for seizures from TBI, and broader application may be appropriate.[21–25]

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SURGICAL MANAGEMENT

KEY POINTS

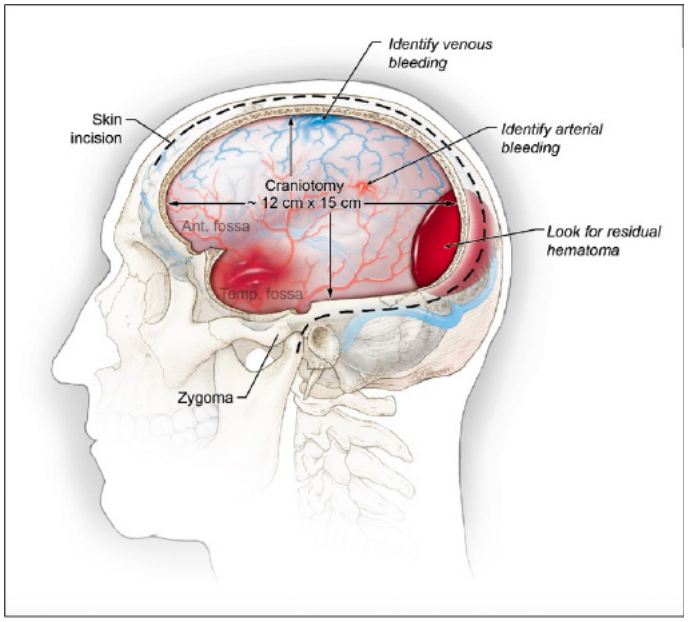
- Evacuate a large traumatic hematoma before neurological deterioration develops, irrespective of the GCS score.
- For evacuation of an acute SDH, perform a large trauma craniotomy to achieve optimal damage control and provide the option for a primary decompressive craniectomy (bone flap left out).
- Following hematoma evacuation, consider if the bone flap can be replaced without compressing the brain by evaluating factors such as burden of concomitant brain injuries, other extracranial injuries, availability of ICP monitoring, and ICU facilities. Leave the bone flap out if replacing it could cause brain compression.
- Secondary decompressive craniectomy is effective in controlling ICP and improves long-term outcome.

Surgical Indications

Surgery for patients with TBI is most commonly performed to evacuate an EDH or SDH or to decrease pressure on the brain resulting from cerebral contusions or intracerebral hematomas. Comatose patients presenting to the ED should be taken to surgery immediately upon arrival if a large hematoma is identified as the likely cause of the coma and the patient has a chance of meaningful recovery. Even if a patient has a relatively high GCS score, evacuate a large (> 25 mL) traumatic hematoma before neurological deterioration develops from hematoma enlargement or brain swelling. A lower threshold for surgical intervention may apply to posterior fossa lesions. Admitted patients who undergo neurological deterioration from delayed development or enlargement of a hematoma require prompt surgical evacuation to prevent further neurological worsening.

In patients with an acute SDH, perform a large craniotomy for optimal damage control, including evacuation of the hematoma, identification of the bleeding source (e.g., bridging veins, temporal base, superficial contusion), and meticulous hemostasis. Concordant with the BTF *Guidelines for the Management of Severe TBI, 4th Edition*, a large craniotomy bone flap (≈ 12 × 15 cm) is created to effectively visualize sources of hemorrhage in the parasagittal, parieto-occipital, and temporo-basal regions.[1] This also maximizes the opportunity for primary and secondary decompression. The 15 cm recommendation may be excessive in some patients with smaller heads. Note that a bone flap of at least 13 cm in the vertical plane provides the opportunity for optimal decompression of the middle fossa. Additional bony removal in the subtemporal region and the sphenoid wing can be considered to augment exposure and decompression (see Figure 2). No role exists for attempted burr hole drainage of solid clots.

Figure 2. Trauma Craniotomy



Courtesy of Ken Probst, UCSF, San Francisco, CA

A large frontotemporoparietal craniotomy provides optimal visualization of the bleeding source and an opportunity for primary or secondary decompression. A large reverse question mark incision is made starting 1 cm anterior to the tragus at the root of the zygoma, coursing just superior to the pinna and extending posteriorly over the parietal bossing, then carried forward linearly to the hairline while staying 1.5–2 cm lateral to midline. The myocutaneous flap is reflected to expose the keyhole and the root of the zygoma. Burr holes are placed to enable a large craniotomy for decompression of the anterior and middle fossa floor.

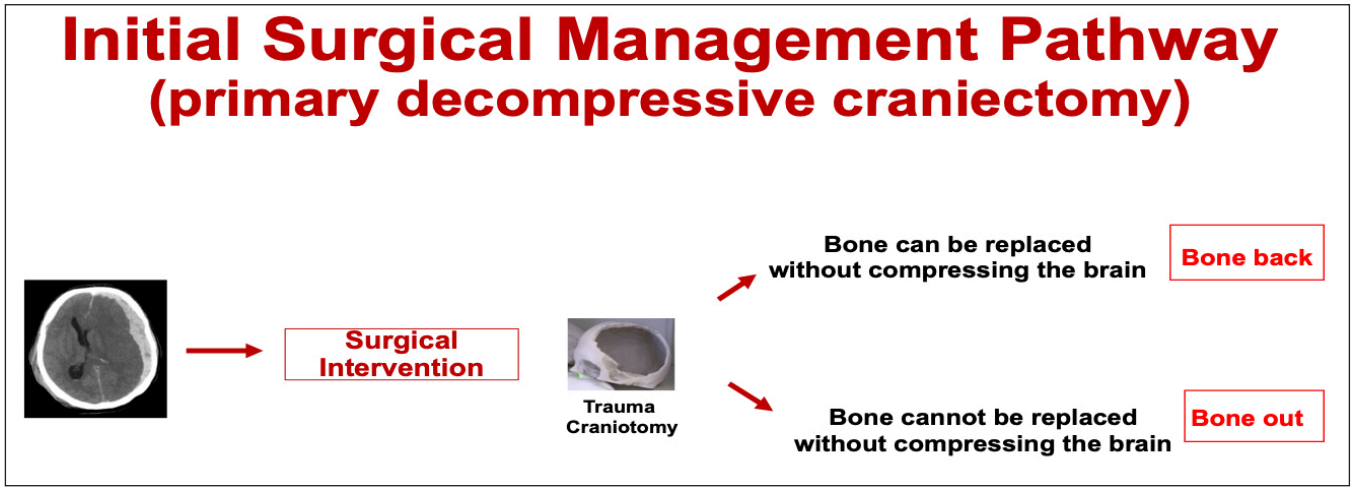
Decompressive Craniectomy

Decompressive craniectomy, in which after performing a large frontotemporoparietal craniotomy the bone flap is not replaced, has recently increased in popularity. Two indications for decompressive craniectomy exist in the context of trauma.

Primary decompressive craniectomy: This procedure involves leaving the bone flap out following acute evacuation of a mass lesion (typically an acute SDH). In the presence of brain swelling, a primary decompressive craniectomy is recommended following evacuation of the mass lesion. However, the bone flap may be replaced if the underlying brain is not compressed and other factors are considered (e.g., burden of concomitant brain injuries, other extracranial injuries, availability of ICP monitoring, and ICU facilities). See Figure 3.

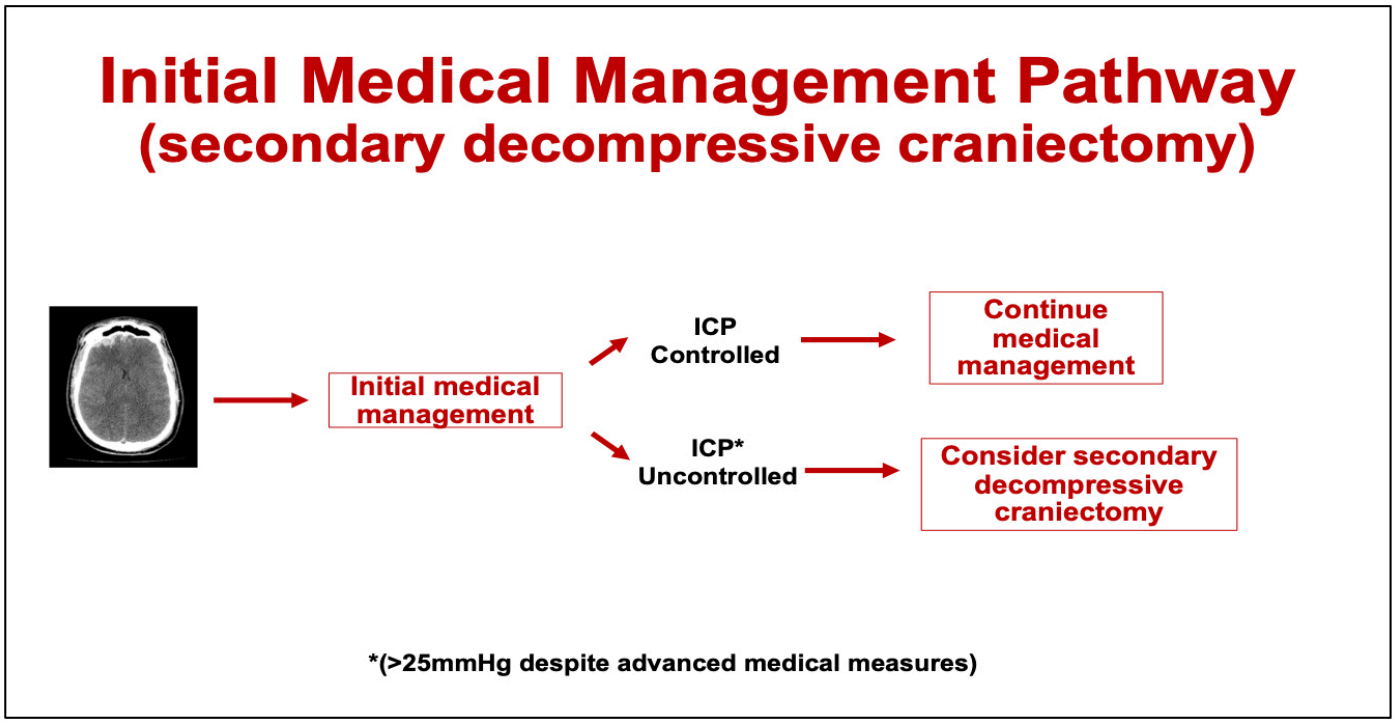
Secondary decompressive craniectomy: This procedure involves removing a bone flap to control brain swelling, as well as elevated ICP that is refractory to medical treatment. Patients with hematomas, contusions, and/or diffuse injury that do not have an indication for immediate surgery are managed medically. However, in the presence of raised and refractory ICP (> 25 mm Hg), secondary decompressive craniectomy was demonstrated to reduce mortality and improve outcome over time (24-month data).[2,3] The RESCUEicp trial predicted that if 100 patients are treated with secondary decompressive craniectomy (compared to conservative management), there are 21 extra survivors with the following functional outcomes: one-third independent outside the home, one-third independent in the home, and one-third dependent (see Figure 4).[2]

Figure 3. Initial Surgical Management Pathway



Courtesy of Geoffrey Manley, M.D., Ph.D., San Francisco General Hospital, UCSF, San Francisco, CA and Peter Hutchinson, F.R.C.S. (Surg. Neurol.) Addenbrooke's Hospital, University of Cambridge, UK

Figure 4. Initial Medical Management Pathway



Courtesy of Geoffrey Manley, M.D., Ph.D., San Francisco General Hospital, UCSF, San Francisco, CA; and Peter Hutchinson, F.R.C.S. (Surg. Neurol.) Addenbrooke's Hospital, University of Cambridge, UK.

Other Surgical Decisions

Traumatic intracerebral hematoma/hemorrhagic contusion: Management for this condition remains controversial. For patients with mass effect and neurological decline, the decision for surgical intervention is more straightforward. However, for patients with smaller lesions, the choice of early surgery to prevent secondary injury is debatable. The STITCH (Trauma) trial, which was prematurely terminated due to slow patient recruitment, demonstrated improved survival in the early surgery group and a trend towards better functional outcome, especially in the subgroup with GCS 9–12.[4] More recently, early surgery versus conservative treatment was studied in the prospective longitudinal CENTER-TBI cohort. For traumatic intracerebral hematoma in patients with GCS 9–12 or an isolated traumatic intracerebral hematoma, early surgery was associated with improved outcome, similar to the STITCH (Trauma) study.[5]

Depressed skull fractures: Depressed skull fractures are commonly surgically elevated if the depression is greater than the thickness of the adjacent skull, especially if located in a cosmetically important area like the forehead. Open depressed skull fractures are usually treated surgically to prevent infection. However, nonoperative management may be attempted in selected cases, limited to those without dural laceration, gross contamination, evidence of infection, or injury to the frontal sinus. In most cases, depressed skull fractures over a dural venous sinus are not treated surgically because of the high risk for uncontrollable hemorrhage.

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NUTRITIONAL SUPPORT

KEY POINT

- Initiate enteral nutrition (EN) support once a patient is hemodynamically stable, ideally within 24–72 hours of injury.
- Achieve full nutritional supplementation within 7 days of injury.
- Postpyloric feeding access is preferred if it can be obtained rapidly without delaying initiation of EN. When obtaining postpyloric access causes delay in EN support, early initiation via gastric access is acceptable.
- Consideration for parenteral nutrition (PN) support is recommended when EN is contraindicated.

Patients with TBI are at risk for significant protein and energy deficits during hospitalization, and they experience significant loss of lean body mass during the critical care phase of recovery.[1] Nutritional support is essential to meet the patient's nutrition requirements, both to prevent the development of malnutrition and to blunt the catabolic effects of TBI.[2,3]

Nutrition Targets

Patients with TBI demonstrate metabolic disturbances lasting 1 week to several months following their injury. Energy expenditure of 120% to 250% of predicted basal expenditure was reported.[4–6] Muscle activity, fever, infection, and additional injury appear to contribute to hypermetabolism, while normothermia protocols may result in energy expenditure below predicted levels.[7,8] Indirect calorimetry is the optimal method to determine caloric targets following TBI. One study of patients with critical illness and trauma found that patients with TBI did not experience increased protein demands compared to trauma patients without TBI, and delivery of protein up to 2 g/kg/day improved nitrogen balance.[9]

Initiating Enteral Feeding

Studies, including a large meta-analysis, demonstrated that early nutritional support is associated with fewer infections and lower mortality.[6,10–14] Initiation of EN within the first two days of admission following TBI was associated with reduced pneumonia and hospital LOS. Early EN is most commonly defined as within 24 to 72 hours of injury. This timing of early EN is recommended in conjunction with the BTF recommendation of achieving full nutritional support within 7 days of injury.[15] The American Society for Enteral and Parenteral Nutrition makes similar recommendations.[16,17]

High-protein EN formulations are preferred to better meet protein targets following TBI. Immune-enhancing enteral formulations may reduce infectious complications and improve nutritional parameters in patients with TBI.[18] Fish oil was shown to reduce inflammatory stress and cellular damage in murine models and small human trials.[19–21] Consider using fish-oil fortified EN formulas unless contraindications exist.

Feeding Methods

Studies specific to patients with TBI demonstrate significant reduction in rates of pneumonia with postpyloric feeding tube placement. However, the level of feeding did not impact other outcomes.[22] The potential benefits of postpyloric feeding must be weighed against the benefits of early EN initiation; avoid delayed initiation of EN in pursuit of postpyloric access.

Consider PN when an absolute contraindication for EN exists and is anticipated to delay initiation of EN support.[16] However, EN is more cost-effective and physiologically correct and is therefore the first-line nutrition support therapy. If EN is contraindicated, initiation of PN support within 72 hours postinjury is recommended.

Glycemic Control

Glycemic targets for adults who are critically ill range from 100 to 180 mg/dL in published guidelines. Hypo- and hyperglycemia are associated with worsened outcomes in observational studies of patients with TBI.[23,24]

Older Adult Considerations

Older adult patients with TBI are at increased risk for nutrition-related sequelae. Rates of malnutrition (protein-energy deficit or undernutrition) can be as high as 62% at admission, and it is associated with higher morbidity (e.g.,

cognitive impairment, infection, depressive symptoms), delayed mobilization, increased LOS, and readmission.[25] Management includes screening and ongoing nutritional status monitoring.[26] The Mini Nutritional Assessment is the most widely used screening tool (https://www.mna-elderly.com/sites/default/files/2021-10/mna-mini-english.pdf).[27,28] The Geriatric Nutritional Risk Index is another nutritional assessment based on serum albumin levels and body mass index.[29–31]

The aims of nutritional intervention include the following:

- Replenishment of protein and energy stores
- Maintenance of functional capacity
- Reduction of malnutrition-associated costs (e.g., LOS, subacute care, and quality of life)[32]

Dysphagia increases the risk of aspiration and malnutrition.[32] The primary risk factor for dysphagia is mechanical ventilation, leading to further complications.[33] Screening entails volume-viscosity swallow testing that can be administered at the bedside.[34]

Pediatric Considerations

Nutrition therapies for pediatric patients with severe TBI must take into account hydration and electrolyte goals to prevent fluid shifts that could worsen cerebral edema.

Equations for predicting energy expenditure may overestimate requirements in severe TBI. Neuroprotective interventions in contemporary TBI management (e.g., sedation, neuromuscular blockade, effective thermoregulation, and seizure control) may depress energy expenditure, potentially even below predicted basal levels.[35–37]

Pediatric-specific data support the following nutrition recommendations consistent with adults:

- Initiate EN support once a patient is hemodynamically stable, ideally within 24 to 72 hours of injury.[38,39]
- Attempt to achieve full nutritional supplementation within 7 days of injury.[38]
- Gastric or postpyloric access are viable modes of EN, although more patients achieve caloric goals with postpyloric feeds, without a difference in symptoms of feeding intolerance.[40]
- In patients for whom EN is contraindicated, consider PN support.

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AIRWAY AND VENTILATION

KEY POINTS

- Early endotracheal intubation and mechanical ventilation are recommended in patients with TBI and reduced consciousness (i.e., GCS < 9), severe agitation, loss of airway protective reflexes, or a GCS > 8 in the presence of thoracic and abdominal injuries.
- Prescribe ventilator settings to assure that arterial pH remains 7.35–7.45, $PaCO_2$ is 35–45 mm Hg (in the absence of intracranial hypertension and/or severe metabolic acidosis), and oxygen saturation is at least 94%.
- Tracheal extubation can be challenging in neurocritical care patients. Consider extubation when intracranial hypertension is resolved, no evolving lesions were documented on the last CT scan, and the patient is able to control upper airway reflexes and cough.

Intubation and Ventilation Management

Early intubation and mechanical ventilation are cornerstones of TBI management in patients with reduced consciousness (i.e., a GCS < 9), severe agitation, and loss of airway protective reflexes. The aim is to avoid hypoxia, control carbon dioxide levels, and minimize the risk of aspiration. During tracheal intubation, protect the cervical spine due to possible associated spinal injuries. Once intubated, ventilate with goals to maintain arterial pH 7.35–7.45, $PaCO_2$ 35–40 mm Hg (in the absence of intracranial hypertension and/or severe metabolic acidosis), and oxygen saturation at least 94%.

- The optimal target range of PaO_2 is 80–100 mm Hg. This could be higher if neuromonitoring (e.g., brain tissue oxygen targeted approaches) suggests it.
- The optimal target range of $PaCO_2$ is 35–45 mm Hg in patients who do not have elevated ICP.

Mild hyperventilation ($PaCO_2$ of 32–35 mm Hg) is suggested as a SIBICC Tier-Two treatment for controlling high ICP or during neurologic worsening (uncal herniation).[1] In the presence of refractory severe intracranial hypertension, or when a threatened or actual herniation is detected (e.g., a dilated unreactive pupil), reduction of $PaCO_2$ to less than 30 mm Hg may be justified as a temporizing measure while other interventions (including surgery) are put in place. However, consider such profound hyperventilation to be a rescue procedure and use it for as short a period as possible, because it can result in arterial spasm and decreased CBF.[1] The $PaCO_2$ levels indicated here may be detected by continuous end-tidal CO_2 monitoring, while recognizing that arterial end-tidal CO_2 gradients vary between patients and individuals over time. In most instances, moderate levels of positive end-expiratory pressure (PEEP) of $\leq$ 10 cm H_2O will not elevate ICP further in the presence of intracranial hypertension. It can be safely applied to maintain oxygenation when accompanied by ICP monitoring.[2]

Rescue therapies for severe/refractory ventilatory failure, such as prone positioning, neuromuscular blockers, and extracorporeal membrane oxygenation (ECMO), have not been systematically studied in the context of TBI. Apply them cautiously and on an individual basis, because monitoring and controlling their effect on intracranial volumes and intracranial bleeding is mandatory.

ECMO is increasingly utilized in severe polytrauma patients with acute respiratory distress syndrome. Compared to venoatrial ECMO, venovenous ECMO without anticoagulation was shown to have a survival benefit in the selected, monitored cases where the patient's systemic oxygenation was unresponsive to conventional management.[3]

Extubation Planning

Tracheal extubation remains challenging.[4] The probability of extubation success increases in the following conditions:

- GCS motor score of 6
- Normal respiratory drive
- Stable intracranial conditions
- Intact airway protective reflexes (vigorous cough, gag reflex, and swallowing attempts)
- Endotracheal suctioning ≤ 2 times per hour

The difficulty with uniformly predicting successful tracheal extubation for patients with TBI means that tracheal extubation may be attempted in some patients while accepting that reintubation may be needed. If tracheal

extubation fails or is not possible due to the absence of safety criteria, the need for tracheostomy must be evaluated.

Older Adult Considerations

As a general rule, the decision-making and management of mechanical ventilation in an older adult with severe TBI is the same as for a younger patient. Consider an individual patient's goals of care when making decisions about the provision of invasive support. Although hypoxia is clearly detrimental to patients of any age with severe TBI, the use of mechanical ventilation to tightly control CO_2 may not be as important in a patient with cerebral atrophy and a relatively lower risk of intracranial hypertension. However, older adult patients may have baseline oropharyngeal dysfunction making early intubation following TBI even more appropriate. Endotracheal intubation and mechanical ventilation in older patients carry the same risks as in younger patients.

Pediatric Considerations

No pediatric-specific literature or guidelines on mechanical ventilation after TBI have been published. A cuffed endotracheal tube is favored for children with TBI who require intubation, in order to facilitate optimal ventilation strategies and minimize risk of aspiration. Overall, the general physiologic considerations motivating ventilation management for children with TBI are similar to those for adults.

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TRACHEOSTOMY

KEY POINT

- Consider all patients with severe TBI for early tracheostomy, within 7 days of injury, when rapid improvement is determined to be unlikely.
- Early tracheostomy can decrease the risk of prolonged mechanical ventilation and pneumonia.

ICU patients with severe TBI often require prolonged mechanical ventilation for the following reasons:

- Attenuated or loss of the pharyngeal protection reflex
- Excessive secretions
- Ventilator dyssynchrony
- Impaired oxygen and CO_2 exchange
- Severe agitation
- Severe associated injuries, including facial, airway, or thoracic injury

When the patient's level of consciousness remains persistently depressed, consider performing a tracheostomy to have a patent airway and to decrease the ventilator-associated risks of pneumonia and ventilator-induced lung injury.

Early Tracheostomy

While no clear evidence exists for survival benefit, early tracheostomy is shown to reduce ICU and hospital LOS in patients with TBI. No absolute contraindications for tracheostomy exist, but relative contraindications include the following: uncontrolled intracranial hypertension, hemodynamic instability, and severe respiratory failure requiring high levels of FiO_2 (> 50%) and PEEP (> 10 cm H_2O).[1] Additional benefits of tracheostomy for patients receiving prolonged mechanical ventilation include improved patient comfort associated with reduced oropharyngeal irritation and improved pulmonary hygiene. These factors might also accelerate liberation from mechanical ventilation.[2] A recent study demonstrated tracheostomy rates in patients with severe TBI to be 31.8%, with 41% of tracheostomies performed within 7 days of injury and 26% performed more than 14 days after injury.[3] This demonstrated substantial differences between participating centers regarding the timing of tracheostomy.[3]

The BTF 4th edition guidelines for patients with severe TBI provide a Level IIA recommendation for performing early tracheostomy to reduce ventilation days. However, the recommendation makes no statement regarding an associated reduction of mortality or pneumonia.[4] Limited evidence exists to recommend either surgical or percutaneous tracheostomy in the setting of TBI, but a percutaneous procedure can be safe and well tolerated. Consider performing an early tracheostomy for patients with severe TBI who are unlikely to be liberated from the ventilator within 7 days.[5]

Older Adult Considerations

Multiple studies reported that older adult patients are less likely to undergo a tracheostomy.[6,7] When tracheostomy is performed in older patients, it is often performed later in the hospital course than for younger patients.[7] This is true despite the fact that tracheostomies in older patients are reported to be associated with lower in-hospital mortality.[7] Both tracheostomy placement and oral intubation are independent risk factors for the development of dysphagia, a common complication in injured older adults.[8] Performing a tracheostomy in an older adult with severe TBI must be weighed against the patient's goals of care.

Pediatric Considerations

Tracheostomy timing for children was studied retrospectively based on a single center and national North American databases.[9] Similar to the adult evidence, early tracheostomy is suggested to decrease ICU morbidity and LOS in pediatric TBI.[9–11] However, less information exists about tracheostomy timing for infants with abusive head trauma.[10] Adolescents likely benefit from similar early tracheostomy strategies as adults.

Children under 10 years old may have a different risk profile for tracheostomy. Therefore, it may be inappropriate to extrapolate the benefits seen in early tracheostomy after TBI from adults and adolescents to younger children and infants. Additionally, the technique and complication profile of tracheostomy in children may be different than in adults. In children, particularly those under 10 years of age, the percutaneous technique is uncommon compared to its frequency of use in the adult ICU setting.[12–14] Airway anatomy and even available tracheostomy equipment are

also different for children. For example, pediatric tubes are single-lumen and not fenestrated, and appropriate tube sizing is much more variable.[13]

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TIMING OF EXTRACRANIAL PROCEDURES

KEY POINTS

- Balance the urgency of operation against the risks posed by intracranial hypertension when making the decision to undertake surgery for extracranial injuries.
- Delay extracranial surgery in patients with or at high risk for intracranial hypertension, except in the context of lifesaving procedures.
- When the patient's ICP is monitored and well-controlled or where raised ICP is not a concern, clinicians may proceed with necessary orthopaedic stabilization and other time-sensitive surgery within 48 hours of admission.
- Avoid laparoscopic procedures, because they raise intra-abdominal pressure and induce hypercarbia.
- Provide careful monitoring during general anesthesia to avoid raised ICP, hypotension, hypoxia, and hypo- or hypercarbia.

The primary determinant of mortality in a polytrauma patient is often the severity of the head injury.[1] Even moderate TBI doubles predicted mortality when associated with extracranial injury.[2] Optimal surgical management of extracranial injuries in polytrauma patients with severe TBI demands a systematic approach emphasizing multidisciplinary involvement and effective communication. Hemodynamic status dictates initial priorities for imaging and management. When the patient is hemodynamically stable, the neurologic injury may take precedence. When the patient is unstable because of hemorrhage from concomitant injury, the primary focus shifts to resuscitation and control of bleeding.

Extracranial Surgical Procedure Planning

Direct the goals of therapy toward the dual tasks of preventing multi-organ failure and mitigating secondary brain injury. A recent large cohort study found significantly worse functional outcomes at 2 weeks and 6 months for patients with CT-positive acute TBI who were exposed to extracranial operations and anesthesia.[3]

Anesthesia considerations: Assure careful monitoring during anesthesia to avoid hypotension, hypoxia, and hypo- or hypercarbia. A single episode of hypotension doubles mortality.[4] When ICP is being monitored, maintain CPP at 60 mm Hg.[5] Because of the adverse effects of inhalational anesthesia on ICP, intravenous (IV) anesthesia is often preferable. While neuraxial regional anesthetic techniques (spinal and epidural anesthesia) are contraindicated in patients with intracranial hypertension, a role may exist for peripheral nerve blocks (whether single shot or continuous) to provide analgesia and facilitate surgery.

Timing of surgical procedures: Damage control orthopaedics—early external fixation after initial stabilization, with delayed definitive treatment—aims to minimize the risk of the so-called neurologic "second hit" that may occur in conjunction with early orthopaedic interventions (early total care).[10–12] The concept of *safe definitive surgery* was recently introduced to strike a balance between the extremes of early total care and damage control orthopaedics.[13] The timing of surgery is optimized through repeated patient assessment, with attention to changing physiology and clinical status (classified as stable, borderline, unstable, or in extremis).

The timing of orthopaedic procedures (primarily long-bone repair) does not appear to have an overall effect on outcomes in patients with severe TBI, with the following provisions.[6–9] In patients with intracranial hypertension, give consideration to delaying trips to the operating room unless lifesaving procedures are required. Perform open laparotomy or open thoracotomy when needed, with adherence to the same general principles of avoiding secondary brain injury. Laparoscopy is generally avoided, especially early on, because it raises intra-abdominal pressure and induces hypercarbia.[14,15] The contribution of hypercarbia to long-term adverse neurologic outcomes is debatable, however. The majority of facial fractures are not life-threatening and do not require emergent intervention; however, such patients may be vulnerable to respiratory distress. Routine ICU procedures (e.g., tracheostomy and percutaneous endoscopic gastrostomy) may be performed once the patient's condition has stabilized. The timing of spine fracture-dislocation surgery may depend on spine stability and the need for emergency spinal decompression in patients with spinal cord injury.

Older Adult Considerations

The average age of polytrauma patients has increased over time.[16] Severe TBI and age > 65 years are known to be independent prognostic factors for mortality during the initial hospital stay. Older adult patients presenting with polytrauma are vulnerable to more severe injury, longer LOS, and a greater likelihood of mortality than younger patients with similar injuries.[16] These findings are associated with geriatric patients having a greater likelihood of comorbid medical conditions, preexisting neurologic or psychiatric diagnoses, and chronic antiplatelet or anticoagulant therapy.[17] Weigh these factors when contemplating extracranial interventions, because they may influence decisions with respect to the timing and the extent of procedures to be performed.

Pediatric Considerations

Children frequently experience polytrauma in association with TBI, and at least a third of children with severe TBI require extracranial surgery.[18] The severity of TBI is also a major determinant of outcome in children with polytrauma, similar to the findings in adults.[19] No definitive data exist to suggest a different management pattern in the surgical care of extracranial injuries for children. Thus, prioritize hemodynamic stability to minimize significant secondary brain injury.[20,21]

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EXTRACRANIAL BLUNT CEREBROVASCULAR INJURY

KEY POINTS

- When a blunt cerebrovascular injury (BCVI) is found, initiate treatment with anticoagulation or antiplatelet agents as soon as the TBI is stable, ideally within the first 24 hours.
- Spine fractures are the single most predictive factor of BCVI, with greatest risk to the vertebral artery.
- Perform liberal screening in older adult patients with risk factors for BCVI, because BCVI in geriatric patients is an independent risk factor for mortality.

Extracranial BCVI has a reported incidence of 2.7% to 7.6% among patients who had CT angiography following blunt force trauma.[1,2] Undetected carotid and vertebral artery injury can lead to delayed therapy and increase the patient's risk of stroke. Patients at high risk of stroke can present with both carotid and vertebral artery injury. Untreated carotid and vertebral artery injuries have a mortality as high as 38% and 18%, respectively.[3,4] Both Denver and Memphis trauma groups have recommended criteria to screen for BCVI (see Box 5).

Spine fractures are the single most predictive factor of BCVI, with greatest risk to the vertebral artery.[3,5,11–13] Older adult patients with low-energy injury mechanisms, including ground-level falls, are also at risk for BCVI.[14] Radiographic screening for BCVI with CT angiography is a sufficient and cost-effective modality, and it is the recommended means of excluding this injury.[15–17] However, for questionable injuries or those that may be amenable to endovascular treatment, formal angiography may be performed.

Even with strict adherence to the Denver and Memphis screening criteria, 20% to 30% of BCVIs are missed.[1,2,18,19] Several studies now recommend universal screening for all patients with major trauma using a whole-body CT (WBCT) scan.[1,2,18] The WBCT includes a non-contrast CT of the head followed by a multi-slice (40- or 64-slice) CT scan incorporating a single IV contrast-enhanced pass from the circle of Willis through the pelvis. This imaging allows screening for BCVI while evaluating the cervical spine, chest, abdomen, and pelvis.[1,2,19] Although some authors question the benefit of a universal WBCT scan for trauma patients, the practice is supported by the American College of Radiology (ACR) Appropriate Use Criteria of CT scans for major blunt trauma.[20,21]

Box 5. Recommended Screening Criteria for BCVI[5–10]

- Scalp degloving injury
- Severe TBI with GCS < 6
- TBI with thoracic injuries
- Neurological exam findings not explained by neuroimaging
- Focal neurological deficit (transient ischemic attack, hemiparesis, vertebrobasilar symptoms, oculosympathetic palsy/Horner syndrome)
- Evidence of cerebral ischemia or vascular territory edema on CT or MRI
- Base of skull fracture with involvement of the carotid canal or petrous temporal bone
- Complex skull fracture (e.g., involving frontal or other sinuses, orbit)
- Le Fort II or III fracture pattern
- Mandible fracture
- Cervical spine fracture
- Arterial hemorrhage from the neck, nose, or mouth
- Neck soft tissue injury (e.g., seatbelt sign, hanging, hematoma)
- Near hanging with hypoxic-ischemic (anoxic) brain injury
- Clothesline-type injury or seat belt abrasion with significant swelling, pain, or altered mental status
- Crepitus in soft tissue of neck
- Cervical bruit in patients < 50 years of age
- Upper rib fractures
- Thoracic vascular injuries
- Blunt cardiac rupture

BCVI Management

Management of BCVI is principally focused on mitigating the risk of thromboembolism, which would result in ischemic stroke.[9,22,23] Treatment options include the use of antiplatelet agents, anticoagulants, and endovascular therapy. Large observational studies identified that treatment with any antithrombotic medication appears to be associated with lower risk of stroke than no treatment, although this has not been tested in large randomized trials.[4,22] Trials of patients with cervical arterial dissection, including but not primarily focused on BCVI patients, have found that antiplatelet therapy and anticoagulation with warfarin (usually with bridging IV heparin until INR is therapeutic) generally perform in a similar manner, although a slight benefit to warfarin may exist.[24–26]

When a BCVI is found, current best practice is to initiate treatment with anticoagulation or antiplatelet agents as soon as the TBI is stable, ideally within the first 24 hours for patients who are not at a high risk for TBI progression and in whom bleeding from extracranial injuries is controlled.[23,27–30] This recommendation is reasonable for patients who have experienced symptoms from cerebral ischemia (e.g., transient ischemic attack or infarction) and for patients asymptomatic from their extracranial BCVI. Remaining questions include, is dual antiplatelet therapy preferred over aspirin alone, and do high-risk features such as intraluminal thrombus or BCVI grade warrant anticoagulation over antiplatelet therapy? Information on the use of direct-acting oral anticoagulants as an alternative to warfarin is limited.

Generally, treatment with antithrombotic agents continues for at least 3 months.[26] Follow-up noninvasive imaging with CT angiography or MRI at 3 months is reasonable to assess healing.[26] Consider reserving endovascular therapy with stenting or coil embolization for nonhealing pseudoaneurysms or recurrent cerebral ischemic events despite antithrombotic therapy.[29] Primary endovascular embolization/sacrifice of an artery affected by BCVI is often not recommended as an initial strategy. This is because of the risk of periprocedural complications[29] and the natural history of healing for many lesions, as long as the patient is protected from thromboembolic events by some form of antithrombotic therapy. However, depending upon the involved vessel and injury grade and configuration, stenting for carotid injuries and stenting or embolic occlusion for vertebral injuries may be safely performed but may also still require adjunctive antiplatelet therapy.[31]

Older Adult Considerations

Data on BCVIs in older adult patients are relatively sparse. BCVIs are classically associated with a high-energy injury mechanism. Older adults are more commonly injured by lower-energy mechanisms, and they may not receive liberal screening for BCVI.[32] However, older adults are at high risk for injuries typically associated with BCVI, such as vertebral body fractures. Although the overall incidence of BCVI is lower in older adults than in younger cohorts, BCVIs are found relatively commonly after ground-level falls.[14] The consequences of these injuries in older adult patients can be devastating. Not only are they more likely to have higher-grade lesions, but BCVI in older patients are also an independent risk factor for mortality.[14,33] Perform liberal screening in older adult patients with risk factors for BCVI.

Pediatric Considerations

Pediatric evaluation for BCVI must consider the additional risk of radiation exposure in children. BCVI prevalence is lower in the pediatric population compared to adults, and application of the Denver criteria would likely overestimate BCVI incidence.[34] The Utah score is a validated BCVI scoring system with high specificity and incorporates risk factors to classify patients as "low" or "high" risk of BCVI-related complication (see Table 5).[35,36] The McGovern modification adds two points for severe injury mechanism related to motor vehicle collision and results in increased sensitivity for BCVI diagnosis.[37]

Table 5. The Utah Score for Assessment of BCVI in Pediatric Patients

Variables	Score
GCS ≤ 8	1
Focal neurological deficits	2
Carotid canal fracture	2
Petrous temporal bone fracture	3
Cerebral infarction on CT	3

A maximum of 11 points are possible. A score ≥ 3 conferred an 18% risk of BCVI, while a score ≤ 2 was associated with less than 3% risk.
From: Ravindra VM, Riva-Cambrin J, Sivakumar W, Metzger RR, Bollo RJ. Risk factors for traumatic blunt cerebrovascular injury diagnosed by computed tomography angiography in the pediatric population: A retrospective cohort study. *J Neurosurg Pediatr*. 2015;15(6):599–606.

Implementation of these risk stratification systems is suggested to identify patients at high risk who need to receive dedicated arch-to-vertex CT angiography. Like the adult recommendations, treatment with antiplatelet or anticoagulation therapy is initiated after BCVI diagnosis, based on intracranial injury stability and extracranial hemorrhage source control. Further evidence is required to identify specific treatment duration recommendations. Treatment should be individualized; however, consider surgery or endovascular therapy for higher-grade injuries (Biffl grade ≥ 3) or for patients with progressive lesions receiving medical therapy.[36–38]

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TIMING OF PHARMACOLOGIC VENOUS THROMBOEMBOLISM PROPHYLAXIS

KEY POINTS

- Venous thromboembolism (VTE) prophylaxis is recommended within 24 hours after injury in patients with low-risk nonoperative TBI, provided the follow-up CT shows no progression of intracranial injury.
- VTE prophylaxis is recommended within 24 to 48 hours after injury in patients with moderate- or high-risk nonoperative TBI, provided the follow-up head CT shows no progression of intracranial injury.
- In patients who have undergone craniotomy or craniectomy, consider initiating or resuming pharmacologic VTE prophylaxis within 24 to 48 hours after surgery if ICH is stable on postoperative CT.
- Low-molecular-weight heparin (LMWH) is preferred over unfractionated heparin (UFH) for prophylaxis in TBI patients.

Trauma patients, particularly those with polytrauma or severe injury patterns, have a significant risk of VTE. Patients with TBI have a high risk of VTE without prophylaxis or when receiving only mechanical prophylaxis.[1,2] Providing pharmacologic VTE prophylaxis for trauma patients with significant injuries is standard practice.[1-3] VTE risk increases for patients with TBI for each day that passes without pharmacologic VTE prophylaxis, and VTE rates increase when trauma patients miss doses of pharmacologic VTE prophylaxis.[3-5] A substantial body of evidence indicates that pharmacologic VTE prophylaxis reduces VTE rates in general trauma and TBI patients, and it may improve outcomes in TBI.[6] Current best practice is to use mechanical prophylaxis on all TBI patients upon admission, regardless of their eligibility for pharmacologic prophylaxis.[3]

For patients with TBI, clinicians must balance concerns for progression of ICH with and without pharmacologic VTE prophylaxis against the known benefits of pharmacologic prophylaxis for reducing VTE risk. A general correlation of TBI severity with risk of ICH progression has been demonstrated.[7,8] Individual patient factors may also affect risk of bleeding or thrombosis, such as congenital or acquired hypercoagulable or coagulopathic states, use of antithrombotic and anticoagulation medications, and acute injury patterns. The modified Berne-Norwood criteria and the Brain Injury Guidelines stratify risk of ICH progression based on mild, moderate, and severe injury patterns, with the Brain Injury Guidelines also accounting for several clinical factors (see Table 6).[7,8]

Table 6. Anatomic Factors and Risk for Intracranial Hemorrhage Progression

Criteria	Low Risk	Moderate Risk	High Risk
Modified Berne-Norwood criteria	No moderate- or high- risk criteria	• SDH or EDH ≥ 8 mm • Contusion or IVH ≥ 2 cm • Multiple contusions per lobe • Scattered subarachnoid hemorrhage • Evidence of progression at 24 hrs	• ICP monitor placement • Craniotomy • Evidence of progression at 72 hrs

Data from: Pastorek RA, Cripps MW, Bernstein IH, et al. The Parkland Protocol's modified Berne-Norwood criteria predict two tiers of risk for traumatic brain injury progression. *J Neurotrauma.* 2014; 31: 1737–1743. doi: 10.1089/neu.2014.3366; Joseph B, Friese RS, Sadoun M, et al. The BIG (Brain Injury Guidelines) project: Defining the management of traumatic brain injury by acute care surgeons. *J Trauma Acute Care Surg.* 2014; 76: 965–969. doi: 10.1097/TA.0000000000000161.

Current evidence supports early initiation of pharmacologic VTE prophylaxis in TBI patients. In the last decade, multiple studies and two systematic reviews have suggested that, in patients with ICH stability reported on follow-up CT scan and regardless of TBI severity, initiation of earlier prophylaxis is associated with reduced VTE rates without clinically significant ICH progression.[6,9–14] Patients with progression of ICH prior to receiving prophylaxis and those undergoing cranial surgery, however, may behave differently and warrant additional observation prior to initiation of prophylaxis.[4,15] While use of pharmacologic VTE prophylaxis in TBI patients continues to be an area of evolving investigation, a reassessment of the available evidence and expert consensus prompted these updated recommendations.

In patients with nonoperative TBI patterns, repeating head CT imaging within 24 hours after the initial CT is recommended to assess ICH stability prior to starting pharmacologic VTE prophylaxis. The possible exception is patients with minimal hemorrhage on initial CT who may not warrant repeat imaging. In hospitalized patients with low risk of ICH (as described in Table 6), consider starting pharmacologic VTE prophylaxis within 24 hours if ICH is stable on repeat CT. In patients with moderate/high risk for ICH progression, consider starting pharmacologic VTE prophylaxis in 24 to 48 hours if ICH is stable on repeat CT.

Patients with an ICP monitor (intraparenchymal or EVD) but without craniotomy/craniectomy may be considered for pharmacologic VTE prophylaxis in the same manner as patients with nonoperative TBI described above. Withholding pharmacologic VTE prophylaxis prior to ICP monitor placement or while the monitor is in place is **not** recommended. Consider continuing pharmacologic VTE prophylaxis without holding doses prior to removal of the ICP monitor. Another option is to coordinate the timing of monitor insertion/removal after one half-life of the drug has passed. In patients who have undergone craniotomy/craniectomy, consider initiating or resuming pharmacologic VTE prophylaxis in 24 to 48 hours after surgery if ICH is stable on postoperative CT. For patients with CT evidence of ICH progression, withholding pharmacologic VTE prophylaxis is recommended until ICH stability is demonstrated on repeat imaging, usually in another 24 to 48 hours.[14,15]

LMWH is considered superior to UFH for VTE prophylaxis in trauma patients without TBI,[1,3] and LMWH is the preferred agent for TBI patients, including those with ICP monitors.[3,16–21] Current evidence suggests that LMWH is associated with lower VTE rates and comparable ICH progression rates when compared to UFH, in both operative and nonoperative TBI patients.[16–21] Current best practice dosing for enoxaparin in general trauma patients is 40 mg every 12 hours.[1] Because of insufficient and specific research of this dosing regimen in patients with TBI, an initial regimen of 30 mg every 12 hours is recommended for patients with TBI. If using dalteparin, standard dosing is recommended. Additionally, consider monitoring anti-factor Xa activity levels to guide subsequent LMWH dosing.[1–3,22] If UFH is chosen for pharmacologic VTE prophylaxis, best practice is to dose at 5000 units every 8 hours. Use of prophylactic inferior vena cava filters is no longer recommended, regardless of the timing of pharmacologic VTE prophylaxis in TBI patients. The indication for inferior vena cava filter placement is the presence of a known VTE in a patient with contraindication for therapeutic anticoagulation.[3]

Monitoring local experience for performance improvement (PI) opportunities is beneficial. PI metrics to consider include:

- Time to initiation of pharmacologic VTE prophylaxis
- Pharmacologic VTE prophylaxis agent used
- Delayed craniotomy/craniectomy rate

Older Adult Considerations

Pharmacologic VTE prophylaxis management in the geriatric population is the same as described for other adults. Keep in mind that altered renal function may affect LMWH dosing or prompt the use of UFH.

Pediatric Considerations

VTE in pediatric trauma patients is very rare in comparison to adult populations. Age is an important VTE risk factor in children; estimates show VTE incidence of 0.09% in patients ages 0–12 years, 0.27% in patients ages 13–15 years, and 0.73% in patients ages 16–21 years.[22,23] Several scoring systems have been proposed to determine the risk of VTE in individual pediatric trauma patients and to inform

decisions regarding use of mechanical and pharmacologic VTE prophylaxis. General risk factors include older age, higher injury severity score, lower GCS, blood transfusion, prolonged central venous catheter use, and major surgery.[23–25] Considering these factors, recommendations include:

- Hospitals need to adopt a published VTE risk assessment tool (e.g., ROCKIT) for pediatric trauma patients, and VTE risk stratification needs to be performed following admission.[26]
- Children at low risk do not require pharmacologic VTE prophylaxis.
- Children at moderate risk need to have mechanical VTE prophylaxis initiated at admission.
- Reserve pharmacologic VTE prophylaxis for patients considered at high risk for VTE.
- Pediatric contraindications to pharmacologic VTE prophylaxis are the same as for adults (regarding presence of ICH, risk of ICH progression, and recent surgery).
- LMWH is the preferred agent for pharmacologic VTE prophylaxis in the pediatric population. Use weight-based dosing in young children.
- While duration of VTE prophylaxis is not well studied, discontinue VTE prophylaxis when the patient is ambulatory in the absence of other thrombogenic factors.

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PHARMACOTHERAPY FOR TRAUMATIC BRAIN INJURY

KEY POINTS

- Patients with TBI at high risk of early posttraumatic seizures (PTS) have a lower incidence of PTS when receiving phenytoin or levetiracetam, compared to those receiving no antiseizure medication (ASM).
- Consider the use of ASM prophylaxis for 7 days following severe TBI to prevent early PTS if risk factors are present; however, its use for more than 7 days to prevent late PTS is **not** recommended.
- Carefully assess patients receiving warfarin or direct-acting oral anticoagulants (DOACs) and initiate drug-specific reversal therapy for those requiring emergent surgery for life-threatening bleeding.
- Consider restarting anticoagulation no later than 14–90 days after TBI, depending on patient-specific risk for thrombosis and bleeding.
- Routine platelet transfusion is **not** recommended for use in reversing antiplatelet agent effects. Use clinical judgment to determine if patients with TBI on antiplatelet agents who are undergoing surgery or invasive procedures with low platelet counts need platelet transfusions to achieve hemostasis.
- Restart antiplatelet agents as early as 4 days after injury, based on assessment of patient-specific risk for thrombosis and bleeding.
- Beta blockers (e.g., propranolol) may be considered for treatment of TBI patients with adrenergic stress or paroxysmal hyperactivity syndrome ("storming"), but adverse effects must also be considered.
- Administer antibiotic surgical prophylaxis based on published guidelines, in conjunction with pharmacist consultation and assessment of ICU antibiograms.
- Antibiotic prophylaxis is not recommended for EVD or intraparenchymal ICP monitor placement, skull-based fractures, CSF leaks, or pneumocephalus, because the prophylaxis may promote growth of drug-resistant bacteria.

Posttraumatic Seizure Prophylaxis

Incidence of PTS: Early PTS (< 7 days) are correlated with severity of TBI injury, and patients with penetrating injuries have the highest incidence.[1,2] Other high-risk patients include those who experience an immediate PTS or have depressed skull fractures, SDH, ICH, GCS < 10, or cortical contusions.[3] Early PTS is also associated with TBI morbidity and mortality, and increased risk of developing post traumatic epilepsy (PTE).[4,5] Findings from an RCT reported early PTS incidence of 14.2% in the placebo group, as compared to 3.6% of patients assigned to phenytoin.[3] However, early seizure prophylaxis did not prevent PTE, highlighting the need for a contemporary randomized clinical study.

PTS prophylaxis: Consider the use of ASM prophylaxis for 7 days following TBI to prevent early PTS if risk factors are present; however, its use for more than 7 days to prevent late PTS is **not** recommended. Seizure prophylaxis is not recommended in TBI patients without intracranial bleeding, or in patients with isolated traumatic subarachnoid hemorrhage.[6,7]

Currently the most studied ASMs for PTS are (fos)phenytoin, levetiracetam, and valproic acid. Of these, phenytoin and levetiracetam appear to be similar in safety and efficacy for early PTS for patients at risk.[8] However, the incidence of early PTS in these studies was low, and superiority of one drug over the other could not be determined.

- **Phenytoin** is an older ASM that requires therapeutic drug monitoring to assure target concentrations are achieved. It is usually monitored 24 hours after initial dosing and once more during the 7 days of prophylaxis in TBI patients. However, phenytoin has many drug-drug interactions, as well as potentially severe adverse drug reactions (ADRs). Phenytoin is also highly bound to albumin, so monitoring albumin and free phenytoin concentrations is essential to guide dosing adjustments. If laboratory assays for free phenytoin are not available, correction of total phenytoin concentrations can be calculated.[9,10]

- **Levetiracetam** is an ASM with a better pharmacokinetic profile and minimal ADRs relative to phenytoin. However, it was observed to have associated behavioral ADRs in both pediatric and adult patients, particularly those with TBI.[11-15] Pyridoxine 50–100 mg daily supplementation may limit these behavioral ADRs.[16]
- **Valproic acid** is **not** recommended for early PTS prophylaxis due to an increased risk of death compared to phenytoin.[17]

Do not continue PTS prophylaxis for more than 7 days in patients with no clinical or EEG seizure activity, or with seizure activity only within the first 24 hours postinjury. Seizure prophylaxis may be continued if seizure activity occurs beyond 24 hours or if the patient was previously receiving medication for a known seizure disorder.

Anticoagulant Management in TBI Patients

Anticoagulant reversal: Consider anticoagulant reversal for patients with TBI who were taking an anticoagulant medication prior to admission, in order to allow them to safely undergo emergent surgery and/or to help prevent hematoma expansion. A specific reversal agent is generally recommended for each available oral anticoagulant medication. If the last dose of a DOAC was within the past 8–12 hours (or the INR is elevated ≥ 1.5 for patients receiving warfarin), the benefits of a reversal agent will most likely outweigh the risks.

When prescribing four-factor prothrombin complex concentrates (4PCCs), some providers choose to use fixed doses of 1500 to 2500 units rather than using weight-based dosing strategies for anticoagulant reversal. Lower doses of 4PCC (10–20 units/kg) are suggested for patients with an INR 1.5–1.9, as higher doses (> 2000 to 3000 units) were associated with increased VTE risk in patients with nontraumatic ICH.[18,19]

> **Note:** If 4PCC is not available and fresh frozen plasma (FFP) is administered, approximately 8–16 units of FFP are equivalent to approximately 20–50 units/kg of 4PCC. The lowest achievable INR for FFP alone is approximately 1.5–1.7; the mean intrinsic INR of FFP is 1.1, but it can range from 0.9–1.3.

Specific anticoagulant reversal recommendations for patients with life-threatening bleeding (all etiologies) are published by the Neurocritical Care Society/Society of Critical Care Medicine, American Heart Association, and American Society of Hematology.[20-22] Acute clinical management of TBI patients admitted on oral anticoagulant medications includes the following:

- Discontinuation of the anticoagulant
- Determination of the DOAC type, dose, time of last dose
- Determination of the impact of DOAC on surgical intervention and reversal strategies, when possible

Laboratory assays are not readily available for DOAC-specific quantitative measurements of anti-Xa activity or DOAC concentrations, nor is there a definitive therapeutic range for DOAC concentrations.[23] More common clinical laboratory measurements that may be elevated if a DOAC was recently administered and have clinically relevant concentrations include the following:

- An activated partial thromboplastin time in patients on dabigatran (thrombin inhibitor)
- Elevations of prothrombin time and activated partial thromboplastin time in patients on Xa inhibitors

Normal values may not rule out potential therapeutic DOAC concentrations.[20,22-24]

> **Note:** Do not delay reversal therapy while waiting for laboratory results in emergent situations when the patient is at high risk for bleeding.

A medical history is very helpful to determine if comorbidities may increase DOAC concentration or prolong DOAC exposure (e.g., advanced age, renal dysfunction, renal failure or dialysis dependence, and drug interactions). TEG may be helpful for qualitative assessment of clot strength and fibrinolysis, but evidence is lacking for its use to support quantitative determination of therapeutic DOAC concentrations.[23,25,26] **Note:** TEG results may not be accurate in patients receiving massive transfusion therapy. A summary of reversal strategies for oral anticoagulation agents can be found in Table 7.

Table 7. Anticoagulation Reversal Strategy for Patients with TBI Needing Emergent Surgery[19,20-22,27]

Oral Anticoagulant Agent	Reversal Strategy
Warfarin	• 2.5–10 mg of IV vitamin K **and:** – If INR is 1.5–1.9, give 15 units/kg 4PCC IV – If INR is 2–3.9, give 25 units/kg 4PCC IV – If INR is 4–6, give 35 units/kg 4PCC IV – If INR is > 6, give 50 units/kg 4PCC IV **-or-** – 1500 units 4PCC (fixed dose) • Recheck INR 1 hour after 4PCC given, if INR is > 1.4, consider administering 2–4 units of FFP • Recheck INR 6–8 hours after 4PCC. If INR is > 1.4, administer another 2.5–10 mg of IV vitamin K
DOACs (rivaroxaban, apixaban, edoxaban)	• If the last dose was administered < 2 hours earlier, consider activated charcoal • Andexanet alfa – If last dose was > 7 hours, administer 400 mg IV bolus followed by 480 mg IV infusion – If last dose was < 7 hours, administer 800 mg IV bolus followed by 960 mg IV infusion • If andexanet alfa is not available, use 25–50 units/kg of 4PCC or a fixed dose of 2000 units • If the last DOAC dose was > 18–24 hours prior to the bleed, a reversal agent may not be beneficial
Thrombin inhibitor (dabigatran)	• If the last dose was administered < 2 hours earlier, consider activated charcoal • Administer two consecutive doses of 2.5 g of idarucizumab IV, with each dose being infused over 10 minutes • If the last dose was > 24 hours prior to the bleed, a reversal agent may not be beneficial • Consider dialysis in patients with renal failure • If idarucizumab is not available, 4PCC or single factor prothrombin complex concentrate PCC 50 unit/kg may be considered

Patients requiring therapeutic anticoagulation prior to admission continue to have an underlying risk of thrombosis. Therefore, consider VTE prophylaxis with subcutaneous heparin or LMWH to prevent further risk of thrombosis in the acute period off anticoagulants. Also consider the benefit versus harm of reversal based on bleeding risk and risk of thrombosis from the underlying disease.

Restarting anticoagulation: The available evidence is insufficient to recommend the optimal timing to restart anticoagulation in patients at moderate to high risk for thromboembolic events (e.g., mechanical valve or left ventricular assist device patients, history of VTE in the last 3 months) but not at a high risk for rebleeding. However, consider restarting anticoagulation earlier than in lower-risk patients (e.g., patients with atrial fibrillation and lower CHA_2DS_2-VASc scores, spontaneous ICH, VTE more than 3 months prior). Available guidelines suggest waiting 2 weeks or less for patients at high risk and 7–8 weeks for low-risk patients, but not more than 90 days after the bleeding event. However, safe restart of anticoagulant medications may occur significantly sooner, especially if traumatic intracranial bleeding is less significant and/or stable on repeat CT imaging.[22,28] This guidance is based on available clinical evidence, and it is dependent on patient-specific thrombosis and bleeding risk factors.

Note: High-risk warfarin patients receiving high doses of vitamin K for reversal (> 2.5 mg) appear to have similar time and magnitude of INR reduction, but the vitamin K (a fat-soluble vitamin) will likely delay warfarin's therapeutic effect for several weeks after restart.[29] In such cases, anticoagulation using LMWH or unfractionated heparin is needed until the effects of the vitamin K have worn off.

Antiplatelet Agent Management in TBI Patients

Reversal of antiplatelet agent effects: The reversal of antiplatelet agent effects in patients with traumatic ICH remains controversial. Few relevant RCTs exist, and conflicting data were reported about the impact on hematoma expansion or neurological outcomes.[30-34] A recent meta-analysis of low-quality data showed no difference in hematoma expansion or need for neurosurgical intervention in patients on single antiplatelet agents when compared to patients on no therapy.[35] Additionally, the most common treatments for reversal of antiplatelet effects (platelet transfusions and desmopressin) are associated with adverse effects that may cause further complications and worse outcomes. A recent study of patients with traumatic ICH found no between-group differences in progression of hemorrhage or rate of neurosurgical intervention in transfusion versus no-transfusion groups.[36] However, a trend toward increased ICU LOS (adjusted odds ratio 1.59, 95% CI 0.74–3.40) and in-hospital death (adjusted odds ratio 3.23, 95% CI 0.48–21.74) was found in those receiving a platelet transfusion.[36] Studies evaluating the combination of desmopressin and transfusion also demonstrated no benefit in hematoma progression or mortality.[37] It is important to note that patients receiving antiplatelet agents who have a low platelet count and undergo invasive procedures (e.g., craniotomy, insertion of a ventricular drain, or insertion of an intraparenchymal ICP monitor) may benefit from preprocedural transfusion of platelets to achieve some degree of circulating functional platelets to promote procedural hemostasis. Postoperative platelet transfusion is not routinely recommended, because antiplatelet medications may continue to affect the functionality of transfused platelets. Patients on preinjury antiplatelet agents without additional risk factors are **not** recommended to receive platelet transfusions for this reason alone.

Important factors to consider when deciding whether to administer therapies reversing preinjury antiplatelet agent effects include antiplatelet agent characteristics and antiplatelet activity monitoring results. Antiplatelet agents are categorized as reversible or irreversible. Irreversible agents have effects throughout the platelet lifespan (approximately 8–20 days). Transfused platelets are also inhibited by these agents until the irreversible agents are eliminated from the blood stream, at about 3–5 times the half-life of the agent.[20,38,39] The antiplatelet agents that have active metabolites (e.g., clopidogrel and ticagrelor) have longer antiplatelet activity. Point-of-care platelet function assays are recommended as an adjunct to standard laboratory and/or coagulation monitoring in patients with suspected platelet dysfunction from preinjury antiplatelet therapy. Platelet function tests help identify patients who may benefit from reversal therapies and decrease the potential risk of thrombosis from unnecessary treatment.[38-40]

Current guidelines suggest that all patients discontinue antiplatelet agents in the acute period postinjury. For patients who require a neurosurgical procedure, consider one single-donor apheresis unit of platelets (equivalent to 6 pooled units or 1 random-donor unit per 10 kg of body weight).[20,40] Desmopressin (0.4 mcg/kg IV) was also suggested for consideration alone or in addition to a platelet transfusion for neurosurgical patients who received aspirin, clopidogrel, or ticagrelor. If desmopressin is administered, monitor for hyponatremia and treat as needed to achieve therapeutic sodium concentrations. Platelet function testing prior to transfusion is recommended whenever possible. For patients with normal platelet function or documented resistance, reversal therapies are **not** recommended. Additional research is needed to confirm benefit of these strategies in patients on preinjury antiplatelet therapies. Until more data are available, platelet transfusion and desmopressin are **not** recommended for patients with TBI who are not candidates for an invasive intervention.

Restarting antiplatelet agents: Consider the reason for antiplatelet therapy when determining if and when to restart antiplatelet therapy in patients after traumatic ICH. Studies support restarting antiplatelet therapy as early as 4 days postinjury, because most posttraumatic hemorrhages occur within 3 days.[41] Risks for acute and delayed ICH after restarting antiplatelet agents must be weighed against the morbidity of thrombotic complications that can have significant clinical consequences. Individual assessment of risk versus benefit must be made for restarting antiplatelet therapy.

Paroxysmal Hyperactivity Syndrome ("Dysautonomia," "Sympathetic Storm")

After TBI, patients can experience loss of inhibitory inputs to sympathetic feedback loops, resulting in symptoms such as hypertension, tachycardia, hyperpyrexia, tachypnea, or diaphoresis. These symptoms can be treated with a variety of agents, including beta blockers (BBKs), benzodiazepines, opioids, alpha-2 agonists, gabapentin, muscle relaxants, and baclofen. Low-quality data suggest that BBKs are associated with decreased mortality in patients with severe TBI who experience paroxysmal hyperactivity syndrome.[42–44] Most of the larger studies to date were observational or retrospective and had the following issues: inconsistency in the dose, beta blocking agent, and timing after injury; variability in patient characteristics and monitoring of adverse events; and whether BBKs were initiated or continued for other comorbidities versus only for TBI adrenergic stress.[42–44] Propranolol, a nonselective BBK, has the most evidence to support its use for these indications. Monitoring for BBK adverse effects, such as bradycardia, hypotension, congestive heart failure, and bronchospasm, is essential, as these effects could be detrimental in the acute period post-TBI.

Disorders of Consciousness

Patients with disorders of consciousness have a prolonged altered consciousness that can be characterized as coma, vegetative state/unresponsive wakefulness syndrome, or minimally conscious state based on their clinical exam. Following assessment and treatment of any confounding factors, amantadine (100–200 mg twice daily) is recommended for adults with vegetative state/unresponsive wakefulness syndrome or minimally conscious state (4–16 weeks postinjury) to accelerate recovery and reduce disability.[45,46]

Antibiotic Prophylaxis

Infection rates reported for patients undergoing ICP monitoring are highly variable. Rates are extremely low for intraparenchymal fiberoptic ICP monitors but may be significantly higher for EVDs. It is essential to develop and follow facility EVD and intraparenchymal bolt insertion and management protocols to decrease the risk of infectious complications.[47] Avoid the use of systemic antibiotic prophylaxis during parenchymal ICP monitor insertion and during the use of parenchymal or ventricular drains to reduce the risk for drug-resistant organisms.[47,48] The most recent BTF and Neurocritical Care Society guidelines recommend the use of antimicrobial-impregnated catheters to prevent ventriculostomy-related infections during EVD monitoring, but these may not be available in every facility.[47,49] A recent meta-analysis also suggested a substantial decrease in CSF infections (from 13.7% to 3.6%) when antimicrobial-impregnated catheters were used, as compared to a standard catheter group.[50] Other strategies to reduce risk of infection include the following[47]:

- Remove ICP monitors and drains as early as clinically possible
- Avoid routine EVD closed-system manipulation
- Avoid CSF sampling unless clinically indicated
- Use aseptic technique

Developing an EVD bundle with an insertion checklist, maintenance worksheet, dressing change procedure, and CSF sampling protocols and techniques is another strategy to reduce ventricular catheter-related infections.[51]

Avoid the use of antibiotic prophylaxis for traumatic skull-based fractures with CSF leaks or pneumocephalus due to the increased risk of promoting drug-resistant organism growth.[52] In patients with open or penetrating skull fractures, consider treatment with broad-spectrum antibiotics with high blood-brain barrier penetration for a maximum of 3 days. Surgical debridement and irrigation are recommended as the standard of care, with perioperative antibiotics for not more than 24 hours.

For surgical prophylaxis, cefazolin is the drug of choice for patients without *methicillin-resistant Staphylococcus aureus*, unless the patient has a documented severe beta lactam allergy. Clindamycin or vancomycin are appropriate alternatives for those with a severe allergy to beta lactams. Clarify any antibiotic allergy preoperatively, when possible, given the superiority of cefazolin to the alternative options. Select the antimicrobial agent and dosing using published guidelines, in conjunction with pharmacist consultation, to optimize therapy.

Older Adult Considerations

Antithrombotic/antiplatelet reversal and restart: Although older adult patients are more likely to receive anticoagulant and antiplatelet agents for comorbidities preinjury, available evidence does not suggest a difference in the risk of worse outcomes for older adult patients with TBI undergoing neurosurgery, despite the use of an anticoagulant or antiplatelet agent.[53–55] The anticoagulant used and the number of antiplatelet agents, however, may impact the risk of worse outcomes. Time to restart of anticoagulants and antiplatelet agents is similar for all patients, regardless of age.

Antibiotic prophylaxis: When selecting an antibiotic and dose for surgical prophylaxis or treatment, older adults' physiologic, pharmacokinetic, and pharmacodynamic changes must be considered to help avoid unwanted adverse effects or toxicity.

Pediatric Considerations

PTS prophylaxis: Pediatric data are in line with adult data as described for PTS prophylaxis. PTS may be more likely to occur in children less than 24 months old, those with severe injury (GCS < 8), and those suffering nonaccidental trauma.[56–60] Despite the growing popularity of levetiracetam for PTS prophylaxis in children with TBI, evidence for its efficacy remains limited, with one recent observational trial demonstrating seizures in 17% of children treated with levetiracetam prophylaxis after TBI.[61] As a result, either levetiracetam or (fos)phenytoin is appropriate for the recommended 7-day course of prophylaxis. Levetiracetam has a more favorable adverse effect profile, and therapeutic drug monitoring is not needed. The most commonly used dose of levetiracetam is 20–40 mg/kg/day, divided into two doses per day. Facilities are encouraged to develop multidisciplinary guidelines, with weight-based dosing, for pediatric PTS prophylaxis.

Antithrombotic/antiplatelet reversal and restart: As in adult patients, consideration of anticoagulant and antiplatelet reversal and restart in pediatric patients requires a thorough risk-benefit analysis for each individual patient before making clinical decisions.

Antibiotic prophylaxis: Pediatric-specific data are limited regarding the use of antimicrobial prophylaxis outside of the perioperative period of EVD placement. Extrapolation of the adult data outlined above and previous studies in similar settings (e.g., hydrocephalus, ventriculoperitoneal shunt failure) support only the use of perioperative antimicrobials.

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PROGNOSTIC ASSESSMENT AND FAMILY COMMUNICATION

KEY POINTS

- Functionally meaningful recovery (i.e., return to independence) may be possible even if consciousness is absent in the first 4 or more weeks and even in patients with a depressed mental status in the initial weeks following TBI.
- Shared decision-making and acknowledgement of prognostic uncertainty are recommended communication approaches with families or surrogates.
- Early withdrawal of life-sustaining therapies may lead to a self-fulfilling prophecy of poor outcome.
- Provide aggressive treatment to patients with severe TBI, including necessary surgical procedures, until the clinical team and the family or surrogate agree that further treatment of this type would not be aligned with the patient's values and preferences.
- A best practice is for each trauma center to develop a brain death determination policy derived from accepted standards and in alignment with local laws and policies.

Prognostic Assessment

Patients with severe TBI are at high risk for death and long-term disability. No current prognostic indicators are precise enough to predict poor outcome (e.g., death, permanent unconsciousness, permanent loss of independence) with high certainty, especially not in the initial weeks postinjury. It is notable that functional outcomes acceptable to the patient and/or family can occur in up to 20% of patients who do not regain consciousness in the first 4 weeks after injury.[1] Statistical models including factors available at the time of initial evaluation (e.g., age, neurological function including GCS score and/or pupillary reactivity, and neuroimaging findings) were developed and validated on large populations of patients with moderate to severe TBI. These models provide some general guidance about predicted outcome. The IMPACT and CRASH TBI statistical models are the most extensively validated and can produce point estimates with CI.[2,3] Using these outcome models for exact prognostication on individual patients is **not** recommended. However, clinicians can use these models to describe the predicted outcome probability as an "estimate only, subject to considerable uncertainty." Experts in clinician-family communication recommend using language that brackets the range of possible patient outcomes by describing both the "best case" and "worst case," as well as the "most likely," scenarios as a way of expressing the uncertainty that is inherent in any prognostication.

Numerous studies including various neurocritical care conditions (e.g., intracerebral hemorrhage, global cerebral ischemia after cardiac arrest, and TBI) reported that worsened patient outcomes are associated with the reflexive default to early care limitations, including do-not-resuscitate orders or withdrawal of life-sustaining therapies, independent of other patient characteristics.[4-6] Other studies found the ability to accurately and precisely prognosticate long-term outcome very early in a patient's course after severe TBI is limited and frequently incorrect, especially in the first days after injury.[7] Factors such as clinician perception of recovery likelihood and hospital-specific practice patterns are sometimes implicated in the wide variability documented in early care limitations. These findings increase the concern that patients with severe TBI will have a "self-fulfilling prophecy" of poor outcomes when aggressive care is not provided.[5,6,8]

Given these concerns, the best practice for patients with severe TBI is to provide a trial of aggressive therapy (e.g., surgical therapy, intensive care, and, if appropriate, placement of an intracranial monitor), if this treatment approach is consistent with patient and/or family goals of care. The previously advocated aggressive care minimum of 72 hours is arbitrary and not based in medical evidence. Recent studies reported the possibility of good outcomes in patients who remain unconscious for 4 or more weeks.[1,9] Exceptions include patients declared brain-dead, those with a preinjury advance directive indicating such interventions are not desired, and when families or surrogates wish to pursue comfort-based measures only. Thus, a longer period of treatment and observation is typically needed to increase certainty regarding prognosis for neurological recovery.[10]

Age is often heavily weighted in prognostic decision-making; however, do not use this factor in isolation or consider it as a valid singular reason for treatment-limiting decisions. Patient frailty, medical comorbidities, persistence of bilaterally unreactive pupils, and lack neurologic

improvement are considerations, in addition to age and TBI severity. Take care to ensure that the pupillary light response is accurate and not confounded by medications or external injury (e.g., orbital trauma). For prognostic assessment, make sure to exclude conditions that confound the neurologic examination (e.g., sedative or analgesic medications, or clinical and nonconvulsive seizures). Standardized neurobehavioral rating scales such as the Coma Recovery Scale–Revised are reported to outperform qualitative bedside examination in detecting consciousness, so consider their use when evaluating prognosis.[11]

Family Communication

Several recent studies highlighted the importance of patient-centered clinician-family communication in the ICU, including patients with severe TBI.[12] These studies revealed that the way most clinicians communicate does not meet the needs of surrogate decision-makers. Making person-value congruent decisions on behalf of the patient must be the main focus for surrogates, yet the shock of sudden, unexpected TBI often leaves surrogates unprepared for decision-making. Shared decision-making is a person-centered process during which the clinician and family work collaboratively to arrive at a decision that the patient would choose for themselves.[13] It respects the clinician's expertise while also integrating the patient's values and preferences. This process is often aided by parties with dedicated time and long-term continuity available for these conversations (e.g., palliative care providers). While still undergoing evaluation in clinical trials, formal shared decision-making tools (decision aids) are being developed, and they have been deemed to be very helpful by families. These tools may be available in the future to support clinician-family communication related to patients with severe TBI.

Communication between treating clinicians and surrogate decision-makers needs to include information about condition, treatment, and prognosis, as well as information on the journey ahead should long-term care be necessary and desired by patients and/or surrogates.[14] Involvement of providers with expertise in palliative care and symptom relief, as well as social services, is often helpful. Acknowledging concerns related to finances, family dynamics, pain, and disability are appropriate aspects of family and patient communication.

Brain Death Determination

State law governs the determination of brain death. Standardized criteria for the determination of brain death exist and should be utilized.[15] Criteria specifically include the following:

- Patients meet prerequisites including cardiopulmonary stability and absence of sedative effects
- Patients have no response to central pain, absent brainstem reflexes, and an inability to breathe independently
- Unless prerequisites for the clinical examination cannot be met, the clinical examination is a priority rather than an ancillary test, such as CBF assessment

Each hospital needs to develop a defined brain death determination policy derived from accepted standards. When relevant, partnering with local organ procurement organizations is appropriate to offer families and patients the opportunity for organ donation.

Older Adult Considerations

An optimal prognostication model for older adult trauma patients with TBI has not been identified, and the IMPACT and CRASH TBI statistical models included patients with a mean age in the 30s.[16] Multiple studies report preinjury frailty as the primary predictor of poor outcomes in older adult patients.[17–20] The *ACS TQIP Palliative Care Best Practices Guidelines* recommend consideration of palliative care consultation for patients who screen as frail to facilitate advance care planning and goals of care discussions.[21]

Pediatric Considerations

Prognostic considerations and family communication may be especially challenging in the case of pediatric TBI. Pediatric-specific prognosis tools do not perform adequately and are not recommended in the context of clinical care. Although direct comparison with TBI in adult populations is challenging, children may recover better than adults with similar injuries because of fewer comorbidities and greater capacity for brain plasticity. Indeed, a recent study found that good recovery (GOS-E score 7 or 8) was observed in 44% of children and 59% of adolescents with severe TBI.[22] For this reason, aggressive therapy in a pediatric ICU is warranted in the vast majority of children with severe TBI.

Little guidance exists for discussing prognosis with parents in early acute care following severe TBI in children. It is important to note that prognosis after abusive head trauma may be different from unintentional head trauma. Regardless of mechanism, providers play an important role in shaping parent reception and synthesis of prognostic information, which shapes families' ability to participate in shared decision-making.[23] Assessing and supporting parent needs during the acute phase of pediatric brain injury may improve parent and child outcomes by increasing parents' ability to participate in hospital care and decreasing psychological distress. In cases where brain death is suspected, use pediatric-specific guidelines.[24]

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EARLY MULTIDISCIPLINARY REHABILITATION IN ACUTE TRAUMATIC BRAIN INJURY

KEY POINTS

- Consider early multidisciplinary rehabilitation interventions on the day of admission, during the initial plan of care, and in conjunction with additional acute care decisions.
- Early multidisciplinary rehabilitation is safe, feasible, and cost-effective for patients with TBI who have not yet achieved medical stability and/or continue to require mechanical ventilation. It can mitigate complications of immobility, critical illness, delirium, and cognitive and psychological disorders.
- Include physical medicine and rehabilitation (PM&R) providers on the primary trauma team to enable follow-up from day of admission.
- Include rehabilitation providers from the specialties of physical therapy (PT), occupational therapy (OT), speech language pathology (SLP), psychology/neuropsychology, social work, and nursing.
- Refer the patient to specialized postacute rehabilitation when medically stabile and cleared for discharge from acute care.
- Patients with GCS 13–15 and prolonged physical, cognitive, and psychological complaints/symptoms need follow-up and referral to multidisciplinary rehabilitation.

Individuals sustaining TBI often experience complex neurological, medical, and polytrauma conditions requiring specialized and coordinated trauma team management. Promoting a positive recovery trajectory after TBI requires intentional and consistent collaboration between trauma and rehabilitation experts. The range of TBI severity can manifest as a spectrum of disturbed consciousness, physical limitations, and deficits in cognition, emotions, behavior, and function. Patients with TBI and a GCS of 13–15 can experience acute or prolonged physical, cognitive, and neuropsychological symptoms. These symptoms can significantly impede daily function and impair participation in school and work activities if appropriate treatment and follow-up do not occur.

Critical illness after moderate or severe TBI can lead to prolonged periods of immobility and mechanical ventilation, increasing the risk of acquiring various comorbidities. Immobility negatively impacts all body systems.[1] Comorbidities can include venous thromboembolism, skin breakdown, contractures, deconditioning, delirium, and systemic syndromes such as ICU-acquired weakness.[2,3] These negative outcomes can persist for years.[3,4] When evidence-based practice guidelines and protocols to manage pain, agitation, delirium, immobility, and sleep[5] (e.g., the ABCDEF bundle) were implemented in the ICU setting, the following patient outcomes were found: decreased mortality, decreased comorbidities, improved functional outcomes, and improved quality of life.[6] Recent evidence supports early rehabilitation for patients with TBI to mitigate the negative impact of immobility, avoid secondary complications, and improve function.[7]

Multidisciplinary Rehabilitation Collaboration

The standards in the 2022 ACS *Resources for Optimal Care of the Injured Patient* direct trauma settings to provide the necessary staffing and resources to support early multidisciplinary rehabilitation and mobilization for patients with moderate to severe TBI, because these interventions foster recovery.[8,9] Implementation of early multidisciplinary rehabilitation positively impacts LOS, reduces healthcare costs and resource use, and maximizes long-term functional outcomes.[4] Rehabilitation specialists are experienced in providing early skilled evaluation and therapeutic interventions, objectively measuring the effectiveness of interventions, monitoring physiologic responses, advancing mobility, and guiding the gradual progression from low- to high-intensity modalities. These interventions facilitate stabilization, promote resumption of functional routines, and quantify patient progression and recovery. They can also support the trauma team through provision of evidence-based recommendations to guide treatment and discharge planning.

The benefits of early rehabilitation are optimized when rehabilitation specialists are integrated into the trauma team. The multidisciplinary team needs to include, but is not limited to, PM&R physicians, nurses, PT, OT, SLP, psychologists/neuropsychologists, and social workers. It is recommended that the PM&R physician be a key member

of the trauma team and be involved in the care of the patient from the day of admission. Early PM&R consultation is associated with greater mobility and cognitive independence, as well as a shorter acute care LOS.[10] PM&R physicians can provide insight into outcome expectations and assist with prognostic communications.

Rehabilitation for GCS 3–12

Early multidisciplinary rehabilitation interventions, provided by PT, OT, SLP, and nursing, can be implemented at the bedside while medical stability is being achieved. Treatment interventions through PT, OT, and SLP for patients with severe TBI presenting with consciousness impairments can focus on serial assessment of LOC, arousal optimization through various modalities of stimulation, environmental adaptation, and early mobilization.[11]

Early mobilization: Early mobilization is defined as initiation of mobilization activities within the first 48 hours of injury, or as soon as neurosurgical, hemodynamic, and respiratory stability are achieved. A multitude of evidence demonstrates the efficacy of early mobilization.[1,4,9,12] See Box 6 for early mobilization activities.

Box 6. Early Mobilization Activities

- Passive range of motion
- Active range of motion
- Bed mobility
- Leg ergometer
- Neuromuscular electrical stimulation
- Upright positioning
- Sitting on edge of bed
- Transfers
- Out-of-bed mobility
- Ambulation
- Resistive exercise and engagement in activities of daily living

These interventions are an essential feature of early rehabilitation in the ICU to mitigate the deleterious impact of immobility, and they are safe and feasible.[12,13] Simple interventions (such as passive movement and splinting) can be implemented soon after admission to maintain joint mobility, reduce contractures, and reduce late burden of disability, even in patients who require ongoing treatment to control ICP or symptoms of paroxysmal sympathetic hyperactivity.[14,15] **Note:** Use caution with more severely injured patients, as some interventions (e.g., mobilization out of bed) are only appropriate once hemodynamic and ventilatory stability are achieved and intracranial hypertension is no longer a significant issue.

Management of posttraumatic confusion and agitation: Moderate or severe TBI can present with posttraumatic confusion and agitation. Agitation is common, occurring in approximately 40% of patients.[16] Acute use of benzodiazepines and typical antipsychotic medications is not recommended, because evidence suggests it can protract neurocognitive recovery. Atypical antipsychotics, as well as beta blockers such as propranolol, can be considered as an alternative in the acute phases of agitation to ensure safety for patients and staff.[17] Multidisciplinary rehabilitation assessment and treatment of posttraumatic confusion and agitation can lead to development of behavioral modification approaches that can increase patient engagement in rehabilitation, minimize dependency, improve safety, and limit the need for pharmacologic interventions.[18]

Interventions to promote resumption of self-care and activities of daily living (ADLs): Evaluation and treatment of dysphagia and other oral motor dysfunction by SLP and OT can improve nutritional intake and normalize eating routines. SLP and OT providers can also evaluate the need for alternative and augmentative communication systems to improve interpersonal interactions and patient autonomy.[19] Evidence from a RCT indicated that retraining for self-care and ADLs can be initiated during posttraumatic confusion, leading to faster improvement in functional independence and shorter LOS.[20]

Rehabilitation for GCS 13–15

Up to 90% of all patients with TBI present with a GCS of 13–15.[21] Symptoms can last for months or years if left untreated and can result in disability. Patients with TBI and GCS of 13–15 experiencing prolonged symptoms benefit from referral to a multidisciplinary rehabilitation team, usually provided in an outpatient or community setting, to support

successful return to lifestyle, including work and school.[21] Rehabilitation specialists (sports medicine, PM&R, PT, OT, SLP, and neuropsychology) can provide a multidisciplinary evaluation and treatment recommendations to address persistent symptoms.

Transition of Care Recommendations

A continuous chain of ongoing, individualized rehabilitation services is recommended beyond the ED, ICU, and acute care, including consideration for coordination and continuity of postdischarge care.[22] In hospitalized patients, begin discharge planning for the next level of care early, following admission to the trauma setting. Postacute care options include long-term acute care hospitals, inpatient rehabilitation facilities, skilled nursing facilities, outpatient rehabilitation programs, and home- and community-based services.[8]

Many patients with moderate or severe TBI have complex, ongoing medical needs that warrant continued medical and nursing management in an inpatient rehabilitation setting. The primary objective is to identify a discharge disposition that has proper support and expertise to meet the medical, functional, and neurobehavioral needs of the patient to promote continued recovery. A growing body of evidence suggests that patients with moderate or severe TBI who have access to specialized postacute rehabilitation services have a higher probability of achieving functional independence and ongoing improvement in long-term outcome.[23,24] Planning the transition from inpatient care to outpatient, community-based services and resources is needed to ensure that patients and families have the necessary support to navigate the healthcare system and manage the patient's recovery.[25]

Older Adult Considerations

Little evidence exists to guide rehabilitation specifically for older adults with TBI. However, the Acute Care for Elders (ACE) unit model brings rehabilitation into the acute care setting. There is substantial evidence that the ACE model improves outcomes among older adults with acute medical conditions and that early mobilization improves outcomes among older adults with hip fracture.[2,7] Furthermore, most studies focusing on early mobilization in adults needing critical care include patients over the age of 60 years.[7,9] Together, the evidence supports early rehabilitation and early mobilization in the older adult TBI population. The acute care rehabilitation plan is ideally developed in consultation with a multidisciplinary team including geriatric medicine expertise, given older adults' increased risk for medical complications, high burden of care, discharge to an institutional setting, and decreased quality of life.[26] Key components of most ACE unit models include all of the rehabilitation strategies, including mobilization, delirium prevention, reduction of inappropriate medications/polypharmacy, and a focus on improving or maintaining function according to individual goals of care.

Pediatric Considerations

Pediatric patients with TBI are at risk for developing critical illness comorbidities and complications related to sedation, immobility, and delirium. A recent review reported global dysfunction in 47% of children at the time of pediatric ICU discharge, with 76% reporting residual disabilities 6 months after discharge.[27] Multidisciplinary rehabilitation of pediatric patients needing critical care was found to be safe, with minimal adverse events; it minimized the number of days on mechanical ventilation, in bed, and in the ICU; and it reduced comorbidities and decreased delirium.[28,29] It was also found to be effective in enhancing functional outcomes and lessening family and caregiver burden in pediatric and adolescent patients with TBI.[30] Pay careful attention to patients with a preinjury comorbid mental or personality condition. Behavioral health medicine would be an appropriate addition to the multidisciplinary rehabilitation team to provide nonpharmacologic and pharmacologic recommendations.

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POSTTRAUMATIC EPILEPSY

KEY POINTS

- Prior to acute care hospital discharge, educate families regarding the signs and symptoms of posttraumatic epilepsy (PTE), including subtle changes in level of consciousness.
- Screen patients for the presence of PTE during the follow-up period and arrange for further diagnostic testing when potential seizure activity exists.
- Patients developing PTE require treatment with ASM and referral to a clinician with expertise in management of PTE.
- Tailor the choice and duration of ASM therapy for PTE to individual patient characteristics, including seizure control, side effects, and other treatment options such as dietary modifications, neuromodulation, and other surgical approaches.
- The incidence of PTE increases over time, so perform ongoing screening of aging adults with a history of TBI, particularly in patients with risk factors for PTE.

Incidence

TBI accounted for about 4% of epilepsy patient diagnoses in earlier population-based studies,[1,2] with other studies citing incidence as high as 20%.[3,4] Late PTS is defined as seizures occurring more than 7 days postinjury. In general, ASM prophylaxis is not recommended to prevent late seizures, because the potential for adverse effects outweighs the risk of seizures for many patients.[5–7] A significant portion of patients post-TBI develop PTE, which carries significant morbidity and mortality, and these patients require treatment.[3,8,9] See Box 7 for factors associated with a higher risk for PTE.

Box 7. Factors Associated with a Higher Risk for Posttraumatic Epilepsy

- Evacuated subdural hematoma (SDH)[3,10]
- Contusion and SDH[3]
- Evacuation of intraparenchymal hematoma[10]
- GCS 3–8[10–12]
- Early seizures (particularly if delayed)[10–12]
- Loss of consciousness or amnesia > 1 day[3]
- Greater time before able to follow commands (> 7 days)[10]
- Skull fracture[3,11]
- Unelevated depressed skull fractures[10]
- Dural penetration[10]
- Nonreactive pupil(s)[10]
- Parietal lesions[10]
- Age > 65 years[2]
- Female sex[11]
- Family history of epilepsy[11]
- History of depression[12]

Furthermore, the cumulative risk (increased incidence over time) of PTE is greater after TBI, especially for severe TBI, but also for moderate TBI.[2] For patients experiencing early seizures, PTE was reported to occur at higher rates among those with intracerebral hemorrhage and greater injury severity.[2] Given that cumulative incidence of PTE increases over time, carefully monitor aging adult patients with a history of TBI, particularly those with risk factors for PTE.

One population-based study found that mild TBI patients had a greater risk of seizures for up to 10 years, compared to the general population (relative risk 2.06–3.51, increasing by age group).[11] However, PTE was found to be most common in patients with more severe injuries (relative risk 4.91–12.24, depending on age group). For both mild and severe TBI, the risk of PTE was highest for those ≥ 15 years of age, and the seizures mostly occurred earlier after injury.

Patients with high risk require family education regarding PTE signs and symptoms, diagnostic vigilance for its detection, and long-term follow-up after TBI by qualified professionals.[13]

Impact of PTE on Outcome

It remains unclear whether patients with PTE have worse mortality and functional outcomes or if patient outcomes are primarily related to their injury severity (which also correlates with PTE development). Some recent studies demonstrated patient outcome effects related to PTE.

In a large prospective cohort study controlling for age, presenting GCS, and imaging findings, patients with PTE demonstrated significantly lower GOS-E scores and performed worse than controls on both the Rivermead Cognitive Metrics and Brief Symptom Inventory-18 scores.[14] This study relied upon a National Institutes of Health stroke-related epilepsy screening tool to identify self-diagnosed seizures. The incidence of self-reported seizures in the TBI group was consistent with prior published reports, and the two control groups had no self-reported seizures, arguing for the reliability of this screening tool for the TBI population. Importantly, the study identified a correlation between self-reported seizures and poor functional outcomes, as well as persistent posttraumatic symptoms.[14] Other studies have reported higher mortality in patients with TBI and PTE compared to TBI patients without PTE when controlling for other factors.[4,15,16] This emerging evidence suggests that the presence of PTE confers additional morbidity and mortality to survivors of TBI.

Treatment Strategies

A discussion regarding the choice and duration of ASM therapy is beyond the scope of this BPG. Initiate treatment for patients experiencing a first late seizure after TBI. Refer the patient to a clinician with appropriate expertise in the management of PTE, because the likelihood of developing recurrent seizures after the first is as high as 86% by 2 years postinjury.[8] The choice and duration of ASM therapy for those with PTE must be tailored to individual patient characteristics, including but not limited to seizure control, side effects, and options for other types of treatment (e.g., dietary modifications, neuromodulation, or other surgical approaches).

Older Adult Considerations

Older adults have a higher risk of falls than younger adults, and TBI due to a fall is reported to have the greatest risk for PTE, regardless of TBI severity.[17] The risk of PTE is also increased in older adults due to comorbidities that impact the risk of seizures (e.g., stroke and dementia). The effects from ASM drug-drug interaction due to polypharmacy can complicate this further.[18,19] Selecting the ASM with the fewest adverse cognitive effects and drug-drug interactions is recommended for management of PTE in the older adult population.

Pediatric Considerations

While children are at higher risk for early seizures than adults after TBI,[20] the development of PTE is less common in the pediatric population, except in cases of abusive head trauma.[21] ASM prophylaxis is not effective for prevention of late-onset seizures in children.[22] Refer children who develop late seizures after TBI to a practitioner with both pediatric and epilepsy expertise, such as a pediatric neurologist.

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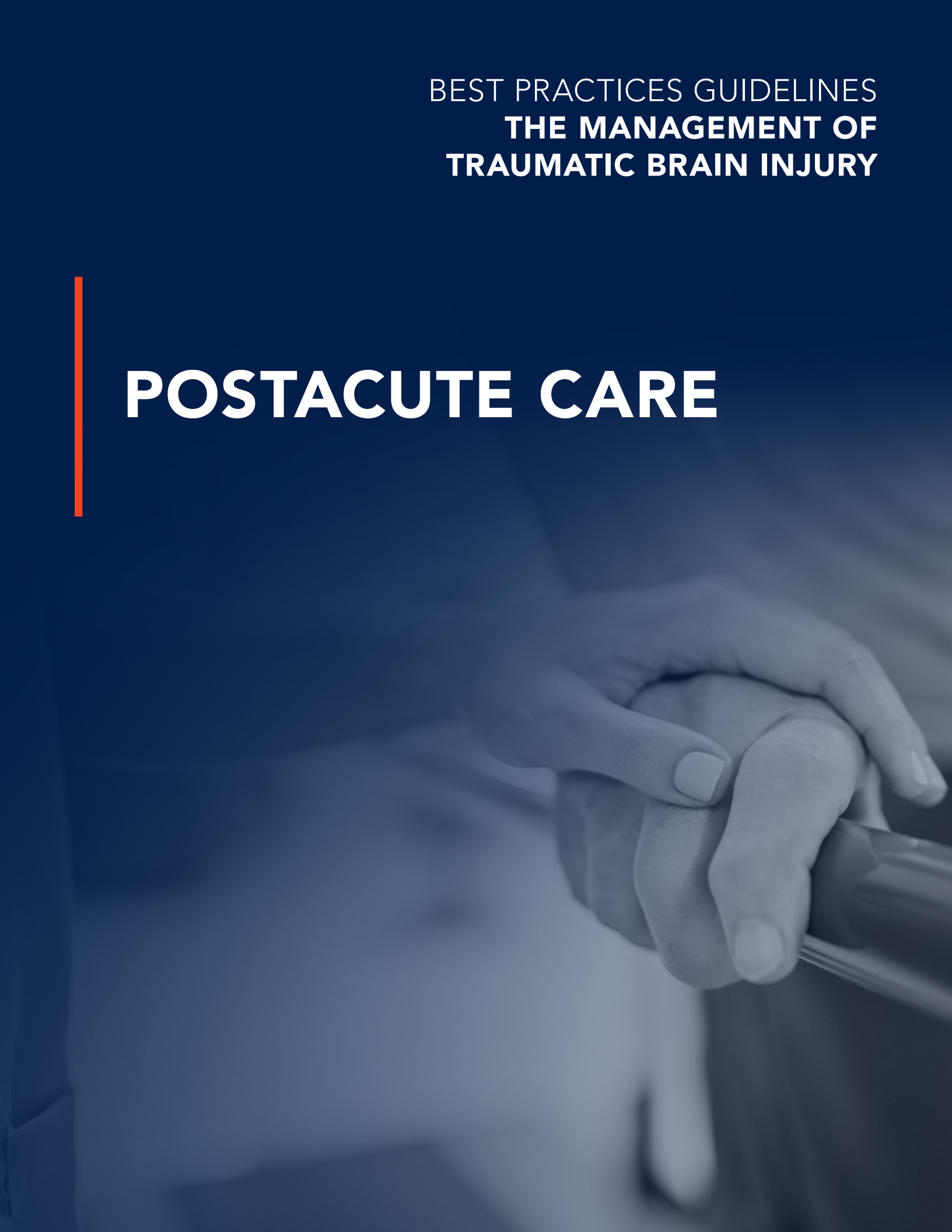
BEST PRACTICES GUIDELINES

THE MANAGEMENT OF TRAUMATIC BRAIN INJURY

POSTACUTE CARE



MANAGEMENT OF PATIENTS WITH GLASGOW COMA SCALE (GCS) SCORE OF 13–15

KEY POINTS

- Although many patients with TBI and GCS 13–15 fully recover over a relatively short period, a sizeable subset have persistent symptoms that negatively impact their ADLs.
- It is estimated that TBI goes undetected and undiagnosed in an estimated 50% of patients presenting to the hospital ED with GCS 13–15 after injury.
- Integration of decision support tools and clinical practice guidelines into the standard clinical workflow is recommended to identify TBI in patients with GCS 13–15 and to facilitate proper evaluation and treatment.
- Follow the broader recommendations of this updated BPG for the acute management of patients with TBI having a GCS 13–15, including diagnostic testing, individualized treatment, discharge instruction, and outcome assessment.
- Educate patients with GCS 13–15 about their injury and recommend outlets for follow-up care for those who experience persistent symptoms. Discuss timing of return to activities (e.g., work, school, and driving), and deliver individualized treatment to restore them to maximal functional capacity.

Incidence

Of the nearly 5 million patients seen in US hospital EDs annually with suspected TBI, approximately 90% have a GCS score of 13–15, or what has historically been classified as *mild TBI*.[1,2] This level of injury is also representative of over 80% of all TBIs among US military service members,[3,4] and millions of athletes worldwide are affected each year by sport-related concussion.[5] Practice guidelines and other helpful resources assist clinicians in the diagnosis and management of patients with TBI and GCS 13–15.[6,7]

Detection and Diagnosis

The acute management of patients with TBI and GCS 13–15 presents several challenges. Most notably, establishing the diagnosis in the ED relies heavily on the subjective report of the patient's signs and symptoms. However, patient history and symptom reporting in the ED are often unreliable due to impairment and can be impacted by numerous factors other than head injury, such as the following:

- Confounding drug or alcohol intoxication
- Co-occurring orthopaedic injury
- Pain management treatment
- Inherent uncertainties in gathering accurate injury history, symptomatology, or mechanism[8]

Great variability can be found in impairment severity, even within the continuum of GCS 13–15 (e.g., a GCS 15 patient with normal neuroimaging and only subtle deficit vs. a GCS 13 patient with extensive pathology on imaging and more severe impairments). The high-volume, high-throughput setting of a hospital ED with primary focus on emergency conditions may not allow for extensive clinical testing (e.g., neurologic or neuropsychological testing) beyond physical examination and head CT to assist in the diagnosis of TBI patients with GCS 13–15. These challenges contribute, in part, to the fact that an estimated 50% of patients with TBI and GCS 13–15 go undetected and undiagnosed in the hospital ED each year.[9–11]

Acute Management

In the acute ED setting, the immediate priority when treating suspected brain trauma, including patients with TBI and GCS 13–15, is identifying those patients at risk for deterioration and potentially in need of urgent neurosurgical intervention. Most patients with TBI and GCS 13–15 have no traumatic intracranial lesions on head CT. However, higher rates of CT abnormalities are reported in patients treated at Level 1 trauma centers and in patients with lower GCS scores.[12] Regardless, head CT remains the standard for identifying ICH in patients with TBI and GCS 13–15. Clinical decision rules exist regarding use of CT imaging for at-risk patients with TBI to reduce the number of unnecessary CT studies performed. Please refer to the Blood-Based Biomarkers section on page 15 regarding the use of neuroimaging and blood-based biomarker testing in the evaluation of patients with TBI and GCS 13–15.

Prognosis and Outcome

Common symptoms in patients with TBI and GCS 13–15 include headache, dizziness, visuo-oculomotor difficulties, cognitive dysfunction, sleep problems, sensory dysfunction, psychological health problems, and others. Typically, symptoms are most severe acutely (within the first few days) and improve gradually over time. A significant percentage of patients achieve full recovery within a relatively short period (days to weeks), but at least half experience persistent cognitive, somatic, and psychological symptoms that negatively impact their normal life activities for months or years after injury.[12,13] Approximately 50% of patients diagnosed with TBI and GCS 13–15 evaluated in the ED do not attain full recovery by 12 months after injury.[12] Combinations of injury (e.g., acute injury severity, pathology on CT, etc.) and noninjury factors (e.g., premorbid psychiatric history, neurologic vulnerability, social distress, etc.) are known to increase risk of prolonged recovery and/or poor functional outcome in these patients.

Follow-Up Care

Provide patients with educational resources about their injury, expected recovery, and outlets for follow-up care. Patients who experience persistent symptoms or difficulties (i.e., longer than 2 weeks postinjury) may need more specific evaluation and treatment targeting their specific symptoms. Supportive care and rehabilitative therapies are effective in treating patients with TBI and GCS 13–15 to restore maximum functional capacity. Systems for follow-up care are admittedly lacking for these patients in the US and around the world. In addition to data demonstrating relatively low detection of patients with TBI and GCS 13–15 in EDs, recent studies indicate that most patients do not receive helpful information resources at time of hospital discharge or any further evaluation and treatment of their injury, even when experiencing persistent symptoms.[14] When possible, such patients need to be seen by clinicians with expertise in the management of TBI. A multispecialty approach is ideal to address the multifaceted sequelae of TBI. Healthcare systems are encouraged to develop coordinated programs for postacute care of TBI patients.

Resources

Consensus guidelines developed by the American Congress of Rehabilitation Medicine (ACRM), the CDC, the US Department of Veterans Affairs and Department of Defense, and the sports medicine community are available for the management of civilians, military service members, and athletes affected by TBI with GCS 13–15 (see Box 8). Providers responsible for the evaluation and management of these specific populations of patients with TBI and GCS 13–15 need to be familiar with existing guidelines and incorporate them into their clinical practice.

Box 8. Current Guidelines and Helpful Resources for Diagnosis, Evaluation, and Management of Patients with TBI and GCS 13–15

The American Congress of Rehabilitation Medicine Diagnostic Criteria for Mild Traumatic Brain Injury. *Arch Phys Med Rehabil*. 2023 Aug;104(8):1343–1355. doi: 10.1016/j.apmr.2023.03.036.

Management of Concussion and Mild Traumatic Brain Injury: A Synthesis of Practice Guidelines. 2020 Feb;101(2):382–393. https://www.archives-pmr.org/article/S0003-9993(19)31305-X/fulltext. Accessed May 31, 2024.

Clinical Guidance for Pediatric Mild TBI. US Centers for Disease Control and Prevention. 2024. https://www.cdc.gov/traumatic-brain-injury/hcp/clinical-guidance/?CDC_AAref_Val=https://www.cdc.gov/traumaticbraininjury/PediatricmTBIGuideline.html. Accessed May 31, 2024.

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Consensus Statement on Concussion in Sport—The 5th International Conference on Concussion in Sport Held in Berlin, October 2016. *British Journal of Sports Medicine.* 2017;51(11):838–847. https://bjsm.bmj.com/content/51/11/838.long.

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Older Adult Considerations

Mild TBI, or TBI in patients with a GCS score of 13–15, occurs frequently in older adults, often resulting from a fall. Studies report that the majority of TBI in older adults (60%–80%) is associated with a GCS score of 13–15.[15–17] Unfortunately, little evidence exists to guide diagnostic or therapeutic decision-making for these injuries in older adults.[18,19]

The evaluation of an older adult patient with mild TBI may be significantly confounded by preinjury cognitive status. Additionally, for older adult patients, a discrepancy of observed GCS is often reported when compared to younger adult patients with similar anatomic injury.[20,21] A GCS score and physical examination cannot reliably exclude significant intracranial pathology in an older adult; therefore, liberal imaging and observation are often recommended.[22–24]

While most older patients with these injuries recover well, TBI with a GCS score of 13–15 is reported to be an independent significant risk factor of death in older adults.[17] Additionally, these injuries may result in long-term changes in self-perception and social life that can persist for years after injury.[25] Such changes can lead to loss of independence and deterioration in quality of life. Older adults who have significant or persistent symptoms that do not improve often benefit from referral to highly specialized rehabilitation.[26,27]

Pediatric Considerations

Approximately 30% of children with TBI and GCS 13–15 will have persistent symptoms 1 month after injury.[28] A recent large-scale observational study identified risk factors (e.g., history of physician-diagnosed migraine) and exam findings (e.g., answering questions slowly) associated with prolonged symptoms.[28] Evidence from observational and intervention trials suggests that early reinstitution of physical activity and early return to school improve outcomes.[29–32] Refer all children with TBI to their primary care clinician for management of return to school and return to activity. Follow-up in a subspeciality clinic, such as neurology or sports medicine, may be warranted in children with risk factors for prolonged recovery. Children with prolonged symptoms (i.e., persistent symptoms at 3 months) may benefit from neuropsychological testing to assess the contribution of both TBI injury and noninjury factors and use this information to aid the patient's return to school and ADLs.

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OUTCOME ASSESSMENT AND QUALITY IMPROVEMENT

KEY POINTS

- Perform a TBI outcome assessment using both global and multidimensional measures, including physical, cognitive, communication, behavioral, psychological, and well-being.
- To assure quality care benchmarking, identify patient-specific factors indicating clinical decline or plateau associated with pathology requiring intervention or treatment, as well as clinical improvement that could be further facilitated by rehabilitation or other treatment.
- Perform a TBI outcome assessment at multiple time points following injury (ideally, between 1 and 3 months, and again between 6 and 12 months) to identify postinjury clinical trajectories and intervene as needed to optimize recovery.

TBI affects multiple domains of function (e.g., physical, cognitive, communication, behavioral, psychological, and well-being), and it is a major cause of long-term disability. Different manifestations and patterns of impairments are patient-specific. TBI outcome trajectories are also heterogeneous, and these can range from improvement to deterioration over many years following injury. Increasing evidence suggests that significant functional recovery from TBI continues well beyond 6 months, extending 10 years or more postinjury.[1]

Individuals hospitalized for TBI need clinical follow-up by medical providers with TBI expertise. Given the dynamic nature of the post-TBI course, with expectations for changes even years after injury, TBI-specific care needs may span months to years. Lifelong follow-up may be beneficial for many patients to optimize outcomes by addressing the screening, monitoring, and management needs of individuals living with chronic brain injury to promote their brain health.[2]

Outcome Assessment

Comprehensive care of patients with TBI requires a multidimensional and longitudinal approach to outcome assessment. This facilitates accurate documentation of the scope of function changes across domains, identification of recovery trends over time, and determination of interventions needed to maximize good outcomes.

It is recommended that healthcare professionals caring for patients with TBI be aware of different outcome assessment measures and their related strengths, limitations, and applicability. Care teams must be adept at interpreting the results of outcome assessments and intervening when needed. For example, place specific emphasis on monitoring for clinical decline given the relationship between TBI, medical, and psychiatric comorbidities (e.g., posttraumatic hydrocephalus, occult seizure, endocrine dysfunction, iatrogenic sedation, major depressive disorder, posttraumatic stress disorder, and neurodegenerative-spectrum conditions).[3–6]

Assessment methods have different strengths and weaknesses, and few can be applied across the full spectrum of TBI severity. A comprehensive brain injury outcome assessment needs to address physical, cognitive, communication, behavioral, psychological, and quality of life domains. The GOS-E is widely adopted for global assessment of function and outcome after TBI. Healthcare professionals administering and interpreting the GOS-E need to be familiar with its limitations (e.g., floor and ceiling effects and the broad range of function represented within discrete categories).[7] Additionally, the different approaches to scoring (i.e., TBI-specific vs. TBI plus peripheral injuries) can lead to different ratings.[7] Global functional outcome measures do not have the precision needed to characterize the heterogeneity of TBI sequelae. When possible, complement global assessment with a multidimensional assessment strategy that addresses additional domains of function to provide a more sensitive and comprehensive approach to TBI care.[8]

Meaningful outcome assessment requires multiple assessment periods to discern the individual's status and recovery path. At a minimum, TBI patients of all severity need a serial standardized outcome assessment consisting of GOS-E administration, ideally between 1 and 3 months and again between 6 and 12 months following injury. The GOS-E is not appropriate for use during the index hospitalization. This recommendation is based on evidence that supports longitudinal monitoring for patients with TBI

to define outcome trajectories suggesting improvement, prolonged plateau, or worsening that may indicate need to intervene to improve outcome.[9] The recommended timeline is suggested to balance the need for serial assessment to acquire prognostically important trajectory data against clinical and operational feasibility. However, individual patients may be selected for more frequent monitoring.

Outcome assessment is important both on the individual patient level and on the broader systems level. Following individual patient trajectories can help identify when recovery is not progressing as expected, thereby indicating the need for further evaluation and treatment. Data obtained at multiple time points aids the clinical team in determining if an individual has plateaued or declined. It can also inform decision-making about the need for further evaluation (e.g., imaging, laboratory evaluation, comprehensive neuropsychological assessment, and driver reevaluation) and treatment (e.g., inpatient rehabilitation, outpatient cognitive rehabilitation program, concussion clinic, and psychological counseling) services. Postdischarge assessments revealing plateau or decline may be an indication of medical or psychiatric conditions that are amenable to intervention or may indicate adverse environmental conditions. On a broader systems level, evaluation of observed versus expected patient outcomes weeks to months after they leave the hospital, within and across trauma programs, can help identify process improvement opportunities in the care delivery system.

Older Adult Considerations

Older adult trauma patients with TBI are at greater risk for complications and poor outcomes after injury, compared to younger patients.[10–13] These outcomes include longer hospital LOS,[10] higher mortality,[10,14,15] greater functional and cognitive decline,[12,14,15] poorer health-related quality of life,[12] more readmissions to acute care,[11] more complications,[11] and discharge to facilities other than home.[11,16] Even with comparatively lower injury severity scores, older patients have the highest rates of hospitalization after injury, mortality, functional decline, and cost of care.[13] Moreover, older adults are at higher risk of secondary complications, including VTE, hemorrhage,[13,17] and neurodegeneration (all-cause dementia, Parkinson's disease).[18] In terms of recovery and disability trajectories after injury, a patient's Functional Independence Measure motor score upon hospital discharge is a strong predictor of global disability as measured by the GOS-E after TBI.[12,19] These statistics highlight the importance of quality improvement (QI) priorities during and after the acute care experience.

Frailty reflects biological aging,[20] and it is a primary predictor of poor outcomes among older patients.[11] This emphasizes the importance of frailty screening upon hospital admission as a crucial QI initiative at all trauma centers.[16,21,22] Because of the range of poor outcomes among older patients, QI monitoring of outcomes after TBI is warranted with risk adjustment for patients' frailty status. Frailty screening leads to increased consultation with an older adult service[23] and higher palliative care referrals.[21] Screening also provides the opportunity for patient/family education regarding measures to mitigate and delay functional decline.[24] Lifestyle modifications to improve post-TBI neurocognitive outcomes include exercise, adequate sleep, and nutrition.[25] Focus rehabilitation strategies on increasing function, balance, coordination, and energy conservation.[12]

Pediatric Considerations

Children with TBI also require ongoing standard assessment following injury. Pediatric outcome assessment tools include but are not limited to the Functional Status Scale and the Pediatric Quality of Life Inventory. Healthcare professionals caring for pediatric patients with TBI need training to administer, interpret, and act upon outcome assessments specific to the pediatric population. Of all traumatic injuries in hospitalized children, 3% are due to nonaccidental trauma, with more than half of these including TBI, either independently or as polytrauma.[26] Accurate diagnoses and close comprehensive outcome assessment are imperative for the optimal care of patients for whom social supports, including their home environment and caregivers, may change.

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TRAUMATIC BRAIN INJURY EDUCATION AND FOLLOW-UP

KEY POINTS

- Treat TBI as both an acute and chronic condition.
- Patients with TBI and their families need targeted education about brain injury, recovery, resources, and follow-up care to enhance safety, coping, follow through, and outcome.
- Healthcare professionals can benefit from TBI education to improve patient care and outcomes.
- Upon discharge from the acute care hospital, ensure that all patients with TBI have the opportunity to follow-up with a clinician experienced in managing TBI. This allows for further evidence-informed education, as well as longer-term screening, surveillance, and treatment as needed.

Across all demographic and socioeconomic strata, TBI remains a leading cause of disability worldwide.[1] For many patients, TBI is a persisting and dynamic condition, not a one-time event.[2] The enormous burden of this condition can have profound implications for patients, their families, and their communities. Patients who present with coma and severe TBI are known to need rehabilitation and long-term chronic care. However, many of these patients do not receive rehabilitation or chronic care from a clinician experienced in managing TBI, and many do not receive any follow-up care because of criteria for healthcare eligibility and benefits. Based on US data gathered during the early 2000s, it was estimated that only 13%–25% of persons hospitalized acutely with moderate, severe, or penetrating TBI received inpatient rehabilitation.[3]

Among patients less severely injured, even fewer receive rehabilitation or a connection with a healthcare professional knowledgeable about TBI. Over the past decade, an increasing body of evidence indicates that patients presenting to trauma centers for evaluation and treatment of mild TBI (GCS 13–15) experience symptoms and impairments that persist beyond the acute and subacute phases of recovery, even though they often do not require intensive acute medical management or hospitalization.[4]

Additionally, nearly 50% of this less severely injured patient population receives no education about their TBI injury at the time of discharge, and they have no form of postacute follow-up care or education.[5]

While current TBI education platforms and resources can be improved and expanded, numerous resources exist (e.g., CDC, Model Systems, and BrainLine).[6–8] TBI education can improve patient outcomes, and encouraging clinician and patient use of these existing resources is important.[9] An important priority for trauma centers is the development of coordinated patient education and follow-up systems.

Healthcare professionals need TBI education to be informed about recent data from large-scale studies demonstrating that long-term patient outcome may not mirror patient presentation. This highlights the need for follow-up patient care and education after TBI. Specifically, many patients with severe injuries can have good outcomes, while many patients with so-called mild injuries can experience persistent problems that negatively impact their life function. Healthcare professionals also need to be educated on patient TBI outcome differences related to sport-related TBI versus community-acquired TBI that results in transfer to a trauma center.

There is a significant shortage of TBI follow-up care systems in the US and worldwide. As a result, the majority of TBI patients do not receive adequate follow-up care.[5] Many symptoms of TBI (e.g., headache, sleep disturbance, various forms of cognitive dysfunction, vestibular dysfunction, spasticity, weakness, sensory changes, decreased stamina, and others) need treatment to prevent disability and improve outcomes after TBI. Outcomes are improved with TBI follow-up and treatment by clinicians experienced in managing TBI.[10] Trauma centers and community healthcare systems are encouraged to facilitate development of coordinated systems for postacute care for TBI patients with providers experienced in managing TBI. Peer-to-peer TBI support opportunities, such as TBI patient support groups, are also important for education and support for individuals and families to manage the challenges faced by their condition, treatment, and recovery.

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BEST PRACTICES GUIDELINES
THE MANAGEMENT OF TRAUMATIC BRAIN INJURY

IMPLEMENTATION AND INTEGRATION OF THE BEST PRACTICES GUIDELINES

GAP ANALYSIS AND EDUCATION PLAN

KEY POINTS

- These best practices recommendations, based upon evidence and expert opinion, are intended as guidance to trauma centers for the care of patients with TBI.
- The trauma medical director (TMD), trauma program manager (TPM), trauma liaisons, registrars, and staff have a leadership role in implementing the *ACS TQP Best Practices Guidelines for the Management of Traumatic Brain Injury*, supporting care of patients with TBI, and monitoring guideline compliance.
- A stakeholder workgroup, receiving its directives from the TMD and the trauma operations committee, implements the best practices recommendations.
- The workgroup reviews the best practices recommendations and completes a gap analysis related to the trauma center's current TBI care.

Implementing recommended best practices in the trauma center begins with the TMD, TPM, trauma liaisons, and registrars as leaders and change agents. These individuals are responsible for the oversight, management, and continuous commitment to improving care within the trauma center and the trauma system, regardless of trauma center designation level. These leaders define the leadership structure, culture, and implementation processes for the BPG that foster stakeholder engagement. This process includes the following:

- The brain injury guidelines interdisciplinary workgroup, with a defined leader and reporting structure, is charged with reviewing the TBI BPG and determining the need to complete a gap analysis that compares current trauma center practices to the recommendations in the *ACS TQP Best Practices Guidelines for the Management of Traumatic Brain Injury.*
- An educational plan is developed for the implementation of the trauma center's TBI management guidelines and for sustaining the new practices.
- Documentation is integrated into the electronic medical record to facilitate reporting consistency and to track outcomes.

Performing a Gap Analysis

The brain injury guidelines interdisciplinary workgroup is charged with comparing current practices to those recommended in the BPG to identify gaps between the two. This gap analysis identifies opportunities to align the trauma center's TBI management practices with the *ACS TQP Best Practices Guidelines for the Management of Traumatic Brain Injury.* Trauma centers that serve as a referral center for brain injuries may choose to not complete the full gap analysis but instead to review the guideline recommendations to identify potential opportunities for improvement. The workgroup, in conjunction with the trauma center's operations committee, establishes the priorities for changes. Progress reports regarding the completion of these identified tasks are provided to the trauma operations committee. Refer to Table 8 for examples of gap assessment recommendations.

Once the gap analysis is completed, the next step is to revise or develop the trauma center's TBI management guidelines for the phases of care provided by the trauma center. The TBI management guidelines are reviewed and approved by the trauma operations committee and the TMD. The operations committee is responsible for the dissemination of and communication about the revised TBI management guidelines to individuals who participate in trauma care.

Interdisciplinary Education Plan Development

The next priority is development of an interdisciplinary education plan for the guidelines that define TBI management needs for each unit and phase of care. This education plan outlines the expectations for the various health professional roles involved in TBI assessment and management, as well as the specific tasks associated with assessment, documentation, interventions, and reassessment. Refer to Table 9 for education plan elements to consider for integration of TBI best practices recommendations.

Table 8. Gap Analysis for Traumatic Brain Injury Best Practices Guidelines

Management Guidelines	Met	Partially Met	Not Met	Priority	Comments
Adherence to published local or regional EMS field triage guidelines for TBI					
Interfacility transfer guidelines and agreements for TBI patients					
Standardized assessment and documentation of GCS components (eye, verbal, motor) across the prehospital and in-hospital settings					
Serial neurologic assessment using GCS and pupillary light reactivity					
Resuscitation guidelines with TBI-specific emphasis on management of blood pressure, airway, and ventilation, including the use of endotracheal CO_2 monitoring					
Trauma activation criteria including criteria for potential traumatic brain injuries					
Specific imaging and reimaging recommendations for TBI					
Age-specific imaging protocols					
Coordination of patient monitoring during diagnostic imaging					
SIBICC or TQIP tiered management of ICP					
ICP monitoring capability and indications					
Analgesia and sedation management guidelines					
Operative indications for brain injury management					
Nutritional risk screening within 24 hours of admission, with corresponding plan for nutritional support					
Recommendations for early tracheostomy					
Coordination of early mobilization					
Concomitant injuries and their priority of coordination with TBI					
Management of comorbidities and prevention of adverse hospital events associated with TBI					
Protocol for BCVI					
VTE prophylaxis modalities and protocols					
Anticoagulant reversal protocols for TBI patients					
PTS prophylaxis protocols					
Guidelines for patient and family discussion of prognostic uncertainty, goals of care, and functional recovery expectations					
Brain death determination protocol					
Behavioral health acute stress support for the patient and family					
Rehabilitation team role in the acute management of brain injuries and transition to rehabilitation services					
TBI education materials for patients and families addressing recovery, long-term effects, and available community resources					
Coordination of discharge from acute care to inpatient rehabilitation facility, when appropriate					
Standardized follow-up for all TBI patients					
Peer-to-peer TBI support opportunities for patients and families					

Table 9. Educational Plan Elements for TBI Best Practices Recommendations

Education Elements	Priority for Education	Targeted Staff
Brain injury pathophysiology		
Triage and transport of TBI patients		
Standardized assessment of GCS and pupillary light response		
Resuscitation of TBI patients, including blood pressure, airway, and ventilation management		
Imaging recommendations and monitoring during imaging		
Utilization of blood-based biomarkers for TBI		
Goals of directed care		
Indications and timing of extracranial procedures		
Role of ICP monitoring and neuromonitoring		
Tiered management of ICP (SIBICC protocol)		
Review of rationale for surgical management		
Nutrition support in TBI patients		
Pharmacotherapy for TBI patients including VTE prophylaxis, seizure prophylaxis, anticoagulation therapy, antiplatelet therapy, and other considerations		
Screening and management of BCVI		
Prognostic uncertainty and family communication regarding goals of care in TBI		
Management of patients with GCS score of 13–15		
Patient education, follow-up, and outcome assessment		
TBI epidemiology and outcome		
Quality indicators for PI		
Trauma Survivors Network information		
Considerations for older adult patients with TBI		
Considerations for pediatric patients with TBI		

IMPLEMENTATION AND INTEGRATION INTO TRAUMA CENTER PERFORMANCE IMPROVEMENT

KEY POINTS

- The interdisciplinary workgroup defines elements of the *ACS TQP Best Practices Guidelines for the Management of Traumatic Brain Injury* to monitor through the trauma Performance Improvement and Patient Safety (PIPS) processes.
- After approval by the trauma PIPS committee, the approved elements are integrated into the existing trauma PIPS plan for compliance monitoring.
- The PI elements of the *ACS TQP Best Practices Guidelines for the Management of Traumatic Brain Injury* are integrated into the current structure and processes of the PIPS plans.

Regional System Integration

A regional system may choose to develop a regional collaborative to review and coordinate TBI care across the region. This collaborative initiative is interdisciplinary and needs to include both rehabilitation and psychosocial services. The TBI collaborative defines its priorities and focus, which may require regional data related to TBI and outcomes.

Potential priorities for development of regional TBI guidelines and related regional commitments include the following:

- Prehospital care, field triage, and destination—requires the trauma center to share data related to TBI injury outcomes
- Early access to rehabilitation—requires the region to identify the various levels and types of rehabilitation services available
- Postacute follow-up for all TBI patients—requires the region to identify clinicians experienced in managing TBI
- Psychosocial and peer-to-peer support—requires the region to identify community resources for patients with TBI

Key Elements for the PI Processes

The interdisciplinary workgroup defines and recommends key elements of the *ACS TQP Best Practices Guidelines for the Management of Traumatic Brain Injury* for integration into the trauma PIPS processes. These recommendations are applicable to the facility's trauma TBI admissions. This includes any direct admissions for the trauma or neurosurgical service. Please refer to Table 10 for PI recommendations and outcome measures for TBI management.

Table 10. Traumatic Brain Injury Management PI Recommendations

Performance Improvement Recommendations	Outcome Measure and Threshold
Documented facility guidelines for neurosurgical urgent evaluation	Neurosurgical evaluation must occur within 30 minutes of request for the following injuries[1]: • Severe TBI (GCS < 9) with head CT evidence of intracranial trauma • Moderate TBI (GCS 9–12) with head CT evidence of potential intracranial mass • Neurologic deficit due to potential spinal cord injury
Consider prehospital transport of patients meeting listed criteria to the most appropriate trauma center with neurosurgical capability[2]	• GCS motor score < 6 • Skull deformity or suspected skull fracture • Signs of basilar skull fracture • Penetrating head injury • Caregiver-reported change from baseline behavior in an infant/child following injury
Consider transferring patients meeting listed criteria to a trauma center with neurotrauma expertise, where available (see Triage and Transport section on page 6)	• Significant intracranial injury (e.g., large SDH, EDH, IPH, IVH) • Displaced skull fracture • Suspected TBI (GCS score ≤ 15) **and** moderate to severe extracranial anatomic injuries, **and/or** inability to monitor for neurological deterioration when intracranial injury is present or suspected
Neurotrauma contingency plan is in place	Must be implemented when neurosurgery capabilities are encumbered or overwhelmed
Monitoring of neurotrauma diversion is reported at least quarterly as part of the PIPS program, if neurotrauma diversion occurs	Diversion initiation (date/time) and discontinuation (date/time) are monitored and reported quarterly as part of the PIPS program
Use of GCS individual components (eye, verbal, and motor scores) as the preferred method of measuring neurological status in TBI patients	Use of individual components of GCS in the prehospital and hospital settings, with frequent serial assessments and notation of changes
Documentation of individual GCS score components (eye, verbal, and motor scores) in the patient care report	All GCS individual components are documented
Pupil assessment documentation	• Clinical assessment is required • Consider use of quantitative pupillometry • Assessments repeated frequently and documented
Hemodynamics assessment documentation	• Age-specific measurement of hemodynamic status (blood pressure management) following acute TBI is required • Assessments repeated frequently and documented
Ongoing standardized neurological assessment and documentation	• Standardized neurological assessment and documentation • Assessments are repeated frequently and documented
Repeat imaging	• Urgent repeat head CT scanning is indicated for a patient of any age with worsening changes on neurologic exam • Repeat head CT is indicated in 6–12 hours after initial imaging when a patient of any age has a persistently altered mental status and initial CT showed traumatic abnormality
Appropriate timeliness and coordination of monitoring during imaging	Per individual facility
Consideration of blood-based biomarker testing for patients to reduce unnecessary CT imaging	Applies to patients ≥ 18 years of age with suspected TBI and a GCS of 13–15 within 12 hours of injury

Performance Improvement Recommendations	Outcome Measure and Threshold
Monitoring to maintain optimal ICP goals	Refer to Table 4 on page 20: Goals of Treatment Recommended Parameters
Monitoring to maintain optimal CPP goal of 60–70 mm Hg	Refer to Table 4 on page 20: Goals of Treatment Recommended Parameters
Timeliness of ICP monitoring in TBI GCS ≤ 8	Recommended in comatose patients (GCS ≤ 8) if evidence of structural brain damage is seen on initial CT imaging, **or** polytrauma patients **and** in patients going to the operating room for acute injuries when clinical exam is limited
ICP monitoring in TBI GCS > 8	Recommended in patients with structural brain damage with high risk for progression (e.g., large/multiple contusions) **and** in cases when knowing ICP might facilitate management of other issues (e.g., earlier extracranial surgery)
Monitoring treatment of brain tissue hypoxia	Maintain $PbtO_2$ ≥ 15 mm Hg
Timely utilization of continuous EEG monitoring for seizure detection and management	Per individual facility
Surgical management	Time to operative intervention (may vary depending on resources)
Craniotomy < 4 hours after arrival for patients with operative indication, excluding ICP monitoring	Ensure delayed craniotomy rates are monitored within the PI program
Early enteral (or parental) nutrition support to attain caloric replacement	Nutritional support is initiated within 3 days
Guidelines include alternate feeding method when EN is contraindicated	PN support is recommended when EN is contraindicated
Documented guidelines to identify TBI patients at elevated risk for nutrition deficiency	Guidelines for specific populations could include pediatric, geriatric, and patients with impaired mobility
Measures to prevent skin breakdown with nutrition plan and protection barrier	Assessment and interventions are documented
Monitoring of electrolytes	Glucose and sodium are monitored
Early mobilization or simple interventions (such as passive movement and splinting) are an integral part of rehabilitation	These elements are implemented within the first 48 hours of injury
Timely endotracheal intubation and mechanical ventilation	Indicated in TBI when patient has • Reduced consciousness, GCS < 9 • Severe agitation • Loss of airway protective reflexes Early endotracheal intubation may be indicated in patients with GCS > 8, particularly in the presence of thoracic and abdominal injuries
Monitoring to maintain normoxia and normocapnia, including continuous endotracheal CO_2 monitoring	• Optimal target range of PaO_2 is 80–100 mm Hg • Optimal target range of $PaCO_2$ without ICP elevation is 35–45 mm Hg
Timely tracheostomy placement	Consider within 7 days of injury
Extracranial BCVI imaging	Consider use of CT angiography to detect potential vertebral artery injury
Extracranial BCVI management and follow-up	Antithrombotic therapy and referral for follow-up are provided at discharge, if warranted
Initiation of anticoagulation or antiplatelet agents when no contraindications exist	Therapy may begin as early as 24 hours postinjury

Performance Improvement Recommendations	Outcome Measure and Threshold
Initiation of VTE prophylaxis	Nonoperative TBI** • GCS 13–15 TBI: initiate within 24 hours • GCS 3–12 TBI: initiate within 48 hours ** Provided follow-up head CT indicates hemorrhage stability Operative TBI • Consider initiating or resuming 24–48 hours after surgery and if ICH is stable upon postop CT scan Monitor: • Time to initiation • Pharmacologic agent used
Initiation of anticoagulant reversal	Refer to Table 7 on page 56 for anticoagulation reversal strategy for TBI patients needing emergent surgery
Initiation of seizure prophylaxis	Early (first 7 days only) prevention of PTS
Documentation surrounding withdrawal of life-supporting treatment	Ensure program is capturing the reason, date, and time of care withdrawal
Documented guidelines for brain death determination	Per individual facility
Psychological support, TBI education, and resources provided to the patient and the family, starting at admission	Per individual facility
Plan available to patients for postacute care of TBI with GCS 13–15, including educational resources and referral guidelines	Provide the following to patients with TBI and GCS 13–15: • Educational resources about their injury • Referral guidelines • Information regarding outlets for follow-up care for those who experience persistent symptoms
Concussion (GCS 13-15) care resources pertinent to the postacute injury period are available	A process is established with criteria identifying patients needing referral for concussion and TBI management services
Rehabilitation consultation	Rehabilitation consultation is ordered within a day of hospital admission
A multidisciplinary service team is a vital component of TBI management	Multidisciplinary service team includes PM&R physician
Incorporation of evidenced-based guidelines to help manage pain and potential complications	Per individual facility; one example is the ABCDEF bundle
Rehabilitation includes a postacute phase for continuation when the patient is medically stabile and cleared for discharge from acute care	Patient is referred to specialized postacute rehabilitation

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APPENDIX A: ACRONYMS

4PCC—four-factor prothrombin complex concentrates

A

ACE—Acute Care for Elders
ACEP—American College of Emergency Physicians
ACR—American College of Radiology
ACRM—American Congress of Rehabilitation Medicine
ACS—American College of Surgeons
ADAPT—Approaches and Decisions in Acute Pediatric TBI Trial
ADLs—activities of daily living
ADR—adverse drug reaction
ASM—antiseizure medication
ATLS—Advanced Trauma Life Support
AUC—area under the receiver operating characteristic (ROC) curve

B

BBK—beta blocker
BCVI—blunt cerebrovascular injury
BPG—best practices guidelines
BTF—Brain Trauma Foundation

C

CBF—cerebral blood flow
CDC—Centers for Disease Control and Prevention
CI—confidence interval
CPP—cerebral perfusion pressure
CREVICE—Consensus-Revised Imaging and Clinical Examination
CSF—cerebrospinal fluid
CT—computed tomography

D

DOAC—direct-acting oral anticoagulants

E

ECMO—extracorporeal membrane oxygenation
ED—emergency department
EDH—epidural hematoma
EEG—electroencephalography
EN—enteral nutrition
EVD—external ventricular drain

F

FDA—Food and Drug Administration
FFP—fresh frozen plasma
FiO_2—fraction of inspired oxygen
FOUR—Full Outline of UnResponsiveness

G

GCS—Glasgow Coma Scale
GOS—Glasgow Outcome Scale
GOS-E—Glasgow Outcome Scale-Extended
GFAP—glial fibrillary acidic protein

H

HRSA—Health Resources and Services Administration

I

ICH—intracranial hemorrhage
ICP—intracranial pressure
ICU—intensive care unit
INR—international normalized ratio
IPH—intraparenchymal hemorrhage
IV—intravenous
IVH—intraventricular hemorrhage

L

LMWH—low-molecular-weight heparin
LOC—loss of consciousness
LOS—length of stay

M

MAP—mean arterial pressure
MRI—magnetic resonance imaging

N

NPV—negative predictive value

O

OT—occupational therapy

P

$PaCO_2$—partial pressure of carbon dioxide
PaO_2—partial pressure of oxygen
$PbtO_2$—partial brain tissue oxygenation
PECARN—Pediatric Emergency Care Applied Research Network
PEEP—positive end-expiratory pressure
pGCS—pediatric version of Glasgow Coma Scale
PI—performance improvement
PIPS—Performance Improvement and Patient Safety
PM&R—physical medicine and rehabilitation
PN—parenteral nutrition
PPV—positive predictive value
PRx—cerebrovascular pressure reactivity index
PT—physical therapy
PTA—posttraumatic amnesia
PTE—posttraumatic epilepsy
PTS—posttraumatic seizures

Q

QI—quality improvement

R

RCT—randomized controlled trial
ROTEM—rotational thromboelastometry

S

S100B—S100 calcium-binding protein
SBP—systolic blood pressure
SDH—subdural hematoma
SIBICC—Seattle International Severe Traumatic Brain Injury Consensus Conference
SLP—speech language pathology
SpO_2—oxygen saturation
SWI—susceptibility-weighted imaging

T

TEG—thromboelastography
TBI—traumatic brain injury
TMD—trauma medical director
TPM—trauma program manager
TQIP—Trauma Quality Improvement Program
TQP—Trauma Quality Program

U

UCH-L1—ubiquitin carboxy-terminal hydrolase L1
UFH—unfractionated heparin
US—United States

V

VTE—venous thromboembolism

W

WBCT—whole-body computed tomography

BEST PRACTICES GUIDELINES
THE MANAGEMENT OF TRAUMATIC BRAIN INJURY

EXPERT PANEL

CHAIR

Geoffrey T. Manley, MD, PhD
Professor and Vice Chairman of Neurological Surgery
Chief of Neurosurgery
Zuckerberg San Francisco General Hospital and Trauma Center
University of California, San Francisco
San Francisco, CA

WORK GROUP MEMBERS

Gregory W. Albert, MD, MPH, FAANS, FACS, FAAP
Lee and Bob Cress Endowed Chair in Pediatric Neurosurgery
Chief of Pediatric Neurosurgery, Arkansas Children's Hospital
Professor of Neurosurgery, University of Arkansas for Medical Sciences
Little Rock, AR

Gretchen M. Brophy, PharmD, BCPS, FCCP, FCCM, FNCS, MCCM
Professor of Pharmacotherapy & Outcomes Science and Neurosurgery
Virginia Commonwealth University
Medical College of Virginia Campus
Richmond, VA

Randall M. Chesnut, MD, FCCM, FACS, FAANS
Professor of Neurological Surgery, Orthopaedics, and Global Health
Director of Neurotrauma Services
University of Washington
Harborview Medical Center
Seattle, WA

Giuseppe Citerio, MD
Professor of Anesthesia and Intensive Care School of Medicine and Surgery
University of Milano-Bicocca
Director, Department of Neuroscience
Director, Neurointensive Care Unit
IRCCS Fondazione San Gerardo dei Tintori
Monza, Italy

Christine S. Cocanour, MD, FACS, FCCM
Associate Dean for Academic Advancements
University of California Davis School of Medicine
Professor of Clinical Surgery
Program Director, Surgical Critical Care Fellowship
Medical Director, Surgical Intensive Care Unit
University of California Davis Health
Sacramento, CA

Arman Dagal, MD, FRCA, MHA
Professor
Division Chief, Neuroanesthesiology and Perioperative Neurosciences
Program Director, Neuroanesthesiology Fellowship
Department of Anesthesiology, Perioperative Medicine & Pain Management
University of Miami Miller School of Medicine
Miami, FL

Bradley A. Dengler, MD, FAANS, FACS
Associate Professor of Surgery
Associate Professor of Neurology
Director, Military Traumatic Brain Injury Initiative
Uniformed Services University
Program Director, Neurological Surgery National Capital Consortium
Bethesda, MD

Raquel C. Gardner, MD
Director of Clinical Research
Joseph Sagol Neuroscience Center
Sheba Medical Center
Ramat Gan, Israel

Joseph T. Giacino, PhD
ACRM Liaison to ACS COT
Professor of Physical Medicine and Rehabilitation
Harvard Medical School
Director, Rehabilitation Neuropsychology
Spaulding Rehabilitation Hospital
Charlestown, MA

Flora M. Hammond, MD, FACRM, FAAPMR
Professor and Chair
Department of Physical Medicine and Rehabilitation
Indiana University School of Medicine
Indianapolis, IN

Odette Harris, MD, MPH
Professor, Neurosurgery
Paralyzed Veterans of America Endowed Professor of Spinal Cord Injury Medicine
Vice Chair, Diversity, Department of Neurosurgery
Director, Brain Injury
Stanford University School of Medicine
Deputy Chief of Staff, Rehabilitation
VA Palo Alto Health Care System
Stanford, CA

Gregory W.J. Hawryluk, MD, PhD, FRCSC
Neurosurgeon, Cleveland Clinic
Adjunct Associate Professor of Neurosurgery
Uniformed Services University
Medical Director and Scientific Advisory Board Chair
Brain Trauma Foundation
Fairlawn, OH

J. Claude Hemphill III, MD, MAS
Professor of Neurology and Neurological Surgery
University of California, San Francisco
Chief, Neurology Service
Zuckerberg San Francisco General Hospital
San Francisco, CA

Michael C. Huang, MD, FAANS
Health Sciences Clinical Professor
Department of Neurological Surgery
University of California, San Francisco
Chief of Neurosurgery Clinical Services
Zuckerberg San Francisco General Hospital &
Trauma Center
San Francisco, CA

Peter Hutchinson, BSc, MBBS, FFSEM, FRCS(SN), PhD, FMedSci
Professor of Neurosurgery
University of Cambridge
Honorary Consultant Neurosurgeon
Cambridge University Hospitals NHS Foundation Trust
Director of Clinical Research
Royal College of Surgeons of England
England

Frederick Korley, MD, PhD
Professor and Associate Chair for Research
Department of Emergency Medicine
Scientific Director, Massey TBI Grand Challenge, Weil Institute
University of Michigan
Ann Arbor, MI

Tiffany LeCroy, MSN, RN, CRRN, FNP-C, ACNS-BC, FARN
Chief Nursing Officer
Director of Intensive Care Unit and Comprehensive Rehabilitation Unit
Shepherd Center
Atlanta, GA

Angela Lumba-Brown, MD
Associate Professor of Emergency Medicine and Pediatrics
Stanford University School of Medicine
Pediatrics, Palo Alto Medical Foundation
Palo Alto, CA

Andrew I.R. Maas, MD, PhD
Emeritus Professor of Neurosurgery
Antwerp University Hospital
University of Antwerp
Belgium

Amelia W. Maiga, MD, MPH
Assistant Professor of Surgery
Division of Acute Care Surgery
Vanderbilt University Medical Center
Nashville, TN

Armaan K. Malhotra, MD
Neurosurgery Resident
Division of Neurosurgery
University of Toronto
Toronto, ON

Rebekah Mannix, MD, MPH
Senior Associate in Medicine
Division of Emergency Medicine
Children's Hospital Boston
Harvard Medical School
Boston, MA

Cathy A. Maxwell, PhD, RN, FAAN
Professor of Nursing
Vanderbilt University School of Nursing
Nashville, TN

Michael McCrea, PhD, ABPP
Professor and Vice Chair
Department of Neurosurgery
Director, Center for Neurotrauma Research (CNTR)
Medical College of Wisconsin
Milwaukee, WI

David K. Menon, MBBS MD PhD FRCP FRCA FFICM FMedSci
Director of Research, University of Cambridge
Honorary Consultant, Neurosciences Critical Care Unit, Addenbrooke's Hospital
Professorial Fellow, Queens' College Cambridge
Department of Medicine
University of Cambridge
Cambridge, United Kingdom

Christopher P. Michetti, MD, FACS, FCCM
Chief of Trauma
Trauma Surgery Program Medical Director
University of Maryland Capital Region Medical Center
Largo, MD

Truman J. Milling Jr., MD
Clinical Professor
Department of Clinical Sciences
Tilman J. Fertitta Family College of Medicine
University of Houston
Houston, TX

Susanne Muehlschlegel, MD, MPH, FNCS, FCCM, FAAN
Professor (PAR) of Neurocritical Care
Departments of Neurology and Anesthesiology/Critical Care Medicine
Neurosciences Critical Care Division
Johns Hopkins School of Medicine
Johns Hopkins Medicine
Baltimore, MD

Brooke Murtaugh, OTD, OTR/L, CBIST
Occupational Therapist
Brain Injury Program Manager
Department of Rehabilitation Programs
Madonna Rehabilitation Hospitals
Lincoln, NE

David O. Okonkwo, MD, PhD
Professor of Neurological Surgery
University of Pittsburgh Medical Center
Pittsburgh, PA

Tolu O. Oyesanya, PhD, RN
Associate Professor of Nursing
Duke University
Durham, NC

Mayur B. Patel, MD, MPH, FACS, FCCM
Vice Chair COT Post-Graduate Education Committee
Chief & Professor, Division of Acute Care Surgery
Ingram Chair in Surgical Sciences
Vanderbilt University Medical Center
Nashville, TN

Stacy Pelekhaty, MS RDN, LDN, CNSC
Senior Clinical Nutrition Specialist
R Adams Cowley Shock Trauma Center
University of Maryland Shock Trauma Center
Baltimore, MD

J. Adair Prall, MD, FAANS, FACS
Director, Neurotrauma Services
Department of Surgery
AdventHealth Littleton
Denver, CO

John Ragheb, MD
Division of Pediatric Neurosurgery
Chief, Department of Surgery
Nicklaus Children's Hospital
Professor of Neurosurgery and Pediatrics
Affiliated Faculty
University of Miami Miller School of Medicine
Miami, FL

P.B. Raksin, MD
Director, Neurosurgery Intensive Care Unit
John H. Stroger Jr. Hospital of Cook County
Associate Professor of Neurosurgery
Rush University Medical Center
Chicago, IL

Claudia Robertson, MD, FCCM
Professor, Department of Neurosurgery
Baylor College of Medicine
Houston, TX

Bryce R.H. Robinson, MD, MS, FACS, FCCM
Chair, ACS COT Performance Improvement Patient Safety Committee
Chair, ACS COT Best Practices Guidelines Committee
Professor of Surgery
University of Washington
Harborview Medical Center
Seattle, WA

Guy Rosenthal, MD
Director of Neurotrauma and Neurocritical Care
Associate Professor of Neurosurgery
Hadassah-Hebrew University Medical Center
Jerusalem, Israel

Andres M. Rubiano, MD, PhD (c), FACS, IFAANS
Chair, Colombian Trauma Committee
Professor of Neurosciences and Neurosurgery
Universidad El Bosque, Bogota, Colombia
Chair, Neurological Surgery Service
Vallesalud Clinical Network
Medical and Research Director
Meditech Foundation
Cali, Colombia

Rachel M. Russo, MD, MS, NHDP-BC, FACS
Lt. Col., US Air Force, MC
Assistant Professor of Surgery
University of California Davis Health
Sacramento, CA
Assistant Professor of Surgery
Uniformed Services University of the Health Sciences
Bethesda, MD

Angelle M. Sander, PhD, FACRM
Professor, H. Ben Taub Department of Physical Medicine and Rehabilitation
Baylor College of Medicine
Director and Senior Scientist, Brain Injury Research Center
TIRR Memorial Hermann
Houston, TX

Alfred Pokmeng See, MD
Assistant Professor
Department of Neurosurgery, Cerebrovascular Surgery and Interventions Center
Boston Children's Hospital
Harvard Medical School
Boston, MA

Deborah M. Stein, MD, MPH, FACS, FCCM
R Adams Cowley, MD Professor of Shock and Trauma
University of Maryland School of Medicine
Director, Adult Critical Care Services
University of Maryland Medical Center
Baltimore, MD

Eiichi Suehiro, MD, PhD
Professor
Department of Neurosurgery
International University of Health and Welfare, School of Medicine
Narita, Japan

Kelli G. Talley, PhD, MPH, OTR/L
Assistant Professor
Department of Rehabilitation Counseling
Virginia Commonwealth University
Richmond, VA

Phiroz E. Tarapore, MD, FAANS
Associate Professor, Department of Neurological Surgery
Zuckerberg San Francisco General Hospital
University of California, San Francisco
San Francisco, CA

Shelly D. Timmons, MD, PhD, FACS, FAANS
Chair and Professor of Neurosurgery
Sanford J. Larson, MD, PhD Endowed Chair
Medical College of Wisconsin
Department of Neurosurgery
Milwaukee, WI

Alex Valadka, MD, FAANS, FACS
Professor, Department of Neurological Surgery
University of Texas Southwestern Medical Center
Chief of Neurosurgery
Parkland Memorial Hospital
Dallas, TX

Steve Willis, PharmD, BCPPS
Clinical Pharmacist Specialist, Pediatrics
Residency Program Director, PGY-1 Pharmacy Practice
Rhode Island Hospital, Hasbro Children's Hospital
Providence, RI

David W. Wright, MD, FACEP
Professor & Chair
Department of Emergency Medicine
Emory University School of Medicine
Attending, Grady Marcus Trauma and Emergency Care Center
Adjunct Faculty, Wallace H. Coulter, Department of Biomedical Engineering
Adjunct Faculty, Nell Hodgson Woodruff School of Nursing
Adjunct Faculty, Rollins School of Public Health
Atlanta, GA

John K. Yue, MD
Resident Physician
Department of Neurological Surgery
University of California, San Francisco
San Francisco, CA

Esther Yuh, MD, PhD
Professor
Department of Radiology and Biomedical Imaging
University of California at San Francisco
San Francisco, CA

ACS TRAUMA QUALITY PROGRAMS MEDICAL DIRECTOR

Avery B. Nathens, MD, PhD, FRCS, FACS
Medical Director of Trauma, Sunnybrook Health Sciences Centre
Professor of Surgery, University of Toronto
De Souza Chair in Trauma Research
Toronto, ON

BPG LEAD NURSE CONSULTANT

Robbie Dumond, MHA, BSN, TCRN, AEMT
Vice President of Operations
UCHealth University of Colorado Hospital
Aurora, CO

BPG NURSE PARTNERS

Tracy Cotner-Pouncy, MSN, RN, TCRN
Senior Director, Trauma Services
UCHealth, North Region
Loveland, CO

Christina McRoberts, MBA, BSN, RN
Pediatric Trauma Coordinator
Hasbro Children's Hospital
Providence, RI

Danielle Sherar, MBA, RN, TCRN
Executive Director of Trauma, Acute Care Surgery and Forensic Services
JPS Health Network
Fort Worth, TX

Matt Wells, MBA, BSN, RN, CEN, CPEN, TCRN
Trauma Program Manager
Pali Momi Medical Center
Aiea, HI

CLINICAL EDITOR

Jane Ball, RN, DrPH
Pediatric Nursing and Trauma System Consultant
Havre de Grace, MD

American College of Surgeons
633 N. Saint Clair St.
Chicago, IL 60611-3295

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