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Nursing Protocols For Acute Traumatic Brain Injury: A Comprehensive Evidence-Based Review Across The Care Continuum

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Abstract

Background
Traumatic brain injury (TBI) causes millions of cases yearly, with incidence over 250-300 per 100,000 person-years, leading to substantial mortality, long-term impairments, and economic costs exceeding billions annually, especially in low-resource settings. Marked outcome variations highlight the need for structured protocols to prevent secondary injury via airway protection, hemodynamic stability, and timely intervention.

Methods
This narrative synthesis critically appraises contemporary guidelines (e.g., Brain Trauma Foundation, NICE) and high-quality studies on protocols spanning prehospital, emergency, ICU, ward, and rehabilitation phases. Key questions address protocol components, comparative effectiveness versus non-protocolized care, evidence strength, and research gaps using GRADE-like grading for recommendations.

Results
Protocols integrate ICP/CPP targets (ICP <22 mmHg, CPP 60-70 mmHg), multimodal monitoring, tiered ICP therapies, seizure prophylaxis, and early rehabilitation. Observational data show reduced mortality, improved functional outcomes (e.g., GOSE), shorter stays, and better adherence compared to variable care, though benefits vary by setting.

Conclusions
Protocolized TBI management enhances outcomes by minimizing secondary injury; future efforts should prioritize precision approaches, resource adaptations, multicenter trials, and biomarkers for personalized care.

Keywords Nursing, Traumatic brain injury, Clinical protocols, Nurses.

Introduction

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide, with a particularly high burden among young adults and older people, and constitutes a major public health and socioeconomic challenge. Acute TBI accounts for millions of emergency visits and hospital admissions annually, with global incidence estimates commonly exceeding 250–300 cases per 100,000 person-years when including mild injuries, and severe TBI responsible for a disproportionate share of mortality and long-term disability. Mortality for severe TBI in contemporary series still ranges around 25–35% despite advances in neurocritical care, while many survivors experience enduring cognitive, behavioral, and physical impairments that limit independence, employability, and quality of life. The economic impact is substantial, combining direct medical costs (acute hospital care, neurosurgery, ICU and rehabilitation) with indirect costs from lost productivity, caregiver burden, and long-term social care needs, and in high-income countries TBI-related expenditures reach tens of billions of dollars annually while low- and middle-income countries face disproportionate morbidity with far fewer resources. These epidemiologic and economic patterns, together with marked international variation in outcomes, underscore the need for structured, evidence-based clinical protocols across the entire acute care continuum for TBI, from scene to community reintegration (Stocker, 2019).

Given the pathophysiology of TBI clinical protocols have emerged as a central strategy to standardize care and minimize preventable secondary brain injury across prehospital, emergency department, intensive care, ward, and rehabilitation settings. In the prehospital phase, protocolized management emphasizes early recognition of severe TBI, airway protection, avoidance of hypoxemia and hypotension, normocapnic ventilation, and timely transport to appropriate trauma centers, as codified in the Brain Trauma Foundation (BTF) 3rd edition prehospital guidelines. Within emergency and ICU environments, structured neurotrauma pathways typically integrate timely neuroimaging, neurosurgical decision-making, multimodal monitoring (intracranial pressure, cerebral perfusion pressure, and often brain tissue oxygenation), tiered therapies for intracranial hypertension, hemodynamic and ventilatory targets, glycemic and temperature control, seizure prophylaxis, and early rehabilitation planning. Ward-based and step-down protocols aim to maintain medical stability, prevent complications (e.g., venous thromboembolism, infections, spasticity), optimize early mobilization, and coordinate multidisciplinary assessment, while rehabilitation protocols and optimal clinical pathways structure cognitive, physical, and psychosocial interventions that continue long after discharge. Across these settings, protocolized care is designed to reduce unwarranted variation, support guideline adherence, and enable system-level quality improvement, providing a framework against which outcomes can be benchmarked and resources aligned (Hawryluk et al., 2023).

Comparative data suggest that protocolized TBI management is associated with better outcomes than non-protocolized or highly variable care, although the magnitude and consistency of benefit can differ by context, injury severity, and health system organization. Observational studies in neurotrauma centers have linked implementation of structured ICU protocols (including ICP- and CPP-guided therapy, standardized sedation and ventilation strategies, and early tracheostomy and nutrition algorithms) with reduced mortality and improved functional outcome compared with historical or non-protocolized cohorts, likely reflecting more reliable prevention and treatment of secondary brain injury. Prehospital guideline implementation has been associated with improved survival and neurologic outcome, while non-protocolized prehospital care often shows wide variability in airway practices, oxygenation and blood pressure targets, and triage decisions. Similarly, integrated clinical pathways that extend beyond ICU to ward and rehabilitation, and that coordinate neurosurgical, neurocritical, rehabilitation, and community services, have been reported to shorten length of stay, enhance functional recovery, and improve participation outcomes compared with fragmented, non-coordinated care. Nonetheless, gaps remain regarding which specific protocol elements drive the greatest benefit, how best to adapt protocols to resource-limited environments, and how to balance individualized precision care with standardized algorithms in diverse TBI populations (Lulla et al., 2023).

Against this backdrop, there is a clear rationale for a comprehensive review that systematically synthesizes contemporary evidence and guideline-based clinical protocols for the management of acute TBI across the full continuum of care. Existing literature is extensive but fragmented, with separate publications focusing on prehospital recommendations, emergency and ICU neurocritical care practices, neurosurgical decision algorithms, and rehabilitation pathways, often targeting specific regions, age groups, or resource settings. Major guideline documents and best-practice

recommendations published by organizations such as the Brain Trauma Foundation, the American College of Surgeons, neurocritical care societies, and national rehabilitation bodies have been updated over the last decade, integrating new evidence on multimodal monitoring, individualized CPP targets, decompressive craniectomy, thromboprophylaxis, seizure prophylaxis, and early intensive rehabilitation, yet their implementation and integration into real-world clinical protocols remain variable. Moreover, recent ICU-focused reviews highlight a trend toward precision, physiology-driven TBI care, but also point to ongoing controversies which necessitate an updated, integrative synthesis (Shen et al., 2025).

Accordingly, the primary objective of this review is to synthesize and critically appraise current evidence and guideline-based clinical protocols for the management of acute traumatic brain injury across the care continuum, encompassing prehospital, emergency department, ICU, ward, and early rehabilitation phases. Key research questions include: (1) What are the principal components and recommended targets of contemporary protocolized care in each phase of acute TBI management, as reflected in recent guidelines, clinical pathways, and high-quality studies? (2) How does protocolized care compare with non-protocolized or less standardized management in terms of mortality, functional outcome, complication rates, resource utilization, and cost-effectiveness, across different health system and resource settings? (3) Which protocol elements show the strongest evidence of benefit, which remain controversial or weakly supported, and where are the major gaps for future research, particularly regarding adaptation to low- and middle-income settings and integration of novel monitoring and rehabilitation technologies? By addressing these questions, the review aims to provide clinicians, protocol developers, and policymakers with an evidence-informed, continuum-of-care perspective that can guide the design, implementation, and refinement of TBI clinical protocols, ultimately supporting more consistent delivery of high-quality acute neurotrauma care and improved outcomes for patients worldwide (Konar et al., 2022).

Definitions and classifications of TBI

Traumatic brain injury (TBI) is classically defined as an alteration in brain function, or other evidence of brain pathology, caused by an external physical force, encompassing a spectrum from transient concussion to coma and death, and is considered “acute” when the inciting mechanical insult and its immediate clinical consequences occur within hours to days of the traumatic event rather than reflecting chronic or degenerative sequelae. Clinical severity is most commonly graded using the Glasgow Coma Scale (GCS) at first contact, with mild TBI defined by a GCS of 13–15, moderate TBI by a GCS of 9–12, and severe TBI by a GCS of 3–8; these thresholds correlate with loss of consciousness and post-traumatic amnesia durations, such that mild injury typically involves loss of consciousness under 30 minutes and amnesia under 24 hours, whereas moderate and severe injuries are associated with longer disturbances of consciousness and far higher early mortality. Mechanistically, TBI arises from diverse external forces: blunt trauma with rapid acceleration–deceleration and rotational components generates focal contusions and diffuse axonal injury; penetrating trauma, including firearm injuries and sharp projectiles, disrupts brain parenchyma and cerebral vasculature along the wound tract; and blast injury combines overpressure waves, secondary shrapnel, tertiary acceleration–deceleration, and quaternary thermal or toxic effects, producing complex mixed patterns of intracranial damage, particularly in military and terrorist contexts (Ginsburg & Smith, 2025).

Beyond simple GCS thresholds, several complementary classification frameworks have been developed to stratify TBI by structural imaging and global injury burden, thereby refining prognostication and guiding therapeutic intensity in neurocritical care. CT-based systems remain central in acute practice: the Marshall classification categorizes head CT into diffuse injury classes I–IV and focal mass lesion categories based on basal cistern patency, midline shift, and presence of high- or mixed-density lesions, while the Rotterdam CT score extends this approach by assigning a 1–6 point ordinal score reflecting basal cistern status, degree of midline shift, traumatic subarachnoid or intraventricular hemorrhage, and presence and type of mass lesion. Both Marshall and Rotterdam scores show significant independent prognostic value for early and in-hospital mortality in moderate–severe TBI cohorts, with multiple validation studies reporting similar areas under the ROC curve and suggesting that Rotterdam, by incorporating additional hemorrhagic features, may offer slightly improved discrimination in patients with diffuse injury; in parallel, global trauma tools such as the Injury Severity Score and head-specific

modifications of the Abbreviated Injury Scale are frequently used in polytrauma to quantify overall injury burden and to support comparative effectiveness research and benchmarking of trauma system performance (Deepika et al., 2015).

The pathophysiological substrate of acute TBI is traditionally divided into primary and secondary brain injury, where primary injury refers to the immediate mechanical damage occurring at the moment of impact and secondary injury encompasses a delayed cascade of biochemical, metabolic, vascular, and inflammatory processes that evolve over minutes to weeks and critically determine neurological outcome. Primary mechanical insults include cortical contusions at coup and contrecoup sites, shearing forces that disrupt axons in deep white matter and corpus callosum producing diffuse axonal injury, and extra-axial or intra-axial hematomas such as epidural, subdural, subarachnoid, and intraparenchymal hemorrhages that compress neural tissue and distort intracranial compartments. These structural lesions immediately alter intracranial biomechanics, compromise microvascular integrity, and generate areas of necrosis and apoptosis that cannot be reversed, yet they also create the milieu in which secondary processes such as excitotoxicity, microvascular thrombosis, and edema can propagate injury into initially viable penumbral regions (Jha et al., 2019).

Secondary injury cascades after TBI are initiated by ionic disequilibrium and glutamate-mediated excitotoxicity, in which excessive release of excitatory amino acids and failure of astrocytic glutamate reuptake drive sustained activation of NMDA and AMPA receptors, intracellular calcium overload, mitochondrial dysfunction, and generation of reactive oxygen and nitrogen species that damage proteins, lipids, and DNA. In parallel, cerebral ischemia and impaired autoregulation lead to heterogeneous regions of hypoperfusion and hyperemia; disruption of the blood–brain barrier and upregulation of transporters such as NKCC1, along with aquaporin-4 changes, contribute to vasogenic and cytotoxic cerebral edema, elevating intracranial pressure (ICP) and reducing cerebral perfusion pressure in a vicious cycle. Neuroinflammation, driven by damage-associated molecular patterns released from injured cells, activates microglia, astrocytes, endothelial cells, and infiltrating leukocytes, resulting in rapid expression of cytokines, chemokines, adhesion molecules, and matrix metalloproteinases that further degrade the blood–brain barrier and expand tissue damage, although some inflammatory signals also participate in repair and plasticity. Clinically, systemic secondary insults such as hypotension, hypoxia, hyper- or hypocapnia, hyperthermia, and dysglycemia amplify these intracranial cascades and have been strongly associated with increased mortality and unfavorable functional outcome, underscoring why contemporary protocols prioritize meticulous avoidance of “secondary hits” through aggressive control of blood pressure, oxygenation, ventilation, and temperature in both prehospital and in-hospital phases of care (Majdan et al., 2015).

Neurological assessment in acute TBI hinges on standardized clinical scales that quantify consciousness and brainstem function, with the Glasgow Coma Scale remaining the cornerstone: eye opening, verbal response, and motor response are scored to produce a total of 3–15, and clinicians often rely particularly on the motor component because of its strong association with outcome and its relative robustness across languages and intubated states. Pupillary reactivity to light provides complementary information on brainstem integrity and raised intracranial pressure, and composite metrics integrating GCS with pupil response have shown stronger associations with 6-month outcome than GCS alone, offering a single integrated ordinal scale that enhances early risk stratification. Large cohort analyses have demonstrated that combinations like field GCS motor score and admission pupillary reactivity yield excellent discrimination for 6-month mortality in moderate–severe TBI, while age, initial GCS, pupillary status, and CT features consistently emerge as the most powerful bedside predictors incorporated into multivariable models (Majdan et al., 2015).

Building on these core clinical and radiological variables, multivariable prognostic models such as IMPACT (International Mission for Prognosis and Analysis of Clinical Trials in TBI) and CRASH (Corticosteroid Randomisation After Significant Head Injury) have been developed and externally validated to estimate risks of mortality and unfavorable functional outcome after TBI, primarily at 6 months. The IMPACT models (core, extended, and lab) typically combine age, GCS motor score, pupillary reactivity, and CT or laboratory variables, whereas CRASH models (basic and CT) incorporate

similar clinical and imaging predictors, and comparative meta-analyses suggest that their discriminative performance is broadly equivalent, with odds ratios for mortality prediction close to unity when models are directly contrasted. Recent validations in contemporary multicenter cohorts indicate that both IMPACT and CRASH maintain acceptable discrimination (AUC roughly 0.77–0.83) for mortality and unfavorable outcome but tend to overestimate risk, explain only a modest fraction of outcome variance, and perform less well beyond 6 months, leading many experts and guideline groups to recommend their use for research, benchmarking, and counseling at the population level rather than for rigid individual prognostication or withdrawal of life-sustaining therapy decisions. In parallel, novel scores that couple clinical variables with physiological data or integrate advanced imaging and biomarkers (for example, the recently proposed MOST mortality score and other emerging machine-learning models) are being explored to better capture the impact of early systemic insults, given robust evidence that even a single episode of hypotension below 90 mmHg, especially when combined with hypoxia, more than doubles the odds of death after moderate–severe TBI and that aggressive prevention of these events is a key modifiable determinant of outcome in prehospital and in-hospital settings (Zarei et al., 2023).

Overview of Guidelines and Protocol Frameworks

Major international and national guidelines on acute traumatic brain injury (TBI) now constitute a multilayered framework spanning the entire continuum of care from the scene of injury through neurocritical care and rehabilitation, with the Brain Trauma Foundation (BTF) guidelines remaining the central international reference for both prehospital and in-hospital management. The latest BTF prehospital guidelines emphasize prevention of secondary brain injury through meticulous avoidance of hypoxia and hypotension, structured airway and ventilation algorithms, and cautious use of hyperosmolar therapy and tranexamic acid, while the adult and pediatric severe TBI guidelines provide detailed recommendations on intracranial pressure (ICP) monitoring, cerebral perfusion pressure (CPP) targets, sedation, osmotherapy, decompressive craniectomy, and venous thromboembolism prophylaxis, all derived from systematic evidence reviews and graded recommendations. In parallel, national frameworks such as the American College of Surgeons (ACS) Trauma Quality Improvement Program (TQIP) best-practice guidelines for TBI integrate BTF recommendations with trauma-system organization, triage, imaging, operative decision-making, and ICU care processes, offering pragmatic algorithms for US trauma centers, whereas professional societies including the Neurocritical Care Society, the Society of Critical Care Medicine, anesthesiology and emergency medicine societies, and national neurosurgical bodies have issued complementary consensus statements on neurocritical care monitoring, sedation and analgesia, airway management, and anesthesia for TBI that further refine practice in specific disciplines. Outside North America, guideline frameworks from the National Institute for Health and Care Excellence (NICE) in the UK and region-specific protocols in Europe and Australasia have adapted similar evidence bases to local resource settings, with a growing emphasis on standardized triage, early CT imaging, regional neurosurgical referral pathways, and structured rehabilitation planning, underscoring the trend toward harmonized yet context-sensitive protocolization of TBI care worldwide (Hawryluk et al., 2023).

The structure and grading of recommendations across contemporary TBI guidelines increasingly align with formal evidence-grading systems such as GRADE, distinguishing between the quality of evidence (high, moderate, low, very low) and the strength of recommendations (strong vs weak/conditional) in order to transparently link clinical directives to underlying data. In the BTF prehospital guideline, for example, strong recommendations are reserved for interventions supported by consistent observational and physiologic data showing harm from secondary insults while more limited or conflicting data on hypertonic resuscitation and prehospital hyperosmolar therapy result in weak recommendations, thereby signaling to systems planners where local adaptation and clinician judgment are particularly important. Across the acute care spectrum, guideline documents explicitly categorize domains such as prehospital scene and transport care, emergency department (ED) resuscitation and imaging, ICU neurocritical care (including ICP/CPP targets, ventilation strategies, seizure prophylaxis, nutrition, temperature management, and infection prevention), neurosurgical decision-making (including decompressive craniectomy and mass-lesion evacuation), and post-acute rehabilitation and long-term follow-up, with each domain containing graded recommendations that facilitate development of

setting-specific protocols in trauma systems, EDs, ICUs, neurosurgical services, and rehabilitation programs (National Academies of Sciences et al., 2022).

Within these graded frameworks, protocolized care pathways and bundled interventions have emerged as key implementation strategies to translate guideline recommendations into consistent bedside practice, particularly for patients with severe TBI who are highly vulnerable to variation in care. Many centers have adopted structured "airway–breathing–circulation–neuroprotection" bundles in the prehospital and ED phases, which typically include early airway control with avoidance of hypoxia and inappropriate hyperventilation, maintenance of normotension and euglycemia, head-of-bed elevation and neutral neck positioning, rapid CT imaging, timely neurosurgical consultation, and early initiation of measures to control ICP, while ICU bundles often layer standardized targets for ICP and CPP, sedation and analgesia protocols, glycemic and temperature control, ventilator strategies to avoid both hypoxia and hypocapnia, early enteral nutrition, and prevention of complications such as deep vein thrombosis and ventilator-associated pneumonia. Evidence synthesized in systematic reviews and practice-based evaluations suggests that such standardized TBI management protocols and care pathways are associated with improved adherence to guideline-recommended care, reductions in in-hospital mortality, and better functional outcomes at 6 months and beyond, even when mortality differences do not always reach statistical significance, implying that protocolization may exert its greatest effect on neurobehavioral recovery and disability rather than survival alone. In pediatric and mixed-age cohorts, implementation of PICU or ICU TBI pathways has been shown to increase compliance with key therapies and to shorten ICU length of stay without excess complications, and more recent learning-health-system initiatives are embedding real-time data feedback and outcome monitoring into TBI care bundles to iteratively refine protocols and align them with evolving evidence on rehabilitation intensity and long-term functional recovery (Chesnut et al., 2023).

Emergency Department Initial Management

Emergency department management of acute traumatic brain injury (TBI) must follow a structured, time-critical protocol that integrates the Advanced Trauma Life Support (ATLS) framework with neuroprotective strategies to prevent secondary brain injury from hypoxia, hypotension, and delayed diagnosis of mass lesions. Across the early care continuum, systematic application of ABCDE principles, detailed neurological assessment, rational imaging pathways, clear neurosurgical triggers, and evidence-based disposition criteria are central to optimizing outcomes for patients with both mild and severe TBI in diverse emergency settings (Dixon et al., 2020).

In the emergency department, initial management of TBI is anchored in the ABCDE primary survey, with rapid identification and correction of life-threatening airway, respiratory, and circulatory compromise while maintaining spinal precautions and simultaneously recognizing intracranial injury patterns. For TBI, ATLS priorities emphasize early airway control in patients with a Glasgow Coma Scale (GCS) score ≤ 8 or those unable to protect the airway, avoidance of hypoxia (targeting oxygen saturation $\geq 94\%$) through supplemental oxygen or endotracheal intubation, and meticulous ventilation to maintain normocapnia and avoid prophylactic hyperventilation except as a brief temporizing measure for signs of impending herniation (Dixon et al., 2020).

Breathing assessment requires immediate evaluation of chest wall integrity, respiratory rate, and bilateral breath sounds, because occult thoracic injuries (e.g., tension pneumothorax, pulmonary contusion) can exacerbate hypoxia and worsen cerebral ischemia, and should be treated in parallel with neuroprotective measures. Circulatory management prioritizes rapid identification of hemorrhagic shock from extracranial sources, aggressive resuscitation with isotonic crystalloid and early blood products when indicated, and maintenance of systolic blood pressure typically $\geq$ 100–110 mmHg in adults to preserve cerebral perfusion pressure and limit secondary brain injury (Dixon et al., 2020).

During the disability component, a rapid neurologic screen (GCS, pupil size and reactivity, gross motor asymmetry) is performed early and then refined after initial stabilization, while exposure and environmental control ensure that other injuries (long bone fractures, abdominal trauma, open skull fractures) are not missed and hypothermia is actively prevented, since coagulopathy and hypotension synergistically worsen outcomes in severe TBI. Early in the primary survey, standardized protocols typically trigger urgent laboratory testing (full blood count, coagulation profile, electrolytes, glucose,

type and screen) and imaging orders (non-contrast CT head with or without trauma pan-scan), integrated with institutional massive transfusion and neurotrauma pathways to minimize door-to-CT and door-to-OR times (Thim et al., 2012).

Neurological assessment in acute TBI is centered on structured, serial application of the GCS, pupillary examination, and motor function testing, which together provide both immediate triage information and powerful prognostic data for 6-month outcome and risk of deterioration. The motor component of the GCS and pupillary reactivity, including their combined use in the GCS-P or related scales, have been shown to correlate strongly with mortality; deterioration in motor score between prehospital and admission assessment or new loss of pupillary reactivity should therefore prompt urgent reassessment for expanding intracranial hematoma or rising intracranial pressure (ICP) (Majdan et al., 2015).
Standardized trauma neurologic examinations in the ED typically include documentation of eye opening, verbal and motor responses, pupillary size and symmetry, extraocular movements where feasible, limb strength and localization to pain, and signs of lateralizing deficits, with repeat "neuro checks" at defined intervals (e.g., every 15–30 minutes initially) to detect early neurological decline. These serial assessments are especially important in patients with initially mild or moderate TBI and intracranial hemorrhage, as clinical deterioration often precedes or parallels radiological progression, guiding decisions about repeat CT and escalation to neurosurgical interventions or ICU-level care (Jain et al., 2025).

Sedation, analgesia, and neuromuscular blockade are frequently required to facilitate airway control, mechanical ventilation, and control of agitation or combativeness in severe TBI, but they also obscure key elements of neurological examination and can mask early signs of herniation or seizure activity. Best practice recommends using short-acting agents when feasible, documenting a detailed baseline neurologic exam before intubation, and coordinating sedation weaning or sedation "holidays" with neurosurgery and critical care when safe, to allow accurate reassessment and avoid misinterpretation of drug-induced unresponsiveness as neurologic decline (Clark et al., 2024).
Non-contrast CT of the brain is the imaging modality of choice for initial evaluation of suspected acute TBI, given its speed, availability, and sensitivity for detecting life-threatening lesions such as epidural hematoma, acute subdural hematoma, traumatic subarachnoid hemorrhage, cerebral contusions, depressed skull fractures, and mass effect with midline shift or herniation. In many major trauma centers, CT is integrated into a whole-body "pan-scan" protocol (head, cervical spine, chest, abdomen, and pelvis) for multi-trauma patients, allowing rapid detection of concomitant extracranial injuries that may drive hemodynamic instability and influence resuscitation priorities (Sharp et al., 2018).
For adults with minor head injury (GCS 13–15), clinical decision rules such as the Canadian CT Head Rule (CCHR) are widely used to identify patients at high risk for clinically important brain injury and reduce unnecessary CT utilization without compromising safety, with multiple studies showing that CCHR implementation can significantly lower CT rates while maintaining high sensitivity for neurosurgical lesions. These rules typically incorporate factors such as age, mechanism of injury, vomiting, amnesia, suspected skull fracture, and signs of basal skull fracture, and their application must be adapted to local protocols and populations, especially in anticoagulated patients or the elderly, who may require lower thresholds for imaging (Sharp et al., 2018).

CT angiography (CTA) of the head and neck is increasingly incorporated into trauma imaging pathways when there is suspicion of vascular injury (e.g., traumatic intracranial aneurysm, carotid or vertebral dissection, penetrating trauma, or skull base fractures involving vascular channels), and can be performed immediately following non-contrast CT in unstable but sufficiently resuscitated patients. Repeat CT brain is generally recommended for patients with neurological deterioration, increasing ICP, or those with high-risk intracranial lesions, while routine scheduled repeat imaging in neurologically stable mild TBI is being questioned, with emerging evidence suggesting that repeat CT should be reserved for patients with severe injury, high-risk radiological patterns, younger age, or new clinical changes rather than used indiscriminately (Beedkar et al., 2024).
Decisions regarding emergent neurosurgical intervention in acute TBI are driven by CT findings, neurological status, and physiologic stability, with classic indications including epidural hematoma causing mass effect, acute subdural hematoma with significant thickness or midline shift, traumatic

intracerebral hematomas with mass effect, and open or markedly depressed skull fractures with underlying contusion or dural violation. Epidural hematomas, often associated with temporal skull fractures and middle meningeal artery injury, typically require urgent craniotomy for evacuation when they are large or associated with declining GCS or anisocoria, as rapid surgical decompression is strongly associated with improved survival and functional outcomes (Khairat et al., 2025).
Acute subdural hematomas with clot thickness greater than standard thresholds (often cited as > 10 mm) or midline shift beyond commonly accepted cutoffs (often > 5 mm), particularly in patients with depressed consciousness, are usually managed with emergent craniotomy or decompressive procedures, while select smaller asymptomatic lesions may be observed with intensive monitoring and interval imaging. Depressed skull fractures, especially those that are open, contaminated, associated with dural tears, or overlying a major venous sinus or focal hematoma, commonly warrant surgical elevation and debridement, and literature on delayed evolving epidural hematomas in the setting of depressed fractures underscores the need for a low threshold for repeat CT and operative management in these high-risk scenarios (Choucha et al., 2025).

ED-to-OR pathways are increasingly formalized through institutional TBI protocols that prioritize rapid neurosurgical consultation, predefined activation criteria, and streamlined transfer processes designed to minimize time from diagnostic CT to skin incision, recognizing that delays to definitive decompression are linked with increased mortality and worse neurologic outcomes. Time-to-intervention metrics, such as door-to-CT, CT-to-neurosurgical decision, and CT-to-OR times, are now common quality indicators; registry-based studies show that prolonged in-hospital delays to surgery, rather than prehospital transport time alone, may be a critical determinant of poor outcomes, particularly in resource-limited settings (Egas Terán & González-Andrade, 2025).
Disposition decisions following initial ED management of TBI rely on integration of injury severity (GCS, CT findings), physiological stability, comorbidities, need for invasive monitoring or ventilatory support, and availability of neurosurgical and critical care resources, with the overarching goal of matching patients to an appropriate level of observation and intervention. Patients with severe TBI, those requiring mechanical ventilation or ICP monitoring, and those with large intracranial hemorrhages or ongoing hemodynamic instability are typically admitted directly to an ICU or dedicated neurocritical care unit, whereas selected moderate TBI patients with stable imaging and physiology may be managed in high-dependency or step-down units with frequent neuro checks (Nishijima et al., 2011).
Mild TBI (GCS 13–15) with normal CT and no high-risk features is often managed with a period of ED observation followed by discharge with clear written instructions, return precautions, and, when indicated, scheduled follow-up for post-concussive symptoms, while patients with intracranial hemorrhage or significant risk factors (e.g., anticoagulation, advanced age, skull fracture) usually require hospital admission for serial neurological assessment. Studies examining ICU admission patterns for mild TBI with traumatic intracranial hemorrhage have found substantial variability and suggest that many such patients who do not receive critical care interventions within the first hours may safely be observed in non-ICU settings, highlighting the need for validated risk stratification tools and institutional protocols to optimize resource utilization without compromising safety (Bonow et al., 2019).

Intensive Care Unit Protocols in Acute TBI

Intensive care unit (ICU) management of acute traumatic brain injury (TBI) is fundamentally directed toward the prevention of secondary brain injury by maintaining adequate cerebral perfusion and oxygen delivery while avoiding intracranial hypertension and systemic complications, using structured protocols that integrate invasive hemodynamic monitoring, intracranial pressure (ICP) and cerebral perfusion pressure (CPP) surveillance, continuous neurological assessment, and organ support within a goal-directed, tiered treatment framework (Konar et al., 2022).
In the neurocritical care setting, the central objective of ICU management after severe TBI is to prevent and promptly treat secondary brain insults such as hypotension, hypoxemia, intracranial hypertension, cerebral hypoperfusion, and metabolic derangements, because these factors are strongly associated with increased mortality and poor neurological outcome. Standardized ICU protocols typically prescribe immediate invasive arterial pressure monitoring for beat-to-beat blood pressure control, central venous access for vasoactive infusions and fluid resuscitation, ICP monitoring in eligible patients, calculation

and targeting of CPP, and the use of multimodality neuromonitoring to individualize therapy and detect evolving secondary injury that is not apparent on clinical examination alone (Konar et al., 2022).
Protocols for ICP and CPP management generally follow guideline-based indications for ICP monitoring, recommending invasive ICP devices in salvageable patients with severe TBI (Glasgow Coma Scale 3–8) and an abnormal CT scan, or in those with severe TBI and a normal CT who exhibit additional risk factors such as age over 40 years, unilateral or bilateral motor posturing, or systolic blood pressure below 90 mmHg, with the aim of reducing in-hospital and early post-injury mortality. Treatment algorithms commonly adopt a threshold-based approach in which sustained ICP values greater than approximately 22 mmHg prompt intervention, while CPP is actively maintained within a target window of about 60–70 mmHg using a tiered escalation that progresses from head elevation, optimization of sedation and analgesia, and cerebrospinal fluid (CSF) drainage, to osmotherapy, controlled hyperventilation, and ultimately decompressive craniectomy for refractory intracranial hypertension (Bögli et al., 2025).

Sedation and analgesia protocols in acute TBI prioritize continuous, titratable agents such as propofol or midazolam in combination with potent opioids to control pain, agitation, and ventilator dyssynchrony, thereby limiting surges in ICP and sympathetic responses, while allowing periodic neurological assessment when safe to do so. Many centers employ structured sedation scales and consider daily sedation interruptions or lightening only when ICP is well controlled and when spontaneous neurological examination is necessary, whereas in patients with unstable ICP or ongoing intracranial crises, deeper continuous sedation is preferred to blunt cerebral metabolic demand and ICP fluctuations. Neuromuscular blocking agents are generally reserved for clearly defined indications such as refractory intracranial hypertension associated with shivering or severe ventilator dyssynchrony, or when achieving lung-protective ventilation is not possible without paralysis, and protocols emphasize careful hemodynamic monitoring and avoidance of prolonged paralysis that could mask seizure activity or delay recognition of neurological deterioration, often pairing neuromuscular blockade with continuous EEG monitoring in deeply sedated, comatose TBI patients (Mathew et al., 2025).
Mechanical ventilation strategies in TBI patients balance lung-protective principles with cerebral physiology, typically using low tidal volumes and adequate positive end-expiratory pressure (PEEP) to prevent ventilator-induced lung injury while closely monitoring their impact on intrathoracic pressure, venous return, and ICP, especially in the setting of concomitant acute respiratory distress syndrome (ARDS). Protocols usually aim to maintain PaO_2 above 80–100 mmHg and avoid hypoxemia, while targeting normocapnia with $PaCO_2$ around 35–40 mmHg under stable conditions, reserving therapeutic hyperventilation to lower $PaCO_2$ (e.g., 30–35 mmHg or lower) as a short-term, rescue measure for acute intracranial hypertension or impending herniation, with strong recommendations against prophylactic or prolonged aggressive hyperventilation because of the risk of cerebral ischemia (Haddad & Arabi, 2012).

Hemodynamic management in severe TBI focuses on maintaining adequate systemic blood pressure to support CPP, with guideline-based thresholds typically recommending systolic blood pressure of at least 100–110 mmHg depending on age and CPP targets of roughly 60–70 mmHg, often achieved through judicious use of vasopressor agents such as norepinephrine as first-line support. Fluid management protocols emphasize euvolemia using isotonic crystalloids, strict avoidance of hypotonic solutions and excessive free water that could exacerbate cerebral edema, and careful attention to serum osmolarity and electrolyte status, sometimes employing slightly hyperosmolar strategies to support ICP control while avoiding fluid overload that may worsen pulmonary function, especially in patients at risk of ARDS (Haddad & Arabi, 2012).
Hyperosmolar therapy is a cornerstone of ICP control in ICU-managed TBI, and protocols typically employ either mannitol or hypertonic saline, selecting agents and dosing based on hemodynamic status, renal function, and serum sodium and osmolarity, for example administering intermittent mannitol boluses (e.g., 0.25–1 g/kg) with close monitoring of serum osmolality and urine output, or using hypertonic saline in bolus or continuous infusion while capping serum sodium (often ≤160 mEq/L) and osmolality thresholds to minimize complications. Temperature management protocols seek to prevent and aggressively treat fever, as hyperthermia exacerbates cerebral metabolism and secondary injury, with contemporary guidelines favoring maintenance of strict normothermia or controlled temperature

management over routine prophylactic hypothermia, given that large randomized trials of early deep hypothermia in severe TBI have not demonstrated consistent outcome benefits and have raised concerns about complications such as infections and coagulopathy (Haddad & Arabi, 2012).

ICU protocols for seizure prophylaxis in acute TBI generally recommend short-term administration of antiepileptic drugs in patients with severe injuries or high-risk features to reduce the incidence of early post-traumatic seizures during the first week after injury, with common practice favoring levetiracetam or phenytoin and limiting prophylaxis to approximately 7 days in the absence of documented seizures. Continuous or intermittent EEG monitoring is increasingly integrated into ICU care for comatose or deeply sedated TBI patients to detect non-convulsive seizures and status epilepticus, enabling timely escalation of antiepileptic therapy and adjustment of sedative regimens; such EEG-based protocols are particularly important when neuromuscular blockade or high-dose sedation obscures clinical seizure manifestations and when unexplained ICP spikes, autonomic instability, or metabolic deterioration raise suspicion for subclinical epileptic activity (Mathew et al., 2025).

Glycemic control protocols in severe TBI favor moderate targets that avoid both hypoglycemia and significant hyperglycemia because tight glycemic control with intensive insulin therapy has been associated with higher risks of hypoglycemia and potential harm in critically ill patients, while uncontrolled hyperglycemia is linked to worse neurological outcomes. ICU care also places strong emphasis on managing serum sodium and osmolarity within ranges that support ICP control and cerebral perfusion, including prompt recognition and treatment of diabetes insipidus or syndrome of inappropriate antidiuretic hormone secretion (SIADH), and on initiating early enteral nutrition using protocols that favor gastric or post-pyloric feeding and implement strategies to reduce ventilator-associated pneumonia, gastrointestinal intolerance, and aspiration risk (Mathew et al., 2025).

Infection prevention is integral to TBI ICU protocols, which routinely incorporate central line bundles, ventilator-associated pneumonia prevention strategies (elevating the head of bed, daily sedation assessment, oral care with chlorhexidine, subglottic suctioning, and early weaning), and catheter-associated urinary tract infection prevention measures, recognizing that nosocomial infections can prolong mechanical ventilation, increase intracranial complications, and worsen overall prognosis. In parallel, comprehensive ICU care pathways address ICU delirium prevention and early mobilization when feasible through structured daily awakening and breathing trials, minimization of benzodiazepine exposure, promotion of normal sleep–wake cycles, early physiotherapy and occupational therapy, and family engagement, all tailored to the unique constraints of severe TBI where ongoing neuromonitoring, ICP status, and surgical considerations may limit the extent and timing of mobilization and neurocognitive assessment (Haddad & Arabi, 2012).

Biomarkers, Imaging Innovations, and Advanced Monitoring

Serum and cerebrospinal fluid (CSF) biomarkers have emerged as key adjuncts to clinical assessment and neuroimaging for the early diagnosis and risk stratification of acute traumatic brain injury (TBI), particularly in the mild and moderate severity spectrum where CT can be normal despite relevant axonal or glial injury. S100B, a calcium-binding protein predominantly expressed by astrocytes, was among the first biomarkers incorporated into clinical algorithms; European guidelines for mild TBI use low serum S100B within a defined time window to safely omit CT scanning in low-risk patients, capitalizing on its very high sensitivity and negative predictive value for intracranial lesions but acknowledging modest specificity and susceptibility to extracranial sources such as bone fractures and soft-tissue trauma. Glial fibrillary acidic protein (GFAP), an intermediate filament protein specific to astrocytes, and ubiquitin C-terminal hydrolase L1 (UCH-L1), a neuronal cell body enzyme, have subsequently shown superior discriminatory performance across the full TBI severity spectrum; both rise rapidly within the first hours after injury, correlate with CT-positive intracranial pathology and clinical severity, and demonstrate better ability than S100B to differentiate mild from moderate–severe TBI, leading to their combination into FDA-cleared blood tests intended to rule out the need for head CT in adults with suspected mild TBI and GCS 13–15. Prospective multicenter kinetic studies indicate that serial sampling of GFAP, UCH-L1, and S100B over the first 24 hours provides dynamic information on ongoing secondary injury processes and is associated with outcome, supporting their integration into protocolized monitoring frameworks where cut-off values measured at fixed time points (for example at emergency department arrival and 6–12 hours post-injury) inform decisions about immediate CT, repeat imaging, observation duration, and potential ICU admission (Oris et al., 2024).

In clinical protocols for mild and moderate TBI, S100B retains a role as a cost-effective, widely available screening tool when sampled within 3–6 hours after injury, with studies reporting near-100% sensitivity for intracranial lesions but low specificity, making it best suited to safely reducing unnecessary CT rather than selecting patients for neurosurgical intervention. GFAP and UCH-L1 have expanded this paradigm by offering a broader sampling window (up to 12 hours in several cohorts), higher specificity than S100B for CT-positive injuries, and stronger associations with diffuse axonal injury, midline shift, and Marshall CT score, which supports their use not only for binary CT-decision rules but also for early risk stratification into low-, intermediate-, and high-risk categories that can be tied to standardized clinical pathways. In moderate TBI (GCS 9–12) and high-risk mild TBI (anticoagulation, age >65, worrisome mechanism), elevated GFAP and UCH-L1 levels can be incorporated into triage algorithms to prioritize rapid CT, expedite transfer to trauma centers, and trigger neurosurgical consultation, while persistently high or rising values beyond 24 hours may flag patients at risk of secondary deterioration who warrant intensive monitoring even in the absence of major CT abnormalities. CSF measurements of these biomarkers, although less practical for routine use, show strong correlations with serum levels and with intracranial pressure and lesion burden in severe TBI, suggesting that lumbar or ventricular sampling in research or highly specialized units can refine mechanistic understanding and guide future protocol refinement that may translate CSF-derived thresholds back into serum-based algorithms (Biberthaler et al., 2021).

Beyond S100B, GFAP, and UCH-L1, a growing panel of candidate serum and CSF biomarkers are being evaluated for added prognostic value and for their ability to capture distinct pathophysiological domains such as axonal degeneration, neuroinflammation, and vascular injury, raising the possibility of multi-analyte signatures that outperform single markers for precision stratification. Systematic reviews and meta-analyses consistently report that higher admission levels of S100B, GFAP, UCH-L1, and NSE are associated with mortality and unfavorable functional outcome in moderate–severe TBI, and that combining glial and neuronal markers yields the best discrimination, which aligns with the concept that their standardized measurement could be embedded into protocolized care bundles: for example, routine sampling at admission, 6 hours, and 24 hours with pre-specified action thresholds for ICU admission, frequency of neuro checks, and timing of follow-up imaging. However, widespread protocol adoption remains limited by analytic variability, preanalytical factors, heterogeneity of published cut-offs, and the lack of randomized trials demonstrating that biomarker-guided algorithms improve hard clinical outcomes, underscoring the current recommendation that these assays be used as adjuncts within structured pathways rather than as stand-alone decision-makers until stronger implementation evidence becomes available (Papa et al., 2015).

Advanced neuroimaging techniques have transformed the understanding of structural and functional abnormalities after TBI and are increasingly considered for integration into clinical pathways, although their routine use in acute protocols remains variable across centers. Diffusion tensor imaging (DTI), which quantifies the directionality and magnitude of water diffusion in white matter tracts, has repeatedly demonstrated microstructural alterations in patients with mild and moderate TBI who have normal or near-normal conventional CT and MRI, supporting its role as a sensitive marker of diffuse axonal injury and a potential adjunct for prognostication and rehabilitation planning. Perfusion imaging modalities, including dynamic susceptibility contrast MRI, arterial spin labeling, and perfusion CT, provide quantitative maps of cerebral blood flow and volume that can identify focal and global hypoperfusion, impaired autoregulation, and ischemic penumbra in the acute phase, thereby informing individualized targets for blood pressure and ventilation management that might be formalized within hemodynamically focused clinical protocols (Smith et al., 2019).

MRI-based protocols that combine conventional sequences (T1, T2, FLAIR, susceptibility-weighted imaging) with DTI, perfusion, MR spectroscopy, and functional MRI offer a multiparametric assessment of contusions, microhemorrhages, white matter tract integrity, metabolic disturbances, and network connectivity, enabling a much richer characterization of injury burden than CT alone. In the acute setting, rapid MRI protocols such as “QuickBrain” or abbreviated trauma MRI have been evaluated as radiation-sparing alternatives to CT for selected pediatric and adult patients, and could be incorporated into protocolized pathways where hemodynamically stable individuals with low to intermediate risk and contraindications to CT contrast are preferentially directed to MRI-based imaging. For moderate and severe TBI, early DTI and susceptibility-weighted imaging have been associated with

long-term functional and neuropsychological outcomes, suggesting that advanced MRI obtained within the first week post-injury could be embedded into prognostic protocols used by multidisciplinary teams to counsel families, stratify patients into rehabilitation trajectories, and select candidates for clinical trials targeting diffuse axonal injury (Hu et al., 2022).

Molecular and functional imaging techniques, including positron emission tomography (PET) and single-photon emission computed tomography (SPECT), add another layer of pathophysiological insight by measuring cerebral metabolism, perfusion, and neuroinflammation, although logistical complexity, cost, and limited availability currently restrict their use to research or highly specialized centers. PET tracers targeting glucose metabolism, amyloid, tau, and neuroinflammatory markers have been used to demonstrate persistent metabolic depression and chronic neurodegenerative changes after TBI, findings that could eventually influence long-term follow-up protocols and neuroprotective strategies if validated in larger cohorts. From a systems perspective, the main challenge for protocolized integration of advanced neuroimaging lies in standardizing acquisition parameters, post-processing pipelines, and reporting frameworks, and then linking specific imaging phenotypes to clearly defined management actions, such as escalation of ICP monitoring in patients with extensive DTI-defined white matter injury or targeted cognitive rehabilitation in individuals with network-level connectivity disruption; several expert reviews therefore advocate for structured TBI imaging pathways that align advanced modalities with clinically meaningful decision points while acknowledging that high-quality evidence for outcome benefit is still emerging (Edlow & Wu, 2012).
Multimodal neuromonitoring has become a cornerstone of advanced neurocritical care in severe TBI, moving beyond sole reliance on intracranial pressure (ICP) and clinical examination to integrate complementary data streams on cerebral oxygenation, perfusion, autoregulation, and metabolism that can be used to tailor truly individualized therapy. Brain tissue oxygen tension ($PbtO_2$) monitoring, typically via a probe inserted into perilesional or at-risk white matter, allows continuous assessment of local oxygen availability; observational studies and expert consensus suggest that maintaining $PbtO_2$ above approximately 20 mmHg is associated with reduced secondary ischemia and may improve outcomes, leading to goal-directed protocols that couple $PbtO_2$ targets with interventions such as optimizing mean arterial pressure and cerebral perfusion pressure, adjusting ventilator settings, transfusion strategies, and sedation depth. Simultaneously, indices of cerebrovascular autoregulation such as the pressure reactivity index (PRx), derived from the correlation between slow waves of ICP and arterial blood pressure, can be used to estimate an “optimal” cerebral perfusion pressure (CPPopt) for each patient; protocols that titrate vasopressors and osmotherapy to maintain CPP near CPPopt, rather than using fixed CPP thresholds, exemplify how multimodal monitoring can drive personalized hemodynamic goals (Carteron et al., 2017).

Cerebral microdialysis (CMD) provides near-continuous sampling of extracellular brain chemistry, including glucose, lactate, pyruvate, glutamate, and glycerol, thereby offering a window into regional energy metabolism, excitotoxicity, and cell membrane degradation that is not captured by ICP or $PbtO_2$ alone. Elevated lactate–pyruvate ratio, low glucose, and high glycerol measured via CMD have been associated with episodes of ischemia, mitochondrial dysfunction, and poor neurological outcome, and recent consensus statements recommend using these metabolic signatures to trigger targeted interventions such as CPP augmentation, red blood cell transfusion, adjustment of ventilatory parameters, or modification of insulin therapy within algorithmic treatment protocols. When combined with $PbtO_2$ and ICP monitoring, CMD can help distinguish between different mechanisms of secondary injury and thus supports more nuanced, protocolized decision-making that avoids overuse of potentially harmful therapies (for example excessive hyperventilation or vasopressor escalation) in patients whose metabolic profile does not indicate ischemia (Casault et al., 2022).
Contemporary multimodal monitoring frameworks increasingly integrate these invasive modalities with non-invasive tools such as transcranial Doppler ultrasonography, near-infrared spectroscopy, and processed EEG, along with advanced analytics and data visualization platforms that display trends and computed indices at the bedside to support real-time protocol adherence. While large randomized controlled trials definitively proving outcome benefit are still limited, accumulating observational evidence and expert consensus have led to pragmatic protocol proposals in which patients with severe TBI and high risk of secondary injury receive tiered monitoring: initial ICP and systemic parameters

for all, with escalation to $PbtO_2$ and CMD in those with refractory intracranial hypertension, unexplained neurological deterioration, or complex lesions. Within such pathways, predefined thresholds for $PbtO_2$, CMD metabolites, and autoregulation indices are linked to specific therapeutic "bundles," and repeated re-evaluation of these metrics over time allows clinicians to adapt interventions as the pathophysiological state evolves, embodying an individualized, data-driven approach to acute TBI management that complements standardized guideline-based care (Hwang et al., 2025).

Rehabilitation and Early Post-Acute Protocols

Transition from the ICU or emergency department to specialized neurorehabilitation services in acute traumatic brain injury (TBI) is increasingly framed as a continuum rather than a discrete handover, with early rehabilitation processes ideally initiated in the hyperacute phase and then escalated as physiological stability is achieved. Current practice guidelines and observational data suggest that transfer to inpatient neurorehabilitation should be considered once intracranial pressure and hemodynamics are stable, neurosurgical issues are controlled, and the patient can tolerate sitting, mobilization, and structured therapy sessions for at least 30–60 minutes per day, typically occurring within days to a few weeks after injury in moderate–severe TBI, while recognizing that early transfer (within 1–2 weeks) is associated with improved functional recovery and reduced length of stay. Alongside medical stability, transfer criteria usually incorporate neurological trajectory (e.g. improving level of consciousness, emergence from coma or disorders of consciousness), respiratory status (ability to participate despite tracheostomy or ventilator dependence), and the availability of a multidisciplinary neurorehabilitation team capable of addressing complex motor, cognitive, behavioral, and communication deficits, as emphasized in recent international and resource-limited settings models of care (Buh et al., 2023).

At the point of transition, standardized functional and disability assessments are essential to characterize baseline status, guide intensity and focus of rehabilitation, and provide metrics for longitudinal outcome monitoring in clinical practice and trials. Widely used tools include global outcome measures such as the Glasgow Outcome Scale–Extended (GOSE) and Disability Rating Scale (DRS), as well as functional instruments including the Functional Independence Measure (FIM) and FIM+FAM (Functional Assessment Measure), which capture motor, self-care, and cognitive domains and can be complemented by more participation-focused tools such as the Community Integration Questionnaire (CIQ) and R-CHART to describe social role and community participation. Evidence from long-term cohort studies indicates that while instruments like the GOSE and DRS are sensitive to broad disability levels, scales emphasizing cognition, neurobehavioral function, and community reintegration (e.g. CIQ, Neurobehavioral Functioning Inventory, employment subscales) may detect persistent deficits years after injury even when FIM and GOSE appear near-normal, underscoring the need to embed multidimensional assessment batteries at transition and to repeat them across the post-acute continuum (Shen et al., 2025).

Early rehabilitation in the ICU and acute ward settings for TBI has shifted from a conservative, "rest until stable" paradigm toward structured, protocolized mobilization and multidisciplinary therapy delivery beginning in the hyperacute phase once intracranial pressure and systemic parameters are adequately controlled. Phase-based models describe a hyperacute ICU phase focused on positioning, passive range-of-motion, chest physiotherapy, and circulation-promoting modalities when intracranial pressure is variable, transitioning to more active bed mobility, sitting, verticalization, and early gait practice as neurologic and cardiorespiratory status permit, with accumulating data suggesting that such early mobilization reduces ICU-acquired weakness, infection, and overall disability without increasing secondary brain injury when carefully titrated. Early physiotherapy protocols emphasize passive and active-assisted range-of-motion of all limbs, static and dynamic stretching of major muscle groups, progressive strengthening of trunk and limb musculature, and early balance and transfer training; occupational therapy introduces self-care retraining, upper-limb function exercises, environmental adaptations, and caregiver education; while speech and language therapy addresses dysphagia management, communication impairments, and early cognitive-linguistic stimulation, including in patients with disorders of consciousness through structured sensory stimulation and command-following paradigms (Shen et al., 2025).

A central goal of these early rehabilitation protocols is prevention of secondary musculoskeletal and integumentary complications such as contractures, heterotopic ossification, pressure injuries, and

generalized deconditioning, which are strongly linked to worse functional outcomes and prolonged hospitalization. Standard bundles in the ICU and acute ward typically incorporate frequent repositioning (at least every 2–4 hours depending on risk level), use of pressure-redistributing mattresses and cushions, heel off-loading devices, prophylactic dressings over high-risk areas (sacrum, heels, trochanters), structured skin assessments, and early sitting and standing programs, alongside individualized range-of-motion regimens and splinting or orthotic use to maintain neutral joint positions and reduce spasticity-related contracture risk. Studies implementing multidisciplinary pressure injury prevention and mobilization protocols in neurocritical populations report reductions in ICU-acquired pressure injuries and acute care length of stay, with therapy programs targeting muscle strength, trunk stability, posture, and safe seating as prerequisites for later functional independence, highlighting that early, intensive, and coordinated rehabilitation within acute care is both feasible and clinically impactful when embedded into standardized pathways (Lovegrove et al., 2020).

Following discharge from inpatient rehabilitation or acute care, comprehensive long-term follow-up pathways are required to monitor evolving neurological, cognitive, behavioral, and psychosocial sequelae of TBI, which may continue to change for years after injury and can show late improvements or deteriorations. Contemporary models advocate tiered, multidisciplinary outpatient services that provide regular reviews by physiatry, neurology, neuropsychology, and therapy disciplines, with scheduled assessments at key milestones (e.g. 3, 6, 12, and 24 months) and flexible re-entry options for patients who develop late-emerging problems such as fatigue, depression, post-traumatic epilepsy, or vocational failure, including for individuals with initially "mild" TBI who remain symptomatic. Within these pathways, standardized outcome measures are repeatedly applied to quantify disability and recovery trajectories: the GOSE and DRS capture global outcome; the FIM and related functional indices describe independence in activities of daily living; and more specialized instruments such as the CIQ, Neurobehavioral Functioning Inventory, and employment and driving status metrics evaluate participation, cognition, and real-world performance, which are increasingly recognized as critical endpoints in TBI survivorship research (Shukla et al., 2011).
Return-to-work, driving, and community reintegration are central rehabilitation goals and require structured protocols that integrate medical, cognitive, psychological, and environmental considerations, rather than relying on isolated clinician judgment or time-based criteria. Evidence-informed approaches recommend graded return-to-work programs with initial work hardening or modified duties, cognitive and fatigue management strategies, and workplace accommodations guided by formal neuropsychological evaluation and functional capacity assessments, combined with ongoing monitoring for failure signals such as excessive fatigue, deterioration in symptom scores, or safety incidents. Driving resumption is usually contingent on seizure control, adequate visual and motor function, and intact attention, executive function, and judgment, often evaluated with standardized off-road cognitive and simulator-based testing in addition to jurisdiction-specific legal requirements, and many guidelines recommend structured driving rehabilitation services where available. Community reintegration protocols frequently encompass community-based rehabilitation programs, peer support groups, caregiver training, and linkages to vocational, educational, and social services, reflecting data that targeted community interventions can improve participation and quality of life after TBI and that long-term functional recovery, including after severe injury, may continue beyond the first post-injury year, justifying sustained follow-up and responsive modification of rehabilitation plans (Shukla et al., 2011).

Future Directions

Future directions in acute traumatic brain injury (TBI) management increasingly center on precision medicine, shifting from guideline-based "one-size-fits-all" algorithms toward protocols tailored to a patient's molecular, physiological, and imaging-defined phenotype across the entire injury continuum, from prehospital triage to neurocritical care and early rehabilitation transitions. Multimodal neuromonitoring platforms that integrate invasive intracranial pressure (ICP), brain tissue oxygen tension, cerebral microdialysis, and continuous electroencephalography (EEG) with systemic hemodynamic and respiratory data are being used to construct individualized "physiologic thresholds," where cerebral perfusion pressure, oxygen delivery, and metabolic targets are dynamically adjusted based on each patient's autoregulatory status and metabolic demand rather than fixed population-

derived cut-offs, laying the groundwork for closed-loop, protocolized interventions that continuously respond to evolving secondary injury patterns. Parallel advances in blood- and cerebrospinal-fluid biomarkers such as glial fibrillary acidic protein, ubiquitin carboxy-terminal hydrolase L1, neurofilament light chain, and panels derived from proteomics, metabolomics, and other "omics" approaches are enabling earlier detection of axonal injury, neuroinflammation, and blood–brain barrier disruption, helping to stratify patients for targeted therapies, refine prognosis beyond traditional scores, and potentially guide protocolized escalation or de-escalation of interventions such as decompressive craniectomy, hyperosmolar therapy, and sedation depth. At the same time, quantitative neuroimaging phenotypes derived from advanced MRI (including diffusion tensor imaging and susceptibility-weighted imaging), CT-based lesion mapping, and positron emission tomography are being combined with high-dimensional clinical and biomarker data using machine-learning models to define biologically coherent TBI endotypes that may respond differently to specific neuroprotective or neuromodulatory strategies, suggesting that future protocols may prospectively assign patients to tailored treatment bundles according to multidimensional risk signatures rather than crude categories like "severe TBI with mass lesion." Long-term, a fully realized precision-medicine paradigm for TBI will likely require interoperable data infrastructures and computational pipelines capable of ingesting real-time bedside monitoring streams, electronic health records, and serial biospecimens, using artificial intelligence to update probabilistic forecasts of cerebral insult and systemic complications, and then embedding these predictions into adaptive clinical pathways that can be tested in platform trials, thereby transforming acute TBI care from reactive management of complications into proactive, individualized prevention of secondary brain injury and its downstream neurodegenerative sequelae (Cruz Navarro et al., 2022).

Because TBI is extraordinarily heterogeneous across mechanisms, health systems, and resource settings, future improvements in protocolized acute management will depend heavily on large, harmonized multicenter consortia that can generate robust, generalizable evidence through observational cohorts, adaptive trials, and implementation studies spanning preclinical, acute, and post-acute phases. Initiatives such as the International Initiative for Traumatic Brain Injury Research and CENTER-TBI illustrate how prospective registries and core studies, built on rigorously defined common data elements (CDEs) that standardize demographic, clinical, biomarker, imaging, and outcome variables, enable sophisticated comparative-effectiveness analyses and allow investigators to examine how variation in monitoring intensity, surgical thresholds, transfusion strategies, and rehabilitation timing translate into patient-centered outcomes across diverse hospitals and countries. Recent preclinical multicenter collaborations have further demonstrated the value of harmonizing protocols and metadata, with consortia like the Translational Outcomes Project in NeuroTrauma aligning hundreds of preclinical and clinical CDEs, developing shared standard operating procedures, and using centralized repositories to support cross-site validation, multivariable phenotyping, and higher-level syndromic classifications that can better inform human protocols and trial design. Building on these foundations, future research priorities include pragmatic, registry-embedded randomized trials that test protocol components (for example, thresholds for ICP-directed interventions, blood pressure or hemoglobin targets, sedation and ventilation strategies, or multimodal monitoring bundles) in routine practice; platform or adaptive designs that allow multiple interventions to be evaluated simultaneously within biologically defined subgroups; and deliberate inclusion of low- and middle-income settings, where resource-adapted protocols and context-specific implementation strategies are critically needed to reduce global TBI-related disability. Central to this agenda will be investment in interoperable data infrastructures, robust governance frameworks for data sharing, and capacity building in underrepresented regions, so that future guidelines and decision-support tools reflect true global diversity in injury patterns, comorbidities, and health-system constraints rather than the experience of a small number of high-income tertiary centers (Wanner et al., 2025).

Emerging evidence underscores that future acute TBI protocols must explicitly incorporate trajectories of functional recovery, community integration, and health-related quality of life, shifting success metrics from short-term survival and ICU-based physiological targets to sustained participation, independence, and psychosocial well-being over years after injury. Longitudinal cohort studies show that patients with mild, moderate, and severe TBI can experience both prolonged recovery and persistent impairments up to at least five years post-injury, with substantial heterogeneity in functional

independence, symptom burden, and life satisfaction, which suggests that prognostic models built solely on early imaging and Glasgow Coma Scale scores are insufficient and that acute management decisions should be evaluated for their downstream impact on long-term outcomes. Systematic reviews and contemporary syntheses of rehabilitation interventions indicate that structured, multidisciplinary programs can improve community participation and functional outcomes, yet access to and timing of these services remain highly variable; consequently, research priorities include embedding rehabilitation consults and early goal setting into acute protocols, defining evidence-based triggers for transfer to specialized rehabilitation, and testing care pathways that extend from emergency admission through post-acute and community phases. Future models are likely to emphasize chronic care and collaborative care frameworks for TBI, with coordinated, person-centered case management, integrated mental health support, and ongoing monitoring for complications such as mood disorders, neurodegenerative changes, and caregiver burden, supported by digital health tools and tele-rehabilitation; these models should be evaluated in terms of cost-effectiveness, equity of access, and their ability to deliver scalable, personalized interventions, especially in pediatric and aging populations where developmental stage or comorbidities profoundly shape recovery (Kim & Colantonio, 2010).

Conclusion

Structured, evidence-based clinical protocols for acute TBI significantly reduce variability in care, lower mortality rates (around 25-35% in severe cases despite advances), and improve functional outcomes compared to non-protocolized approaches across prehospital, emergency, ICU, and rehabilitation settings. While observational data support benefits like shorter ICU stays and better neurologic recovery, gaps persist in optimal ICP/CPP thresholds, resource-limited adaptations, and integration of precision tools such as biomarkers (e.g., GFAP, UCH-L1) and advanced imaging. Future directions should prioritize multicenter trials, machine learning for endotyping, and global harmonization to enhance protocol implementation and long-term patient quality of life.

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