Reprint from The Review of DIABETIC STUDIES

The Review Of
DIABETIC
STUDIES OPEN ACCESS

Multidisciplinary Management of Traumatic Brain Injury: Advances in Laboratory Assessment, Diagnostic Imaging, Emergency Care, Nursing, and Physical Rehabilitation

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Abstract

Traumatic brain injury (TBI) is a complex, heterogeneous condition whose clinical trajectory is shaped less by the initial insult than by the quality and coordination of care delivered across the continuum. Effective management demands an integrated multidisciplinary approach in which laboratory assessment, diagnostic imaging, emergency medicine, nursing, and physical rehabilitation function as a synchronized system rather than isolated specialties. Advances in laboratory medicine—particularly serum biomarkers such as glial fibrillary acidic protein (GFAP), ubiquitin C-terminal hydrolase L1 (UCH-L1), neurofilament light (NfL), and S100B—are reshaping triage by offering rapid, objective tools for detecting intracranial injury, guiding CT decisions, and predicting outcomes in ways that complement, rather than replace, clinical judgment. Meanwhile, modern neuroimaging, including high-resolution CT, advanced MRI sequences (susceptibility-weighted, diffusion tensor, and functional imaging), and emerging point-of-care modalities, has improved the ability to characterize structural damage, identify diffuse axonal injury, and prognosticate recovery. Together, these diagnostic advances inform time-sensitive emergency interventions that must be executed with precision amid physiological instability.Emergency care and nursing practice form the operational core of acute TBI management, where the priorities of preventing secondary injury—hypoxia, hypotension, hyperthermia, hypercapnia, and intracranial hypertension—depend on meticulous, protocol-driven monitoring and rapid escalation. Specialized nursing assessment, including serial Glasgow Coma Scale evaluation, pupillary monitoring, and neuroprotective bundle compliance, is instrumental in early detection of deterioration and prevention of complications such as delirium, pressure injury, and hospital-acquired infection. As patients transition from acute stabilization to recovery, physical rehabilitation becomes central to maximizing functional independence, with early mobilization, vestibular and balance training, cognitive-motor retraining, and individualized exercise prescription shown to improve outcomes and reduce long-

term disability. Sustained progress ultimately relies on coordinated discharge planning, family engagement, and continuity of care that bridges disciplines and care settings. The future of TBI management lies in standardizing biomarker and imaging pathways, embedding evidence-based protocols, and fostering interprofessional collaboration that places the patient's neurological and functional recovery at the center of every decision.

Keywords: traumatic brain injury, multidisciplinary management, serum biomarkers (GFAP, UCH-L1, NfL, S100B), neuroimaging, computed tomography, magnetic resonance imaging, emergency care.

Introduction

Traumatic brain injury (TBI) is a complex and heterogeneous neurological condition caused by an external mechanical force applied to the head, producing temporary or permanent impairment of brain function. Its clinical spectrum ranges from mild concussion to severe, life-threatening intracranial injury, and it remains a leading cause of mortality, disability, and socioeconomic loss worldwide. Contemporary management has moved beyond a purely neurosurgical or neurocritical care model toward an integrated, multidisciplinary framework that coordinates laboratory medicine, diagnostic imaging, emergency and prehospital care, nursing, and physical rehabilitation across the entire continuum of recovery [1]. The Global Burden of Disease 2021 estimates indicate that, although age-standardized incidence and disability rates have declined in some regions, the absolute number of individuals living with TBI continues to rise because of population growth and ageing; approximately 69 million people are estimated to sustain a TBI annually, including 5.48 million severe cases [2]. The epidemiological landscape has also shifted, with falls accounting for an increasing proportion of cases, particularly among older adults, and with a disproportionate burden concentrated in low- and middle-income countries where access to organised trauma systems remains limited [2]. The BOOTStraP framework illustrates how prehospital, emergency, surgical, and intensive care interventions can be stratified and adapted to different resource settings, thereby supporting coordinated multidisciplinary care even where advanced technologies are unavailable [3]. A systematic review and meta-analysis of contemporary multidisciplinary strategies further concluded that clinical benefits depend on highly specific applications, including early haemostasis, carefully selected decompressive surgery, and formal inclusion of structured, goal-directed multidisciplinary rehabilitation, rather than on any single universal intervention [4].

Pathophysiological Basis and Rationale for Multidisciplinary Intervention

The distinction between primary and secondary brain injury provides the conceptual foundation for all therapeutic efforts. Primary injury refers to the immediate mechanical disruption of neurons, glia, blood vessels, and axonal tracts at the moment of impact and is largely irreversible. Secondary injury, by contrast, is a dynamic and potentially modifiable process that unfolds over minutes, hours, and days after trauma. Its principal components include excitotoxicity from excessive glutamate release, intracellular calcium overload, generation of reactive oxygen species, mitochondrial permeability transition, activation of microglia and astrocytes with release of pro-inflammatory cytokines, infiltration of peripheral immune cells, and disruption of the blood–brain barrier. Recent work has identified a self-amplifying ferroptosis–neuroinflammation feedback loop in TBI: neuroinflammation promotes ferroptosis through the IL-6/JAK2/STAT3–hepcidin axis and impairment of the system Xc^-/glutathione/GPX4 antioxidant system, while ferroptotic cells release damage-associated molecular patterns that further activate neuroinflammatory signalling via TLR4/NF-κB [5]. Mitochondrial dysfunction and inflammatory responses in brain cells also reinforce one another, creating a feed-forward loop that perpetuates tissue damage and offers multiple potential targets for intervention [6]. These mechanistic insights have direct clinical implications. Because secondary injury evolves over time, every component of the multidisciplinary team has a window of opportunity to intervene: the laboratory can detect biochemical evidence of injury before imaging becomes abnormal, the emergency physician can prevent hypoxia and hypotension that amplify the cascade, the nurse can maintain physiological stability and recognise early neurological deterioration, and the rehabilitation specialist can harness neuroplasticity during the critical

recovery phase. The effectiveness of this continuum, however, depends on the precise coordination of these roles rather than their isolated execution [1,4].

Advances in Laboratory Assessment: Fluid Biomarkers of Brain Injury

Laboratory assessment of TBI has traditionally been limited to non-specific parameters such as blood glucose, electrolytes, coagulation profiles, and inflammatory markers, which support general critical care but do not directly reflect brain tissue injury. The most transformative recent development has been the validation of blood-based biomarkers of cerebral origin, which now offer a rapid, non-invasive, and physiologically informative complement to neuroimaging. Recent technological reviews emphasise that point-of-care and multiplex assay platforms are accelerating the translation of these biomarkers from research settings into emergency and critical care practice [7]. Three biomarkers have achieved the strongest evidence base: glial fibrillary acidic protein (GFAP), ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), and the calcium-binding protein S100B. GFAP is an intermediate filament protein expressed predominantly in astrocytes, and its release into blood reflects astroglial injury and disruption of the blood–brain barrier. UCH-L1 is a neuronal protease released following neuronal damage and has a diagnostic window that extends to approximately 12 hours post-injury, making it suitable for patients who present later to medical attention. S100B, historically the most extensively studied biomarker, offers excellent negative predictive value for intracranial injury and is particularly useful for ruling out clinically significant lesions, but its specificity is limited in older patients and in those with extracranial injuries, and it requires early sampling, ideally within three hours of trauma [8]. Serum dynamics studies of BD-Tau, neurofilament light (NfL), GFAP, UCH-L1, p-Tau181, and S100B have further clarified how these markers behave across concussion and mild TBI, supporting their combined use for diagnosis and monitoring [9]. Direct comparisons have shown that GFAP demonstrates superior diagnostic performance relative to UCH-L1 and S100B in detecting intracranial injury on computed tomography (CT), and that UCH-L1 does not provide meaningful incremental value beyond GFAP alone in some cohorts; a prospective cohort of over 1,000 patients confirmed that GFAP and UCH-L1 perform comparably to S100B in detecting intracranial injury, while also highlighting the influence of age, haemolysis, neurodegenerative disease, and extracranial fractures on biomarker interpretation [10]. The clinical utility of these biomarkers extends beyond diagnosis to prognostication. A prognostic modelling study of young TBI patients demonstrated that GFAP, UCH-L1, S100B, and NfL are associated with injury severity and recovery outcomes, supporting their incorporation into multidimensional prognostic algorithms [11]. Inflammatory markers, including interleukin-6 (IL-6) and total tau, have also been shown to correlate with plasma NfL, GFAP, UCH-L1, S100B, and subacute three-tesla MRI measures of lesion volume and white matter injury, suggesting that laboratory assessment can bridge the gap between molecular injury and structural neuroimaging [12]. Emerging biomarkers such as NfL, IL-6, microRNAs, and exosomal cargo are under active evaluation and may further refine diagnostic and prognostic precision, although their clinical validation is not yet complete [7,9]. Table 1 summarises the principal characteristics of the established and emerging biomarkers.

Table 1. Principal Fluid Biomarkers in Traumatic Brain Injury

Biomarker	Cellular Origin	Diagnostic Window	Principal Clinical Utility	Key Limitations
GFAP	Astrocytes	Up to 12 h	Detection of intracranial injury; superior performance to UCH-L1 and S100B in some cohorts	Age-dependent thresholds; influence of extracranial injury
UCH-L1	Neurons	Up to 12 h	Neuronal injury detection; complementary to GFAP	Limited incremental value beyond GFAP alone in certain populations
S100B	Astrocytes, Schwann cells	< 3 h ideally	Excellent negative predictive value; rule-out of significant intracranial lesions	Low specificity in older adults and

				polytrauma; requires early sampling
NfL	Axons	Days to weeks	Axonal injury quantification; prognostic modelling	Not yet validated for acute clinical decision-making
IL-6	Immune cells, glia	Hours	Neuroinflammatory monitoring; correlation with imaging lesion burden	Non-specific; influenced by systemic inflammation

Diagnostic Imaging: From Conventional CT to Multimodal Neuroimaging

Non-contrast computed tomography (CT) remains the first-line imaging modality in acute TBI because of its speed, accessibility, and sensitivity for surgically significant lesions such as intracranial haemorrhage, mass effect, midline shift, and skull fracture. Clinical decision rules—most notably the Canadian CT Head Rule, the New Orleans Criteria, and the PECARN guidelines for children—have been developed and validated to rationalise CT utilisation, reduce unnecessary radiation exposure, and identify patients who require urgent neurosurgical evaluation. However, these rules have structural limitations in special populations, including children, older adults, and patients receiving anticoagulants, for whom modified thresholds and decision tools are required [13]. Furthermore, conventional CT is relatively insensitive to diffuse axonal injury, microstructural white matter damage, and subtle metabolic derangements that may underlie persistent post-concussive symptoms. Magnetic resonance imaging (MRI) offers superior tissue contrast and has become indispensable for detecting lesions that are occult on CT. Conventional MRI sequences, including T2-weighted, fluid-attenuated inversion recovery (FLAIR), and susceptibility-weighted imaging (SWI), improve the detection of contusions, petechial haemorrhages, and traumatic axonal injury. Advances in diffusion MRI, particularly diffusion tensor imaging (DTI) and its newer variant neurite orientation dispersion and density imaging (NODDI), allow quantification of axonal integrity and orientation dispersion, revealing injury invisible to standard DTI in mild TBI [14]. Quantitative susceptibility mapping (QSM) has been shown to quantify chronic iron deposition linked to post-traumatic neuroinflammation, while functional MRI (fMRI) confirms specific network disruptions that correlate with cognitive deficits. Magnetic resonance spectroscopy (MRS) provides metabolic information, and magnetoencephalography (MEG) and quantitative electroencephalography (qEEG) offer functional and electrophysiological characterisation. Recent reviews of microstructural, metabolic, and artificial intelligence–driven advances in TBI neuroimaging indicate that multimodal imaging is necessary for precise TBI biotyping, because different pathophysiological mechanisms—axonal injury, vascular injury, inflammation, and metabolic dysfunction—are best captured by complementary modalities [15]. Positron emission tomography (PET) remains largely a research tool in TBI but is increasingly used to investigate cerebral metabolism, neuroinflammation, and tau deposition in chronic phases. Table 2 compares the principal imaging modalities.

Table 2. Comparative Profile of Neuroimaging Modalities in Traumatic Brain Injury

Modality	Principal Strengths	Principal Limitations	Typical Clinical or Research Role
Non-contrast CT	Rapid; widely available; detects haemorrhage, mass effect, fractures	Radiation exposure; low sensitivity for diffuse axonal injury and microstructural damage	First-line acute triage; surgical decision-making
Conventional MRI (T2, FLAIR, SWI)	Superior soft-tissue contrast; detects contusions and petechial haemorrhage	Longer acquisition time; limited availability in acute emergencies	Lesion characterisation; detection of occult injury

DTI / NODDI	Quantifies white matter integrity and axonal orientation dispersion	Protocol variability; lack of standardised thresholds	Detection of traumatic axonal injury; mild TBI research
QSM	Quantifies iron deposition and microbleeds	Post-processing complexity; limited clinical validation	Investigation of chronic neuroinflammation and neurodegeneration
fMRI	Reveals functional network connectivity and cognitive correlates	Sensitivity to patient cooperation and motion	Mapping of network disruption; cognitive outcome research
MRS	Provides metabolic information (e.g., N-acetylaspartate, choline)	Limited spatial resolution; technical demands	Metabolic characterisation of injured tissue
PET	Enables molecular imaging of metabolism, inflammation, and proteinopathy	High cost; limited availability; radiation	Chronic TBI pathophysiology and biomarker validation

Emergency Care: Prehospital and Early Hospital Management

The emergency phase of TBI care is defined by the imperative to prevent secondary injury. The Brain Trauma Foundation and the American College of Surgeons' Best Practices Guidelines provide the foundational framework, emphasising avoidance of hypotension (maintenance of systolic blood pressure above 90 mmHg) and hypoxia (maintenance of oxygen saturation above 90%) during prehospital transport and resuscitation. The 2023 third-edition prehospital guidelines for TBI management provide domain-wise recommendations spanning prehospital systems, transport destination decisions, neuroimaging capabilities, and ICP monitoring, specifying that patients with suspected moderate-to-severe TBI should be transported directly to facilities with immediately available CT neuroimaging, prompt neurosurgical care, and the ability to monitor and treat intracranial hypertension [16]. These physiological targets are not merely supportive measures; hypotension and hypoxia are among the most powerful independent predictors of mortality and poor neurological outcome after TBI, and their prevention requires coordinated action by emergency medical services, trauma teams, and receiving emergency departments [16]. Pharmacological adjuncts in the emergency setting have been clarified by recent randomised evidence. Tranexamic acid (TXA) has been shown to reduce head injury–related mortality in mild-to-moderate TBI when administered within three hours of injury, and current guidance suggests that a 2 g intravenous bolus may be considered before imaging in patients without active extracranial bleeding [17]. The prehospital and field management of TBI further requires protocolised airway control, cervical spine protection, prevention of hypoxia and hypotension, and rapid triage to an appropriate trauma or neurosurgical centre; field providers therefore function as the first link in the multidisciplinary chain of survival [18]. Decompressive craniectomy is highly effective for refractory intracranial hypertension and mortality reduction, although it increases survival with severe disability in patients with diffuse injury, necessitating careful patient selection and shared decision-making [16]. In contrast, several interventions that appeared promising in preclinical studies—including progesterone, citicoline, and prophylactic hypothermia—have not demonstrated consistent benefit in phase III randomised controlled trials, underscoring the heterogeneity of TBI and the need for targeted, mechanism-specific therapies [4,16]. The emergency management of TBI is therefore best understood as a protocolised, physiology-driven, and resource-adapted process in which the emergency physician, neurosurgeon, intensivist, and prehospital provider function as an integrated team [3,16,18].

Nursing Care: Continuous Surveillance, Early Rehabilitation, and Family Integration

Nursing occupies a unique position within the multidisciplinary team because nurses provide continuous, 24-hour surveillance of neurological status, physiological parameters, and patient responses to therapy. In the emergency department, integrated nursing interventions—including continuous monitoring, systematic

neurological assessment, patient and family education, and early motor function training—have been associated with enhanced recovery and improved functional outcomes [19]. The nurse is often the first clinician to detect subtle signs of neurological deterioration, such as a decline in the Glasgow Coma Scale score, pupillary asymmetry, or changes in respiratory pattern, and timely escalation of these findings is critical for preventing irreversible secondary injury [19]. Beyond acute surveillance, nursing has become a principal vehicle for early rehabilitation. A prospective cohort study of patients with severe TBI (Glasgow Coma Scale ≤ 8) demonstrated that early rehabilitation nursing initiated within 48 hours of physiological stabilisation was associated with superior neurological recovery over 18 months. The intervention comprised psychological support, cognitive intervention, and motor rehabilitation, and it produced significantly higher Glasgow Coma Scale scores, Fugl-Meyer Assessment scores, Functional Independence Measure scores, and Glasgow Outcome Scale–Extended scores, alongside lower neurological deficit scores, compared with routine nursing; the proportion of patients achieving good recovery (GOSE 7–8) was 36.84% in the early rehabilitation nursing group versus 20.00% in the control group at 18 months [20]. These findings align with the broader recognition that rehabilitation should not be deferred until after acute care is complete but should begin as soon as physiological stability permits [20]. Nursing interventions also address the neurobehavioural and psychosocial consequences of TBI. Successful neurobehavioural management emphasises a structured and predictable daily routine that mirrors pre-injury activities, with nursing staff establishing consistent schedules for medication administration, self-care, and toileting [21]. Evidence-based nursing interventions have further been shown to improve recovery in patients undergoing haematoma evacuation, and theory-driven nursing models—such as Orem's self-care theory and Levine's conservation model—have been applied to enhance limb function, balance, nutritional status, and psychological resilience in TBI rehabilitation [22]. Family education and involvement are integral to these approaches, as caregivers require preparation for the long-term behavioural, cognitive, and physical needs of the survivor [19,21].

Physical Rehabilitation: From Early Mobilisation to Technology-Assisted Recovery

Physical rehabilitation is the domain in which the functional consequences of TBI are most directly addressed, and it is increasingly recognised as a continuous process that begins in the neurointensive care unit and extends through inpatient and community-based settings. Early mobilisation and structured multidisciplinary neurorehabilitation have been associated with improvements in functional independence, progression to assisted ambulation, cognitive function, and quality of life, even in severe cases such as craniocerebral gunshot injury. The acute–critical–comprehensive three-stage standardised TBI rehabilitation unit has been shown to improve one-year Glasgow Outcome Scale scores and reduce Disability Rating Scale scores, supporting the concept of staged rehabilitation that mirrors the phases of recovery [23]. The evidence base for specific rehabilitation strategies has been clarified by systematic review and meta-analysis. Structured outpatient rehabilitation and high-intensity gait training are favourable for functional and symptom-related outcomes, whereas many acute-phase neuroprotective pharmacological strategies have not translated into functional benefit. A comprehensive review of rehabilitation approaches for TBI concluded that combining conventional and technology-assisted rehabilitation, guided by patient-centred strategies, can enhance recovery in moderate-to-severe TBI, while identifying gaps in longitudinal studies, predictors of individualised treatment success, cost-benefit evaluation, and management of comorbidities such as post-traumatic stress disorder [24]. Integrated care models are recommended because multidisciplinary rehabilitation needs cannot be met by a single discipline; a case study using the Computer Assisted Rehabilitation Environment (CAREN) demonstrated improvements in gait, balance, and coping through integrated treatment across disciplines [24]. The International Classification of Functioning, Disability and Health (ICF) framework has been increasingly adopted to structure rehabilitation assessment and goal-setting. In severe TBI, ICF-based functional profiling identifies deficits in mental functions, neuromusculoskeletal and movement-related functions, and activities of daily living, and it guides the formulation of individualised goals addressing arousal, orientation, motor control, communication, swallowing, and daily function [25]. This framework facilitates structured assessment, interdisciplinary communication, and patient-centred goal-setting, all of which are

essential for coordinating physical therapy with occupational therapy, speech-language pathology, neuropsychology, and nursing [25]. Technology-assisted approaches—including virtual reality, wearable biosensors, telemedicine, and artificial intelligence–driven training—are emerging as promising adjuncts, although high-quality trial data and implementation standards remain limited [24]. Table 3 summarises the principal rehabilitation domains and their associated interventions and outcomes.

Table 3. Domains of Physical Rehabilitation in Traumatic Brain Injury

Rehabilitation Domain	Representative Interventions	Principal Outcome Measures	Evidence Highlights
Early mobilisation and positioning	Progressive sitting, standing, and transfer training initiated in neurocritical care	Functional Independence Measure; GOSE	Associated with improved functional independence and shorter length of stay
Gait and balance training	High-intensity gait training; task-specific balance exercises	6-minute walk test; Berg Balance Scale; gait velocity	Favorable effects on functional and symptom-related outcomes
Upper-limb and motor control	Task-oriented practice; constraint-induced movement therapy principles	Fugl-Meyer Assessment; Action Research Arm Test	Improvements in motor impairment and functional use
Technology-assisted rehabilitation	Virtual reality; CAREN; robotic-assisted gait training	Gait parameters; balance; patient-reported coping	Integrated technology-assisted treatment improves gait, balance, and coping
ICF-based goal setting	Interdisciplinary functional profiling and individualised goal formulation	ICF qualifiers; goal attainment scaling	Facilitates communication and patient-centred rehabilitation planning

Integration Across the Continuum: Toward a Coordinated Multidisciplinary Model

The evidence reviewed above converges on a single conclusion: no single discipline can adequately address the needs of a patient with TBI. The laboratory identifies biochemical injury and prognosis, imaging defines structural and functional lesions, emergency care prevents the physiological insults that amplify secondary injury, nursing maintains stability and initiates early rehabilitation, and physical rehabilitation restores function and participation. The systematic review and meta-analysis of contemporary multidisciplinary strategies concluded that clinical benefits are heavily dependent on highly specific applications—early haemostasis, carefully selected decompressive surgery, and formal inclusion of structured, goal-directed multidisciplinary rehabilitation—rather than on any single universal intervention [4]. This finding reinforces the need for protocolised, context-sensitive care pathways that integrate prehospital services, emergency departments, neurosurgery, neurocritical care, and rehabilitation [1,3]. The BOOTStraP framework exemplifies this integrated approach by providing stratified algorithms that span prehospital transport, emergency care, neurosurgical decision-making, and critical care, with resource-sensitive adaptations for low- and middle-income countries [3]. Similarly, multimodal imaging frameworks and the growing validation of fluid biomarkers support a diagnostic pathway in which laboratory and imaging data are interpreted together to characterise the dominant injury mechanism—axonal, vascular, inflammatory, or metabolic—and to guide targeted therapy [7,9,15]. Nursing and rehabilitation are no longer regarded as downstream services but as essential components of the acute and subacute care continuum, with early rehabilitation nursing and early mobilisation producing measurable improvements in neurological and functional outcomes [20,23]. The future of TBI management lies in the further development of integrated care pathways that embed biomarker-guided triage, multimodal imaging, physiological optimisation, early rehabilitation, and long-term community support within a single coordinated system [1,4,16,24].

Conclusion

Traumatic brain injury is a dynamic and heterogeneous condition whose outcome is shaped not only by the initial mechanical insult but also by the quality and timeliness of care delivered across multiple domains. Laboratory assessment has been transformed by blood-based biomarkers—GFAP, UCH-L1, and S100B—that can rapidly identify intracranial injury, reduce reliance on CT, and inform prognosis. Diagnostic imaging has evolved from conventional CT to multimodal MRI and advanced techniques that reveal microstructural, metabolic, and functional injury invisible to standard modalities. Emergency care has become protocolised and resource-sensitive, with clear physiological targets, evidence-based pharmacological adjuncts such as TXA, and stratified algorithms that can be implemented across diverse healthcare settings. Nursing has emerged as a continuous surveillance system and a driver of early rehabilitation, with prospective evidence demonstrating sustained neurological and functional benefits. Physical rehabilitation, guided by the ICF framework and increasingly assisted by technology, restores function and participation through structured, goal-directed, and interdisciplinary interventions. The overarching lesson is that these domains are interdependent: the full benefit of any single advance is realised only when it is embedded within a coordinated multidisciplinary system. Strengthening that system—through protocol development, workforce training, equitable resource allocation, and multicentre research—represents the most promising pathway toward reducing the global burden of TBI.

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