

Biomarkers in Traumatic Brain Injury: From Molecules to Machine Learning

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Background: Accurate diagnosis and prognostication in traumatic brain injury (TBI) remain challenging. While CT imaging and clinical scores are current standards, blood biomarkers may provide objective adjuncts by detecting intracranial injury and predicting outcomes.

Materials and Methods: A narrative review was conducted using PubMed, Cochrane Library, and other biomedical resources accessible via NHS OpenAthens, focusing on blood-based, imaging, and physiological biomarkers with diagnostic or prognostic relevance in TBI.

Results: Glial fibrillary acidic protein (GFAP), S100B, and ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) are consistently associated with mortality and poor neurological outcomes. Across prospective studies and systematic reviews, GFAP has shown strong association with CT-positive intracranial lesions, with AUROC values typically ranging from 0.74 to 0.98. However, heterogeneity in assay platforms, sampling times, and threshold definitions limits immediate standardisation. Notably, combined measurement of GFAP and UCH-L1 is FDA-authorised to aid CT triage in adults with mild TBI, underscoring the translational potential of biomarker-based diagnostics. In moderate-to-severe TBI, a multi-marker panel (S100B, GFAP, MCP-1) predicted 6-month outcomes (AUC 0.83) and mortality (AUC 0.87), though without significant improvement over S100B alone. Importantly, S100B is limited by lack of brain specificity, as extra cranial trauma can elevate levels, supporting the complementary role of GFAP and other markers. Beyond biochemical assays, diffusion tensor imaging (DTI) and physiological monitoring (intracranial pressure, brain tissue oxygenation) provide additional prognostic information.

Conclusion: Biochemical, imaging, and physiological biomarkers collectively improve diagnostic and prognostic accuracy in TBI, though variability and lack of standardised cut-offs constrain clinical adoption. Large multicentre validation studies remain a priority. Emerging applications of AI and machine learning for multimodal data integration, together with structural biology tools such as AlphaFold to guide biomarker assay design, may accelerate translation of biomarker-guided risk stratification into routine clinical care.