

From Statistical Association to Clinical Utility: Refining the Prognostic Credibility of Diffusion Tensor Imaging in Traumatic Brain Injury

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ABSTRACT

Introduction: Diffusion tensor imaging (DTI) has emerged as a key tool for detecting microstructural white matter changes after traumatic brain injury (TBI), particularly in cases of subtle traumatic axonal injury not evident on conventional neuroimaging. **Objective:** This work critically analyzes the prognostic credibility of DTI in TBI, emphasizing the transition from statistical association to clinical utility. **Methodology:** A critical narrative literature review was conducted, focusing on meta-analyses, systematic reviews, scoping reviews, and longitudinal studies concerning DTI and TBI prognosis. **Results and Discussion:** Evidence consistently shows an association between DTI-derived metrics, especially fractional anisotropy and mean diffusivity, and functional, cognitive, and clinical severity outcomes. However, the strength of this association does not automatically translate into routine prognostic applicability. Significant barriers persist, including protocol heterogeneity, equipment variability, differences in post-trauma acquisition timing, diverse analytical methods, modest sample sizes, and limited external validation. Recent reviews indicate that DTI possesses robust biological plausibility and potential predictive value, especially when integrated into multimodal models incorporating clinical variables, severity scales, and other biomarkers. **Conclusion:** DTI has moved beyond being merely a promising experimental marker, but its prognostic credibility still requires methodological refinement to achieve broad clinical utility. The field's advancement depends less on demonstrating new associations and more on proving reproducibility, incremental value, and real impact on decision-making.

Keywords: Prognosis; Diffusion tensor; Traumatic brain injury.

INTRODUCTION

Traumatic brain injury (TBI) remains a significant public health problem, associated with high mortality, prolonged disability, and great heterogeneity in clinical presentation. Even in patients with subtle findings on computed tomography or conventional magnetic resonance imaging, significant microstructural damage can occur, especially in the context of traumatic axonal injury. This dissociation between the clinical picture and traditional structural imaging contributes to prognostic difficulty across different spectra of TBI.

In this scenario, DTI emerged as an advanced magnetic resonance technique capable of inferring white matter integrity through the directional behavior of water diffusion. Metrics such as fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity began to be used to investigate axonal damage, demyelination, and microstructural disorganization after trauma. Over recent years, a significant body of studies has accumulated, showing that alterations in these measures are associated with worse cognitive performance, greater initial severity, and poorer functional outcomes in adults with TBI (Bandak et al., 2018; Ward et al., 2018).

However, association is not synonymous with clinical utility. A biomarker can show a statistical relationship with an outcome and still not improve individual prognostic accuracy, not alter decision-making, or not be reproducible outside the research environment. This point is central to the contemporary debate on DTI in TBI. Recent reviews emphasize that the field has matured enough to move beyond merely asking whether DTI detects relevant changes and to start asking whether these changes are sufficiently consistent, standardizable, and clinically useful to guide prognosis in real-world scenarios (Grant et al., 2023; Paolini et al., 2025).

Thus, this work addresses an essential question for translational research in neurotrauma: how to refine the prognostic credibility of DTI so that it advances from the domain of association to that of clinical utility. The objective is to critically analyze the prognostic credibility of diffusion tensor imaging in traumatic brain injury, discussing its biological bases, the current body of associative evidence, its methodological limitations, and the requirements for its more consistent clinical incorporation.

METHODOLOGY

This is a critical narrative review, guided by contemporary scientific literature on DTI and prognosis in TBI. Priority was given to synthesis studies and works with greater clinical and methodological relevance, including meta-analyses, systematic reviews, scoping reviews, and longitudinal studies. The analysis focused on four axes:

1. Association between DTI metrics and clinical, functional, or cognitive outcomes;
2. Relationship between microstructural changes and trauma severity;
3. Technical and methodological limitations that reduce reproducibility;
4. Potential of DTI in multimodal prognostic models.

The critical interpretation was constructed with a translational focus, valuing not only associative significance but also aspects of generalization, standardization, clinical applicability, and incremental value compared to traditional prognostic variables.

RESULTS AND DISCUSSION

Available evidence supports that DTI is sensitive to relevant microstructural changes after TBI, even in situations where conventional imaging is limited in demonstrating diffuse axonal injury. In adults, meta-analyses have shown that changes in fractional anisotropy and other metrics vary according to trauma severity and are related to cognitive outcomes, especially in domains such as memory, processing speed, and executive functions (Bandak et al., 2018; Ward et al., 2018). This strengthens the technique's plausibility as a prognostic marker.

However, the most important point in recent literature is that this biological consistency is not enough to justify routine clinical use. The review by Grant et al. (2023) emphasizes that, although DTI and other diffusion-based techniques have prognostic potential, there is still a considerable gap between promising findings and clinical applicability. In other words, the literature shows that DTI often "associates," but does not always "add" something measurable to clinical practice.

This gap stems from multiple factors. First, there is great technical heterogeneity among studies: differences in magnetic field strength, number of diffusion directions, spatial resolution, artifact corrections, and post-processing methods make direct comparison between cohorts difficult. Second, there is significant analytical diversity, with studies using region-of-interest approaches, whole-brain analyses, tract-based spatial statistics, and mixed strategies, which increases the variability of results. Third, the timing of post-trauma acquisition varies widely, and the microstructural pathophysiology of TBI is not static; thus, the interpretation of the same metric may differ between acute, subacute, and chronic phases.

Another central problem is the predominance of small, often single-center samples with heterogeneous populations. Many studies group mild, moderate, and severe TBI, while others select very specific clinical subsets, making extrapolation difficult. Furthermore, not all adequately adjust for relevant confounders, such as age, sedation, comorbidities, extracranial injuries, post-trauma time, and image quality. These factors reduce the robustness of prognostic inference.

The review by Paolini et al. (2025) reinforces this point by describing DTI as a promising neurological predictor, yet still dependent on greater methodological consistency. Convergent, reviews on mild TBI and post-concussion syndrome show that DTI can capture relevant changes, but findings remain heterogeneous and do not always converge to a uniform prognostic pattern (Khong et al., 2016). A longitudinal study by Zhang et al. (2019) adds an important dimension: the relationship between DTI and outcome can be dynamic, varying over time, which reinforces the need for more refined temporal models.

Another important conceptual advance is the shift from an isolated focus on imaging to multimodal strategies. Recent reviews on traumatic axonal injury argue that DTI will likely have greater value when integrated with serum biomarkers, clinical scales, conventional structural findings, and possibly other quantitative neuroimaging modalities (Lampros et al., 2023). This reasoning is consistent with contemporary prognostic practice, where a single marker is rarely useful alone; clinical value generally emerges when it improves discrimination, calibration, or risk stratification within composite models.

Thus, the central question is no longer to demonstrate that DTI has a biological basis or associative relevance. This is already reasonably established. The true challenge is methodological and translational: defining reproducible protocols, validating models in multiple centers, establishing incremental utility, and demonstrating decisive impact. Until these steps are sufficiently consolidated, DTI will remain stronger as an investigational biomarker than as a routine clinical prognostic tool.

CONCLUSION

Diffusion tensor imaging holds a prominent position in the investigation of microstructural injury after traumatic brain injury and shows a consistent association with functional, cognitive, and clinical severity outcomes. Its biological plausibility is robust, especially in the context of traumatic axonal injury.

However, DTI's prognostic credibility is not yet fully refined to justify widespread adoption in clinical practice. Technical heterogeneity, methodological variability, limited external validation, and insufficient demonstration of incremental value remain central obstacles.

The real advancement of the field will depend on prospective multicenter studies, standardization of acquisition and analysis, adequate temporal stratification, and integration of DTI into multimodal prognostic models. More than producing new correlations, the next step must demonstrate the extent to which DTI improves concrete clinical decisions in TBI patients.

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