

ABSTRACT NO:32
NARRATIVE REVIEW**Glymphatic dysfunction following traumatic brain injury: Mechanism of waste clearance and Emerging therapeutic targets**Rameen Suhail¹, Tooba Imran², Zainab Mehtab³, Nimra Shabeer⁴**Abstract**

Objective: Traumatic brain injury (TBI) affects millions annually, contributing to mortality and neurological deficits. The glymphatic system, the brain's perivascular waste-clearance network, has been implicated in injury mechanisms following TBI. This narrative review expands current evidence on the mechanisms of glymphatic dysfunction, imaging biomarkers and therapeutic targets.

Method: We conducted a literature search in PubMed to screen relevant studies on glymphatic dysfunction following TBI. Of 114 initially identified articles, 45 met the inclusion criteria. Following the exclusion of 13 articles due to unavailable full text, a total of 32 articles were included in the final review.

Result: The reviewed literature demonstrated that TBI leads to glymphatic dysfunction, which may be associated with complications such as oedema, neuroinflammation and persistent neurological deficits.

Initial studies established the glymphatic system's role in the clearance of exogenous molecules, however, recent evidence has expanded this role to clearance of endogenous proteins and TBI-associated biomarkers including GFAP, NfL, tau and amyloid- β .

TBI-induced alterations in AQP4 polarization were associated with impaired clearance of excess fluid and neurotoxic metabolites. Emerging evidence suggests its role in astroglial migration and identifies it as a potential therapeutic target; experimental omega-3 supplementation shows potential in partially restoring AQP4 polarity.

Poor sleep quality was linked with an enlarged perivascular space (ePVS) burden in patients with mTBI, as the system shows marked efficiency during sleep.

Promising non-invasive methods include advanced MRI techniques, such as intrathecal (IT) contrast-enhanced MRI and DTI-ALPS.

Therapeutic strategies targetting adrenergic regulation, cerebral oedema, and sleep may be beneficial in enhancing glymphatic function.

Conclusion: Our review highlights the disruption of glymphatic function as part of TBI pathophysiology and focusses on diagnostic tools and emerging treatment modalities. Further human studies are required, as most evidence comes from murine models. Moreover, studies are needed to assess therapeutic interventions involving hypothermia and aquaporin-4 on TBI-induced glymphatic dysfunction.

Keywords: Glymphatic dysfunction; traumatic brain injury; waste clearance.

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