Using Blood Biomarkers To Determine Intracranial Injury Seen on CT/MRI following mild Traumatic Brain Injury

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Background

Mild traumatic brain injury (mTBI) is one of the leading causes of injury worldwide,[1] and those with concurrent traumatic intracranial findings on CT or MRI (CT+ or MRI+), are at increased risk of persistent complications.[2,3] Low-cost and reliable identification of patients with potential intracranial injury in the emergency room, such as through utilizing blood-based biomarkers, could drastically improve patient triage protocols. Further, accurate knowledge of the temporal profiles of biomarkers in those with intracranial findings versus those without could provide valuable information about disease progression and could be used in litigation for instance, as many mTBI patients do not seek medical attention during the acute injury phase. The aim of this study is to use machine learning techniques to determine whether blood-based biomarkers at different timepoints after mTBI can predict intracranial injury on CT and MRI scans taken during the acute phase, which is the best timepoint to uncover traumatic intracranial findings. Biomarkers associated with central nervous system (CNS) damage (GFAP, NFL, tau) and inflammation (IFNγ, IL-8, Eotaxin, MIP-1β, MCP-1, IP-10, IL-17A, IL-9, TNF, FGF-basic PDGF and IL-1ra) are longitudinally assessed.

Methods

Patients with mTBI (n = 207; 16-60 years) were defined as having a Glasgow Coma Scale (GCS) score between 13-15, loss of consciousness (LOC) < 30 min and post-traumatic amnesia (PTA) < 24 hours. MRI and CT scans were obtained within 72 hours. Blood was drawn at admission (between 24-72 hours), 2 weeks, 3 months and 12 months post-injury. Linear mixed models were used to assess the temporal profiles of single biomarkers in CT+/MRI+ and CT-/MRI- groups, along with group differences at each timepoint. The optimal combination of biomarkers for predicting intracranial findings on MRI/CT at each timepoint was determined using elasticnet regression.

Results

Linear mixed models revealed that GFAP and NFL at admission and 2 weeks were significantly elevated in both CT+ and MRI+ groups compared to CT- and MRI-. NFL was also elevated at 3 months in CT+ and MRI+ groups. MIP-1β, IP-10 were significantly reduced at all timepoints in both CT+ and MRI+ groups, while eotaxin and IL-9 were significantly reduced in the MRI+ group only. FGF-basic was significantly reduced at 3 months and 12 months only in the MRI+ group. Elasticnet revealed the optimal combination of biomarkers for predicting CT+ at both admission and 2 weeks was GFAP, NFL, MIP-1β, IP-10, eotaxin and IL-1ra. The same biomarkers – excluding IL-1ra – were selected for the MRI+ models at admission and 2 weeks. At 3 months, NFL, MIP-1β and IP-10 were the optimal combination for CT+ and NFL, MIP-1β and IP-10, eotaxin and IL-9 were the optimal combination for MRI+. At 12 months, MIP-1β and IP-10 were most predictive of CT+ and MIP-1β and IL-9 were most predictive of MRI+.

Conclusions

Our study shows that GFAP and NFL, at both acute and subacute stages of injury are the most useful biomarkers for reliably predicting intracranial injury, while NFL also demonstrates diagnostic specificity at chronic stages. Inflammation being lower in those with intracranial injury than those without is a novel finding, which could have implications for our understanding of inflammation following mTBI.

References

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