

The Potential of MicroRNAs as Diagnostic and Prognostic Biomarkers for Mild Traumatic Brain Injury: A Systematic Review and Meta-analysis

Introduction At least 80% of traumatic brain injuries (TBI) are classified as mild. Repetitive mTBI might lead to long-term cognitive and behavioural alterations, or even increasing risks of neurocognitive disorders. Current diagnostic techniques have little benefit for patients with no obvious brain lesions. Altered expression of miRNAs in humans' biofluids are related to the pathological processes of TBI and can be a molecular signature.

Objectives Investigate the potential of miRNAs as diagnostic and prognostic biomarkers for mTBI.

Methods This study was reported following the PRISMA criteria. Literature search was carried out in PubMed, ScienceDirect, and ProQuest for relevant articles published prior to January 2021. Both qualitative and quantitative analyses was conducted to determine the diagnostic and prognostic value of miRNAs. The quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS).

Results Ten clinical studies reported various miRNAs from serum/plasma, cerebrospinal fluid, and saliva as potential diagnostic and prognostic biomarkers. miRNAs secured from the saliva had the highest diagnostic accuracy (Pooled AUC=0.843; 95% CI [0.802,0.883]; I²=0%; P<0.001). The diagnostic accuracy was higher among paediatrics and athletes (AUC>0.850) who were more vulnerable to head trauma without apparent lesions on neuroimaging. A common miRNA reported across studies, miR-92a, had very good diagnostic accuracy, even when used as a single biomarker (AUC>0.890). Qualitative studies showed that the concentration of miR-425, miR-103a-3p, miR-219a-5p, miR-302d-3p, miR-422a, miR-518f-3p, miR-520d-3p, miR-93, miR-

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191 and miR-499 were correlated with patients' clinical outcome. All of the included studies showed good quality in terms of selection, comparability, and outcome domains.

Conclusion The present study suggested the use of salivary miRNAs as an early diagnostic tool for mTBI. Even though its prognostic value was still undermined, miR-92a was a promising candidate for future diagnostic biomarkers in mTBI.