Panels of MicroRNA predict head CT lesions following mild traumatic brain injury

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Background: There is an urgent need for robust triage tools to guide emergency department head CT use following mild traumatic brain injury (mTBI). Circulating microRNA represent a promising but underexplored class of biomarkers for this purpose. In the present study, we aimed to identify candidate microRNA predictors of acute intracranial CT abnormalities following mTBI.

Methods: A subcohort of 54 mTBI patients, comprising 27 with CT-detectable lesions (CT+) and 27 without (CT–), was selected from the prospective, multicentre AIM-TBI study. Plasma samples (median = 3 hours) and head CT scans were obtained within 24 hours of mTBI. Plasma microRNA expression was quantified using small RNA sequencing (RNA-Seq). An extensive ensemble feature selection pipeline combined with machine learning was used to identify top-performing microRNA subsets of size one, two or three predictive of CT lesions.

Results: No individual microRNA was significantly differentially expressed between CT-groups at the significance threshold for multiple comparisons. The best performing single microRNA was miR-324-5p which predicted the presence of CT lesions with 32.6% [25.9-39.4] specificity at 100% sensitivity (AUC 0.57 [0.51-0.62]). The addition of miR-760 further improved specificity to 48.1% [40-56.2] at 100% sensitivity (AUC 0.67 [0.61-0.74]). No further improvement of panel specificity was obtained with the addition of a third microRNA.

Conclusion: The reported specificity of the miR-324-5p + miR-760 panel is comparable to the extensively validated glial fibrillary acidic protein + ubiquitin carboxyhydrolase L1 biomarker panel. This suggests that combining both panels may greatly reduce false positives and reduce unnecessary head CT usage. Although external validation of findings is necessary, this work supports further investigation of microRNAs as clinically relevant biomarkers in the context of (m)TBI. Improved understanding of the biological background of identified microRNA could provide novel insights into mTBI pathophysiology.