

## Severity of pre-existing cerebral small vessel disease is associated with outcome after traumatic brain injury

Nils Henninger, MD<sup>1,2\*</sup>, Saef Izzy, MD<sup>1</sup>, Raphael Carandang, MD<sup>1,3</sup>,  
Wiley Hall, MD<sup>1,3</sup>, Susanne Muehlschlegel, MD, MPH<sup>1,3,4</sup>

Departments of Neurology (1) and Psychiatry (2), Surgery (3), and Anesthesia/Critical Care (4)  
University of Massachusetts Medical School, Worcester, MA

**\*Correspondence to:** Nils Henninger, MD  
Departments of Neurology and Psychiatry  
University of Massachusetts Medical School  
55 Lake Ave, North  
Worcester, MA 01655  
Tel: (774) 455-3760  
Fax: (508) 856-2811  
E-mail: [nils.henninger@umassmed.edu](mailto:nils.henninger@umassmed.edu)

### Abstract

**Background and purpose:** It is now well accepted that traumatic white matter injury constitutes a critical determinant of post-traumatic functional impairment. However, the contribution of *pre-existing* white matter rarefaction on outcome following traumatic brain injury (TBI) is unknown. Hence, we sought to determine whether the burden of pre-existing cerebral small vessel disease related white matter rarefaction (leukoaraiosis) is independently associated with outcome after TBI.

**Methods:** We retrospectively analyzed consecutive, prospectively enrolled patients of  $\geq 50$  years ( $n=136$ ) that were admitted to a single neurological-trauma intensive care unit. Supratentorial white matter hypoattenuation on head CT was graded on a 5-point scale (range 0-4) reflecting increasing severity of leukoaraiosis. Outcome was ascertained according to the modified Rankin Scale (mRS) and Glasgow outcome scale (GOS) via telephone interview at 3 and 12 months, respectively.

**Results:** After adjustment for other factors, leukoaraiosis-severity was significantly associated with a poor outcome at 3 and 12 months as defined as mRS 3-6 and GOS 1-3, respectively. The independent association between leukoaraiosis and a poor outcome remained when the analysis was restricted to patients that survived to 3 months, had moderate-to-severe TBI (enrolment Glasgow Coma Scale [GCS]  $\leq 12$ ;  $p=0.001$ ), or had mild TBI (GCS 13-15;  $p=0.002$ ), respectively.

**Conclusion:** We provide first evidence that pre-existing cerebral small vessel disease independently predicts a poor functional outcome after closed head TBI. This association is independent of other established outcome predictors such as age, comorbid state as well as intensive care unit complications and interventions. This knowledge may help improve prognostic accuracy, clinical management, and resource utilization.