Towards Early Prediction of Vasospasm and Death Following Severe Traumatic Brain Injury

Abstract 2327

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Severe traumatic brain injury (sTBI) is associated with high rates of morbidity and mortality. Early identification of patients at highest risk of death or post-traumatic vasospasm, which can lead to secondary brain injury and worse outcome, is desirable to guide management and allocate resources.

The purpose of this study was to evaluate whether serum inflammatory and neuronal markers detected early in the injury process can improve upon the ability of known prognostic variables in identifying these patients.
METHODS

Patient Recruitment

• Study design: prospective, observational cohort study

• Inclusion criteria: adult patients with severe traumatic brain injury (Glasgow Coma Score ≤ 8) and radiographic evidence of brain injury

• Daily serum samples collected and analyzed for a 41-point array of inflammatory and neuron-specific markers

• Patients screened for vasospasm with daily transcranial dopplers (TCDs)

Data analysis

Machine learning techniques were used to create Random Forest models optimizing prediction of the two primary endpoints: vasospasm and death.

Potential predictive features:

• standard demographic variables

• radiographic severity of brain injury (Marshall Classification of TBI and Rotterdam CT Score)

• serum markers obtained in the first 24-72 hours post-injury
• 53 patients (41 male)
• Median age 35 years (range 18-77y)
• Exponential Injury Severity Score
  Mean: 33.8 (range 11-36)
43 (68%) patients developed vasospasm
median day of onset= 4 (range 1-10)

Worse radiographic severity (Rotterdam CT score), lower pulse rate and lower potassium on admission were predictive of vasospasm.
AUC= 0.79, Sensitivity= 0.72, Specificity= 0.80
Low SBP on admission, higher levels of eotaxin, IL-6, IL-1RA and lower levels of serum alpha-synuclein predicted mortality. 
AUC= 0.83, Sensitivity= 0.85, Specificity= 0.82

• 10 patients died
• Median day of death= 8 (range 5-20)
• Serum inflammatory and neuronal proteins can augment the predictive ability of clinical variables in identifying patients at risk of death.

• Serum proteins did not enhance predictive models for vasospasm. It is known that inflammatory cascades and cytokine levels are dynamic after trauma; serum proteins measured closer to the day of vasospasm detection (rather than on admission) may enhance model performance.

Future work will:
• Illustrate the evolution of biomarker arrays after head injury
• Vary the timepoint of variables used for model creation after injury
• Apply machine-learning techniques to predict other relevant outcomes (e.g. elevated intracranial pressure, complications after cranioplasty, long-term functional outcome)
SUMMARY POINTS

• Preliminary studies show promise for utilizing serum inflammatory and neuron-specific proteins to enhance predictive models of outcomes following severe traumatic brain injury.

• Identifying clinical and serum proteins with ability to predict specific outcomes would be most beneficial for triage efforts in resource poor settings, such as the active combat zone.

• Ultimately the performance of predictive models will have to be evaluated in a prospective cohort for validity and generalizability.