Widely Used Clinical Predictors do not Account for Outcome Variability in Mild Traumatic Brain Injury

1. **Background**
   - Of the approximately 1.4 million individuals in the US who undergo medical treatment for traumatic brain injury (TBI) each year, more than 1.1 million sustain mild TBI (mTBI).
   - Outcome following mTBI is variable, with 10-20% of mTBI cases having poor long-term outcome.
   - The reasons for this variability remain unknown and the ability to accurately prognosticate mTBI outcome is severely limited.
   - Studies have not specifically investigated this phenomenon.

2. **Research Participants**
   - An unselected series of head trauma patients were prospectively recruited at Ben Taub General Hospital, a level-1 trauma center in Houston TX.
   - Criteria for enrollment included:
     1. Diagnosis of non-penetrating TBI;
     2. Lowest post-resuscitation Glasgow Coma Scale (GCS) > 13;
     3. Computed tomography (CT) scan of the brain performed < 24 hours post-injury;
     4. No surgery under general anesthesia during hospitalization;
     5. Arrival to the hospital < 24 hours post-injury;
     6. Blood alcohol level < 200 mg/dL;
     7. Age > 16 years;
     8. Fluent in English or Spanish;
     9. Residing in the hospital catchment area, Harris County, TX;
     10. Not an undocumented resident, incarcerated, homeless, or on active military service;
     11. No spinal cord injury;
     12. No other pre-existing condition preventing standard medical treatment for traumatic brain injury (TBI) each year, more than 1.1 million sustain mild TBI (mTBI).
     13. No history of substance dependence, mental retardation, psychotic disorders, receiving treatment for depression at the time of injury, or other CNS disturbance;
     14. No other pre-existing condition preventing standard administration and interpretation of the outcome measures.

3. **Procedure**
   - Participants were recruited in the EC or during their acute hospitalization.
   - Diagnosis of TBI was made by EC trauma physicians and GCS ratings were made by EC trauma physicians and/or staff;
   - Modified ISS ratings were made by an AIS-certified research nurse based on thorough medical record review;
   - Evaluations at 3 ± 1 month after injury included face-to-face interviews;
   - Only the three-month data are presented here.

4. **Data Analysis Design/Methods**
   - We analyzed data from subjects with mTBI with negative head CT findings at 24 hours post-injury and without sources of secondary gain at follow-up (litigation or compensation).
   - We compared two groups based on results of the Glasgow Outcome Scale-Extended (GOS-E) assessed at 3 months post-injury:
     - Upper Good Recovery (UGR; n = 116, 57.1% of the sample) and Lower Moderate Disability (LMD; n = 21; 10.3% of the sample).

5. **Results**
   - **Variable**
     - **Upper Good Recovery**
       - Age (years) 28.0 (9.8)
       - Gender M 75.9%
       - Modified ISS 3.6 (4.8)
       - GCS in ER 14.9 (0.4)
       - Mechanism of Injury MVA (56.0%)
       - Blood Alcohol in ER (mg/dL) 0.0 (0.1)
       - Education (years completed) 11.8 (2.4)
       - Occupation Level Professional (8.6%)
       - History of Premorbid Alcohol Abuse 20.7%
       - History of Premorbid Substance Abuse 0.86%
       - Past Major Depressive Episode 6.9%
   - **Lower Moderate Disability**
     - Age (years) 32.9 (10.0)
     - Gender M 57.1%
     - Modified ISS 3.0 (4.3)
     - GCS in ER 14.7 (0.6)
     - Mechanism of Injury MVA (81.0%)
     - Blood Alcohol in ER (mg/dL) 0.0 (0.1)
     - Education (years completed) 10.6%
     - Occupation Level Managerial (14.6%)
     - History of Premorbid Alcohol Abuse 38.1%
     - History of Premorbid Substance Abuse 4.76%
     - Past Major Depressive Episode 38.3%
   - **Statistic**
     - F = 4.3, p = .04
     - F = 0.38, p = .54
     - F = 2.52, p = .11
     - X² = 5.29, p = .38
     - X² = 0.002, p = .68
     - X² = 15.38, p < .0001
     - X² = 7.53, p = .18
     - X² = 3.0, p = .08
     - X² = 1.88, p = .17
     - X² = 16.77, p < .0001
     - X² = 20.8, p < .0001

6. **Conclusions**
   - The analysis demonstrates that some of the most widely used predictors of outcome following mTBI account for only a small fraction of the outcome variance.
   - Recent studies have suggested that advanced imaging may have some prognostic value.
   - Further studies are needed to dissect the factors associated with outcome variability and to develop more effective prognostic tools and therapies in mTBI.