**Concussion Guidelines Step 1: Systematic Review of Prevalent Indicators**

**Supplemental Content 7**
**Evidence Table. Included Studies For Key Question 4 – Imaging and Biomarker Publications – Medium Potential for Bias, Inclusive Case Definitions, Fixed Time Points – N = 7**

| Reference | Inclusion Criteria | Signs Reported | Symptoms Reported | Neurologic or Neurocognitive Tests | Imaging | Biomarkers | Signi-ficance Measure | Time-point | Data |
|---|---|---|---|---|---|---|---|---|---|
| Geyer 2009[1]<br>Hospital<br>Pediatrics | Mild TBI Group:<br>- GCS 13 – 15 or F-GCS 17 – 19<br>- absence of focal neurological signs, and<br>- at least one of: LOC < 15 min., amnesia, nausea, vomiting, somnolence, headache, dizziness, or impaired vision<br>Contusion Group:<br>GCS 15 or F-GCS 19 and no clinical signs | GCS 14, 15<br>LOC<br>Amnesia | Vomiting<br>Headache<br>Nausea<br>Somnolence<br>Dizziness<br>Impaired vision | | | S100B<br>NSE<br><br>Measured in E.D. (patients included if presented within 6 hours of injury)<br>Range for blood draw – 1.5 to 6 hours<br><br>Compared two groups:<br>Mild TBI N = 95<br>Contusion N = 53<br><br>No significant relationship between GCS and S100B or NSE. | ANCOVA for differences in markers between groups<br><br>Spearman correlation coefficients | Fixed | Means |
| Ono 2007[2]<br>Hospital<br>Adults, Adolescents, and Pediatrics | - GCS ≥ 14 | GCS<br>LOC<br>Amnesia | Headache<br>Nausea/ Vomiting | | CT<br><br>Admitted within 6 hours of injury and CT scan occurred after initial examination.<br>N = 1,064<br>CT+ N = 50<br>4.7%<br><br>Proportions:<br>18/50 (36%) with CT+ had GCS 14; 134/1014 (13.2%) with CT- had GCS 14<br>19/50 (38%) with CT+ had headache; 144/1014 (14.2%) with CT- had headache<br>14/50 (28%) with CT+ had Nausea/Vomiting; 66/1014 (6.5%) with CT- had Nausea/Vomiting<br>35/50 (70%) with CT+ had LOC/amnesia; 274/1014 (71.4%) with CT- had LOC/amnesia<br><br>Odds of CT+ for Signs (Multivariate analysis) Odds Ratio (95% CI) p value:<br>GCS=14 0.69 (0.31-1.54) p=0.372<br>Headache 9.30 (4.22-20.47) p < 0.001 | | Logistic regression | Fixed | Means and Odds ratios |

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| | | | | | Nausea/vomiting 4.67 (2.02-10.78) p < 0.001<br>LOC/Amnesia 4.89 (2.31-10.37) p < 0.001 | | | | |
| Papa 2012[3]<br>Hospital<br>Adults | - GCS 9 - 15 (data separated for GCS 13 – 15)<br>- Either LOC, amnesia, or disorientation | GCS<br>LOC<br>Amnesia | | | | Serum levels of UCH-L1<br><br>Measured within 4 hours of injury<br>PCE N = 86 (GCS 13-15)<br>Control #1 – Uninjured volunteers N = 176<br>Control #2 – Injured patients admitted to E.D. N = 23.<br><br>PCE patients had sign. greater levels of UCH-L1 than trauma controls (p = 0.006). | ANOVA and Games-Howell post hoc test | Fixed | Means |
| Papa 2012[4]<br>Hospital<br>Adults | - GCS 9 - 15 (data separated for GCS 13 – 15)<br>- Either LOC, amnesia, or disorientation | GCS<br>LOC<br>Amnesia | | | | Serum levels of GFAP-BDP<br><br>Measured within 4 hours of injury<br>PCE N = 97 (GCS 13-15)<br>Control #1 – Uninjured volunteers N = 176<br>Control #2 – Injured patients admitted to E.D. N = 23.<br><br>PCE patients had significantly greater levels of GFAP-BDP than trauma controls (p = 0.011). | ANOVA and Games-Howell post hoc test | Fixed | Means |

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| Saadat 2009[5]<br>Hospital<br>Adults | - GCS ≥ 13 | GCS 15<br>GCS 14<br>GCS 13<br>Amnesia<br>RTA > 15 m. | Nausea<br>Dizziness<br>Vomiting<br>Abnormal behavior<br>Blurred vision | Pupil size or reflex<br>Nystagmus | CT<br><br>Admitted within 12 h of injury and CT scan occurred after initial examination.<br>N = 318<br><br>Proportions:<br>20/318 (6.3%) had CT+<br><br>GCS 15 – 89.5%<br>14 – 8.6%<br>13 – 12%<br><br>Sign. association of CT with Risk Factors:<br>GCS < 15<br>Vomiting<br>Amnesia for trauma<br>RTA > 15 m.<br>(significance level not reported)<br><br>No significant associations with CT:<br>PTA, abnormal behavior, nausea, headache, dizziness, pupil size or reflex, nystagmus, blurred vision | | Chi-squared<br>t-tests | Fixed | Proportions and Associations |
| Smits 2007[6]<br>Hospital<br>Adults | Presentation within 24 h of injury<br>- GCS 13 – 14 or GCS 15 and at least one of:<br>- LOC<br>- Short term memory deficit<br>- Amnesia for event<br>- Seizure<br>- Vomiting<br>- Headache<br>- Intoxication<br>- Use of anticoagulants<br>- Coagulopathy<br>- Evidence of injury above clavicles<br>- Neurologic deficit | GCS 13, 14<br>Anterograde Amnesia<br>PTA<br>LOC<br>Seizure | Headache<br>Vomiting | Neurologic deficit | Admission within 24 h of injury and CT “asap” after admission.<br><br>N = 3,181<br>CT+ N = 243<br>7.6%<br><br>Association of CT and Neurosurgery with GCS:<br>135/2,462 with GCS 15 had +CT (5.5%)<br>10/2,462 with GCS 15 had neurosurg. (0.4%)<br>77/568 with GCS 14 had +CT (13.6%)<br>5/568 with GCS 14 had neurosurg. (0.9%)<br>31/151 with GCS 13 had +CT (20.5%)<br>2/151 with GCS 13 had neurosurg. (1.3%)<br>Sign. NR<br><br>Odds of +CT for Signs/Risk Factors – Odds Ratio (95% CI):<br>GCS 13 3.9 (2.4-6.6) | | Multivariable logistic regression<br>Chi-squared<br>Mann-Whitney U<br>Unpaired 2-tailed t-test<br>Odds ratios<br>(Nagelkerke’s $R^2$) | Fixed | Proportions |

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| | | | | | GCS 14 2.1 (1.4-2.9)<br>Anterograde Amnesia 1.5 (1.1-2.2)<br>Vomiting 2.4 (1.7-3.5)<br>PTA < 4 h 1.6 (0.6-4.5)<br>PTA ≥ 4 h 7.5 (1.5-3.7)<br>LOC 1.8 (1.3-2.5)<br>Neurologic Deficit 1.5 (1.0-2.3)<br>Headache NR | | | | |
| Turedi 2008[7]<br>Hospital<br>Adults and Pediatrics | LOC or Amnesia, and GCS 13 – 15 | GCS<br>LOC<br>Amnesia<br>Seizure | Headache<br>Vomiting | Asymmetric Pupils<br>Focal neurological finding | CT Scans<br><br>Within 3 hours of trauma<br>N = 240<br>High Risk N = 120<br>Low Risk N = 120<br>CT+ N = 47<br>19.6%<br><br>High Risk Group: LOC, amnesia, vomiting, suspected skull fracture, multi-trauma, headache, asymmetric pupils, focal neurological findings, seizures, coagulopathy and GCS score of 14 or 15 (I think this is a typo – I think it should say 13 or 14).<br><br>Associations of CT with Risk Category:<br>High Risk N = 39 (32%) CT+<br>Low Risk N = 8 (6%) CT+<br>p < 0.0005<br><br>Associations of CT with Individual Risk Factors:<br>Significant Correlations for Abn. CT with vomiting. NSD for amnesia or headache. Insufficient data for analysis of other signs.<br><br>Odds of CT+:<br>OR for Abnormal CT Findings (95% CI):<br>Vomiting 4.61 (2.20-9.64) p = 0.0001<br>Amnesia 0.89 (0.32-2.48) NSD<br>LOC 1.52 (0.46-4.99) NSD<br>Headache 2.51 (0.54-11.62) NSD | | Chi-squared with Yates correction | Fixed | Correlations based on Proportions |

ANCOVA = Analysis of Covariance, ANOVA = Analysis of Variance, CI = Confidence Interval, CT = Computerized Tomography, ED = Emergency Department, F-GCS = Glasgow Coma Scale (for children <12 years), GCS = Glasgow Coma Scale, GFAP-BDP = Glial Fibrillary Acidic Protein Breakdown Products, LOC = Loss of Consciousness, NSD = No Significant Difference(s), NSE = Neuron-specific enolase, PCE = Potential Concussive Event, PTA = Post-Traumatic Amnesia, RTA = Retrograde Amnesia, UCH-L1 = Ubiquitin C-terminal hydrolase

**REFERENCES**


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