Evaluation of the Combined Prehospital Hypoxia-Hypotension “Depth-Duration Dose” and Mortality in Major Traumatic Brain Injury

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Background

- Prehospital hypoxia and hypotension dramatically increase mortality in TBI

Why is So Little Known?

- Linkage of detailed EMS data to TC outcomes is challenging →
  - TC-based registries have little or no prehospital data
  - Even those that do have EMS data...typically only have one recorded measurement from the field
Previous Reports on “Dose”

- EPIC Study Database:
  - Extensive EMS data including all recorded BPs... and associated times... linked to comprehensive trauma center data
  - We defined the “Depth-Duration Dose” for hypoxia and for hypotension
  - Reported the separate dose-effects of hypoxia and hypotension

Case Example 2: Hypoxia Depth-Duration Dose

aOR for death vs. Log₂ dose: 1.22
Doubling of dose ➔ 22% increase in the odds of death
The Next Logical Step

- Obviously, hypoxia and hypotension are not mutually exclusive
- Question: Is there a way to meaningfully evaluate the “combined” dose effects in patients with either hypoxia or hypotension or both?
Approach

- In major TBI, evaluated the association between mortality and the dose of prehospital hypoxia and hypotension.

- LR was used to determine the association between odds of death and the doses of hypoxia and hypotension.

- A dose "score" was defined by combining the fitted effects of both hypoxia and hypotension.

- Thus, the model simultaneously accounts for adjusted death risk for patients with either hypoxia or hypotension or both.

Results

- Pre-implementation cohort: 16,711
  - 8469 met inclusion criteria
- 6682 (78.9%) had at least two EMS SBPs and SpO2s with recorded times
  - Hypoxia only: 418
  - Hypotension only: 319
  - Both: 112
Unadjusted mortality rate increases consistently across the quartiles of the dose score.

Adjusted mortality: In patients with either hypoxia or hypotension or both:
- Nearly linear function
- One SD ↑ of dose score → 63% ↑ odds of death

Limitations
- Observational
- Association doesn’t prove cause
- Does not prove that treating hypoxia or hypotension improves outcome
- One of the main study hypotheses
**Discussion**
- The separate models for dose revealed remarkably similar patterns
- So...at the cellular level...is this just two ways of looking at the same issue?

**What About Combined Effects?**
- For both hypoxia and hypotension...at the cellular level...the primary physiological insult is inadequate oxygen delivery
- Some have hypothesized that the combined effect of hypoxia and hypotension would not add significantly to the individual effect...since they "look similar" at the cellular level

**What About Combined Effects?**
- Does this mean that the addition of one to the other will have little or no effect since the neuron is already experiencing oxygen deprivation regardless of which physiological insult is present?
Our findings provide strong evidence that hypoxia and hypotension depth/duration have an additive effect on TBI mortality. The findings also show that the effects of hypoxia and hypotension are far more complex than is inferred by the current "dichotomous" literature.

The combined "dose" of hypoxia and hypotension is strongly...and essentially linearly...associated with mortality. This model allows "co-mingling" of hypoxia and hypotension doses both separately, and in combination.

Summary: Given all of the issues that impact survival...it's remarkable how dramatically these two factors...occurring in the field...influence final outcomes in TBI.
Future Considerations

- We plan to use the post-implementation cohort from EPIC as a dataset for validating and optimizing the model.

Special thanks to the EPIC Partners

Arizona Fire Departments and EMS Agencies

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Unadjusted and adjusted ORs for death for hypoxia or hypotension or both:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neither</td>
<td>4.4</td>
<td>6.1</td>
</tr>
<tr>
<td>Hypoxia Only</td>
<td>2.5</td>
<td>3.0</td>
</tr>
<tr>
<td>Hypotension Only</td>
<td>6.6</td>
<td>8.1</td>
</tr>
<tr>
<td>Both Conditions</td>
<td>13.2</td>
<td></td>
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</table>
Future Considerations
- Does this have future clinical implications?
- Calculation of hypoxia dosage requires real-time computer support
- These findings point to the potential need for monitors that can calculate the dose in real-time and potentially help with clinical decision support

Methods: Patients
- Inclusion:
  - Major TBI: CDC Barell Matrix Type 1
  - Pre-implementation cohort
  - SBPs: ≤200mmHg
  - Age ≥10

The Excellence in Prehospital Injury Care (EPIC) Study
- Statewide, 9-year, before-after system evaluation of the impact of implementing the National EMS TBI Guidelines throughout Arizona
- 125 agencies and the 8 level I trauma centers participating
- Will enroll over 22,000 major TBI patients