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Pre-Hospital Intubation is Associated with Increased Mortality After Traumatic Brain Injury

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Background. Early endotracheal intubation in patients sustaining moderate to severe traumatic brain injury (TBI) is considered the standard of care. Yet the benefit of pre-hospital intubation (PHI) in patients with TBI is questionable. The purpose of this study was to investigate the relationship between pre-hospital endotracheal intubation and mortality in patients with isolated moderate to severe TBI.

Methods. The Los Angeles County Trauma System Database was queried for all patients > 14 y of age with isolated moderate to severe TBI admitted between 2005 and 2009. The study population was then stratified into two groups: those patients requiring intubation in the field (PHI group) and those patients with delayed airway management (No-PHI group). Demographic characteristics and outcomes were compared between groups. Multivariate analysis was used to determine the relationship between pre-hospital endotracheal intubation and mortality.

Results. A total of 2549 patients were analyzed and then stratified into the two groups: PHI and No-PHI. There was a significant difference noted in overall mortality (90.2% versus 12.4%), with the PHI group being more likely to succumb to their injuries. After adjusting for possible confounding factors, multivariable logistic regression analysis demonstrated that PHI was independently associated with increased mortality (AOR 5, 95% CI: 1.7–13.7, P = 0.004).

Conclusions. Pre-hospital endotracheal intubation in isolated, moderate to severe TBI patients is associated with a nearly 5-fold increase in mortality. Further prospective studies are required to establish guidelines for optimal pre-hospital management of this critically injured patient population. © 2011 Elsevier Inc. All rights reserved.

Key Words: traumatic brain injury; pre-hospital intubation; mortality; outcomes.

INTRODUCTION

Traumatic brain injury (TBI) is the most common cause of death and disability in trauma patients, affecting over 1 million Americans per year. Most of these disabilities are a direct result of secondary injury processes following the initial mechanical insult [1, 2]. Secondary injury processes include systemic hypotension and hypoxia, which are known to play a critical role in the development of irreversible tissue damage. Hypoxia in TBI patients has shown to be significantly associated with increased morbidity and mortality and is also a strong predictor of poor neurological outcomes [3–7]. Additionally, hypoventilation and resultant hypercapnia can lead to cerebral vasodilation and subsequent exacerbation of intracranial hypertension. In order to prevent secondary brain injury from hypoxia and hypercapnia, aggressive pre-hospital airway control has been advocated [1, 3, 8]. However, despite multiple studies, the benefit of pre-hospital intubation (PHI) remains unproven [9–11].

To our knowledge, the role of PHI has not been evaluated in an urban trauma setting where transport times remain relatively short compared with those in a more rural environment. We hypothesized that pre-hospital endotracheal intubation for patients with isolated moderate to severe TBI in this environment would be rare, and would be associated with poor outcomes.
METHODS

This is a retrospective database review of the Los Angeles County Trauma System Database, consisting of 5 Level I and 8 Level II trauma centers. The 13 trauma centers consist of 5 Level I adult centers in the more densely populated areas surrounded by seven Level II centers, with one pediatric Level I center, covering an area of approximately 4079 square miles and providing care for approximately ten million people. As part of the county trauma system policy, transport times are required to be less than 30 min. This database contains 110,297 medical records from the years 2005 to 2009. All data provided by the Los Angeles County Database is de-identified and in strict compliance with the Health Insurance Portability and Accountability Act of 1996.

Our study population consisted of all patients presenting with isolated moderate to severe TBI (head AIS ≥ 3, all other AIS < 3) who required intubation either in the pre-hospital period (PHI) or in the emergency room (No PHI). Patients who were dead on arrival, died in the emergency department, were found to have non-survivable injuries (any AIS = 6), had missing intubation data, or less than 14 years of age were excluded from our analysis.

Data abstracted for the two study groups included demographic characteristics, mechanism of injury, systolic blood pressure (SBP), and Glasgow Coma Scale (GCS) on admission, Injury Severity Score (ISS), and Abbreviated Injury Scale (AIS) of the head. The primary outcome of interest was the difference in mortality between the PHI and No-PHI groups.

To compare the PHI with the No PHI cohort, contingency tables were created for each data set and statistical analysis was performed using χ² with Yates correction or Fisher exact test for dichotomous variables, and Student’s t-test or Mann-Whitney U test or analysis of variance (ANOVA) for continuous variables. Continuous variables are described as means ± standard deviations (SDs). To calculate the adjusted odds ratios (AOR) and the 95% confidence intervals (CI) for the differences in mortality and complication rate between the PHI and No PHI groups variables that on bivariate analysis were significant at the 0.2 level were selected as covariates and entered in a multivariable logistic regression model. Due to a noticeable difference in baseline characteristics between the two patient groups, a propensity score model was created to test our logistic regression model. Propensity scores were calculated for each patient to determine the expected risk of mortality based upon available variables. These scores were then combined into a logistic regression model containing only the propensity scores and intubation status to determine the propensity AOR for mortality. To identify factors independently associated with PHI, all potential risk factors that were significant at P < 0.2 were entered into a stepwise forward logistic regression analysis from which AOR and 95% CI were derived.

All statistical analyses were performed using the Statistical Package for the Social Sciences for Macintosh, ver. 18.0 (SPSS Inc., Chicago, IL). This study was determined to be exempt from institutional review board (IRB) approval by the Cedars Sinai Medical Center IRB.

RESULTS

During the study period, 2366 patients with isolated moderate to severe TBI requiring intubation were identified. Of note, only 61 patients (2.6%) were managed with PHI, which is lower than other reports in the literature [9–12]. Table 1 depicts the study population and compares the characteristics between the PHI and No PHI groups. Though the two groups were demographically similar, the injury and physiologic parameters vary significantly with the PHI group presenting with a higher severity of injury. The crude outcomes between the two groups are presented in Table 2. The overall mortality for the study population was 14.4%. There was a marked difference noted in overall mortality (90.2% versus 12.4%, P < 0.001), with the PHI group being almost 65 times more likely to succumb to their injuries. In-hospital complications occurred in 10.9% of the cohort. There was no significant difference between the PHI and No PHI groups (11.5% versus 10.8%, P = 0.9). The similarities in complication rates may have been due to the overall high mortality seen in the PHI group.

After performing multiple logistic regression to adjust for differences in baseline characteristics (Table 3), the PHI group demonstrated significantly higher mortality compared to the No PHI cohort (AOR 5, 95% CI: 1.7–13.7, P = 0.004). Similar findings were also seen when using our propensity score model, the AOR for the PHI group was found to be 6.8 (95% CI: 2.3–19.6, P = 0.001). However, the Hosmer-Lemeshow statistic was found to be significant for this propensity model likely due to the small number of patients that required PHI. Again, after adjustment no differences were found for in-hospital complications between the two study groups.

Forward stepwise logistic regression was used to identify independent risk factors for PHI by including variables that were significant at the P < 0.2 level into a regression model (Table 4). The presence of a GCS ≤ 8 upon admission (AOR 71.4, 95% CI 9.4–500) and emergency department hypotension (SBP < 90, AOR 62.5 95% CI 33.3–111.1) were the strongest predictors for need of a pre-hospital airway followed by penetrating mechanism of injury (AOR 3.0, 95% CI 1.6–5.7).

DISCUSSION

Our review of an urban countywide database found that PHI for isolated moderate to severe TBI occurred rarely (2.6%) and was associated with significantly increased mortality (AOR 5, 95% CI: 1.7–13.7, P = 0.004). Although a secure airway to optimize oxygenation and control ventilation with a secure airway are well known to improve outcomes in hospitalized TBI patients, numerous studies in the literature have demonstrated results similar to those in the current investigation by suggesting that pre-hospital intubation in severe TBI patients is associated with worse outcomes [8–11, 13].

Murray et al. [8] evaluated 714 patients with severe TBI and determined that in the pre-hospital setting, intubated patients had a significantly higher relative risk of mortality when compared to nonintubated (RR = 1.74, P < 0.001) and unsuccessfully intubated severe
TABLE 1
Comparison of Demographics and Clinical Characteristics Between Study Groups

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 2366)</th>
<th>Pre-hospital intubation (n = 61)</th>
<th>Post-hospital intubation (n = 2305)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) mean ± SD [median]</td>
<td>37.8 ± 23.8 [35.0]</td>
<td>35.9 ± 18.2 [30.0]</td>
<td>38.1 ± 24.2 [35.0]</td>
<td>0.472</td>
</tr>
<tr>
<td>Age ≥ 55 y</td>
<td>24.3% (576/2366)</td>
<td>14.8%</td>
<td>24.6%</td>
<td>0.095</td>
</tr>
<tr>
<td>Male</td>
<td>71.0% (1,609/2366)</td>
<td>82.0%</td>
<td>76.3%</td>
<td>0.304</td>
</tr>
<tr>
<td>Blunt mechanism</td>
<td>81.1% (2068/2366)</td>
<td>39.3% (24/61)</td>
<td>88.7% (2,044/2305)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>134.6 ± 38.3 [137.0]</td>
<td>45.0 ± 63.2 [0]</td>
<td>137.2 ± 34.5 [138.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypotension on admission (SBP &lt; 90 mmHg)</td>
<td>6.3% (147/2348)</td>
<td>73.8% (45/61)</td>
<td>4.5% (102/2287)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCS mean ± SD [median]</td>
<td>11.6 ± 4.3 [14.0]</td>
<td>3.3 ± 1.1 [3]</td>
<td>11.7 ± 4.2 [14.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCS ≤ 8</td>
<td>23.3% (594/2366)</td>
<td>98.3% (58/59)</td>
<td>23.7% (536/2258)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Head AIS</td>
<td>4.0 ± 0.8 [4.0]</td>
<td>4.8 ± 0.5 [5.0]</td>
<td>4.0 ± 0.8 [4.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ISS mean ± SD [median]</td>
<td>18.3 ± 7.2 [17.0]</td>
<td>26.7 ± 8.4 [26.0]</td>
<td>18.4 ± 7.0 [17.0]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ISS ≥ 16</td>
<td>66.7% (1700/2549)</td>
<td>93.4% (57/61)</td>
<td>71.3% (1,643/2305)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transport time (min) ± SD [median]</td>
<td>13.2 ± 6.9 [12.0] (1,553/2366)</td>
<td>11.5 ± 7.5 [9.0] (47/61)</td>
<td>13.3 ± 6.8 [12.0] (1,506/2305)</td>
<td>0.073</td>
</tr>
</tbody>
</table>

ISS = injury severity score; GCS = Glasgow Coma Scale; AIS = Abbreviated Injury Score; SBP = systolic blood pressure.

TBI patients (RR = 1.53, P = 0.008). Bochicchio et al. [13] later confirmed these findings in 191 patients with severe TBI by demonstrating that PHI was associated with significantly longer hospital (20.2 d versus 16.7 d), ICU length of stays (15.2 d versus 11.7 d), and nearly twice the mortality rate (23% versus 12.4%). In the largest study to date, Davis et al. [10] evaluated 13,625 moderate to severe TBI patients and found that PHI was associated with a significant increase in mortality compared with intubation immediately upon hospital admission (57.6% versus 29.3%). In their study, 19.3% of all patients underwent PHI, a significantly higher rate than observed in the current study. This may reflect the difference in transport times as San Diego County trauma systems have six trauma centers that cover a similar geographic distance that the 13 trauma centers in Los Angeles County do.

In contrast to the above findings, Winchell and Hoyt [12] evaluated 671 patients with severe TBI and found that field intubation was associated with a significant decrease in mortality (57% to 36%). A subgroup analysis of 351 isolated severe TBI patients also showed a significant decrease in mortality for those patients intubated in the pre-hospital setting (50% to 23%). However, in addition to the small sample size, a multivariable logistic regression analysis to adjust for confounding factors such as injury severity, hypotension, and age was not performed, which limits the conclusions that can be made from this study.

Although our findings showed that PHI is associated with worse outcomes in patients with isolated moderate to severe TBI, we did find however, that a GCS ≤ 8 upon admission (AOR 71.4, 95% CI 9.4–500), hypotension in the Emergency Department (SBP < 90, AOR 62.6, 95% CI 33.3–111.1), and having a penetrating injury (AOR 3.0, 95% CI 1.6–5.7) were all independent predictors for the need for a pre-hospital airway. It is important for us to emphasize that the relationship between pre-hospital intubation and resultant mortality is not causal but associative. These patients represent a select group of TBI patients who are at a high risk for death and require heightened clinical vigilance.

Thus, in moderate to severe TBI patients, balancing the benefit of a secure airway in the pre-hospital setting with the risk of worse outcomes due to sub-optimal conditions, delays in transport, esophageal intubations, or injuries during intubation is challenging. Perhaps rigorous training in various airway management techniques by emergency pre-hospital providers could prove to be beneficial. Rapid sequence intubation (RSI) is defined as the rapid administration of sedative agent(s) plus a rapid-onset neuromuscular blocking drug and is

TABLE 2
Crude Outcomes by Pre-Hospital Intubation

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Pre-hospital intubation</th>
<th>Post-hospital intubation</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>14.4%</td>
<td>90.2%</td>
<td>12.4%</td>
<td>64.7 (27.6–151.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Complication rate</td>
<td>10.9%</td>
<td>11.5%</td>
<td>10.8%</td>
<td>0.9 (0.4–2.1)</td>
<td>0.876</td>
</tr>
</tbody>
</table>

The P values for the categorical variables were derived from the χ² or Fishers exact test.
considered standard of care in severe TBI patients in the hospital setting [14]. In a recently published prospective, randomized, controlled trial, Bernard et al. [15] found that in adult patients with severe TBI, pre-hospital RSI by paramedics improved functional neurologic outcomes at 6 mo compared with intubation in the hospital. Despite these recent findings, the use of RSI by paramedics requires additional training, which is costly; requires skills maintenance as use of RSI in patients with severe TBI is infrequent, and the risk of a failed intubation in the pharmacologically paralyzed patient or an unrecognized intubation of the esophagus could be fatal [16]. Additionally, alternative rescue airway methods such as the laryngeal mask airway; which require less skill and training to place yet serves as a viable emergency airway alternative, should be emphasized in emergency provider training [17]. Perhaps end-tidal carbon dioxide monitoring (EtCO2) combined with point of care arterial or capillary blood gas values could assist in maintaining a PaCO2 in the 35–40 mmHg range as recommended by the Brain Trauma Foundation Guidelines [14]. Recent positive military experience involving air evacuation of critically ill soldiers with TBI requiring mechanical ventilation using computer automation for control of respiratory parameters may lead to novel techniques in civilian population [18].

There are several limitations to our study. As in all retrospective database studies, the design of the trauma registry used for data analysis limits the conclusions that can be established. Differences in the level of training and skill of airway management between paramedics in the pre-hospital setting and physicians in the hospital setting exist, which could not be accounted for [19]. The use of intubation medications, as well as therapies directed at treating intracranial hypertension for both study groups and their effects on outcome is unknown. We also were not able to obtain important respiratory parameters such as respiratory rate, oxygen saturation, or arterial blood gas values in our study. Potential complications that commonly occur during pre-hospital intubations such as multiple attempts, desaturations, aspiration events, or possible deaths related to intubation were not recorded [20]. The potential impact of pre-hospital time data to determine delays in treatment were not captured for all of our patients, limiting the conclusions that can be drawn from this data. Evaluating the actual length of survival as well as functional outcomes utilizing a standardized scale such as the Extended Glasgow Outcome Score would strengthen the study and should be investigated in future studies. Finally the limited number of patients in our study population limits the veracity our findings.

Despite these limitations, our findings from a county-wide database suggest that pre-hospital endotracheal intubation for isolated moderate to severe TBI patients rarely occurs in an urban setting and is associated with a nearly 5-fold increase in mortality. Further prospective studies are needed to establish new guidelines for optimal pre-hospital management of this critically injured patient population.

### REFERENCES


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**TABLE 3**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted odds ratio (95% CI)*</th>
<th>Adjusted P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality %</td>
<td>5.0 (1.7–13.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>Propensity score mortality %</td>
<td>6.8 (2.3–19.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Complication rate %</td>
<td>1.5 (0.6–3.9)</td>
<td>0.397</td>
</tr>
</tbody>
</table>

**Variables that were included:** mechanism of injury, mean admission SBP, hypotension on admission (SBP < 90 mmHg), mean admission GCS, admission GCS ≤ 8, head AIS, mean injury severity (mean ISS), and severe injury (ISS > 16).

CI = confidence intervals; ISS = Injury Severity Score; GCS = Glasgow Coma Scale; AIS = Abbreviated Injury Score; SBP = systolic blood pressure.

All Variables with a P value < 0.05 were included in the multivariable analysis.

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**TABLE 4**

<table>
<thead>
<tr>
<th>Step</th>
<th>Variable</th>
<th>Adjusted odds ratio (95% CI)*</th>
<th>Adjusted P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>GCS ≤ 8</td>
<td>71.4 (9.4–500)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>Hypotension (SBP &lt; 90)</td>
<td>62.5 (33.3–111.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>Penetrating Injury</td>
<td>3 (1.6–5.7)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Variables that were included:** age > 55, mechanism of injury, systolic blood pressure, hypotension on admission (SBP < 90 mmHg), admission GCS ≤ 8, head AIS, and severe injury (ISS > 16).

CI = confidence intervals; ISS = injury severity score; GCS = Glasgow Coma Scale; AIS = Abbreviated Injury Score; SBP = systolic blood pressure.

All Variables with a P value < 0.2 were included in the multivariable analysis.


