Determinants of Mortality in Patients With Severe Blunt Head Injury

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**Context:** Head injury is the leading cause of traumatic death in the United States.

**Hypothesis:** A set of clinical parameters available soon after injury can be used to accurately predict outcome in patients with severe blunt head trauma.

**Design:** Validation cohort study.

**Setting:** Urban level I trauma center.

**Patients and Methods:** Data from patients with severe blunt head injury, as defined by inability to follow commands, were prospectively entered into a neurological database and analyzed. The impact on survival of 23 potentially predictive parameters was studied using univariate analysis. Logistic regression models were used to control for confounding factors and to assess interactions between variables, whose significance was determined by univariate analysis. Goodness of fit was calculated with the Hosmer-Lemeshow c statistic. The predictability of the logistic model was evaluated by measuring the area under the receiver operating characteristic curve (AUC).

**Results:** Logistic regression analysis revealed that 5 risk factors were independently associated with death. These variables included systemic hypotension in the emergency department, midline shift on computed tomographic scan, intracranial hypertension, and absence of pupillary light reflex. A low Glasgow Coma Scale score and advanced age were found to be highly correlated risk factors that, when combined, were independently associated with mortality. The model showed acceptable goodness of fit, and the AUC was 80.5%.

**Conclusions:** Systemic hypotension and intracranial hypertension are the only independent risk factors for mortality that can be readily treated during the initial management of patients with severe head injuries. When used together, Glasgow Coma Scale score and age are significant predictors of mortality.

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HEAD INJURY is the leading cause of traumatic death in the United States.\(^1,2\) The identification of reliable indicators of outcome after head injury is critical to appropriate counseling of family members and use of resources. Multiple studies have defined the major predictors of outcome after head injury.\(^3,12\)

The neurosurgical service at Ben Taub General Hospital (Houston, Tex) maintains a comprehensive database with more than 267 fields. Data on all patients with severe head injury, defined as inability to follow commands (Glasgow Motor Scale [GMS] score \(\leq 3\)), are entered into this database. A GMS score of 5 or less is the inclusion criteria because it is simple to use and avoids the difficulty of calculating a Glasgow Coma Scale (GCS) score in intubated patients. The GMS has also been shown to have an excellent correlation with mortality.\(^13\)

The purpose of this study was to determine which of a comprehensive set of prospectively collected variables, available soon after injury, were predictive of mortality in a uniform population of patients with head injury. Logistic regression analysis was used to ensure that variables found to be associated with mortality were statistically independent.

**RESULTS**

Of the 418 consecutive patients from the database who were screened, 26 were excluded because a GOS score was not recorded at discharge. Twenty-four patients had head Abbreviated Injury Scale scores of less than 5. The head Abbreviated Injury Scale scores in this group ranged from 2 to 4, and none of these
PATIENTS AND METHODS

Patients with severe head injury, defined as a GMS score of 5 or less, admitted to the American College of Surgeons–accredited level I trauma center at Ben Taub General Hospital from April 1994 through March 2000 were eligible for the study. Only patients admitted to the neurosurgical intensive care unit were included. These patients were prospectively entered into a neurosurgical database. Patients with a blunt mechanism and a head Abbreviated Injury Scale score of 5 were subsequently analyzed.

Patients were managed by standardized protocols that emphasize immediate evacuation of large mass lesions and prevention and rapid treatment of secondary insults. Computed tomographic (CT) scans of the head were obtained for all patients as soon as possible after arrival in the emergency department or immediately after the findings from the neurologic examination worsened. All research protocols were approved by the Baylor Affiliates Review Board for Human Subject Research (Baylor University, Houston).

National Library of Medicine PubMed literature searches were performed using the phrases “head injury,” “outcome and trauma,” and “outcome.” These searches produced 1353 articles. Pertinent articles that revealed statistically significant outcome measures routinely obtained in our practice were used as the basis for choosing the study variables. The literature search identified 23 commonly measured variables that are predictive of outcome.

The impact on survival of these 23 potentially predictive parameters was studied. The variables included demographic characteristics, findings prior to hospitalization, findings from emergency department physical examination, findings from laboratory studies, presence of extracranial injuries, CT findings, the need for craniotomy, initial intracranial pressure (ICP), and initial cerebral perfusion pressure. Glasgow Outcome Scale (GOS) scores were calculated at discharge, 3 months after injury, and 6 months after injury.

Scoring on the GOS was performed by a neuropsychiatric technician who was trained and supervised by a neuropsychologist. The evaluations were performed on a blinded basis. All GOS scores were obtained within 2 weeks of the scheduled end point.

Variables were initially analyzed using univariate analysis. Analysis with a χ² test was performed on all variables except when the predicted value of a cell was less than 5. In these cases, the Fisher exact test was used. Cutoff values for numerical variables were based on accepted values from the literature, and 95% confidence intervals (CIs) were used to determine significance.

Variables that were found to be significantly associated with mortality were then analyzed with logistic regression to control for confounding factors and assess interactions among variables. The Hosmer-Lemeshow c statistic14 was used to calculate the goodness of fit of the final logistic model. The receiver operating characteristic (ROC) curve was plotted, and the area under the curve (AUC) was calculated with SPSS 10.0 software (Statistical Product and Service Solutions; SPSS Inc, Chicago, III). The ROC curve presents the relationship between sensitivity and specificity by plotting the true-positive rate (sensitivity) against the false-positive rate (1–specificity) as the cutoff level of the model varies. The AUC is based on a nonparametric statistical sign test that compares the probability of events between pairs of patients who experience the event and those who do not. The AUC may be interpreted as the probability that given any 2 subjects, one who dies and one who survives, the model would assign a higher probability of death to the one who dies. It is a measure of the overall classification performance of a diagnostic test or prognostic model.15

The severity of head injury is depicted in Figure 1, which shows the GOS scores at discharge and 3 months after injury. The GOS scores were available for all patients at discharge and for 327 patients (89%) at 3 months after injury. Mortality was 38% at discharge and 43% at 3 months, and 28% of the deaths occurred within 24 hours of admission. The median time to death was 3 days, with the earliest death occurring 1.7 hours after admission. Of patients with an available GOS score at 3 months, 22% had a good outcome, defined as either a good recovery or a moderate disability. The GOS scores were available for 294 patients at 6 months after injury. Mortality was 50% at 6 months, and 29% of patients had a good outcome.

Only 7 of the variables were not significantly associated with mortality (Table 1). These variables were sex, race, need for craniotomy, time to craniotomy, platelet count, blood alcohol level, and the presence of extracranial injuries. None of 6 patients with a partial thromboplastin time of 50 seconds or more survived. The odds ratio for this variable was infinity, and the CI could not be calculated, so the Fisher exact test was used instead. Partial thromboplastin time was a significant predictor of mortality (P=.003).

The remaining 16 variables were then subjected to logistic regression. Five risk factors were found to be independently associated with death. These risk factors included systolic blood pressure of 90 mm Hg or less in the emergency department, midline shift of 5 mm or more on CT scan, opening ICP of 15 mm Hg or more, and absence of pupillary light reflex in one or both eyes. Scores of 8 or less on the GCS and age of 35 years or older were highly correlated with mortality (Figure 2). Mortality increased significantly in older patients with low GCS scores. Although all possible combinations of risk factors were tested in the logistic regression model, this was the only combination that produced this effect. The risk factors that are independently associated with death are shown with their relative risks and 95% CIs in Table 2.

Only those patients in whom all 6 of the significant variables were recorded (n=213) were included in the

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This study is a comprehensive examination of the variables that are potentially predictive of outcome in a uniform group of patients with blunt head injuries. Systolic blood pressure of 90 mm Hg or less in the emergency department was the single risk factor most highly associated with mortality. This variable was considered positive if it occurred at any point during the emergency department stay: before, during, or after resuscitation. Hypotension has previously been found to be highly predictive of outcome.\(^8,10-18\) This finding is extremely pertinent for several reasons. First, hypotension can be treated during the initial assessment of patients with blunt head injuries. Second, strategies that incorporate limited resuscitation to induce permissive hypotension and thus diminish bleeding, hypothermia, and coagulopathy should be approached with caution in patients with severe head injuries. These strategies have been shown to be effective in patients with penetrating torso injuries and may also be appropriate in patients with blunt trauma.\(^19\) Alternative strategies that incorporate limited resuscitation with elevation of blood pressure using pressor agents should be studied in hypotensive multiple-trauma patients with head injuries. Whichever strategy is used, additional caution should be exercised to avoid cyclic hyperperfusion or maintenance of systemic blood pressure in excess of preinjury levels, because this may result in increased bleeding and mortality. Elevated ICP has also been associated with mortality.\(^7,20\) This is the only other risk factor detected by this study that is readily treatable in the early period after injury.

The only CT finding that was independently associated with mortality was a midline shift of 5 mm or more. The presence and degree of midline shift are predictors of outcome in patients with severe head injuries.\(^21-24\) This phenomenon has been recently studied at our institution by Valadka et al.\(^25\) In that study, a midline shift of more than 5 mm was associated with diminished cerebral metabolic rate of oxygen and, therefore, depressed cerebral metabolism. Depressed cerebral metabolism was independent of the cause of the midline shift, and patients who had midline shifts had worse outcomes than those who did not. The study by Valadka et al also revealed a significant correlation between midline shift and ICP. Patients with midline shifts had a mean ICP of 20.1 mm Hg, whereas those without midline shifts had a mean ICP of 17.0 mm Hg. Based on this finding, we used ICP of 15 mm Hg or more as the cutoff for our study, as opposed to the typical value of 20 mm Hg found in the literature. The logistic regression analysis was performed using both values, and there was no significant difference in the model results.

Age and GCS score were found to be highly correlated risk factors for death. Younger patients with the same GCS scores did better than older patients. A similar finding was noted in a study by Quigley et al\(^26\) published in 1997. This group examined patients with very severe head injuries as defined by a GCS score of 3 to 5. They found that the oldest survivor with a GCS score of 3 was aged 30 to 39 years, the oldest survivor with a GCS of 4 was aged 40 to 49 years, and the oldest survivor with a GCS of 5 was aged 50 to 59 years. Our results reveal that the association of age and GCS score with mortality persists beyond a GCS score of 5. Narayan et al\(^27\) also found that age alone is predictive of outcome in 66% of cases, but when age is combined with other factors, the predictive value increases significantly.

The presence of extracranial injuries was not a risk factor for mortality in this study. A similar conclusion was reached by Baltas et al\(^27\) who found that in patients with a GCS score of 8 or less, there was no difference in mortality between those with Injury Severity Scale scores of 9 or less and those with scores greater than 9. Mortality in patients with severe head injuries appears to be determined by the severity of the intracranial trauma and not other factors.

Similarly, the need for craniotomy was not predictive of outcome. This finding differs from that reported by Marshall et al,\(^28\) which was based on the Traumatic Coma Data Bank. In their study, patients with evacuated masses were found to have a higher overall mortality rate than patients with nonevacuated masses. However, patients with nonevacuated lesions, diffuse injuries, and more than 5 mm of midline shift had worse outcomes than patients with evacuated lesions. The infor-
mation that is most predictive of mortality may be whether midline shift is present or absent.

Sex, race, and alcohol intoxication have all been previously shown to affect outcome in patients with trauma and head injury.29-31 This study differs from prior work in that none of these 3 variables was found to be predictive of outcome.

This study was limited by the necessity to include only those patients who had all of the potentially predictive variables present in the final logistic regression model. As a result, 112 patients were not included in the final analysis. The primary reason for absence of data was the lack of a recorded ICP. Reasons for the lack of an ICP measurement included death before placement of a monitor and the absence of a clinical indication for a monitor, which explains the improved mortality in the final group as compared with the overall population. However, despite the loss of a large number of patients in the final analysis, the model showed increased performance with the inclusion of ICP as evidenced by an increase in the AUC.

Another limitation of the study was the use of mortality at discharge as the primary outcome measure as opposed to GOS score at 6 months, which is a stan-

Table 1. Potentially Predictive Variables for Mortality After Severe Head Injury*

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients†</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>368</td>
<td>2.3 (1.2-4.3)</td>
</tr>
<tr>
<td>Sex</td>
<td>368</td>
<td>1.0 (0.6-1.8)</td>
</tr>
<tr>
<td>Hispanic, Asian, or black vs white</td>
<td>368</td>
<td>0.8 (0.5-1.2)</td>
</tr>
<tr>
<td>Injury type</td>
<td>368</td>
<td>2.8 (1.8-4.3)</td>
</tr>
<tr>
<td>Time to craniostomy</td>
<td>179</td>
<td>0.6 (0.3-1.1)</td>
</tr>
<tr>
<td>Systolic blood pressure  ≤ 90 mm Hg</td>
<td>362</td>
<td>3.5 (1.8-7.2)</td>
</tr>
<tr>
<td>Prothrombin time  ≥ 18 s</td>
<td>191</td>
<td>5.9 (1.2-29.1)</td>
</tr>
<tr>
<td>Partial thromboplastin time  ≥ 50 s</td>
<td>190</td>
<td>Infinity‡ (NA)</td>
</tr>
<tr>
<td>Platelet count  ≤ 10^10/µL</td>
<td>230</td>
<td>2.4 (0.7-8.0)</td>
</tr>
<tr>
<td>Blood ethanol  ≥ 100 mg dL</td>
<td>267</td>
<td>0.9 (0.5-1.5)</td>
</tr>
<tr>
<td>Prehospital hypoxia</td>
<td>360</td>
<td>1.6 (1.1-2.5)</td>
</tr>
<tr>
<td>Prehospital hypotension  ≤ 90 mm Hg</td>
<td>360</td>
<td>2.8 (1.6-4.8)</td>
</tr>
<tr>
<td>GCS score  ≤ 8</td>
<td>368</td>
<td>2.6 (1.5-4.5)</td>
</tr>
<tr>
<td>Extracranial injury Present vs absent</td>
<td>368</td>
<td>0.8 (0.4-1.7)</td>
</tr>
<tr>
<td>Pupil abnormality</td>
<td>368</td>
<td>2.8 (1.6-4.9)</td>
</tr>
<tr>
<td>Dilatation  (≥ 5 mm) of either pupil or anisocoria  (≥ 2 mm) vs normal</td>
<td>349</td>
<td>4.3 (2.5-7.2)</td>
</tr>
<tr>
<td>Light reflex Absent or sluggish in either pupil vs normal</td>
<td>349</td>
<td>4.3 (2.5-7.2)</td>
</tr>
<tr>
<td>Craniotomy</td>
<td>368</td>
<td>1.5 (0.96-2.2)</td>
</tr>
<tr>
<td>Absent, small, or enlarged vs normal</td>
<td>322</td>
<td>2.5 (1.5-4.2)</td>
</tr>
<tr>
<td>Ventricle asymmetrical vs symmetrical</td>
<td>324</td>
<td>2.9 (1.8-4.8)</td>
</tr>
<tr>
<td>Gistern space Abnormal (absent or compressed) vs normal</td>
<td>326</td>
<td>5.3 (3.0-9.6)</td>
</tr>
<tr>
<td>Midline shift Present vs absent</td>
<td>325</td>
<td>3.8 (2.3-6.3)</td>
</tr>
<tr>
<td>Intracranial pressure  ≥ 15 mm Hg</td>
<td>233</td>
<td>4.0 (2.2-7.4)</td>
</tr>
<tr>
<td>Cerebral perfusion pressure  ≥ 60 mm Hg</td>
<td>231</td>
<td>3.3 (1.7-6.6)</td>
</tr>
</tbody>
</table>

*Variables analyzed with univariate analysis. OR indicates odds ratio; CI, confidence interval; NA, not applicable; and GCS, Glasgow Coma Scale.
†Number of patients for whom the variable was recorded.
‡The OR could not be calculated because only 6 patients had a partial thromboplastin time greater than 50 seconds and none of them lived.
With mortality, only hypotension and elevated ICP can be readily treated during the initial management of patients with severe head injuries.

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REFERENCES