A model for predicting delayed intracranial hypertension following severe head injury

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A graph is presented for predicting delayed intracranial hypertension (intracranial pressure (ICP) greater than 30 mm Hg) for severely head-injured patients, based on a logistic regression model. Data gathered during the first 24 hours of patient observation are used to predict patient status during the subsequent 48 hours. The best predictor out of 10 factors analyzed was the peak ICP level during the first 24 hours (p < 0.0001). Other predictors used in the final model were the presence of hypotension (p = 0.045) and abnormal ventricles—defined as ventricles which were either absent, small, or enlarged (p = 0.086). Error rates of 24% and 20% were obtained initially and by means of a separate cross-validation group, respectively. Use of a conservative cut point (25% estimated chance of developing excess ICP) for designating high-risk patients provided a procedure with sensitivity of 86% to 89% for the two groups.

KEY WORDS • abnormal ventricle • hypertension • intracranial pressure • prognosis • severe head injury • National Traumatic Coma Data Bank

There is strong evidence that increased intracranial pressure (ICP) after head injury is associated with poor outcome. Miller, et al., noted increased morbidity with moderate elevation of ICP to more than 20 mm Hg. Uncontrollable ICP is uniformly fatal. Therefore, a model that is able to predict which patients have a high risk of developing intracranial hypertension is desirable. To be relevant in the clinical management of patients, such a model should be simple, sensitive, and specific, and based on information available shortly after injury. We believe the graphic method presented below meets these criteria, with the possible exception of high specificity.

Clinical Material and Methods

In an effort to study severe head injury in the United States, the National Institute of Neurological and Communicative Disorders and Stroke and six medical centers joined in a cooperative prospective study. In the pilot phase of this prospective study (January 1, 1980, through May 31, 1982), data were collected on 581 patients. These data were stored in a common computerized data base, the National Traumatic Coma Data Bank. Information retrieved from this Data Bank is the basis for the development of this model.

Entry into the Data Bank is restricted to trauma patients of all ages who either had a Glasgow Coma Scale (GCS) score of 8 or less following resuscitation at a Center hospital or deteriorated to that level within 48 hours of injury. The data from the first 325 patients entered into the Data Bank were used for developing the predictive model ("training group"). The subsequent 256 patients were used as a test or cross-validation group to determine whether the model had a predictive value for patients not used in the model derivation ("test group"). This splitting of the sample into the two groups was made at a natural break point in data entry, which occurred at a time when the data collection instruments were revised. Cross-validation of predictive models is important since, if many predictors are tried, a model that works well initially may not provide reproducible results on a new group of patients.

The following variables, noted within the first 24 hours after initial data collection for each patient, were used as potential predictors: age, lowest GCS score, highest ICP peak, amount of brain structure shift as determined by computerized tomography (CT), abnormal ventricular size as identified by CT (absent, small, or enlarged), hypoxia (\(pO_2 \leq 60\) mm Hg), hypo- or hypercarbia (\(pCO_2 < 30, 31 \text{ to } 49, \text{ or } 50+\) mm Hg), hypotension (systolic blood pressure less than 90 mm Hg), bradycardia (heart rate less than 45 beats/min),
and the number of seizures. If information on any one of these variables was not present during the first 24 hours of a patient's admission, that patient was excluded from the analysis of that variable. That is, no attempt was made to estimate missing data based only on the information that was present.

Excess ICP was defined as any sustained value of 30 mm Hg or greater. Thus, patients who developed transiently elevated ICP to above 30 mm Hg (for example, increases associated with pulmonary care) were not considered to have developed a sustained rise in ICP. This level of excess ICP was chosen based on the observations of Eisenberg, et al., which were used in the development of this model. In that paper, the authors demonstrated the adverse influence on outcome of an ICP of greater than 30 mm Hg.

The period considered most desirable for a predictive model was the first 24 to 72 hours following hospital admission. Any patient whose sustained ICP exceeded 30 mm Hg during the first 24 hours was excluded. Patients with a maximum ICP exactly equal to 30 mm Hg were included in the model fitting in order to add precision, but were not included in the model evaluation. Table 1 shows the number of patients by group and reason for exclusion from the analysis.

Two processes were used to eliminate potential predictors. Standard statistical tests (for example, ordered and unordered chi-squares) were used first to eliminate any variables which were not significantly related at the 10% level to the development of high ICP. This was followed by the use of stepwise logistic regression to eliminate any variables that were not significant at the 10% level by the latter analysis. The backward elimination procedure was used: all predictors were first entered and then one by one were eliminated by the likelihood ratio chi-square test if they were not statistically significant at the 10% level. At each step the least significant variable was eliminated.

The logistic model may be written as follows:

\[ \log \left( \frac{P}{1 - P} \right) = C' + \sum (CX) \]

where \( P \) = probability of developing a high ICP. The C's are computed constants and the X is the predictor. The logistic equation may be inverted to obtain estimated probabilities or percent chance of high ICP for varying values of the predictors.

For both training and test groups, the following operating characteristics of the model were determined: sensitivity (percent of those who developed high ICP who were predicted by the model to develop it), specificity (percent of those who did not develop high ICP who were predicted by the model to not develop it), predictive value of a positive test (percent of those predicted to develop high ICP who did develop it) and predictive value of a negative test (percent of those predicted to not develop a high ICP who did not develop it).

The training, test, and combined groups were used to fit logistic models. A simple graph by which one can quickly estimate a patient's chances of developing high ICP without making any mathematical calculations was constructed using the training group model.

### Results

Both the training and test groups had virtually the same percentage of patients who developed high ICP in the 24- to 72-hour period: 34% and 31%, respectively. Table 2 shows the ICP status for those patients included in the analysis.

The initial statistical analysis eliminated age, GCS score, hypoxia, hypo- and hypercarbia, bradycardia, and seizures from consideration as potential predictors. Table 3 shows the p values for those predictors included in the logistic regression analysis of the training group.

### TABLE 2

<table>
<thead>
<tr>
<th>Status of Intracranial Pressure</th>
<th>Patient Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Training</td>
</tr>
<tr>
<td>max ICP during first 24 hrs ≥ 30 mm Hg</td>
<td>4</td>
</tr>
<tr>
<td>developed high ICP between 24 &amp; 72 hrs</td>
<td>55</td>
</tr>
<tr>
<td>did not develop high ICP during first 72 hrs</td>
<td>101</td>
</tr>
<tr>
<td>total cases</td>
<td>160</td>
</tr>
</tbody>
</table>

* For explanation of patient groups see text.

### TABLE 3

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Coefficient (C)</th>
<th>Coefficient (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICP high during first 24 hrs</td>
<td>-0.173</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>size of ventricles on CT</td>
<td>-0.360</td>
<td>0.086</td>
</tr>
<tr>
<td>hypotension</td>
<td>0.506</td>
<td>0.045</td>
</tr>
<tr>
<td>brain shift on CT</td>
<td>+</td>
<td>0.58</td>
</tr>
<tr>
<td>constant</td>
<td>3.285</td>
<td>NA</td>
</tr>
</tbody>
</table>

* For explanation of "training group" see text. ICP = intracranial pressure; CT = computerized tomography; (C) = computed constant; P = probability of developing a high ICP; NA = not applicable.

† Excluded from the model because of lack of statistical significance.
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Highest ICP in the first 24 hours was by far the best predictor of delayed elevated ICP. Shift of brain structures was not a significant predictor when the three more potent predictors were included in the model. The goodness-of-fit test ($p = 0.61$) indicated an adequate fit of the data to the model.

Table 4 shows the performance of the model using the highest ICP in the first 24 hours, hypotension, and ventricular size as determined by CT as predictors for the training group. The lowest error rate for prediction obtained for the training group used a cut point (estimated percent chance of developing high ICP) of 47.5%. The results were comparable for the test and the training groups; nevertheless, the sensitivity was inadequate (< 60%) for both groups (Table 4). In order to reduce the rate of false negatives, the cut point was reduced to 25%. While this more stringent cut point of 25% provided high sensitivity and a low rate of false negatives, it was at the expense of reduced specificity and an increase in overall error rate. Table 4 shows that the revised cut point results were well reproduced in the test group.

By fitting the model to the data for the combined groups, it was hoped that an improvement in operating characteristics could be achieved. However, in the present study no improvement was obtained. Therefore, for simplicity, only the training group model is presented. This model is summarized in the graph (Fig. 1). Observe that only three lines are presented when, in fact, four could be obtained using all possible hypotension and ventricle categories. Only three lines are drawn because there was a close correspondence between the two lines for prediction of patients who had only one unfavorable condition. The midline between the two lines is shown.

For ICP greater than 25 mm Hg, the lines are shown as dashes. This is to indicate the increasing unreliability of the graph the closer the ICP is to 30 mm Hg. In the neighborhood of 30 mm Hg, the estimated chances of developing high ICP are likely to be much higher than that given by the graph, so these values should be read as “at least the value given by the graph.”

The graph is easy to use. For example, in an instant one can determine that a patient in hypotension with abnormal ventricles and a maximum ICP in the first 24 hours of 18 mm Hg has an estimated two-thirds chance of developing elevated ICP in the subsequent 48 hours.

**Discussion**

Although ICP monitoring has increasingly become part of the standard management of the patient suffering severe head injury, there are still a considerable number of neurosurgeons who continue to be reluctant to use it. This is in part because some patients who suffer such injuries will not have elevated ICP; consequently, there are questions as to the value of monitoring.

The performance of one-time measurements of either the initial intraventricular pressure or the subarachnoid pressure is impractical. The development of a noninvasive method to predict elevated ICP is important and highly desirable. While the method described here requires the determination of the initial ICP, it can yield an early prediction of the likelihood of sustained elevation of ICP in patients, with and without abnormal ventricles and a maximum ICP in the first 24 hours of 18 mm Hg has an estimated two-thirds chance of developing elevated ICP in the subsequent 48 hours.

**TABLE 4**

<table>
<thead>
<tr>
<th>Actual ICP</th>
<th>Predicted ICP: Training Group</th>
<th>Predicted ICP: Test Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>47.5% Cut Point</td>
<td>25.0% Cut Point</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>low</td>
<td>90</td>
<td>11</td>
</tr>
<tr>
<td>high</td>
<td>24</td>
<td>21</td>
</tr>
<tr>
<td>total</td>
<td>114</td>
<td>32</td>
</tr>
<tr>
<td>sensitivity</td>
<td>46.7%</td>
<td>84.4%</td>
</tr>
<tr>
<td>specificity</td>
<td>89.1%</td>
<td>62.3%</td>
</tr>
<tr>
<td>predictive value +</td>
<td>65.6%</td>
<td>50.0%</td>
</tr>
<tr>
<td>predictive value -</td>
<td>78.9%</td>
<td>90.0%</td>
</tr>
<tr>
<td>overall error rate</td>
<td>24.0%</td>
<td>30.0%</td>
</tr>
</tbody>
</table>

**FIG. 1.** Estimated percent change of a patient developing elevated intracranial pressure (ICP) by highest ICP during the first 24 hours, appearance of the ventricles, and systolic blood pressure (in mm Hg).
selected risk factors such as systemic hypotension and abnormal ventricles as demonstrated by CT scanning. On the basis of this predictive model, a patient whose highest ICP is 10 mm Hg and who has normal ventricles and a systolic blood pressure in excess of 90 mm Hg during the first 24 hours has a probability of less than 10% for developing an ICP greater than 30 mm Hg. Thus, in such a patient, invasive monitoring could be discontinued within a relatively short period of observation. In patients with adverse risk factors, however, the model indicates that monitoring should be continued for a longer period.

This demonstrates that multiple noninvasive variables can be used in conjunction with the level of ICP during the first 24 hours to develop a predictive index of the risk of developing intracranial hypertension. These observations are important, as Mayhall, et al, have recently shown that the length of time that ICP is continuously recorded by ventricular catheter correlates directly with the risk of infection. If a ventricular catheter is used to monitor ICP, the predictive model described here would have immediate clinical application.

It should be noted that some variables which are likely to be useful in prediction were not available during the development of this model, or their application in clinical practice was considered difficult. In the former instance, the appearance of the basal cisterns was only noted in the last group of patients collected (the test group) and thus, no training model could include it.

The predictive value of shift of brain structures noted on initial CT scanning is limited. The major problem is that some patients who undergo surgery for mass lesions have an unpredictable postoperative course in which the ICP is highly variable. Although a substantial number of these patients will develop intracranial hypertension, many will not. Consequently, shift, when considered alone, is not predictive because ICP is rarely measured in patients with operable lesions until after surgery.

The logistic model is clearly inadequate for ICP values close to 30 mm Hg since at this level the chance of high ICP must be 100%. The lines for each hypotension and ventricle group cross the 30-mm Hg line well below 100% (Fig. 1). Other mathematical functions will be tried in future work. Nevertheless, the logistic model should be of practical use because any patient with ICP close to 30 mm Hg (such as 25 to 30 mm Hg) will automatically be identified at high risk by the neurosurgeon, as well as by the logistic model. To obtain a sensitive method we advocate a conservative cut point as was used in Table 4 (25%). As a tool in patient management, a graph will be of greatest value for intermediate (5 to 20 mm Hg) values of ICP. For patients with ICP values less than 10 mm Hg and no other adverse predictors, the chances are less than 1 in 10 of developing high ICP. However, in a patient with an initial ICP of 10 mm Hg, a systolic blood pressure below 90 mm Hg, and abnormal ventricles as seen on CT, a substantially greater risk of developing later intracranial hypertension is present. This immediately indicates to the treating physician the need for an increased level of vigilance in such a patient.

The usefulness of hypotension as a predictor may be an indicator of the transitory nature of any prediction model. In the training group (excluding those with a highest ICP level of 30 mm Hg in the first 24 hours), 18% had hypotension. The corresponding value for the test group was 11%. Although this difference was not statistically significant, it suggests that as knowledge of the importance of hypotension became available, the Centers may have tried more vigorously to treat hypotension, either in the prehospital or the hospital phase. In summary, as the importance of any controllable predictor becomes known, the utility of that predictor may be reduced by good patient management, and therefore that factor will cease to be a significant predictor.

This graphic model may ultimately alter the time at which standard therapy for elevated ICP is instituted. If one takes, as an example, the patient with an initial ICP of 15 mm Hg but with small ventricles and a systolic blood pressure of less than 90 mm Hg, the graph estimates that the likelihood of developing an ICP of greater than 30 mm Hg is approximately 50%. Bellegarrigue and Ducker have hypothesized that earlier treatment of more modest elevations in ICP, namely at levels greater than 15 mm Hg, rather than waiting for the ICP to reach 25 mm Hg, may reduce the ultimate incidence of uncontrolled ICP. Given that fact, it might be logical to institute therapy earlier in patients who are known to be at high risk, based on this predictive model. In the future we intend to test this hypothesis.

Furthermore, recent evidence has suggested that ICP's as low as 18 to 20 mm Hg may be deleterious in some patients. Specifically, in patients with temporal lobe lesions there appears to be a substantially greater risk of herniation at relatively low pressures when compared to patients with high parietal or simple frontal lesions. Incorporating more information from the CT scan into such a predictive model may permit the identification of patients at greater risk and could lead to earlier institution of measures — either surgical or medical — to control ICP in such patients. Thus, a predictive model such as we have presented here could have substantial value in tailoring therapy to individual patients. This initial attempt has produced a graph which has immediate clinical application and demonstrates that the probability of developing better predictive indices of elevated ICP is substantial.

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