Relationship of “dose” of intracranial hypertension to outcome in severe traumatic brain injury

Clinical article

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Object. It has recently been suggested that the degree of intracranial pressure (ICP) above the treatment goal can be estimated by the area under the curve (AUC) of ICP versus time in patients with severe traumatic brain injury (TBI). The objective of this study was to determine whether the calculated “ICP dose”—the ICP AUC—is related to mortality rate, outcome, and Marshall CT classification.

Methods. Of 135 patients (age range 1–82 years) with severe TBI treated during a 5-year period at the authors’ institution, 113 patients underwent ICP monitoring (84%). Ninety-three patients with a monitoring time > 24 hours were included for analysis of ICP AUC calculated using the trapezoidal method. Computed tomography scans were assessed according to the Marshall TBI classification. Patients with Glasgow Outcome Scale scores at 6 months and > 3 years were separated into 2 groups based on outcome.

Results. Sixty patients (65%) had ICP values > 20 mm Hg, and 12 (13%) developed severe intracranial hypertension and died secondary to herniation. A multiple regression analysis adjusting for Glasgow Coma Scale score, age, pupillary abnormalities and Injury Severity Scale score demonstrated that the ICP AUC was a significant predictor of poor outcome at 6 months (p = 0.034) and of death (p = 0.035). However, it did not predict long-term outcome (p = 0.157). The ICP AUC was significantly higher in patients with Marshall head injury Categories 3 and 4 (24 patients) than in those with Category 2 (23 patients, p = 0.025) and Category 5 (46 patients, p = 0.021) TBIs using the worst CT scan obtained.

Conclusions. The authors found a significant relationship between the dose of ICP, the worst Marshall CT score, and patient outcome, suggesting that the AUC method may be useful in refining and improving the treatment of ICP in patients with TBI. (DOI: 10.3171/JNS/2008/109/10/0678)

Key Words • dose–response relationship • intracranial hypertension • intracranial pressure • secondary brain insult • severe head injury

Intracranial hypertension remains a major cause of death and disability in patients with TBI. Elevated ICP can lead to ischemia, cerebral herniation, and death. Current clinical guidelines recommend monitoring ICP in all patients with TBI who have GCS scores ≤ 8 and abnormal CT scan results.3,11 At most institutions the treatment goal is to avoid ICP > 20 mm Hg.3,9,11,12 However, intracranial hypertension above this value develops in about 45–80% of patients with TBI.12,15

Despite the widespread use of ICP monitoring, the precise threshold at which a patient requires treatment for ICP and the impact of the duration of intracranial hypertension remain unknown. The resurgence of decompressive craniectomy for the treatment of intracranial hypertension has focused new attention on the issue of optimal timing of surgery for ICP control.20 The authors of some previous studies have shown a relationship between intracranial hypertension and outcome,9,12,15,19 whereas others have not shown such a relationship,4 or found one only with the mortality rate.1

Although other methods have been used, the most commonly applied method for describing the degree of intracranial hypertension has been to calculate the mean

Abbreviations used in this paper: AUC = area under the curve; CPP = cerebral perfusion pressure; GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; ICP = intracranial pressure; ISS = Injury Severity Scale; TBI = traumatic brain injury.
Dose of intracranial pressure and outcome

ICP. In general, these methods are relatively crude and may not allow a precise determination of the effect of the physiological insult. Recently, secondary brain injuries have been characterized using a method that accounts for the cumulative extent and duration of these episodes. The method computes a “dose” of secondary brain injury as the cumulative AUC above, or below, a defined physiological threshold. This method more accurately reflects the impact of secondary brain insults on outcome than previous methods because it takes into account both the level and duration of the insult.

The aim of this study was to compute the “dose” of ICP above the treatment goal of 20 mm Hg in a group of patients with severe TBI and correlate this with outcome. We also compared the ICP dose to the Marshall CT Classification score that has previously been shown to correlate with the development of intracranial hypertension.

**Methods**

The neurosurgical department at the University Hospital of Trondheim, Norway, serves a population of 660,000 inhabitants in an area where most patients must be transported by air ambulance. Medical records from a 5-year period between January 1, 1998, and December 31, 2002, were reviewed to identify patients with severe head injuries (146 patients). Patients were included if they had GCS scores \( \leq 8 \) before sedation and intubation or later during testing. Patients with GCS scores \( > 8 \) before intubation were also included if the pupils were dilated and the CT scan showed worsening. In 11 patients the exact value of GCS score prior to intubation could not be determined, but the patients were unconscious and had scores \( \leq 8 \). Traumatic injury was demonstrated in all patients on CT scanning.

Patients with GCS scores of 3, bilaterally fixed and dilated pupils on admission, and CT confirmation of cerebral herniation were excluded if they were deemed clinically unsalvageable and no further treatment was performed (9 patients). Patients who died of other injuries within the first 24 hours after TBI were also excluded (2 patients).

**Treatment of Severe Head Injury and Intracranial Hypertension**

Because \( < 15\% \) of patients reach the emergency department at our hospital within 30 minutes, they usually undergo intubation and sedation in the field or at a local hospital prior to transfer. Air ambulances in Norway are staffed with experienced anesthesiologists who perform the initial neurological examination at the scene. If the initial CT scan at the receiving hospital does not indicate severe head trauma, sedation is discontinued so that a new neurological examination, and possibly extubation, can be performed.

During the study period, patients were routinely sedated with opiates and benzodiazepines, and their heads were elevated at 15–20°. The ICP goal was \( \leq 20 \) mm Hg and the CPP goal was \( \geq 60–70 \) mm Hg. Emergency surgery was performed in cases of mass lesions, and patients who received ventricular drainage usually drained continuously except during periods of ICP measurement.

Although the European Brain Injury Consortium guidelines for treatment of severe head injury were followed, no specific protocol-driven therapy using the staircase procedure for treatment intensity was instituted during the time of the study. Our standard treatment for patients who have an elevated ICP for \( > 5–10 \) minutes included head repositioning, increased sedation, alteration of ventilation, and optimization of blood pressure. If no decrease in ICP was observed, hyperosmolar intravenous therapy was then instituted. Patients were given mannitol (in 85% of the patients with elevated ICP in this study) or hypertonic saline (48%). Early in the study period, some patients (33%) also received steroids. Based on European Brain Injury Consortium guidelines published in 1997 this treatment has since been removed from our guidelines. Hyperventilation (\( < 4.5 \) kPa/35 mm Hg) and barbiturate coma (in 65% of patients) were used deliberately, and some patients were treated with hypothermia at \( < 35° \) (28%) or lumbar drainage of cerebrospinal fluid (8%). Large decompressive craniectomies were not used in our patient population, but medium-sized bone flaps were not always replaced after hematoma evacuation (15%). Since the end of the study period in December 2002, barbiturate coma, hypothermia, and lumbar drainage are seldom used because decompressive craniectomy is now the preferred treatment for intractable intracranial hypertension in our department.

In determining how many days the patients were treated for intracranial hypertension, we defined the end point as the day when treatment to reduce ICP was discontinued. Thus, the patients did not necessarily have increased ICP or undergo treatment every day during this interval.

**Intracranial Pressure Monitoring**

In 44% of patients, monitoring was done with an intraparenchymal ICP monitoring device (Codman or Spiegelberg sensor), in 20% it was done through the external ventricular drain, and both methods were used in 36% of patients. If values from both devices were available, the values from the intraparenchymal device were normally presented. The zero level for external drainage was set at the level of the foramen of Monro.

The hourly data entry records kept by the bedside nurse were used, and the highest value was chosen if multiple values were recorded per hour. All values related to procedures were excluded. If a value was missing, the previous value or the value nearest in time was used. Intracranial pressure was usually monitored for 1–3 days after it seemed to have stabilized below 20 mm Hg and the patients were no longer sedated. Sedation was prolonged in some patients due to pulmonary complications.

Eighteen patients were excluded from the study for the following reasons: ICP monitoring started \( > 72 \) hours postinjury; ICP monitoring time \( < 24 \) hours; inadequate records for the patient available for \( > 24 \) hours; technical problems occurred with the ICP device; or the time of injury was unknown.

**Area Under the Curve and ICP Dose**

The trapezoidal method was used to calculate the
AUC from a graph of ICP versus time (Fig. 1). The AUC where the 20-mm Hg threshold is exceeded represents the ICP “dose.”

We did not include values recorded after CPP progressively started to decrease below 40 mm Hg or if ICP progressively increased above 50 mm Hg to exclude terminal data (in patients dying of severe intracranial hypertension). However, to avoid including patients with only a few values, 1 patient with < 12 values collected before terminal data was excluded. Thus, 93 patients fulfilled the inclusion criteria.

The patients were divided into 4 groups depending on the “dose,” or amount, of ICP measured above the treatment goal of 20 mm Hg: no dose (0 mm Hg*hour), low dose (> 0–75 mm Hg*hour), moderate dose (> 75–200 mm Hg*hour), and high dose (> 200 mm Hg*hour). For example, a value of 75 mm Hg*hour corresponds to values of 25 mm Hg during 15 hours, and a value of 200 mm Hg*hour to values of 30 mm Hg during 20 hours.

Marshall Head Injury CT Classification

The Marshall CT classification for TBI was developed to identify patients at risk for intracranial hypertension and poor outcome. A neuroradiologist and a neurosurgeon trained in Marshall classification reviewed the CT scans. In each patient, both the first and worst CT were used in this study. Hematoma volume calculations were obtained by multiplying length × width × height and dividing the product by 2. If multiple hematomas were present, the sum was calculated.

Outcome Assessment

A trained rehabilitation physician who was not involved in the acute care of the patients collected GOS scores at 6 months after the injury from medical records and follow-up interviews. Long-term GOS scores were prospectively collected in structured interviews conducted > 3 years postinjury by direct contact or telephone interview with the patient and/or relatives. One patient who died of another disease < 6 months after the head injury was not included in the outcome analysis; 2 patients who died during the first year of other causes not related to TBI were only included in the 6-month outcome analysis; and in 1 patient who died in a new accident, the GOS score at 23 months was used for long-term GOS score. The GOS scores were divided into poor (1–3) and favorable (4–5) outcomes.

The Regional Committee for Medical Research Ethics, Health Region IV, Norway, approved the study.

Statistical Analysis

Patient demographics and injury characteristics are presented as percentages, both median and range. Nonparametric tests were used for categorical data and for the ICP AUC because it was not normally distributed: Kruskal–Wallis for > 2 groups, followed by the Mann–Whitney U-test.

Logistic regression analysis was performed with the following admission variables and ICP AUC as explanatory variables, and poor outcome as the dependent variable: the GCS score before intubation, age (listed in 10-year categories), ISS score, pupillary abnormalities (normal vs unilateral or bilateral dilation), and ICP AUC (values divided by 10). In the multiple regression models we added the relevant variables with a significance level < 0.10. All tests were considered statistically significant at a probability value < 0.05.

Results

The characteristics of the 93 patients who met the inclusion criteria are presented in Table 1. The median age was 34 years, and most patients were male (81%) and had been injured in traffic accidents (49%). Five patients had GCS scores > 8 before intubation, but their conditions later deteriorated to ≤ 8; 31% had pupillary abnormalities on admission.

Intracranial Pressure Dose Estimated by ICP AUC

The median time until the start of ICP monitoring was 9 hours (range 3–66 hours). In 3 patients the monitoring was started 48 hours postinjury, but all 3 had long monitoring times exceeding 6 days, and eventually died of intractable intracranial hypertension. The median monitoring time was 10 days (range 1–28 days). Treatment of increased ICP was stopped, on average, 9 days postinjury.
Dose of intracranial pressure and outcome

TABLE 1
Demographics and injury characteristics in 93 patients*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>female/male ratio</td>
<td>18:75</td>
</tr>
<tr>
<td>median age in yrs (range)</td>
<td>34 (1–82)</td>
</tr>
<tr>
<td>mechanism of injury</td>
<td>45 (49)</td>
</tr>
<tr>
<td>traffic accident</td>
<td>33 (36)</td>
</tr>
<tr>
<td>fall</td>
<td>3 (3)</td>
</tr>
<tr>
<td>assault</td>
<td>7 (8)</td>
</tr>
<tr>
<td>other</td>
<td>5 (5)</td>
</tr>
<tr>
<td>median GCS score before intubation (range)</td>
<td>6 (3–14)</td>
</tr>
<tr>
<td>pupillary abnormalities</td>
<td>19 (21)</td>
</tr>
<tr>
<td>unilat dilation</td>
<td>9 (10)</td>
</tr>
<tr>
<td>median ISS score (range)</td>
<td>25 (9–50)</td>
</tr>
<tr>
<td>median NISS score (range)</td>
<td>41 (9–75)</td>
</tr>
<tr>
<td>traumatic SAH</td>
<td>56 (60)</td>
</tr>
<tr>
<td>multiple contusions</td>
<td>41 (44)</td>
</tr>
<tr>
<td>worst Marshall CT Category</td>
<td>23 (25)</td>
</tr>
<tr>
<td>2</td>
<td>21 (23)</td>
</tr>
<tr>
<td>3</td>
<td>3 (3)</td>
</tr>
<tr>
<td>5 (surgery on a mass lesion)</td>
<td>46 (50)</td>
</tr>
</tbody>
</table>

* Values represent number of patients unless otherwise indicated. Values in parentheses are percentages unless otherwise indicated. Abbreviation: NISS = New Injury Severity Scale; SAH = subarachnoid hemorrhage.

(range 1–16 days). One patient continued to receive treatment until the 25th day postinjury.

The ICP AUC values were calculated and the patients were divided into 4 groups (see Methods): 33 had no ICP dose (36%), 26 had low dose (28%), 18 had a medium dose (19%), and 16 had a high dose (17%). The relationship between ICP AUC and mean ICP values is presented in Fig. 2. All but 3 patients had mean ICP values ≤ 20 mm Hg.

Marshall Head Injury CT Classification and ICP Dose

The patients were divided according to their Marshall CT classification (Categories 2–5) based on analysis of their worst CT scan (Table 1). Fifty-six percent of the patients with Marshall Category 2 TBIs had an ICP dose > 20 mm Hg (> 0 mm Hg*hour), 71% of patients with Marshall Category 3 had a dose of elevated ICP, and 100% with Category 4 had an increased dose of ICP. Of patients with Marshall Category 5 injuries (evacuated mass lesions), 63% had an elevated ICP dose. Due to the low number of patients with Marshall Category 4 head injuries, the data in these patients were analyzed together with those with Category 3 TBIs. There was a significant difference between ICP AUC in the patients with Marshall Category 3 and 4 TBIs (130 mm Hg*hour, range 0–753 mm Hg*hour) compared with Category 2 (9 mm Hg*hour, range 0–431 mm Hg*hour; p = 0.025) and Category 5 (27 mm Hg*hour, range 0–423 mm Hg*hour; p = 0.021). Five patients had a first CT scan of Marshall Category 2 with subsequent worsening to Category 3 or 4. There was no significant difference between the ICP AUC in the Marshall classification groups based on the first CT scan (p = 0.191).

Dose and Patient Outcome

Twelve patients died of intractable intracranial hypertension between Days 2 and 15 postinjury. Nine other patients died of sequelae after head injury. Thus, the 6-month mortality rate was 23%. As shown in Table 2, the dose of ICP was an independent predictor of death in a multiple regression analysis (p = 0.035).

Outcomes of patients in groups of different ICP AUC are presented in Fig. 3. Patients with a poor outcome at 6 months had a significantly increased ICP AUC compared to patients with a favorable outcome (42 mm Hg*hour, range 0–753 mm Hg*hour vs 2 mm Hg*hour, range 0–431 mm Hg*hour; p = 0.045). A multiple regression model also demonstrated AUC as an independent predictor of poor outcome, after adjusting for GCS score, age, pupillary abnormalities, and ISS score (p = 0.034, Table 2).

Long-term outcome (median follow-up 62 months) was not significantly associated with ICP AUC (p = 0.157, Table 3). Ten of 31 patients with a GOS score of 3 at 6 months, improved to GOS score 4 at long term. There was a tendency

**TABLE 2**
Multiple logistic regression of admission variables and ICP AUC with poor outcome or death as the dependent variable*

<table>
<thead>
<tr>
<th>Variable</th>
<th>GOS Score at 6 Months</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>1.05</td>
<td>1.003–1.10</td>
<td>0.034</td>
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</tr>
<tr>
<td>GCS score</td>
<td>0.74</td>
<td>0.57–0.96</td>
<td>0.022</td>
<td></td>
</tr>
<tr>
<td>pupillary abnormality age</td>
<td>4.66</td>
<td>1.16–18.70</td>
<td>0.030</td>
<td></td>
</tr>
<tr>
<td>ISS score</td>
<td>1.04</td>
<td>0.97–1.11</td>
<td>0.294</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mortality Rate</th>
<th>OR</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>1.04</td>
<td>1.003–1.10</td>
<td>0.035</td>
<td></td>
</tr>
<tr>
<td>GCS score</td>
<td>0.76</td>
<td>0.57–1.02</td>
<td>0.070</td>
<td></td>
</tr>
<tr>
<td>pupillary abnormality age</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>ISS score</td>
<td>1.45</td>
<td>1.07–1.95</td>
<td>0.015</td>
<td></td>
</tr>
</tbody>
</table>

* An odds ratio > 1 increases probability of poor outcome or death; an odds ratio < 1 decreases probability of poor outcome or death. Abbreviations: CI = confidence interval; NA = not applicable; OR = odds ratio.
for these patients to have a higher ICP AUC than the patients that continued to have a GOS score of 3 (98 mm Hg*hour, range 0–753 mm Hg*hour versus 17 mm Hg*hour, range 0–529 mg Hg*hour; p = 0.066). In the group of 10 patients that improved, none had bilateral dilated pupils on admission. In the group of patients that did not improve, 5 of these had such pupil abnormalities and no or low AUC.

**Discussion**

In this study we demonstrate a significant relationship between ICP “dose” above the treatment goal, measured by AUC, and outcome and mortality rate at 6 months. There are several studies on intracranial hypertension and outcome, and some authors have observed a relationship,\(^9\)\(^12\)\(^19\) while others have not.\(^1\)\(^4\)\(^17\) The diverging results are probably dependent on the method of calculating the ICP dose and other methodological issues, such as differences in inclusion criteria of patients for monitoring, differences in exclusion of patients with low monitoring times, and exclusion of terminal data for patients who die after herniation. Finally, standard outcome measures for TBI are crude and may vary.

We chose to use the AUC method, because it takes into account both the level of ICP insult as well as the duration of the ICP increase.\(^2\) The concept of a “dose” of secondary insult is clinically intuitive and has been applied to several types of secondary brain injuries. In a recent study by Hemphill et al.\(^6\) the method seemed to better demonstrate a relationship to outcome in head-injured patients with hypotension than when only events were counted. Others have also tried to include both the level of the elevated ICP and the duration in estimates of the degree of intracranial hypertension. Resnick et al.\(^17\) used peak ICP, mean ICP, and the percentage of time with elevated ICP, whereas Elf et al.\(^5\) counted the number of insults above a certain ICP level and the time spent within the insult threshold divided by good monitoring time. Good monitoring time was calculated by subtracting the data judged to be invalid for various reasons from the total monitoring time. Furthermore, Marmarou and associates\(^12\) used proportions of ICP measurement > 20 mm Hg and mean ICP. However, in contrast to the previously mentioned methods, the method of calculating the AUC combines all of this information in 1 value as a summary measure. One objection to such a summary measure could be that patients with shorter pressure peaks > 30 mm Hg might have the same ICP AUC as patients with values in the range of 21–25 mm Hg for longer periods of time. By choosing higher thresholds as 25 mm Hg or 30 mm Hg, it is easy to recalculate the ICP AUC. Thus it is possible to analyze the importance of different thresholds for outcome. In a similar manner the CPP AUC can be calculated, and different thresholds can be used.

The ICP AUC was not a predictor of long-term outcome. This is in agreement with some other studies in which ICP increase was related to 1-year outcome.\(^5\)\(^17\) However, in the study of Resnick et al.\(^17\) only 37 patients with prolonged intracranial hypertension were included. In most previous studies the 6-month outcome is presented, but we know that patients can improve after the initial 6 months such that those from the severe disability group may change to the moderate disability group.\(^1\) This fact could explain why a significant relationship was not observed at long-term follow-up. Interestingly, we observed that patients who did not improve had a lower ICP dose than those who did, although this difference did not reach statistical significance. Firsching et al.\(^5\) have argued that brainstem lesions detected on MR imaging are a strong predictor of outcome. These lesions might be primary lesions as well as secondary after herniation because of late surgery of a mass lesion. Such patients may have a CT scan without compressed basal cisterns and midline shift and no development of severe intracranial hypertension.\(^5\) Thus they might have a poor outcome despite a low ICP dose.

The estimated ICP dose related significantly to the Marshall worst classification but not to the first CT scan. Servadei et al.\(^18\) suggested that 1 of 6 patients with a diffuse injury will demonstrate significant CT evolution and argued that worst CT should be recommended in clini-

![Fig. 3. Graph demonstrating the number of patients with favorable and poor outcomes at 6 months in 4 groups with different doses of ICP AUC: no dose (0 mm Hg*hour), low dose (> 0–75 mm Hg*hour), moderate dose (> 75–200 mm Hg*hour), and high dose (> 200 mm Hg*hour).](image-url)
Dose of intracranial pressure and outcome

cal studies of moderate and severe head injury. Poca et al. also reclassified their Marshall classification in their study, but they thereby sometimes changed from a worst CT to a better CT scan. They found an increased risk of high ICP for patients with Marshall classifications 3, 4, 5, and 6. In our study, when comparing ICP AUC, patients with Category 5 injuries did not seem to be at high risk of intracranial hypertension compared to patients with Categories 3 and 4. To evaluate the estimated ICP dose it would be more appropriate to use the worst classification, and thus it is not surprising to find that the initial CT did not relate to ICP dose. In a recent study, Hiler et al. showed that the initial CT scan in patients with TBI correlated significantly but weakly to ICP during the first 24 hours of monitoring, but not to mean ICP over the total time of intensive care. The fact that we calculated a higher ICP dose in patients with Marshall worst classification Categories 3 and 4 compared with Categories 2 and 5 could support the use of ICP AUC to estimate the dose of intracranial hypertension in patients with severe head injury.

Only patients with monitoring times > 24 hours were included in our study to avoid a small individual sample size for these analyses. Some studies have included patients with short monitoring times: > 6 hours and > 12 hours, whereas Marmarou et al. and Elf et al. included only patients with monitoring times > 42 and 54 hours, respectively. In the latter study the authors also excluded the records obtained in the last 24 hours in patients who died after herniation and found that ICP insults did not predict outcome. A large number of patients who die after herniation will influence the prediction of a dichotomized outcome if high ICP values in the terminal phase are included in the analysis. Therefore, we also excluded terminal data. However, we did not want to exclude values between 30 and 50 mm Hg before the obvious increase of ICP during herniation. Therefore, for most patients the excluded values were < 24.

In our study 84% of the treated patients with severe TBI underwent ICP monitoring, but only 65% of monitored patients needed treatment of intracranial hypertension. Several other outcome studies have reported a higher percentage of patients with intracranial hypertension, probably due to the selection of patients for ICP monitoring and the fact that continuous data collection might reveal shorter episodes of ICP > 20 mm Hg that can be missed when hourly recorded values are recorded. All patients with an ICP AUC > 0 received treatment to avoid severe intracranial hypertension, and most patients received this treatment for a long period of time. Thus, the ICP dose would probably have been increased for many patients without treatment, as also noted by Elf et al. in their study. Five of our patients died of intracranial hypertension > 8 days after the injury, and Unterberg et al. also showed that more than one-third of the patients had delayed intracranial hypertension or long-lasting elevation of ICP. These authors argued that monitoring should be prolonged because ICP elevations may develop in patients after the initial 3–4 days. Thus, the monitoring time is important in calculating the ICP dose to predict the outcome, and a long monitoring time explains why most of our patients had a mean ICP < 20 mm Hg despite having large ICP AUC values.

There are limitations in the present study because it is a retrospective study and the number of patients is limited. However, the long-term outcome data were prospectively collected.

Furthermore, the ICP registrations are manually collected hourly, a method that still is the most used in clinical practice. We used peak values during the hourly registration if > 1 value was recorded. Hemphill and colleagues compared the results of secondary insults by the use of AUC when ICP was measured every minute via a custom data acquisition system, and when ICP was calculated from the medical records, usually recorded hourly. These hourly records tended to underestimate the number of total events and consequently the AUC. However, the trapezoidal interpolation we used to calculate AUC seemed to be the best method for the hourly records. Thus, our calculated ICP AUC is a first approximation of the true AUC. In addition, it would also be of interest to calculate the CPP AUC. Although the focus of our study was the ICP AUC and its relationship to the Marshall brain injury classification and patient outcome, future studies should explore the utility of calculating the “dose” of other physiological and laboratory variables such as CPP, temperature, and serum glucose. It should also be noted that the stratification of the dose of ICP in this study was arbitrarily defined and therefore may not have been the optimal breakpoints, but it does illustrate the potential of this measure to predict clinical outcome. Further studies with additional patients and more data will be required to better determine AUC thresholds using techniques such as receiver operating characteristic curves.

Conclusions

We found a significant relationship between the dose of intracranial hypertension measured by ICP AUC, mortality rate, and 6-month outcome. A relationship between ICP dose and the worst Marshall CT classification was also observed, giving further support to the use of this method for evaluating TBI. Our results suggest that this method may be useful in refining and improving the treatment of ICP in patients with TBI, and therefore prospective studies using high frequency data (1-minute measurements) should be performed to further determine the utility of the concept.

Disclosure

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