Impact of ICP instability and hypotension on outcome in patients with severe head trauma

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This study describes the relationship between raised intracranial pressure (ICP), hypotension, and outcome from severe head injury. The study is based on information derived from the Traumatic Coma Data Bank where ICP records from a relatively large number of patients were available to help delineate the major factors influencing outcome. From the total data base of 1030 patients, 428 met minimum monitoring duration criteria for inclusion in the present analysis. Outcome was classified according to the Glasgow Outcome Scale score determined at 6 months postinjury. Arrays of comparably defined summary measures describing the patient's course were considered for ICP, blood pressure (BP), central perfusion pressure, and therapy intensity level. For instance, the array of ICP summary descriptors included the proportion of ICP readings greater than x, for x = 0 to 80 mm Hg by increments of 5 mm Hg. A total of 187 candidate summary descriptors were considered. A stepwise ordinal logistic regression was used to select the subset of candidate summary descriptors that best explained the 6-month outcome.

As established previously, age, admission motor score, and abnormal pupils were each highly significant in explaining outcome. Beyond these factors, the proportion of hourly ICP readings greater than 20 mm Hg was next selected and was also highly significant in explaining outcome (p < 0.0001). In addition to the ICP factor, the cutoff point of 20 mm Hg was selected by the procedure as most indicative of outcome. With these four factors modeled, the next selected factor was the proportion of hourly BP readings less than 80 mm Hg. Again, the BP factor was highly significant in explaining outcome (p < 0.0001). As with the ICP factor, the BP cutoff point of 80 mm Hg was objectively selected as most indicative of outcome. In summary, the incidence of mortality and morbidity resulting from severe head trauma is strongly related to raised ICP and hypotension measured during the course of ICP management. Moreover, these ICP and BP factors provide a better indication of outcome than the similarly defined factors of central perfusion pressure or therapy intensity level.

KEY WORDS • Traumatic Coma Data Bank • head injury • coma • outcome • intracranial pressure • blood pressure

Recent studies have linked sustained high levels of ICP with high rates of morbidity and mortality.16,21,26 Such studies support the notion among some investigators that aggressive treatment of ICP is essential to reduce the risk of mortality and improve neurological outcome.
in severe head trauma. Yet, other investigators question the emphasis of treating raised ICP and maintain that treatment should focus on factors related to brain ischemia.\(^{27,28}\) Sustained elevation of ICP may have direct effects upon the neural tissue despite adequate perfusion.

It is difficult to directly measure the putative influence of raised ICP and ischemia on outcome because of the multiplicity of other factors involved. Age, admission motor score (derived from the Glasgow Coma Scale\(^{29}\) score), and admission pupillary response have been shown to be good predictors of outcome.\(^5\) The presence of a mass lesion and other secondary insults such as shock or hypoxia superimposed on the primary structural damage may also contribute to prognosis.\(^{19}\) Furthermore, an array of treatment strategies may be involved with varying success. Except for age and treatment, these factors are interrelated indicators of severity of either initial or secondary injury.

This investigation attempts to more precisely describe the relationship of raised ICP and other factors to outcome by attempting to simultaneously account for effects of age and initial injury severity. The study sample is taken from the Traumatic Coma Data Bank (TCDB) where relatively large numbers of patients are available to help delineate the major factors influencing outcome.

**Clinical Material and Methods**

**Clinical Material**

The TCDB contains data on 1030 patients with severe head trauma. Pertinent characteristics of these patients have been described more fully by Foulkes, et al.\(^8\) In this study, we excluded patients who arrived brain-dead, patients with gunshot wounds, and those with monitoring durations of less than 4 hours. Monitoring duration in the remaining 654 patients ranged from 4 hours to more than 10 days.

The variability in monitoring duration poses a problem in precisely assessing raised ICP. An assessment based on many hours of monitoring is expected to be more precise than an assessment based on only a few hours of monitoring. The problem is further complicated by the fact that monitoring duration is related to the patient’s severity of injury. Therefore, we set minimum monitoring criteria designed to assure a reasonably precise assessment of raised ICP. Monitoring must have begun before 18 hours postinjury and must have continued through at least 60 hours postinjury. These criteria defined a reasonable clinical sample for assessing treatable ICP. They assured a minimum of 42 hourly ICP observations per patient, measured during an early postinjury critical period of treatment opportunity. Of the 654 patients available for ICP analysis, 428 met the minimum monitoring criteria.

**Patient Assessment**

All patients analyzed in this subsample were managed according to the protocol detailed previously.\(^4\) Information on early postinjury neurological assessment was gathered in the TCDB hospital emergency room after cardiopulmonary stabilization.

The 6-month outcome was classified according to the five Glasgow Outcome Scale\(^{13}\) (GOS) ordinal categories: good recovery, moderately disabled, severely disabled, vegetative, or dead. For the surviving patients, the GOS score was determined at follow-up neurological examination which was scheduled as close as possible to exactly 6 months postinjury (the allowable time window ranged from 4 to 8 months postinjury).\(^8\) The GOS vegetative and dead categories were combined because the vegetative patients were quantitatively indistinguishable from the dead patients.

The management protocol for the TCDB sample included hourly measurements of ICP and blood pressure (BP). In brief, ICP was defined as the digitally averaged ICP indicated on the bedside monitor and recorded by a nurse at the end of each hour. An analogous technique was used to record “end-hour” BP. The 24-hour day was subdivided into six 4-hour “blocks” for assessment of the therapy intensity level directed toward ICP management.\(^4,16\)

**Statistical Methods**

The intensive care unit (ICU) management protocol results in a plethora of data for each patient. There is no general agreement as to an optimum list of ICP descriptors or of other factors collected during ICU management, with regard to quantiative description or frequency of sampling. In this study, a number of summary measures were developed to describe the patient’s course. These descriptors include counts of various events of putative importance with means and variability measures, each defined over the patient’s entire course of ICU monitoring. Our approach has been to consider all of these newly defined descriptors as candidates for outcome indicators.

Since monitoring duration varies across patients, proportion measures were obtained by dividing each count measurement by the number of hours monitored. Sixteen descriptive measurements were defined as the proportion of ICP measurements greater than \(x\), for \(x = 0\) to 80 mm Hg by increments of 5 mm Hg. For therapy intensity level, 14 measures were defined as the proportion of therapy intensity level measurements greater than \(x\), for \(x = 0\) to 14 by increments of 1. For central perfusion pressure (CPP), 24 measurements were defined as the proportion of CPP measurements above \(x\), for \(x = 0\) to 120 mm Hg by increments of 5 mm Hg. For BP, two arrays of summary variables were defined. The upper array was defined as the proportion of time BP was greater than \(x\), for \(x = 120\) to 200 mm Hg by increments of 5 mm Hg. It was intended to measure the detrimental effect of hypertension. The lower array was defined as the proportion of time BP was lower than \(x\), for \(x = 120\) to 20 mm Hg by increments of 5 mm Hg. This calculation measured the detrimental effect of hypotension.
Descriptive measurements based on means were created analogous to each of the proportion measurements for ICP, BP, therapy intensity level, and CPP. For example, 17 descriptors were defined as the mean of all ICP measurements greater than x, for x = 0 to 80 mm Hg by increments of 5 mm Hg. These means assessed the magnitude of ICP elevations as well as their frequency. For ICP, BP, therapy intensity level, and CPP, the summary measurements assessing variability were the variance of all of each patient’s hourly measurements, the maximum observed, and the minimum observed.

In addition to this extensive list of candidate regressors we added gender, presence of intracranial lesion, whether surgery was performed for an intracranial lesion, admission hypoxia, and admission hypotension. In total, 187 candidate regressors were included in the analysis.

A stepwise ordinal logistic regression procedure was used to select a subset of the candidate descriptors that best explained the 6-month ordinal outcome in our ICP-monitored subsample. Previous reports have indicated that age, admission motor score, and admission pupillary response (number of abnormal pupils) are good predictors of the 6-month outcome. The motor score and abnormal pupils variables provide a crude indication of the severity of the initial injury. The age variable may reflect the biological capability for recovery from such a severe trauma. We forced these variables into each putative model considered by the logistic regression procedure. Thus, the analysis actually considers each of the candidate descriptors to discern which provide additional information about outcome beyond what is available from admission motor score, and abnormal pupils.

The logistic regression analysis assumes that each descriptor affects outcome at the same rate over its entire range. That is, the logistic transform of the outcome probability is modeled as a linear function of each included descriptor. This assumption was checked using empirical plots of group outcome proportions versus each descriptor.

### Results

**Description of Patients in ICP Study**

The study group included 428 patients (75% males) admitted to the TCDB in whom ICP was monitored within 18 hours postinjury and continued at least through 60 hours postinjury. The primary diagnosis included 202 (47%) patients with surgical mass lesions (Table 1). Duration of ICP monitoring ranged from 42 to over 240 hours among the 428 patients. Approximately 50% of the patients were monitored for 5 days or more.

The age range for the 428 patients in this analysis was 1 to 85 years and 33% of the patients were young adults aged between 20 and 30 years. The full range of admission motor scores was represented, but only 10 patients followed commands on admission. Forty percent of patients presented with both pupils abnormal and 10% with one pupil abnormal. Normal pupils were observed in 40% of the sample, and the remaining 10% of pupil responses were not recorded.

**Outcome**

About 32% of the 428 patients in this analysis had favorable outcomes (good or moderate disability) while 49% had poor outcomes (severe disability, vegetative, or dead). In 20% of the group, the 6-month outcome was not available; most of these patients were ineligible for follow-up review because of institutionalization. A small number of patients missed the 6-month follow-up window for scheduling reasons, or their whereabouts were unknown.

The cumulative effect of missing data reduced the number of patients available for analysis of outcome to 295. Examination of histograms for age, admission motor score, abnormal pupils, and outcome correlated with missing data status revealed no trends to distinguish those patients with missing data from those with complete observations.

**Modeling Results**

The logistic regression assumption was reasonably well satisfied for each of the initial descriptors, except for age. There was an apparent discrepancy for ages between about 18 and 24 years, where the outcome-age relationship was more severe than would be expected with the linear relationship exhibited by the remainder of the sample. An exploratory search seemed to rule out alcohol and mechanism of injury as possible explanations. We elected to model age without transformation.

**Outcome and ICP**

Age, admission motor score, and abnormal pupils on admission were each highly significant in explaining outcome in the sample (p < 0.0001). Beyond these variables, the proportion of ICP measurements greater
greater than 20 mm Hg (denoted "p(ICP > 20)") was then selected (Fig. 1). This factor was also highly significant in explaining outcome (p < 0.0001). With these four regressors modeled, the next selected factor was the proportion of BP measurements below 80 mm Hg (denoted "p(BP < 80)"). The p(BP < 80) factor was also highly significant (p < 0.0001) (Fig. 2). With these five factors modeled, no other candidate regressor offered substantial additional information about outcome.

In addition to the p(ICP > 20) descriptor being the best of the candidate descriptors for explaining outcome, it is also interesting to note that the explanatory power* of the ICP proportion variables peaked at 20 mm Hg and was less for all other cutoff points. This result suggests that detrimental effects of ICP elevation occur at levels around and above 20 mm Hg.

An analogous situation existed at the second step, where p(BP < 80) was selected. Among the p(BP < x) descriptors, the explanatory power peaked at 80 mm Hg and was less for all other cutoff points. This finding suggests that detrimental effects of compromised BP occur at levels around and below 80 mm Hg.

Table 2 shows the parameter estimates and associated summary statistics for the five-factor model. It can be seen from the parameter estimates that higher values of age, admission abnormal pupils, p(ICP > 20), and p(BP < 80) are each associated with more severe outcome; while higher admission motor scores are associated with less severe outcome.

Estimated outcome probability versus p(ICP > 20) is plotted in Fig. 3 for each outcome group. To simplify the presentation, the other modeled factors were fixed at the following values: age = 30 years, admission motor score = 3 (flexion), abnormal pupils = 1, and p(BP < 80) = 0. Ninety-five percent asymptotic confidence

* "Explanatory power" is defined as the magnitude of the score statistic adjusted for the factors already modeled.
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![Graphs](Image)

**FIG. 3.** Plots of estimated outcome probability versus proportion of intracranial pressure measurements more than 20 mm Hg (p(ICP > 20)) for each outcome group. To simplify the presentation, the other modeled factors were fixed at the following values: age = 30 years, admission motor score = 3 (flexion), abnormal pupils = 1, and proportion of blood pressure measurements less than 80 mm Hg (p(BP < 80)) = 0. Ninety-five percent asymptotic confidence bands are plotted around each curve.

bands are plotted around each estimated outcome probability curve. Note that the vertical axis intercept identifies the estimated outcome probability when p(ICP > 20) = 0 also. In general, as p(ICP > 20) increases, more favorable outcomes (good or moderate disability) become less likely while worse outcomes (vegetative or dead) become more likely.

Figure 4 shows the additively modeled relationship of both p(ICP > 20) and p(BP < 80) on the estimated probability of a vegetative/dead outcome. This figure represents three dimensions. The substantial effect of hypotension is readily evident from the front-to-back upward sloping of the surface. The impact of ICP elevation is apparent from the right-to-left upward sloping of the surface.

**Discussion**

Our results suggest that the mortality and morbidity resulting from severe head trauma are strongly related to raised ICP and hypotension. In addition to the *a priori* modeled factors of age, admission motor score, and admission pupillary response, a total of 187 candidate descriptors of outcome defined by the GOS were considered in the stepwise analysis. As expected, age, admission motor score, and admission pupillary response were highly significant in explaining outcome.

Modeled alone, these three factors correctly explained 46% of the observed outcomes. Beyond these three, the factor most indicative of outcome was the proportion of ICP measurements greater than 20 mm Hg (p < 0.0001). Although critical ICP levels from 0 to 80 mm Hg in increments of 5 mm Hg were tested, the ICP level of 20 mm Hg emerged with the highest level of significance. This finding suggests that the detrimental effects of ICP elevation occur above the 20 mm Hg level. With the p(ICP > 20) factor added to the model, the next most indicative measure of outcome was the proportion of BP measurements less than 80 mm Hg (p < 0.0001). Again, low BP critical levels from 120 to 20 mm Hg in increments of −5 mm Hg were available as candidates. Yet, the BP level of 80 mm Hg emerged with the highest level of significance. The implication is that the detrimental effects of hypotension occur below the 80-mm Hg BP level. The full model with age, admission motor score, admission pupillary response, p(ICP > 20), and p(BP < 80) correctly explained 53% of the observed outcomes.

As stated earlier, the variability in monitoring duration caused problems in the analysis because the monitoring duration tends to be related to the patient's severity of injury. Patients with shorter monitoring duration tended to those who died shortly after admission. Patients with an intermediate monitoring duration tended to those less severely injured who
never evidenced ICP problems and whose ICP catheters were removed early to reduce infection risk. Longer monitoring durations occurred in patients with ICP instability either early in their clinical course or as a result of secondary injury. Patients in the first group typically have too few ICP values for reliable assessment of ICP instability. The minimum monitoring criteria used to define the patient sample helped to assure reliable assessment of ICP instability, yet selectively removed more of the early deaths. This consequence may be desirable because the resulting patient sample contains those whose injury allows reasonable time for ICP treatment.

This work began with reducing the tremendous volume of hourly monitoring data available for each patient. A patient monitored for 5 days produced 120 hourly observations for ICP, BP, and CPP, as well as 30 4-hour block measurements of therapy intensity level. Each patient’s ICP variance descriptor was simply the sample variance of all the hourly ICP observations. This was considered an indirect measure of the patient’s volume/pressure stability; however, it was only poorly related to outcome.

It was interesting that therapy intensity level measurements were not significantly related to outcome in this analysis. It seemed logical that the intensity of therapy directed toward ICP management should be maximum in patients with a tight brain and predisposed to ICP elevation and instability. However, since a uniform management protocol for the severely head-injured patient was not adopted within the TCDB, this hypothesis could not be adequately addressed. For example, the thresholds for initiation of ICP treatment varied among the TCDB centers from 15 to 25 mm Hg. Furthermore, some of the centers were engaged in randomized clinical trials applying therapies that could affect ICP. With a uniform study plan, we would expect that the therapy intensity level association with outcome would be apparent, as shown by Maset, et al. These investigators showed a close association between therapy intensity level and ICP. From their data, the temporal course of therapy intensity level and ICP in a hospital-based sample was closely linked during the first 5 days postinjury. A comparable measure of the proportion of time therapy intensity level is above a set threshold might be the feature of choice for such an analysis.

Despite the wide application of ICP monitoring in the neurosurgical ICU, relatively few studies have addressed the relationship between ICP and outcome. Miller, et al., were among the first to report on the influence of ICP upon outcome in head-injured patients. Normal ICP in their study was defined as 10 mm Hg or less. In their series of 160 patients, 39% had mass lesions and 61% had diffuse brain injury. The main ICP feature selection included the ICP level upon admission and whether ICP exceeded 20 mm Hg at any time in the 5 days postinjury. Among patients in whom ICP remained below 20 mm Hg, a favorable outcome (good or moderate disability) was observed in 77%; in contrast, only 47% of the patients had favorable outcomes when ICP exceeded 20 mm Hg but was controlled. In a later expanded series of 225 patients, these investigators confirmed the significant correlation between raised ICP and poor outcome and extended the analysis to several other clinical variables. The contribution of ICP alone was not considered in their analysis.

Marshall, et al., utilized thresholds of 15 and 40 mm Hg to describe the ICP in a series of 100 head-injured patients. Normal ICP was defined as an ICP less than 15 mm Hg. They observed a favorable outcome in 77% of the patients with no mass lesion and an ICP less than 15 mm Hg. In contrast, only 37% of patients in that study with ICP exceeding 40 mm Hg for 15 minutes or more had favorable outcomes.

Other workers studied the effect of ICP upon outcome in a series of 127 head-injured patients in whom ICP treatment was initiated at 25 mm Hg and in a subsequent series of 106 patients in whom ICP treatment started at 15 mm Hg. The overall mortality rate for the group treated for ICP above 25 mm Hg was 46% compared to 28% in the patients treated at the 15-mm Hg threshold.

In their analysis, Gaab and Haubitz used ICP histograms of head-injured patients, similar to the techniques employed by Janny, et al., they emphasized that, in addition to magnitude, the duration of ICP elevation is important. They reported that the ICP was of greater prognostic value than the duration of coma. Similarly, McGraw, et al., studied a series of 293 head-injured patients using a stepwise linear regression analysis, and found that the primary predictor of outcome was the average ICP over the entire monitoring period.

Nordby and Gunnerod studied 130 patients accumulated over a 4-year period and analyzed the association between outcome and the initial ICP measured epidurally. In this series, none of the patients with a normal initial ICP (defined as ICP < 15 mm Hg) developed an ICP increase leading to brain tamponade. A subsequent ICP rise to 40 mm Hg signified a high-risk group and progression to brain tamponade. The comparison of outcome groups with an ICP higher or lower than 20 mm Hg was statistically significant (p < 0.001) and is in general agreement with the results of this study.

Analysis of ICP and outcome in all of the studies described thus far have been restricted to comparisons of high, low, controlled, and unstable ICP with outcome. The data were reported with a general awareness of the strong influence of age, injury severity, and other factors known to be of strong prognostic value. However, with the exception of the report by McGraw, et al., no attempt was made to isolate the contribution of ICP to outcome. Our study takes into consideration the factors of age, admission motor score, and admission pupillary response. The ICP curves shown in Fig. 3 demonstrate more specifically how ICP influences

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outcome. These results are consistent with an earlier report by Eisenberg, et al.,7 who studied the ICP trends of 581 comatose patients in the pilot TCDB project. In this preliminary study, it was concluded that elevated ICP (> 30 mm Hg), prehospital shock, and hypoxia were predictive of outcome. The effect of ICP upon outcome was not attributed to initial GCS score or patient's age.

Pitts, et al.,23 studied the predictive value of ICP during the first 24 hours of monitoring using a linear logistic regression procedure. These investigators showed that outcome was linearly related to ICP based upon a weighted ICP value extracted from the first 24 hours of monitoring in 88 head-injured patients. As in our study, they found that age, admission motor score, and pupillary response were strongly related to outcome. However, these variables were not isolated to more clearly delineate the contribution of ICP. It is also interesting to note that, although several workers have demonstrated that the age factor is strongly prognostic,4 Alberico, et al.,4 found no difference in outcome among adult and pediatric groups in whom ICP exceeded 20 mm Hg but was controlled. In the analysis by these researchers, the percentage time that ICP measured above 20 mm Hg was not considered, yet ICP elevation above 20 mm Hg seemed to be a more critical factor than age.

Several investigators hold the view that CPP is the critical parameter that determines outcome.25 The argument was put forth by Tsutsumi, et al.,30 that identical ICP values with different arterial pressures do not represent similar conditions of intracranial hypertension. They determined the highest and lowest ICP and CPP of 104 head-injured patients and correlated these values with outcome, concluding that 40 mm Hg was the critical lower limit of CPP and 40 mm Hg was the critical high limit for ICP. In our analysis, CPP did not emerge as a significant factor; however, the proportion of BP readings less than 80 mm Hg was highly significant. These findings indicate that hypotension is strongly related to outcome and does not necessarily imply a concomitant reduction in CPP.

The presence of hypotension and hypoxia upon admission have been addressed by a number of researchers.19-21,24 The influence of these secondary insults in the TCDB sample is addressed in another report.4 Initially, we believed that the hypotension factor emerging from this analysis was attributed to patients who were hypotensive upon admission and in whom stabilization was difficult. However, the stepwise procedure selected the p(BP < 80) factor as more informative than all other candidates, including admission hypotension. Furthermore, subsequent analysis of the 428 patients in this sample revealed that adding admission hypotension to the five-factor model in Table 2 did not significantly improve explanatory power. A more detailed study of the influence of posttraumatic hypotension with the attendant complications introduced by barbiturate coma is now the subject of a separate investigation.

Conclusions

We have found that the mortality and morbidity resulting from severe head trauma are strongly related to raised ICP and hypotension measured during the course of ICU management. In addition to the factors of age, admission motor score, and admission pupillary response, the factor most indicative of outcome was the proportion of ICP measurements greater than 20 mm Hg. The next most significant factor was the proportion of BP measurements less than 80 mm Hg. It is suggested that the deleterious effects of traumatic injury occur beyond these critical values.

References

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