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Original Article

Impact of Intracranial Pressure and Cerebral Perfusion Pressure on Severe Disability and Mortality After Head Injury

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Abstract

Objective: To investigate the relationships between intracranial pressure (ICP), cerebral perfusion pressure (CPP), and outcome after traumatic brain injury.

Material and Methods: A retrospective analysis of prospectively recorded data from 429 patients after head injury requiring intensive treatment on the Neuroscience Intensive Annex and the Neuro Critical Care Unit, Cambridge, UK.

ICP, CPP, and arterial blood pressure (ABP) were continuously recorded. Mean values of pressures were compared to outcome assessed at 6 months after injury (using the Glasgow Outcome Scale).

Results: The mortality rate was greater in those having mean ICP greater than 20 mmHg (17% below versus 47% above; $p < 0.0001$). The mortality rate was dramatically increased for CPP below 55 mmHg (81% below versus 23% above; $p < 0.0001$). For values of CPP greater than 95 mmHg, favorable outcome was less frequent (50% below versus 28% above; $p < 0.033$). The rate of severe disability showed the tendency to increase with CPP ($r = 0.87$; $p = 0.02$), suggesting that a higher CPP does not help in achieving favorable outcomes.

ICP was greater in those who died in comparison to those who survived (27 ± 19 mmHg versus 16 ± 6 mmHg; $p < 0.10$–7), and CPP was lower (68 ± 21 versus 76 ± 10 mmHg; $p < 0.0002$). There was no difference between mean ICP and CPP in good/moderate and severe disability outcome groups.

Conclusion: High ICP is strongly associated with fatal outcome. Excessive CPP seems to reduce the probability of achieving a favorable outcome following head trauma.

Key Words: Head injury; outcome; intracranial pressure (ICP); cerebral perfusion pressure (CPP).

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Introduction

In the past 10 years, several changes have occurred in the management of head-injured patients. These are mainly related to the introduction of highly specialized neuro-intensive care units that have been shown to reduce the risk of mortality after brain trauma *(10,18)*. The application of monitoring methods for the early detection of treatable ischemic complications and the introduction of protocols to prevent or reduce secondary insults to the brain have been reported to improve the

outcome of these patients *(9,18,23)*. In this context, the choice of a neuromonitoring system able to support the clinical management is important. Several modern and advanced forms of brain monitoring have recently been studied and compared to more traditional techniques *(11,15,17,22–25)*, but intracranial pressure (ICP) and mean arterial blood pressure (ABP) monitoring still form a crucial framework for neurocritical care monitoring *(16,27,21)*. Although there is no class-1 evidence that monitoring of ICP has a potential to improve outcome *(16)*, there is a consensus that without this modality the management of severely head-injured patients is far from optimal. The overwhelming evidence of ICP as predictor of outcome and its power to detect and follow episodes of intracranial hypertension has assured its central role in the treatment of head injury patients *(17,20)*. Moreover, cerebral perfusion pressure (CPP) and ICP have become a therapeutic target to prevent potentially life-threatening cerebral hypoperfusion *(12,14,19)*. Therefore, several protocols for the management of acutely head-injured patients are based on a CPP-oriented therapy *(23)*, an ICP-oriented management *(9,19)*, or a mixture of both *(18)*.

Since September 1991, a bedside computer-supported system has been used *(5)* in our Neurosurgical Critical Care Annex (until 1993) and subsequently in our Neurosciences Critical Care Unit (NCCU) from 1994 onward. Its purpose was to continuously monitor physiological parameters such as ICP, ABP, and CPP. The system provides 1-minute averaged values for the monitored variables and calculates indices, which are potentially useful for the interpretation of cerebral hemodynamics after brain trauma. Over this period, various strategies, medications, and protocols have been used, the most important being the introduction of a CPP/ICP-oriented protocol aiming to standardize the pre-existing level of treatment and to optimize the quality of patient care *(18)*.

This large dataset has been used to examine our 10 years of experience in post-head injury monitoring and to review the information that can be gathered with a continuous recording of ABP, ICP, and CPP in patients after traumatic brain injury. Some particular aspects such as the relationship between Glasgow Coma Score and outcome *(1)*, influence of gender *(2)* and age *(6)* on outcome, and usefulness of ICP waveform analysis to predict the complications associated with intracranial hypertension *(3)* have already been published. The aim of this retrospective analysis was to investigate the relationships between the averaged monitored brain pressures and mortality, severe disability, and favorable outcome rates.

Patients and Methods

This retrospective analysis is based on 492 head-injured patients admitted to the NCCU between January 1992 and December 2001. Only patients with invasive monitoring of ICP and ABP over a period longer than 12 hours and connected to a bedside computerized system were included in the study. It is important to emphasize that the studied group is not representative for all admissions to the unit. Patients who have been admitted and discharged promptly, or died soon after admission, are not included in the analysis.

Patients were sedated, mechanically ventilated, and paralyzed in order to maintain ICP below 25 mmHg. Systemic hypotension was treated with fluids and vasoactive drugs. CPP was targeted to above 60–70 mmHg to avoid secondary ischemic insults. Episodes of intracranial hypertension were treated with mild hyperventilation ($PaCO_2$ > 4.0 kPa), moderate hypothermia, boluses of mannitol, and thiopentone. An external ventricular drain was inserted when feasible, depending on the size of ventricles on the computed tomography scan. The introduction of a standard ICP/CPP-oriented protocol for head injury in 1997 consisted of a more aggressive management of intracranial hypertension and a stricter control of ABP, aiming at minimizing the detrimental effects of hypoperfusion on brain tissue *(18)*.

Data were analyzed retrospectively as part of the standard clinical audit and no additional intervention was associated with the bedside computer data capture of the monitored variables.

Monitoring and Data Analysis

ICP was monitored by an intraparenchymal probe (Camino ICP transducer in 12 patients or Codman ICP MicroSensors in 446 patients) or through a ventricular drain and an external pressure transducer (Baxter, 34 cases prior to 1994). ABP was monitored invasively. Signals were sampled from the analogue output of the monitors at 30 Hz, digitized (12 bits analogue-to-digital converter), analyzed as 6-second averages, and subsequently converted to 1-minute averages.

Data from every patient were summarized as mean values of the physiological parameters (ICP, ABP, and CPP) after manual check and rejection of artifacts. Terminal data were excluded (e.g., in patients dying from severe intracranial hypertension) and in periods of weaning from the ventilator. Outcome was graded 6 months after injury according to the Glasgow Outcome Scale (GOS) *(8)*. Mean values were compared with *t*-tests when data were normally distributed; the Mann-Whitney U-test was used to compare medians of parameters that were not normally distributed. The χ^2 test was used for comparisons of outcome rates.

Results

Of 492 patients included in the computer-supported monitoring, 429 were suitable for analysis, with adequate quality of the continuous recording of ICP and ABP and reliable outcome follow-up. Mean age was 34 (±16.7 years) and median admission Glascow Coma Scale (GCS) score was 6 (range 3 to 15; 20% of patients had an initial GCS higher than 8); 21% of the patients were female. Overall, 28% of patients had a good outcome, 21% were moderately disabled, 22% severely disabled, 2% remained in a persistent vegetative state, and 27% died.

Outcome as a Function of Brain Pressures

Outcome rates were distributed unevenly along the observed range of ICP (*see* Figure 1). Mortality showed a clear breakpoint, increasing from 17 to 47% when averaged ICP increased above 20 mmHg ($p < 0.0001$; the exact threshold of ICP that minimized the *p*-value of the difference in mortality rate was 23 mmHg). This was mirrored by a decrease in good/moderate outcome rate. Severe disability did not show any remarkable changes dependent on ICP (Figure 1).

The relationship between CPP and the mortality rate revealed two areas where mortality rate increased (*see* Figure 2). For CPP

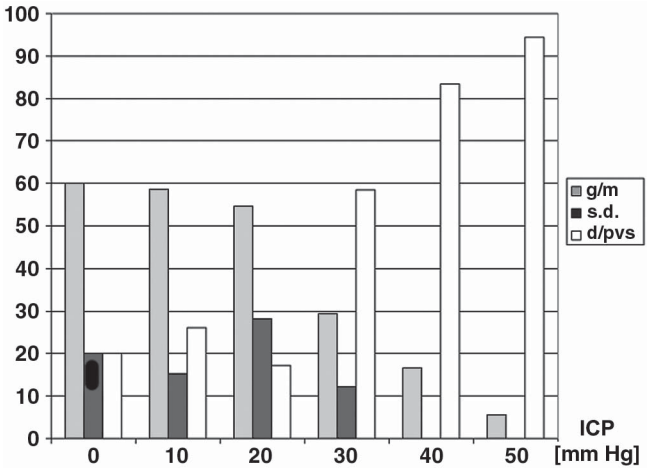

Fig. 1. Mortality and persistent vegetative state (d/pvs) rate, rate of favorable outcome (g/m), and rate of severe disability (s.d.) expressed as a function of ICP.

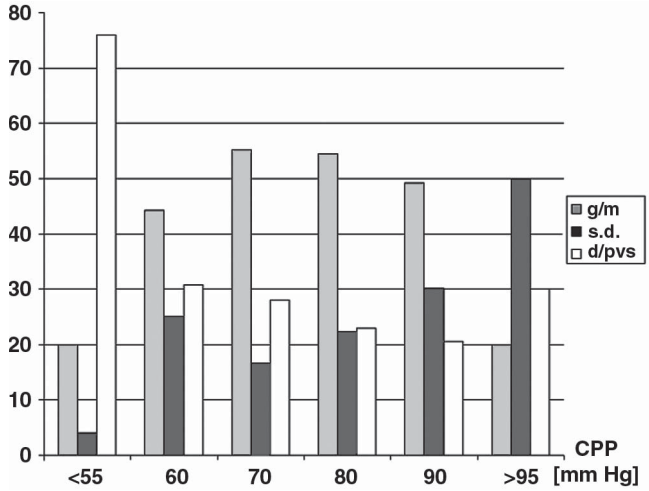

Fig. 2. Mortality and persistent vegetative state (d/pvs) rate, rate of favorable outcome (g/m), and rate of severe disability (s.d.) expressed as a function of CPP.

less than 55 mmHg, mortality was 81%, whereas for CPP greater than 55 mmHg was only 23% ($p < 0.0001$). For CPP greater than 95 mmHg, mortality was 30%, whereas for CPP less than it was 20%, although this difference was not significant ($p = 0.46$).

However, a CPP greater than 95 mmHg had a detrimental effect on good and moderate outcome. For CPP above 95 mmHg, the rate of good and moderate outcome was 28%, whereas less than 95 mm Hg, it was 50% ($p < 0.033$).

The severe disability rate showed a tendency to steadily increase with CPP ($r = 0.87$; $p = 0.02$), suggesting that either the greater CPP does not help in achieving favorable outcome or that these patients had more severe injury, requiring greater intensity of treatment (Figure 2).

ICP, CPP, and ABP in Different Outcome Groups

Distribution of measured pressures in the different outcome groups are presented in Figure 3. In patients who died compared with those who survived, there are significant differences in the monitored parameters. Mean ICP was higher (27 ± 19 mmHg versus 16 ± 6 mmHg; $p < 0.10–7$), and CPP was lower (68 ± 21 versus 76 ± 10 mmHg; $p < 0.0002$). There were no significant differences in ABP between the outcome groups.

Discussion

Methodological Issues

In this retrospective analysis, we have considered all the patients included in our multimodality neuromonitoring program over the past 10 years, which represents 30 to 40% of the total number of the severely head-injured patients admitted to our NCCU. Every patient admitted to the NCCU and receiving invasive monitoring of ICP and ABP was potentially eligible to be studied. On arrival in hospital, 20% of the monitored patients had a GCS more than 8, but all included patients developed a severe neurological deterioration at some stage of their hospitalization requiring invasive cerebrovascular monitoring and active medical treatment according to our guidelines *(18)*. Patients whose monitoring period was short were excluded from the analysis; for example, patients who died soon after admission and patients whose neurological conditions did not require further invasive monitoring.

Our database does not contain information regarding intensity of treatment. Multiple protocols have been used over long periods, and their direct comparison using retrospective data is virtually impossible. Whether the specific management can influence the outcome can be only addressed with prospective trials.

Continuous Monitoring of ICP and CPP

The result of this analysis reconfirms ICP as one of the most important predictors of mortality after brain trauma, but it also points out the limitation of this parameter as a tool to differentiate between patients who survive with favorable outcome and patients who survive with severe disability. The same clear cut-off between patients who died and patients who survived is observed for CPP; however, the significance level of the difference between averaged CPPs in those who died and those who survived is less than for ICPs.

The averaged ICP and CPP of ABP is an alternative to the evaluation of the percentage of time for ICP and CPP above and below certain critical thresholds *(4)* or counting insults *(13)*. Our choice of total monitoring mean values was intentional in order to keep the results of our audit simple and understandable. In this group of patients, there is a strong correlation between the percentage of time when ICP was above 20 or 25 mmHg and averaged ICP (in both cases $R > 0.9$). Therefore, it seems much more natural to compare averaged ICP with outcome than any nonlinearly transformed variable (percentage of time above a given threshold). Moreover, simple averaging is more useful where threshold values of brain pressures are to be studied.

Our results confirm many previous findings *(4,13,15)* suggesting that high ICP is associated with greater mortality rate. The threshold for increased ICP lies between 20 and 30 mmHg (*see* Figure 1). However, exact threshold for ICP only

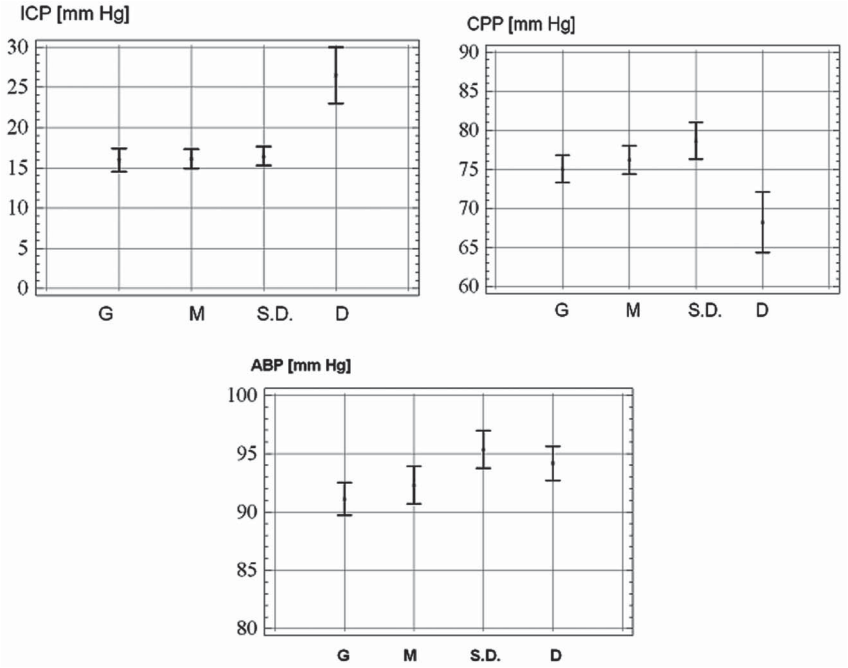

Fig. 3. Mean values and 95% confidence intervals (individual) for monitored parameters in different outcome groups. ICP, intracranial pressure; CPP, cerebral perfusion pressure; and ABP, mean arterial blood pressure.

makes sense when statistical analysis of a large amount of data is considered. In individual cases, both mean ICP, CPP, but also other indices such as brain compensatory reserve or pressure reactivity *(3,24)* are more useful. More accurate analysis (receiver operator curve or probabilistic analysis) suggests exact threshold of 23 mmHg. It does not change the clinical implications of our review, particularly the statement that any sustained increase in ICP more than 20 mmHg should be managed actively.

Low CPP, but lower than 55 mmHg (not 60 or 70 mmHg *[23]*) is associated with greater mortality rate. This threshold involves only a few patients in whom CPP-oriented management has failed (only 5%).

The lower values of CPP observed in patients who died were mainly related to the higher values of ICP, as no significant difference was found between mean values of ABP in the different outcome groups. Juul et al. *(14)* have already shown the lack of significant correlation between the level of CPP and outcome when CPP is kept higher than 60 mmHg. This does not lessen the importance of maintaining stable hemodynamic conditions after brain trauma, but it points out the limit of the importance of CPP as a therapeutical target when dealing with head-injured patients.

What was surprising is the finding that a high CPP (>95 mmHg) may reduce the rate of favorable outcome. Although the significance of this finding is not very strong ($p < 0.033$), it may suggest that an excessive increase of ABP with vasopressors may be detrimental. Low ICP and CPP within the range of 50 to 90 mmHg are clinical findings that seem to justify the main assumptions of the Lund concept *(9)*. Our study is based on material gathered over a long time interval and has not been influenced by one consistent protocol. Our policy has changed few times over this period, to finish with a mixed CPP- and ICP-oriented protocol *(18)* in 1997. The use of vasopressors to increase CPP became more frequent (in recent years this tendency has been moderated). This resulted in an increase in mean CPP from 68.3 ± 15.1 mmHg to 80.1 ± 10.6 mmHg post-1997; $p < 0.00001$; and slight, although nonsignificant, reduction of ICP from 20.2 ± 14.8 mmHg to 17.4 ± 8.3 mmHg; $p = 0.39$ (*see* Figure 4). More than three times as many patients with CPP greater than 95 mmHg were from the period 1997 to 2002 ($n = 10$) than pre-1997 ($n = 3$). After 1997, there was no significant difference between mean ICP in those having CPP greater than 95 mmHg and less than 95 mmHg (18.7 ± 9.3 mmHg versus 17.7 ± 9.5 mmHg; $p > 0.05$). Therefore it seems to be likely, although we do not possess direct proof, that high CPP was an effect of a more generous use of vasopressors.

Unfortunately, with this retrospective material there were no data suggesting how easy it was to control ICP and CPP. Character of distribution of mean values of ICP and CPP in different outcome groups (Figure 3) remained unchanged after 1997; however, there was a change in thresholds for high ICP and low CPP maximizing incidences of death. Threshold of ICP decreased from 25 mmHg to 22 mmHg after introduction of protocol. Threshold of CPP increased from 54 to 68 mmHg.

In summary, our survey confirms that ICP and CPP are important to identify patients at a high risk of dying. The relationship between the brain pressures and the timing of treatment could be of particular interest and should be investigated prospectively. Also "optimization" of CPP to this individual needs requires prospective study *(24)*. In clinical practice, we normally treat episodes of intracranial hypertension and systemic hypotension at an early stage in order to maintain ICP

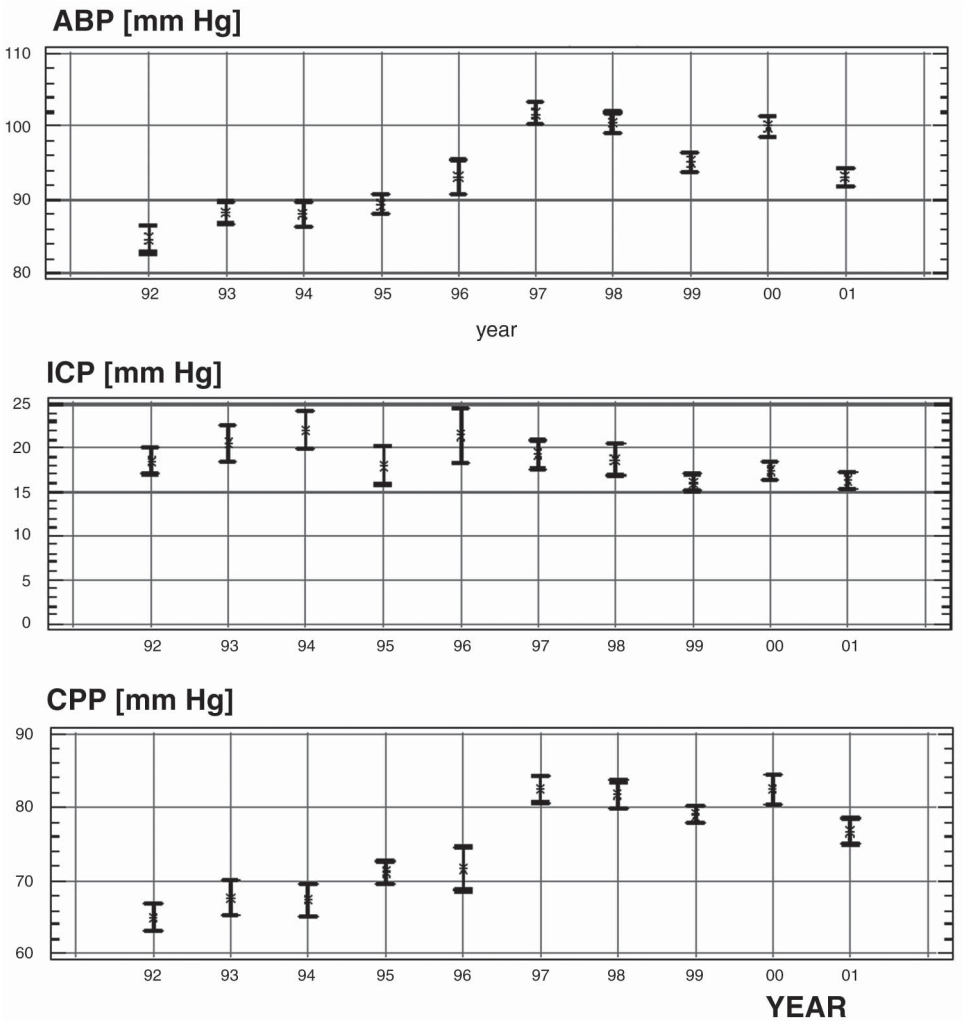

Fig. 4. Mean values and 95% confidence limits of averaged arterial blood pressure (ABP), ICP, and CPP in different years when the survey was done. There was a visible increase in ABP and CPP between 1996 and 1997, when the integrated CPP/ICP-oriented protocol *(18)* was introduced.

and CPP within the range established by the guidelines, but the clinical decision when to start a more aggressive treatment (either medical or surgical) is sometimes difficult *(29)*.

Conclusion

Intracranial hypertension determines life or death following head injury. High values of ABP, which may be justified in the presence of episodes of increased ICP, may be detrimental in patients with normal ICP.

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