Original articles

Cognitive and Psychosocial Outcome in Survivors of Severe Traumatic Brain Injury: Correlations with Cerebral Perfusion Pressure, Frontal Lobe Damage and Somatosensory Evoked Potentials

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ABSTRACT

Objective: *To correlate neuropsychological outcome in patients after severe traumatic head injury, with neurophysiological and neuroradiological data collected during the intensive care unit (ICU) period of care.*

Methods: *Patients admitted to Waikato Hospital ICU with severe traumatic head injury were studied. Respiratory difficulty at the accident site, admission Glasgow Coma Score (GCS), anatomic traumatic brain disruption as quantified by a cerebral computed tomography score, prolongation of the central conduction time (CCT) of somatosensory evoked potentials and the percentage time that the cerebral perfusion pressure was less than 70 mmHg (%CPP < 70) were measured. Neuropsychological outcome was assessed, in terms of cognitive and behavioural function, by the Controlled Oral Word Association (COWA) test (performed by the patient) and Head Injury Behaviour rating scale (HIBS, performed by their caregiver) respectively, one year following injury.*

Results: *Sixty-eight patients with a median post-resuscitation GCS of 6 were able to complete the neuropsychological follow up. Most patients had significantly impaired cognitive and behavioural function (mean COWA = 32 and HIBS = 9.7). Cognitive function did not correlate significantly with behavioural function (COWA vs HIBS, r = -0.14, p = 0.27). There were no significant correlations between either GCS (r = 0.15, p = 0.28) or estimates of respiratory difficulty at the accident scene and neuropsychological outcome. Poor cognitive outcome (COWA) was correlated with %CPP < 70 (r =-0.41, p = 0.005) and prolonged CCT (r = 0.26, p = 0.03). There was an insignificant correlation between the CT score and cognitive outcome (frontal lobe score vs COWA, r = -0.12, p = 0.33). However, the group of patients with the most severe frontal lobe injury tended to have a worse behavioural outcome as assessed by the HIBS.*

Conclusions: *Behavioural outcome as quantified by the caregiver (HIBS) does not correlate well with the degree of cognitive impairment as measured directly from the patient (COWA). Severely head injured patients with poor neurophysiological indicators (%CPP < 70 or prolonged CCT) have a poor neuropsychological outcome. However, anatomical disruption of the brain as estimated by the frontal lobe CT score correlated poorly with outcome.* (**Critical Care and Resuscitation 2000; 2: 246-252**)

Key words: Head injury, outcome, neuropsychological assessment

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There are many potential end-points that may be used to measure clinical outcome after severe traumatic brain injury. Of the numerous studies addressing this issue, most have concentrated on either prediction of survival, or have used the Glasgow Outcome Score (GOS) as a coarse predictor of functional outcome.[1-3] Clinical criteria such as pupillary response and brainstem reflexes, and adjunctive modalities, such as evoked potentials and cerebral imaging techniques, have been advocated to predict death.[4-6] However, this does not allow the survivors to be well categorised in terms of functional outcome. While the GOS has the advantage of simplicity, there are a number of problems with its use. Firstly, the GOS has not been formally compared with other methods of evaluating cognitive and psychosocial function commonly used by psychologists. Secondly, both survivors and non-survivors are included in the GOS (which may well be inappropriate, as many of the predictive factors will no longer be significant if applied purely to survivors). Thirdly, the GOS assumes a continuous transition from GOS 1 to GOS 5, whereas there is no evidence to support this, with most studies merging the GOS 4 and GOS 5 groups into one group, usually called "good" outcome.[5,7]

The disability occurring after severe traumatic brain injury can be thought of in three categories: 1) physical, 2) cognitive, and 3) behavioural or social. It has been suggested that it is the social dysfunction which has the greatest impact on the patient's quality of life.[8] Physical disability can potentially be overcome with the use of specialised appliances, but the extent of social and cognitive dysfunction will determine the ability of the individual to function acceptably in society. Various studies[9-11] have demonstrated a strong relationship between frontal lobe damage and poor performance with tests of verbal fluency. Such tests have previously been shown to be a sensitive indicator of cognitive dysfunction. Frontal lesions, regardless of side, tend to depress fluency scores with left-sided lesions resulting in lower word production. Social dysfunction has also been correlated with frontal lobe damage, particularly the pre-frontal regions.[8] With this in mind, it would seem more appropriate to measure the 'quality' of outcome using a scale specifically designed to measure frontal lobe neuropsychological functioning.

We wished to identify those clinical factors recorded during the patient's period in the ICU that could correlate with cognitive and behavioural outcome to add clarity to the prognostic information we can give to relatives, and to gauge the level, or indeed appropriateness, of support that would be required for rehabilitation.

METHODS

Patient Selection.

Patients who were admitted to Waikato Hospital ICU from 1993 to 1996 with severe brain trauma were studied. The inclusion criterion was brain trauma in patients who were expected to require sedation and controlled ventilation for over 24 hr as part of the management of the head injury.

Patients were excluded from the study if they had sustained a severe head injury previously, had neurological pathology or an active psychiatric disorder.

The study was approved by the regional ethics committee, and informed consent for somatosensory evoked potential testing and follow-up was required from the next of kin. The clinical management of the patients has been previously described in detail,[12] and was similar to that described in a recent consensus conference report.[13] The patients were sedated and ventilated to achieve PaO_2 >150 mmHg and a $PaCO_2$ ranging from 30 to 35 mmHg. Treatment for elevated intracranial pressure included mannitol, hypertonic saline, increased sedation and moderate hypothermia (33° to 35°C). If these therapies failed, thiopentone infusion and/or dihydroergotamine were used. We attempted to maintain the cerebral perfusion pressure above 70 mmHg using intravenous fluids and noradrenaline infusions.

The following set of variables were used to assess outcome:

1. Admission Glasgow Coma Scale (GCS) score.
2. Assessment of respiratory difficulty at the scene of the accident. A clinical estimate was recorded by the attending paramedic. Respiratory difficulty was deemed significant, or otherwise by assess-ments of respiratory effort, airway obstruction and cyanosis.
3. An ordinal scale based on the CT appearance of the brain (Table 1) was used to quantify the extent of macroscopic anatomic disruption of the brain. The number and timing of scans were determined by the clinical need. For the purposes of the study, only those scans within the first 72 hr of admission were reviewed. Of these, only the last scan was scored. The scoring system did not account for extra-axial collections (which were all drained when present and clinically significant) prior to the 'scored' CT. Two scores were recorded independently: for the brain as a whole, and for the frontal lobes.
4. Cerebral perfusion pressure (CPP) was recorded every 30 minutes and was calculated from measur-

ements of intracranial pressure (ICP) using the Camino Bolt 420 system (Camino Neurocare Inc. San Diego, California) and mean arterial pressure (MAP) using continuous direct intra-arterial pressure measurements. The percentage time that the CPP was less than 70 mmHg (called the %CPP < 70) was used as a measure of inadequate cerebral perfusion. CPP monitoring was discontinued when ICP had remained stable, without treatment, for 24 hr.

Table 1. Grading scale for the radiological appearance of the brain after severe head injury

'Normal' Score = 0	• No radiological abnormality apparent
'Mild' Score= 1	• Contusion or intracerebral collection < 1 mL • Localised oedema or necrosis • No midline shift • No petechial haemorrhages • No evidence of generalised pressure effect
'Moderate' Score= 2	• Contusion or intracerebral collection > 1 but < 3 mL • Evidence of generalised pressure effect (ventricles / cisterns compressed but patent) • Less than 3 mm midline shift • Any evidence of petechial haemorrhages
'Severe' Score= 3	• Contusion or intracerebral contusion > 3 mL • Extensive pressure effect (ventricular / cisternal / sulcal effacement) • Greater than 3 mm midline shift • Multiple widespread petechial haemorrhages

Any single feature, when present, determines the severity grade.

5. Somatosensory evoked potentials (SSEP) were performed using the median nerve as described by Hume.[14] The central conduction time (CCT) was recorded as the mean of studies from either side. A normal CCT was taken as less than 7 milliseconds. If there was unilateral absence of the cortical component of the SSEP (giving a false impression of a good conduction time), the CCT was scored as being the time of the SSEP present on the other side (i.e. biased to good outcome).

Outcome measures

Neuropsychological assessments were performed at one year post injury. Outcome was assessed with relation to cognitive performance and behavioural disorder. Cognitive ability was tested directly from the patient by the controlled oral word association (COWA) test.[8] The behavioural disorder was tested indirectly by the primary caregiver using the head injury behaviour scale (HIBS).[15]

The COWA test is a test of verbal association fluency which measures frontal lobe function and goal-directed behaviour. The mean (± SD) COWA score for a normal population has been quoted as 44.8 (±5.8). It consists of three word-naming trials in which the patient is required to produce orally as many words as possible beginning with a given letter of the alphabet, excluding proper nouns, numbers, and the same word with different suffix. The letters F, A and S were used and patients were given 60 seconds to complete each trial. The COWA score is the total number of words produced over the three trials. A total score less than 20 would indicate an individual with minimal ability to initiate day to day activities.

The HIBS is derived from a 20 item questionnaire that requires the caregiver to identify changes in the patient's behaviour since the brain injury. The score obtained represents the frequency of various behavioural problems and can range from 0 (no change) to 20 (most affected). High scoring patients (i.e. > 8) were generally described by their caregivers as exhibiting behaviour associated with loss of emotional control, such as impatience, childishness, impulsive-ness, and excessive sensitivity. Psychometric evaluation of the HIBS has provided evidence for its reliability and validity as a measure of behavioural and emotional problems following traumatic brain injury.[15-18]

Statistical analysis

Univariate correlations between variables were quantified using Spearman's rank correlation (r). A p value of < 0.05 was considered statistically significant.

RESULTS

One hundred and twenty three patients enrolled in the study. The median post-resuscitation GCS for these patients was 6 (range 3 to 11). At 12 months post injury 25 patients died (20.3%), 10 were lost to follow up, and 14 were less than 16 years of age. Of the remaining 74 adults, 6 were too impaired to reliably complete the COWA test, leaving 68 to form the study group. The mean (± SD) age was 26 (± 14) years. Eighteen of the subjects were female.

Eighty three percent of the patients were victims of road trauma. Respiratory difficulty, as clinically estimated by paramedics at the accident scene, was common (50%), and 21% of patients were intubated at that point

by ambulance staff. In 76% there was a delay of at least 2 hr between the time of the accident and the first CT scan. The mean duration of stay in the ICU was 10.7 days, and in hospital was 42 days.

Outcome

The mean (± SD) COWA was 32 (± 14), with the 25th and 75th centiles at 20 and 40 respectively. The mean (± SD) HIBS was 9.7 (± 5.3), with the 25th and 75th centiles at 6 and 14 respectively. The outcome as measured directly from the patient (COWA) did not correlate significantly with the outcome as perceived by the caregiver (HIBS) (r = -0.14, p = 0.27) implying that cognitive disruption of the patient did not necessarily result in behavioural disturbances (as perceived by the caregiver).

Explanatory variables

As the results for the whole-brain score were identical to the frontal lobe score, only the frontal lobe score was reported. Twenty-two patients had a frontal lobe CT score of zero, 9 had a score of 1, 25 had a score of 2, and 12 had a score of 3. Four patients had unilaterally absent central conduction.

Correlations

Estimates of respiratory difficulty did not correlate significantly with either COWA or HIBS. This may be explained by the fact that information with regard to duration and extent of respiratory difficulty after head injury is difficult to estimate reliably at the scene of an accident. This lack of objectivity invalidates further analysis in this clinical setting.

The COWA did correlate statistically significantly with %CPP < 70 (r = -0.41, p = 0.0005) and mean CCT (r = -0.26, p = 0.03, figures 1 and 2). However, while the correlation of CCT and COWA has achieved statistical significance, the relationship is weak. Observing the scatterplot of CCT vs COWA, it can be seen that if the three most prolonged CCT points are removed, the correlation becomes insignificant (r = -0.19, p = 0.22). The COWA did not correlate significantly with the GCS (r = 0.15, p = 0.28), or frontal lobe score (r = - 0.12, p = 0.33, figures 3 and 4).

There were no patients in whom there were bilaterally absent CCT's who were able to be scored (all died, or the brain injury was too severe to score COWA). The HIBS did not correlate significantly with the frontal lobe score when using the whole data set (Figure 5). However, if the HIBS for those patients with the most severe frontal lobe injury (score 3) were compared with score = 2 and score = 0 groups, there was a statistical difference (using a post-hoc test, Fishers Least Significant Difference).

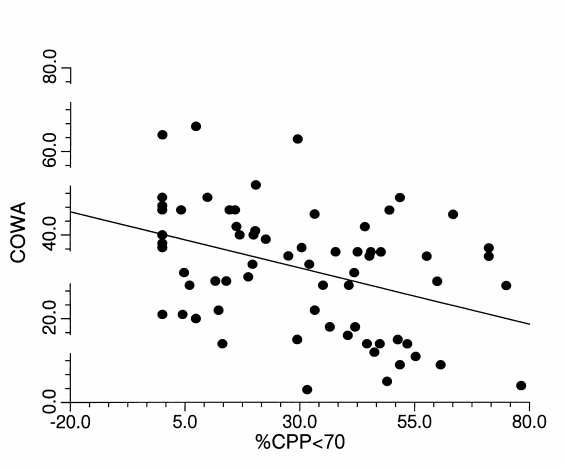

Figure 1. Scatter plot of controlled word association (COWA) score vs percentage time the Cerebral Perfusion Pressure < 70 mmHg (%CPP < 70).

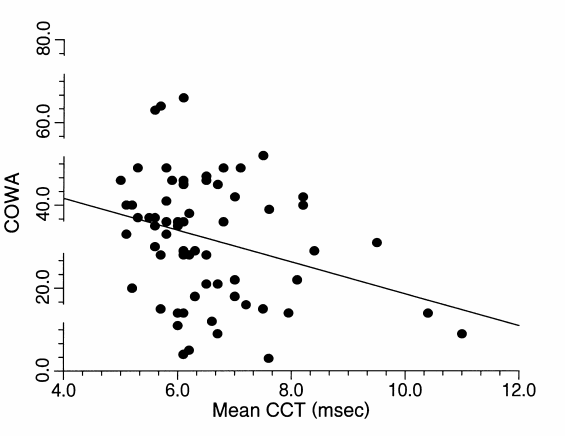

Figure 2. Scatter plot of controlled word association (COWA) score vs Central Conduction Time (CCT).

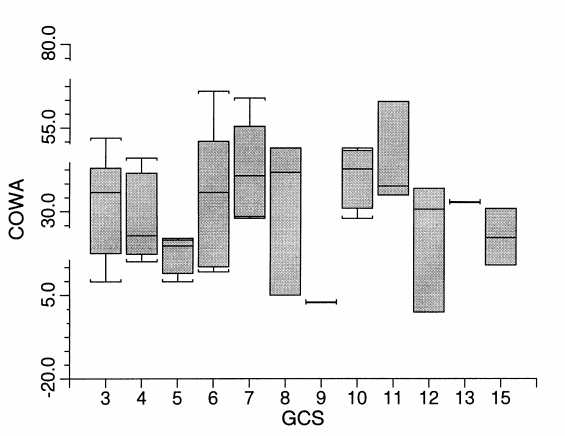

Figure 3. Box plot of controlled word association (COWA) score vs Glasgow Coma Score (GCS).

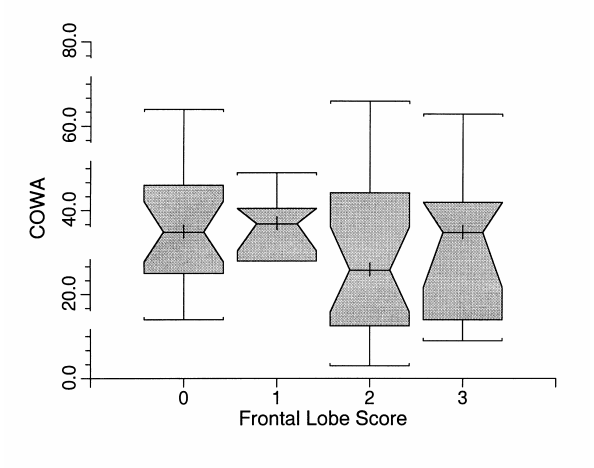

Figure 4. Box plot of controlled word association (COWA) score vs CT frontal lobe score. This graph is presented in the form of notched box plots. The notches are used to make comparisons among the different batches. If the notches of two boxes do not overlap, then it can be assumed that the medians are significantly different (the notches are constructed to demonstrate the 95% confidence limits of the median score).

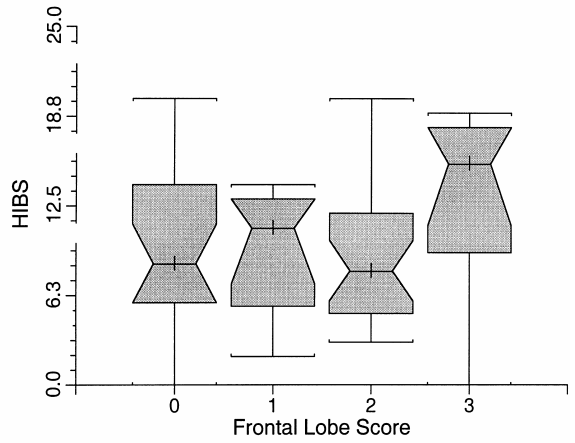

Figure 5. Box plot of the head injury behaviour scale (HIBS) vs CT frontal lobe score. This graph is presented in the form of notched box plots. The notches are used to make comparisons among the different batches. If the notches of two boxes do not overlap, then it can be assumed that the medians are significantly different (the notches are constructed to demonstrate the 95% confidence limits of the median score).

This raises the question of a non-linear relationship between structural damage (as estimated by the frontal lobe CT score) and behavioural disturbances with only the most extreme frontal lobe damage causing measurable worsening of behaviour of the patient.

Our results suggest that a GOS 4 and GOS 5 are indistinguishable in terms of cognitive outcome as measured by a general intelligence test (the Weschler Adult Intelligence Scale, GOS 4 vs GOS 5, p = 0.24, t-test).

DISCUSSION

Previous work has demonstrated that CT scoring is useful in predicting survival.[2,5] We have studied only the survivors, thus removing those factors determining mortality. Taken overall, cognitive (COWA) and psychosocial (HIBS) function at one year post-injury did not correlate with the radiological appearance of the brain within 72 hr of severe brain injury. However, severe frontal lobe damage may be weakly associated with a slightly more impaired psychosocial function as perceived by the caregiver.

We can only assume that the intricate cerebral physiological processes involved in cognition and behaviour cannot be assessed in terms of gross radiological anatomical changes alone. These findings may simply be explained by fact that cerebral CT is a poor indicator of physiological integrity. The functional unit of the brain is the neurone, and CT has been shown to have limited effectiveness at detecting axonal injury.[1,19] Some sources[20] suggest that less than 20% of the total amount of axonal shear will be demonstrable on CT (as indicated by petechial haemorrhages at the grey-white interface). In contrast, cerebral contusions are well demonstrated on CT but may not necessarily be associated with axonal shear and thus have the potential for good functional recovery. The use of imaging techniques that may be more sensitive in detecting axonal shear (magnetic resonance imaging and positron emission tomography) in this setting has not been fully explored, mainly because of logistical difficulties in performing these scans in the critically ill patient.

We found a significant correlation between neuropsychological outcome and CPP contrasting with the findings of Lannoo *et al*.[21] Normal cognitive outcome did not occur in any of our study group if the CPP was less than 70 mmHg for more than 50% of the monitoring period. Signorini *et al*[22] have tried to quantify the impact of these secondary cerebral insults. They implemented automated data collection to record the relevant physiological variables. We, however, have used a 30 minute manual recording of MAP, ICP and CPP. This has been shown previously to be sufficiently accurate,[23] and has the added benefit of allowing one to manually review the record and reject artifact.

Lannoo *et al*,[21] attempted to correlate outcome with the absolute time that the CPP was less than 70 mmHg. However, their data may have been skewed by one patient who had multiple episodes of low CPP, yet had a good outcome. In contrast, we have used the percentage time of the total period of ICP monitoring in which the CPP was less than 70mmHg. We did not explore which

determinants of a low CPP were more significant (i.e. low MAP, high ICP or both) as this has been addressed elsewhere.[22]

We have demonstrated a weak 'one-sided' correlation between CCT and neuropsychological outcome at one year. Normal cognitive function did not return in patients whose CCT was greater than 8 milliseconds. No prediction of outcome could be made if the CCT was normal (i.e. both good and bad outcome occurred). Expressed in the language of formal logic, we can say that a prolonged CCT is sufficient (but it is not necessary) to result in a poor outcome. Our findings are at variance with those of Pohlman *et al*[24] who found SSEPs a reliable indicator of both good and bad outcome (as measured by GOS). The SSEP is a measure of the integrity of the axonal systems between the cervicomedullary junction and the cerebral cortex. Unless a discrete brainstem lesion is seen on the CT, delay or absence of the SSEPs is commonly indicative of diffuse axonal injury.

Somatosensory evoked potentials are a product of thalamocortical connections which represent less than 1% of cortical afferents. Thus, it seems reasonable that a prolonged CCT will be correlated with a poor neurological outcome. The reverse is not true. A normal CCT is a comment on the physiological integrity of the 1% of cortical afferents (thalamocortical), and thus does not exclude severe cortico-cortical axonal injury. Kane *et al*[25] have addressed this issue by studying the long latency components of event-related potentials. These event-related potentials are generated by subcortical-cortical and cortico-cortical circuits, and their presence is suggestive of the integrity of a more extensive network of connections.

In summary, behavioural outcome as quantified by the caregiver (HIBS) did not correlate well with the degree of cognitive impairment as measured directly from the patient (COWA). Severely head injured patients with poor neurophysiological indicators (i.e. %CPP < 70 over 50%, or prolonged CCT) have a poor neuropsychological outcome. However, anatomical disruption of the brain as estimated by the frontal lobe CT score was poorly correlated with outcome.

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