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# Cerebral Autoregulation and Outcome in Acute Brain Injury

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*The purpose of this study was to examine the relationship between Czosnyka and others' Pressure Reactivity Index (PRx) and neurologic outcome in patients with acute brain injury, including traumatic brain injury (TBI) and cerebrovascular pathology. PRx measures the correlation between arterial blood pressure and intracranial pressure waves and may reflect cerebral autoregulation in response to blood pressure changes. A negative PRx reflects intact cerebrovascular response, whereas a positive PRx reflects impaired response. Positive PRx has been shown to correlate with poorer outcome in individuals with TBI, but these findings have not been confirmed by replication in other studies, nor have PRx values been reported for individuals with cerebrovascular pathology. In this study, PRx was determined in 52 patients with TBI (n = 27) or cerebrovascular pathology (n = 25). Hierarchical linear regression was used to evaluate the contribution of PRx to outcome, controlling for age and Glasgow Coma Scale score. Analysis of all subjects together did not support the previously reported relationship between PRx and outcome. However, for those with TBI, positive PRx was a significant predictor of negative outcome (P = 0.03). For those with cerebrovascular pathology, the effect was not significant (P = 0.10) and was in the opposite direction. For individuals with TBI, PRx may provide useful information related to cerebral autoregulation that is predictive of outcome. The meaning of PRx in individuals with cerebrovascular*

*pathology is unclear, and further study is needed to examine the paradoxical findings observed.*

**Key words:** Cerebral autoregulation, brain injury, neurologic outcome

**T**he common denominators of the management of acute brain injury, whether traumatic or related to cerebrovascular pathology, are the maintenance of adequate cerebral perfusion and the prevention of secondary brain injury. Secondary brain injury occurs minutes, hours, or days after the primary injury as a result of pathophysiologic events, also called secondary insults (Jones and others 1994). Secondary insults may be of intracranial origin, such as intracranial hypertension, or of systemic origin, such as arterial hypotension. A majority of secondary insults contribute to ischemia and are associated with poorer outcome (Jones and others 1994; Chesnut 1995; Wald 1995). Secondary insults occur frequently despite current intensive care management (Miller and others

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1977; Miller and others 1981; Andrews and others 1990; Marmarou and others 1991; Cortbus and others 1994; Jones and others 1994), and their effect may be particularly detrimental when adaptive responses that normally act to maintain cerebral perfusion are impaired.

Cerebral autoregulation is an adaptive mechanism that maintains a relatively constant blood flow to the brain despite changes in systemic arterial blood pressure (ABP). Cerebral autoregulation is impaired after brain injury and may be one of the mechanisms rendering the brain more vulnerable to secondary, potentially preventable, ischemic injury (Steiger and others 1994; Czosnyka and others 1996; Newell and others 1996; Czosnyka and others 1997; Junger and others 1997; Newell and others 1997). Acute perturbations in hemodynamic status that would normally be compensated for when autoregulation is intact may contribute to cerebral ischemia and secondary brain injury when autoregulation is impaired.

Ongoing clinical monitoring of the relationship between ABP and intracranial pressure (ICP) may provide clinically available relevant information about cerebral autoregulation, allowing earlier identification of deteriorating status and risk for secondary brain injury. The Pressure Reactivity Index (PR<sub>x</sub>) is a continuous measure of cerebrovascular response to ABP changes that can easily be implemented as a part of bedside computerized monitoring systems. PR<sub>x</sub> has been demonstrated to correlate with outcome in individuals with traumatic brain injury (Czosnyka and others 1997), but these findings have not yet been confirmed by replication in other studies, nor has the use of PR<sub>x</sub> been examined in individuals with cerebrovascular pathology.

The purpose of this study was to examine the coupling between ABP and ICP waveform data (as a measure reflecting cerebral autoregulation) and its relationship with neurologic status at hospital discharge.

### **Cerebral Autoregulation and Nursing Care**

Critically ill patients with brain injury respond differently to routine nursing care activities and environmental stimuli in relation to maintaining normal ICP and cerebral perfusion pressure (CPP) (Shalit and Umansky 1977; Mitchell and Mauss 1978; Mitchell and others 1981; Tsementzis and others 1982; Muwaswes 1984; March and others 1990; Kirkness

1992; Rising 1993). Responses differ not only among individuals but also within individuals over time. Cerebral autoregulation may be a significant factor contributing to the ability to compensate for changes in CPP and, therefore, to the risk of secondary brain injury (Bouma and Muizelaar 1992; DeWitt and others 1995). Continuous knowledge of autoregulatory status may be helpful in predicting those individuals with decreased cerebral autoregulation who are at greater risk of secondary brain injury from episodes of decreased cerebral perfusion in response to nursing care activities and environmental stimuli.

### **Cerebral Autoregulation and Intracranial Dynamics**

Cerebral autoregulation involves changes in cerebrovascular resistance in response to changes in systemic blood pressure to maintain a relatively constant blood flow to the brain over a range of mean ABPs from 60 to 150 mm Hg (Cold 1990). The exact mechanism of cerebral autoregulation remains unclear, although myogenic, metabolic, and neurogenic mechanisms have been proposed (Kontos 1981; Strandgaard and Paulson 1984; Paulson and others 1990; Aaslid 1992). Regardless of the exact mechanism, the autoregulatory response of cerebral blood vessels to changes in systemic blood pressure has been clearly demonstrated in animal and human studies. When autoregulation is fully intact, an increase in ABP leads to constriction of cerebral resistance vessels so that a stable cerebral blood flow is maintained. A decrease in ABP conversely leads to cerebral vasodilation to maintain flow. Cerebral autoregulation generally is not viewed as an all-or-none phenomenon. Evidence suggests that the autoregulatory response is impaired to varying degrees in individuals with traumatic brain injury; for example, the response may have a delayed onset or may not completely restore blood flow to its previous level (Newell and others 1997).

When autoregulation is impaired, there is a diminished or absent response of cerebral resistance vessels to changes in ABP. An increase in ABP then results in an increase in cerebral blood flow due to the lack of compensatory changes in cerebrovascular resistance and vessel diameter. This contributes to an increase in cerebral blood volume and ICP. Particularly when intracranial compliance is poor, minor increases in

blood volume may cause significant increases in ICP (Obrist and others 1984). A decrease in ABP conversely can lead to decreased cerebral blood flow, blood volume, and ICP.

ICP is a function of the combined pressures exerted by the brain, blood, and cerebrospinal fluid within the rigid skull. Other factors, such as venous and cerebrospinal fluid volume, are assumed to influence how ABP changes affect ICP, but ICP responses to changes in ABP are evident clinically and may provide meaningful information about autoregulatory status. The ICP pulse waveform emanates from the cerebrovascular bed, and evidence suggests that phasic changes in ICP are related to fast circulatory adjustments (Portnoy and others 1982; Obrist and others 1984). The vascular mechanism has been identified as an important factor in ICP changes after severe head injury (Marmarou and others 1987). ICP has been shown to vary directly with blood pressure when autoregulation is impaired, and the lack of a concomitant significant change in cerebral metabolic rate of oxygen leads to the conclusion that changes in ICP can be explained by changes in cerebral blood volume due to cerebral vasoconstriction or dilatation (Bouma and others 1992).

Spectral analysis has been used to characterize the transfer of the ABP signal to the ICP signal, and findings support the hypothesis that the degree of transfer between these signals is related to cerebral autoregulatory state (Chopp and Portnoy 1980; Portnoy and others 1982; Lin and others 1991). Greater transfer between the ABP and ICP occurs when autoregulation is diminished or absent and ABP changes are not attenuated as they would normally be when autoregulation is intact. The technical challenges of spectral analysis preclude its use in routine ongoing clinical monitoring at this time.

## PRx

An alternative and more clinically practical method of assessing the transfer of the ABP signal to the ICP signal involves the calculation of the correlation between the raw waveforms. Czosnyka and others (1997) developed PRx as a method of continuous monitoring of the correlation between slow ABP and ICP waves as a measure of global cerebral autoregulation in patients with traumatic brain injury (TBI).

PRx, as a standardized correlation coefficient varying between  $-1$  and  $+1$ , allows for comparison between patients. A positive PRx reflects a positive correlation between slow ABP and ICP fluctuations and is interpreted as an indicator of decreased cerebrovascular response to ABP changes. A PRx value of 0 indicates no correlation between slow ABP and ICP fluctuations, with changes in cerebrovascular resistance fully compensating for changes in ABP so that a constant cerebral blood flow is maintained. A negative PRx also indicates a normally reactive cerebrovasculature, with an inverse correlation between ABP and ICP waveforms; for example, an increase in ABP provokes vasoconstriction that decreases cerebral blood volume and, therefore, ICP. Overshoot of the compensatory mechanisms or a time delay in the feedback loop may accentuate this inverse correlation.

## Materials and Method

This study extended data gathering and analysis from a previous study examining the use of ICP waveform analysis and a measure of cerebral autoregulation to predict critically ill individuals with acute intracranial pathology who are at risk for sustained elevations of ICP (Mitchell and others 1998).

### Design

This study is a descriptive correlational study examining the relationship between PRx (as a measure of cerebral autoregulation) and ICP, CPP, Glasgow Coma Scale (GCS) score at the time of study and at discharge, and Glasgow Outcome Scale score. PRx was used as a variable in inferential model-building analyses aimed at predicting individuals with decreased cerebral autoregulation who are at risk for adverse physiologic responses that could threaten cerebral perfusion and neurologic outcome.

### Sample

Data were collected over two 12-month periods on a convenience sample of 52 patients, age 18 and older, who had intracranial pathology requiring invasive ICP and ABP monitoring in ICUs at a university teaching hospital.

Individuals were excluded if they were hemodynamically unstable, defined as baseline systolic ABP less than 90 mm Hg, baseline heart rate greater than 130 beats per minute, or baseline arterial oxygen saturation less than 90%.

## Measures

Invasive ABP recordings were obtained via radial artery catheters with the wrist maintained at heart level. ICP measures were obtained from CAMINO Laboratories (San Diego, CA) fiber-optic catheter-tipped transducers with dedicated CAMINO monitoring equipment input to the bedside monitoring equipment. ICP-monitoring catheters were located intraparenchymally and referenced to atmospheric pressure prior to insertion.

CPP is an important clinical measure reflecting the pressure gradient driving cerebral perfusion and is the difference between the mean arterial and venous pressures of brain blood flow (Head Injury Guidelines Task Force 1996). CPP is calculated by subtracting mean ICP from mean ABP ( $CPP = MAP - ICP$ ) ( $MAP = \text{mean arterial pressure}$ ).

The GCS is a quantitative measure of level of consciousness with a score ranging from 3 in an unconscious individual to 15 in an alert and oriented individual (Teasdale and Jennett 1974).

The Glasgow Outcome Scale is a widely used and reliable means to assess outcome after brain injury (Jennett and Bond 1975). The scale has 5 categories, with a higher score indicating better outcome.

## Procedure

Approval for the study was obtained from the University of Washington Institutional Review Board. The data were obtained from the clinical records and data generated by the bedside monitoring equipment. The ICP and ABP signals from the bedside monitors were split to a computer and recorded on the computer's hard drive.

The data were obtained from monitoring sessions carried out between 12:00 PM and 6:00 PM within the first 24 to 74 hours following admission to the ICU. Attempts were made to allow for uninterrupted monitoring for up to 50 minutes with excess stimuli minimized. Nursing or medical care activities were carried

out if necessary and records kept of the care and time they were given. Demographics and other relevant data were obtained from the charts. Charts were reviewed after discharge for GCS and Glasgow Outcome Scale scores at time of discharge.

## Data Analysis

The PRx was computed using the algorithm described by Czosnyka and others (1997). The PRx measures zero-lag cross-correlation between the ABP and ICP series, focusing on coherent variation on a time scale that is longer than 5 seconds and shorter than 200 seconds. The data were preprocessed by removing linear trend spanning 500-second segments and by summarizing the series into 5-second averages to minimize cardiac and respiratory cycle influences. Within each subject's record, a succession of moving estimates of the simple zero-lag linear correlation between the ABP and ICP series were computed based on a sliding window with a span of forty 5-second intervals (200 seconds). These were averaged into a composite PRx representing the record. If a subject had multiple records, these were averaged into a single summary PRx value.

Because a majority of variables were not normally distributed, Spearman's rank correlation test was used to examine the linear correlation between PRx and physiologic and outcome variables. Significance level (2-tailed) was set at  $P = 0.05$ .

Because prior studies have reported the use of PRx only in traumatic brain injury, data were analyzed for all subjects together as the combined diagnostic group and then separately for the 2 major diagnostic subgroups to assess diagnostic category differences. The diagnostic subgroups were TBI ( $n = 27$ ) and cerebrovascular pathology ( $n = 25$ ), including aneurysm (postoperative clipping,  $n = 14$ ; subarachnoid hemorrhage with no surgery,  $n = 3$ ), postoperative arteriovenous malformation resection ( $n = 4$ ), and miscellaneous cerebrovascular ( $n = 4$ ).

## Results

The sample consisted of records from 35 men (67%) and 17 women (33%) (Table 1). Ages ranged from 20 to 92 years, with a mean of 48.5 years. The sample was primarily Caucasian, reflecting the demo-

**Table 1. Subject Characteristics**

	Mean	SD	Range
Age (years)	48.3	16.6	20–92
Mean arterial blood pressure (mm Hg)	94.3	12.3	59–129
Mean intracranial pressure (mm Hg)	12.0	8.2	–5–35
Mean cerebral perfusion pressure (mm Hg)	82.4	14.6	45–120
Glasgow Coma Scale score at time of study	8.5	4.0	3–15
Glasgow Coma Scale score at discharge	10.5	6.0	0–15
Glasgow Outcome Scale score at discharge	2.1	1.4	0–4
Days in hospital	18.1	12.2	2–60
Degree of elevation of head of bed	15.3	12.8	0–30
Arterial oxygen saturation (%)	98.8	1.7	94–100

NOTE: Male  $n = 35$  (67%), female  $n = 17$  (33%).

graphics of the area. Mean GCS score at the time of monitoring was 8.5 (range 3–15). Thirty-four subjects (65.4%) were ventilated.

When TBI and cerebrovascular subgroups were examined, they did not differ significantly in mean ABP, age, baseline ICP, median ICP and CPP throughout monitoring, GCS at time of study or discharge, or arterial oxygen saturation. The TBI subgroup had a significantly higher heart rate (mean = 95,  $SD = 20$ ) than the cerebrovascular subgroup (mean = 82,  $SD = 17$ ) ( $P = 0.016$ ). There were more women in the cerebrovascular subgroup than in the TBI subgroup (15 vs. 2), reflecting the higher incidence of cerebral aneurysms in women (Mathieu and others 1996) and TBI in men (Miller and others 1981; Bowers and Marshall 1982).

## PRx

For the combined diagnostic group, PRx ranged from –0.46 to +0.79, with a mean of 0.3934, a standard deviation of 0.2487, and a median of 0.4057 (Table 2). Subgroups of TBI and cerebrovascular pathology were also examined. There was no significant difference in the mean of PRx between subgroups using the independent samples  $t$  test ( $P = 0.604$ ), but the lowest PRx and largest range of PRx occurred in the cerebrovascular subgroup.

Nineteen patients in the cerebrovascular subgroup had a PRx of greater than 0.20, the critical value above which the chance of unfavorable outcome was high in

**Table 2. Pressure Reactivity Index (PRx)**

Diagnostic Subgroup	n	Mean PRx	Median PRx	SD	Range
Traumatic					
brain injury	27	0.4107	0.4140	0.1916	0.07–0.78
Cerebrovascular	24	0.3740	0.3968	0.3037	–0.46–0.79
Traumatic					
brain injury and cerebrovascular	51	0.3934	0.4057	0.2487	–0.46–0.79

Czosnyka and others' (1997) study. Of these, 16 had a discharge GCS score of 13 to 15. In the TBI subgroup, 21 patients had a PRx greater than 0.20, and 11 of these had a discharge GCS score of 13 to 15. Five patients in the cerebrovascular subgroup had a PRx below 0.20, where the chance of good outcome should be favorable, but only 1 had a discharge GCS score above 9. Six patients in the TBI subgroup had a PRx of 0.20 or less. Of these, 4 had a discharge GCS score of 14 or 15. A clear pattern to the relationship between PRx and outcome is elusive, with individuals having both better and worse outcomes than would be predicted based on PRx.

## Combined Group Correlations

The linear correlation between PRx and physiologic and outcome variables was examined using Spearman's rank correlation test (Table 3). For the combined diagnostic group, there was a significant correlation between PRx and baseline ICP ( $r = 0.308$ ,  $P = 0.021$ ) and between PRx and median ICP throughout the period of monitoring ( $r = 0.37$ ,  $P = 0.005$ ). For both diagnostic groups together, PRx was not significantly correlated with GCS score at time of study, age, heart rate, median ABP or CPP during monitoring, or discharge GCS or Glasgow Outcome Scale scores.

In the subgroup analysis, PRx remained significantly correlated with median ICP during monitoring in the cerebrovascular subgroup ( $r = 0.463$ ,  $P = 0.023$ ), but the correlation was no longer significant in the TBI subgroup ( $r = 0.343$ ,  $P = 0.080$ ). PRx was not significantly correlated with any other physiologic or outcome variables in the subgroup analysis.

Further analysis was carried out to assess whether there was a correlation between the presence of a subarachnoid hemorrhage and PRx, since sub-

**Table 3. Nonparametric Combined Group Correlations**

	Median Pressure Reactivity Index (PRs)	
	Correlation Coefficient	<i>P</i> Value (2-tailed significance)
Age	-0.141	0.310
Diagnostic subgroup	0.032	0.823
Glasgow Coma Scale score at time of study	0.058	0.671
Glasgow Coma Scale score at time of discharge	-0.009	0.948
Glasgow Outcome Scale score	-0.059	0.670
Heart rate	-0.083	0.541
Baseline intracranial pressure	0.308	0.021
Median arterial blood pressure	0.036	0.792
Median cerebral perfusion pressure	-0.131	0.336
Median intracranial pressure	0.367	0.005

arachnoid hemorrhage was present in both groups, although of different etiology. In the TBI subgroup, 15 individuals suffered traumatic subarachnoid hemorrhage, and in the cerebrovascular subgroup, 14 individuals suffered aneurysmal subarachnoid hemorrhage. The presence of subarachnoid hemorrhage of either etiology was correlated with lower GCS score at discharge ( $r = -0.329$ ,  $P = 0.014$ ). No significant correlation between PRx and subarachnoid hemorrhage was found in the combined group or the subgroups of traumatic and aneurysmal subarachnoid hemorrhage.

### Linear Regression

Hierarchical linear regression was used to assess the value of PRx in predicting neurologic outcome at time of hospital discharge (Table 4). Age and GCS at the time of study were included in the base model (model 1), since both are well-identified predictors of outcome (Miller and others 1981; Marshall and others 1991; Vollmer and Dacey 1991; Steiger and others 1994; Temkin and others 1995; Mamelak and others 1996; Resnick and others 1997). The 2 major variables of diagnostic subgroup and PRx were added to the model (model 2), with no significant change in the fit of the overall model. Model 2 requires that the slope of the linear relationship between PRx and GCS be equal for both diagnostic subgroups and, thus, does not reflect subgroup differences. A diagnostic subgroup by

PRx interaction term ( $DXGRP \times PRx$ ) was then added to the model (model 3) to assess subgroup differences in the relationship between PRx and outcome. This interaction term allows the model to fit a separate slope for each diagnostic subgroup. Adding the term resulted in an improved fit of the overall model, implying that the relationship between PRx and outcome is different in the diagnostic subgroups. The overall model was significant ( $P < 0.001$ ), as were diagnostic subgroup and the diagnostic subgroup by PRx interaction terms ( $P = 0.028$  and  $P = 0.003$ , respectively). PRx by itself was not a significant predictor of outcome ( $P = 0.176$ ).

A similar linear regression model was computed using the Glasgow Outcome Scale score rather than GCS score at discharge as the dependent variable. Similar results were obtained, as would be expected because of the strong correlation between Glasgow Outcome Scale score and GCS score at discharge ( $r = 0.957$ ,  $P < 0.001$ ).

When the data were divided into the 2 diagnostic subgroups, linear regression demonstrated that within the TBI subgroup, high PRx was a significant predictor of negative outcome ( $P = 0.029$ ). Within the cerebrovascular subgroup, PRx was not a significant predictor ( $P = 0.098$ ) and the predictive trend was in the opposite direction, with higher PRx associated with better outcome. Figure 1 presents a partial regression plot of PRx controlled for GCS at the time of study and age versus GCS at discharge controlled for GCS at time of study and age. This plot clearly displays the difference in the slope of the regression lines for the 2 diagnostic subgroups. GCS and PRx on this plot cannot be interpreted as absolute values owing to our controlling for GCS and age at time of study.

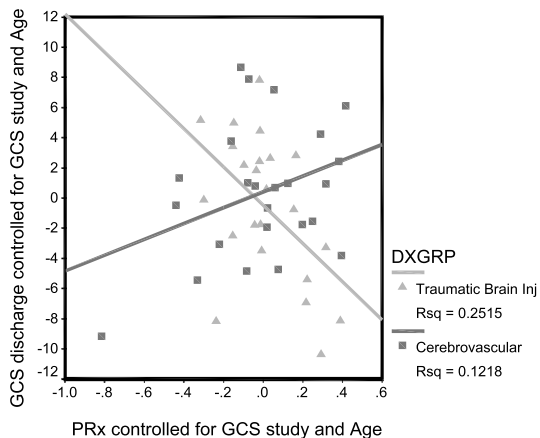
### Discussion

Czosnyka and others (1997) examined the relationship between PRx and neurologic outcome in a population with TBI and reported that a positive PRx correlated with poorer outcome at 6 months following injury. The critical value for averaged PRx over the entire period of monitoring was +0.2, with PRx greater than this value associated with an 81% chance of unfavorable outcome. Individuals with an averaged PRx of less than -0.2 all had favorable outcomes. The currently reported study extends the use of PRx to a com-

**Table 4. Regression Model**

	Dependent Variable	Predictors	Predictor Significance	Model Significance	Model $r^2$	$r^2$ Change	Significance
Model 1 (base)	Glasgow Coma Scale score at discharge	Age Glasgow Coma Scale score at study	$P = 0.002$ $P < 0.001$	$P < 0.001$	0.461	0.461	0.000
Model 2	Glasgow Coma Scale score at discharge	Age Glasgow Coma Scale score at study PRx DXGRP	$P = 0.002$ $P < 0.001$ $P = 0.969$ $P = 0.448$	$P < 0.001$	0.469	0.007	0.747
Model 3	Glasgow Coma Scale score at discharge	Age Glasgow Coma Scale score at study PRx DXGRP DXGRP $\times$ PRx	$P < 0.001$ $P < 0.001$ $P = 0.176$ $P = 0.028$ $P = 0.003$	$P < 0.001$	0.573	0.104	0.003

NOTE: PRx = Pressure Reactivity Index. DXGRP = diagnostic subgroup, DXGRP  $\times$  PRx = diagnostic subgroup by PRx interaction term.

**Figure 1. Partial regression plot.**

NOTE: PRx = Pressure Reactivity Index, GCS = Glasgow Coma Scale, DXGRP = diagnostic subgroup.

bined population of individuals with TBI and cerebrovascular pathology. The relationship between PRx and outcome reported by Czosnyka and others was not well supported in this sample when the analysis was carried out on the combined data from both major diagnostic subgroups. A significant diagnostic subgroup by PRx interaction term ( $P = 0.003$ ) in the linear regression model implied strong subgroup differences in the slopes of the relationship between PRx and outcome.

Separate analysis was carried out with the data divided into subgroups of TBI and cerebrovascular pathology. The association between high PRx and poorer outcome in TBI reported by Czosnyka and others (1997) was supported by the linear regression analysis of the TBI subgroup but not the cerebrovascular subgroup. Czosnyka and others' multiple linear regression model for outcome prediction, with admission GCS and age in the base model, increased the  $r^2$  value from 30% to 42% when PRx was added as a 3rd variable ( $P < 0.001$ ). In this study, with the regression model including GCS at time of study, age, PRx, and diagnostic subgroup terms, adding the PRx by subgroup interaction term increased the  $r^2$  value from 47% to 57% ( $P = 0.003$ ).

The subgroup analysis demonstrates a different association between PRx and outcome for the 2 subgroups, suggesting that the differing pathology influences cerebral autoregulation in different ways. For the TBI subgroup, the results are consistent with the simplified model of increased transmission of ABP pulse changes to the ICP pulse if the ABP changes are not buffered by autoregulatory changes. Although the findings were not statistically significant, the trend toward the association of a higher PRx with better outcome in the cerebrovascular subgroup is paradoxical.

It is possible that delayed cerebral vasospasm contributed to the poorer outcome in the cerebrovascular



subgroup. Eight patients in this subgroup had cerebral vasospasm documented by angiography or transcranial Doppler ultrasonography. Vasospasm resulting in cerebral ischemia is the leading cause of death and disability after subarachnoid hemorrhage from aneurysmal rupture (Kassell and others 1985). Cerebral vasospasm occurs in 40% to 70% of individuals following subarachnoid hemorrhage and leads to increased vascular resistance, impaired autoregulation, and sustained narrowing of the arteries at the base of the brain (Kassell and others 1985). The typical onset of cerebral vasospasm is 3 to 21 days following hemorrhage, most often between 4 and 14 days (Fisher and others 1980; Kistler and others 1983). In the present study, monitoring was carried out before cerebral vasospasm would be expected to occur. Those with decreased cerebral autoregulation at the time of study may have been less likely to develop increased cerebrovascular resistance resulting in cerebral vasospasm later on.

PRx was positively correlated with ICP ( $r = 0.366$ ,  $P < 0.001$ ) in Czosnyka and others' (1997) study as well as in both the combined group ( $r = 0.357$ ,  $P = 0.005$ ) and the cerebrovascular subgroup ( $r = 0.463$ ,  $P = 0.023$ ) in this study. The correlation between PRx and ICP in the TBI subgroup was not significant ( $r = 0.343$ ,  $P = 0.080$ ). There would seem to be a specific relationship between increased ICP and cerebral autoregulation, since there was not a significant correlation with CPP, so the pressure gradient driving cerebral perfusion was not the major factor in determining PRx. Higher ICP may be associated with a tighter, less compliant brain and greater transmission of the ABP pulse pressure across the cerebrovascular bed. When autoregulation is absent, cerebral blood vessels may be dilated as compared to when autoregulation is present, contributing to increased blood volume and increased ICP (Chan and others 1992). This supports PRx as an indicator of the state of cerebral autoregulation.

Whereas median ICP was significantly correlated with PRx in the cerebrovascular subgroup, neither median ICP nor PRx were significant predictors of outcome for this group. It would be expected that individuals with high ICP might also have poorer autoregulation and, therefore, a higher PRx, which the correlation of ICP and PRx supports. ICP was generally within normal limits or only slightly elevated (mean = 10,  $SD = 9$ ) in this group, so severe increased

ICP was not a major factor in outcome, reflected in the lack of a significant correlation between ICP and outcome. ICP is used in the analysis both as a single value reflecting an individual's ICP (median ICP) and as a variable in the PRx computation, which represents the correlation between dynamic changes in ICP and ABP. The PRx computation removes the median ICP value because the index focuses on the coupling of changes in ABP to changes in ICP, not ICP level. Median ICP and PRx can therefore have both shared and distinct information contributing to outcome prediction.

The cerebrovascular subgroup had a significantly higher heart rate compared to the TBI subgroup. Although heart rate could potentially have an association with PRx through its influence on blood pressure, it was not significantly correlated with either blood pressure or PRx in the combined group or in the subgroups. The difference in heart rate between the 2 subgroups does not appear to have a direct influence on the predictive value of PRx on outcome.

There are differences in variables used in this and Czosnyka and others' (1997) study that could contribute to differences in the results. Czosnyka and others assessed outcome at 6 months postinjury, whereas outcome was assessed at hospital discharge in this study. Although these measures are related, they are not equivalent. The outcome status of a significant proportion of individuals with severe TBI changes in the first 6 months postinjury, with the majority demonstrating improvement (Choi and others 1994). It would be expected that a proportion of patients in this study would have shown improvement in outcome at 6 months postinjury.

GCS at admission was used in Czosnyka and others' (1997) analysis, whereas GCS at time of study was used in this analysis. Although changes in GCS scores can occur within 72 hours of admission, significant improvement or deterioration in GCS scores is not likely in the majority of patients. Particularly in the TBI population, most patients would remain intubated and sedated. A majority of patients in this study were studied within 24 to 48 hours of admission, minimizing the difference in the timing of the GCS scores between the 2 studies.

The population in Czosnyka and others' (1997) study had GCS scores ranging from 3 to 13, with a mean of 6, whereas in this study, GCS scores ranged from 3 to 15, with a mean of 8.5. This difference could

be related to an actual difference in severity of subjects' condition or to all patients in Czosnyka and others' study reportedly being intubated and, therefore, receiving only 1 point for the GCS verbal score. In the present study, only 65% of patients were intubated. Because of the known predictive value of initial GCS score on outcome, GCS was controlled for in the linear regression analysis that examined the predictive value of PRx on outcome.

The average age of the population in this study was 10 years older than that in Czosnyka and others' (1997) study (46 years vs. 36 years); thus, a poorer overall group outcome would be predicted in this study. To address the influence of age on outcome, age was controlled for in the linear regression analysis.

### Conclusion

Impaired cerebral autoregulation is known to occur following acute brain injury and may be one of the mechanisms contributing to secondary brain injury by making the brain more vulnerable to events such as decreases in ABP or increases in ICP. Human and animal studies support the hypothesis that there is greater transmission of the ABP pulse to the ICP pulse with impaired autoregulation. PRx is a dynamic measure of global cerebrovascular response to changes in ABP that may have important clinical applications. The calculation of PRx is not complex and could be incorporated relatively easily into current clinical monitoring systems.

PRx may be particularly useful to nurses as an indicator of individuals with acute TBI who are at increased risk for adverse responses to routine care activities, such as positioning or suctioning. A critically ill individual's physiologic state is dynamic, and PRx may provide an indication of a trend of deteriorating cerebral autoregulation and allow earlier initiation of nursing interventions.

PRx may also provide a useful guide for individualized CPP management. The optimal CPP level in individuals with acute brain injury remains unclear, but it is likely that the injured brain requires a higher than normal CPP to maintain adequate perfusion and that the threshold can change as the patient's clinical status changes. PRx can provide ongoing information about whether an individual's CPP is being maintained

within the range over which cerebral autoregulation is present.

The meaning of PRx in a population with cerebrovascular pathology is unclear and remains to be elucidated. Findings from this and Czosnyka and others' (1997) study support the potential value of PRx in the clinical management of acute TBI. Further study to correlate PRx with another measure of cerebral autoregulation and to verify the correlation of PRx and outcome could provide additional validation of the meaning and usefulness of this measure. It is of particular interest to assess the feasibility and impact of continuous monitoring of cerebral autoregulation on dynamic nursing decision making and care. The value of PRx in predicting individuals at risk for adverse cerebrovascular responses to routine care procedures as a basis for the development and testing of interventions to prevent or minimize these events needs to be further explored.

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