Cerebral arteriovenous oxygen difference: a predictor of cerebral infarction and outcome in patients with severe head injury

PETER D. LE ROUX, M.B., CH.B., M.D., DAVID W. NEWELL, M.D., ARTHUR M. LAM, M.D., F.R.C.P.C., M. SEAN GRADY, M.D., AND H. RICHARD WINN, M.D.

Departments of Neurosurgery and Anesthesiology, Harborview Medical Center, University of Washington, Seattle, Washington

✔ Jugular bulb oxygen monitoring can be used to estimate the adequacy of cerebral blood flow to support cerebral metabolism after severe head injury. In the present study, the authors studied the cerebral arteriovenous oxygen difference ($AVDO_2$) before and after treatment in 32 head-injured patients (Glasgow Coma Scale scores ≤ 8) to examine the relationships among $AVDO_2$ and cerebral perfusion pressure (CPP), delayed cerebral infarction, and outcome. Fifteen patients (Group A) underwent craniotomy for hematoma evacuation and 17 (Group B) received mannitol for sustained intracranial hypertension (intracranial pressure > 20 mm Hg, > 10 minutes). Radiographic evidence of delayed cerebral infarction was observed in 14 patients. Overall, 17 patients died or were severely disabled. Cerebral $AVDO_2$ was elevated before craniotomy or mannitol administration; the mean $AVDO_2$ for all patients before treatment was 8.6 ± 1.8 vol%. Following craniotomy or mannitol administration, the $AVDO_2$ decreased in 27 patients and increased in five patients (mean $AVDO_2$ 6.2 ± 2.1 vol% in all patients; 6 ± 1.9 vol% in Group A; and 6.4 ± 2.4 vol% in Group B). The mean CPP was 75 ± 9.8 mm Hg and no relationship with $AVDO_2$ was demonstrated. Before treatment, the $AVDO_2$ was not associated with delayed cerebral infarction or outcome. By contrast, a limited improvement in elevated $AVDO_2$ after craniotomy or mannitol administration was significantly associated with delayed cerebral infarction (Group A: $p < 0.001$; Group B: $p < 0.01$). Similarly, a limited improvement in elevated $AVDO_2$ after treatment was significantly associated with an unfavorable outcome (Group A: $p < 0.01$; Group B: $p < 0.001$). In conclusion, these findings strongly indicate that, despite adequate cerebral perfusion, limited improvement in elevated cerebral $AVDO_2$ after treatment consisting of either craniotomy or mannitol administration may be used to help predict delayed cerebral infarction and poor outcome after traumatic brain injury.

KEY WORDS • traumatic brain injury • arteriovenous oxygen difference • intracranial pressure • cerebral ischemia • outcome

NEUROPATHOLOGICAL studies demonstrate that cerebral ischemia is frequently found in patients who die after head injury.[19] In addition, cerebral infarction is observed on sequential computerized tomography (CT) scans in disabled survivors.[31] Intracranial hypertension is also a common occurrence after severe head injury and may contribute to cerebral ischemia by reducing cerebral perfusion pressure (CPP); however, the relationship among intracranial pressure (ICP), CPP, and the development of cerebral ischemia is not consistent.[24,33,50] This discrepancy may result, in part, from other factors not reflected in either ICP or CPP, such as disturbed autoregulation,[2,14,34] traumatic vasospasm,[29] or neurochemical changes such as elevated excitatory amino acids,[1] which may adversely influence cerebral blood flow (CBF) or tissue oxygenation and contribute to infarction.

Several techniques have been developed to determine the adequacy of CBF after severe head injury. Although it does not measure absolute CBF values, jugular bulb oxygen monitoring provides an estimate of the adequacy of CBF to support cerebral metabolism by measuring the balance between oxygen delivery and consumption. Previous investigators have demonstrated that in the absence of infarction or necrosis, the cerebral arteriovenous oxygen difference ($AVDO_2$) and CBF are inversely related.[37,43] The present study of severely head injured patients was undertaken to examine: 1) the $AVDO_2$ response to craniotomy or mannitol administration; 2) the relationships among $AVDO_2$, ICP, and CPP; and 3) the associations between $AVDO_2$ and delayed cerebral infarction and outcome. Our results demonstrate that there was a poor relationship between CPP and $AVDO_2$. However, limited improvement in an elevated $AVDO_2$ following craniotomy for traumatic mass lesions or mannitol administration for intracranial hypertension was significantly associated with delayed cerebral infarction and poor outcome. By

contrast, a large improvement in $AVDO_2$ was associated with favorable outcome and no evidence of delayed cerebral infarction.

Clinical Material and Methods

Patient Population

During a 12-month period, 32 patients with severe traumatic brain injury (postresuscitation Glasgow Coma Scale[51] [GCS] scores of ≤ 8) admitted to our institution within 8 hours of injury were prospectively evaluated. There were 21 males and 11 females in the group, ranging in age from 14 to 79 years (median 34.5 years). The patients fulfilled the following criteria: 1) isolated nonpenetrating head injury; 2) normal blood pressure; 3) normothermia; 4) hematocrit above 30%; and 5) survival more than 24 hours after admission. Two groups were identified: Group A (15 patients) underwent craniotomy for evacuation of a traumatic mass lesion and Group B (17 patients) demonstrated no mass lesion on a CT scan but received a mannitol infusion for sustained intracranial hypertension (ICP > 20 mm Hg, > 10 minutes) despite adequate sedation and ventilation.

Case Management

All patients were managed according to a standard protocol that emphasized prompt evacuation of intracranial mass lesions and prevention of secondary cerebral insults. Patients suffering severe head injury were initially evaluated and aggressively resuscitated, including intubation and mechanical ventilation, by paramedics in the field. On admission to the emergency department, the patients were hemodynamically stabilized and, after initial evaluation, all underwent cranial CT scanning. Patients with surgical mass lesions were taken directly to the operating room for hematoma evacuation. All patients were admitted to the neurosurgical intensive care unit and their cases were managed according to a standard protocol designed to prevent secondary insults. This protocol included: 1) intubation and mechanical ventilation to maintain PaO_2 at above 100 mm Hg and $PaCO_2$ at 30 to 35 mm Hg; 2) volume replacement with albumin and crystalloid boluses to maintain systolic blood pressure at more than 100 mm Hg and central venous pressure between 5 cm and 10 cm H_2O; 3) maintenance of normal serum glucose and electrolyte levels and a hematocrit of between 30% and 40%; and 4) treatment of increased ICP (> 20 mm Hg) in the following sequence: sedation (morphine sulfate), muscle paralysis (pancuronium therapy), head elevation (10–30°), and moderate hyperventilation ($PaCO_2$ maintained at 25–30 mm Hg). If a patient's ICP remained elevated (> 20 mm Hg, > 10 minutes) despite these measures, an intravenous bolus of 20% mannitol was administered over 10 to 15 minutes (0.5–1 g/kg).

Physiological Measurements

The following physiological parameters were continuously monitored: arterial blood pressure through a radial arterial catheter; arterial oxygen saturation (SaO_2) by pulse oximetry; end-tidal CO_2 using a capnometer installed through the endotracheal tube; temperature mea-
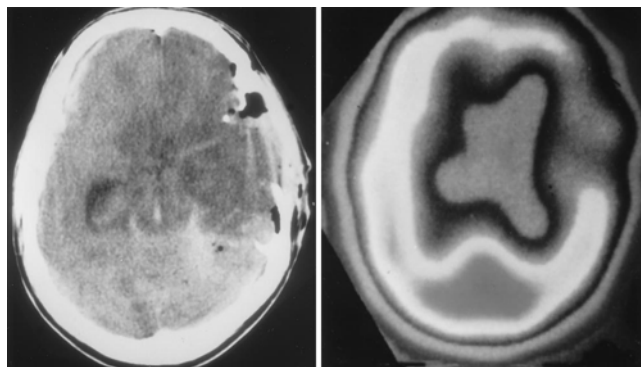

FIG. 1. Computerized tomography *(left)* and single-photon emission CT *(right)* scans illustrating radiographic changes of delayed cerebral infarction. There was histological confirmation of this radiological diagnosis in four patients who underwent autopsy.

sured through an esophageal temperature probe in the operating room or by tympanic thermometer in the intensive care unit; and ICP through a fiberoptic parenchymal intracranial pressure monitor (Camino Laboratories, San Diego, CA). The level of cerebral perfusion was calculated as the difference between the mean arterial blood pressure (MABP) and ICP (CPP = MABP − ICP). All parameters were recorded in a computerized database and were correlated with the $AVDO_2$ measurements.

Determination of Cerebral Arteriovenous Oxygen Difference

To measure jugular venous oxygen saturation ($SjVO_2$), a 5.5-in-long 16-gauge catheter was inserted percutaneously into the internal jugular vein.[22] The catheter tip, confirmed by x-ray film, was positioned in the jugular bulb. The catheter was placed on the side of the mass lesion to be evacuated or, in Group B patients, in the dominant jugular vein based on a CT assessment of the jugular foramen.[12] The ICP monitor was placed ipsilateral to the jugular catheter. Arterial (radial) and retrograde jugular venous samples were obtained simultaneously: 1) at skin incision and skin closure in patients undergoing craniotomy and 2) before and 30 minutes after completing intravenous mannitol administration. The samples were used to determine pH, PaO_2, $PaCO_2$, O_2 saturation, and hemoglobin (Hb) (Corning 170 blood gas analyzer; Corning Medical Instruments, Medfield, MA). The $AVDO_2$ was calculated according to the following formula: $AVDO_2 = Hb \times 1.34$ $(SaO_2 - SvO_2) + 0.003 (PaO_2 - PvO_2)$.

Diagnosis of Delayed Cerebral Infarction

Cranial CT scans (model GE 9800; General Electric Medical Systems, Milwaukee, WI) were obtained in all patients at admission, shortly after surgery or mannitol infusion (1–2 hours), on a daily basis for 3 days, and 1 week after admission. A low attenuation region conforming to a vascular territory identified on CT scanning was regarded as radiographic evidence of delayed infarction if an area of hypoperfusion in the same region was identified on a nuclear medicine single-photon emission CT scan obtained using ^{99m}Tc-hexamethylpropyleneamine oxime

| Characteristic | No. of Patients | |
	Group A (15 patients)	Group B (17 patients)
median age in yrs (range)	50 (23–79)	31 (14–79)
sex (male/female)	9:6	12:5
admission GCS score		
3–5	10	13
6–8	5	4
type of injury		
diffuse head injury	0	12
single/multiple contusion(s)	0	3
intraventricular hemorrhage	0	2
subdural hematoma	7	0
intracerebral hematoma	6	0
cerebral swelling	2	0
mean ICP posttreatment (mm Hg)	13 ± 3.2	22 ± 8.3
mean CPP posttreatment (mm Hg)	80 ± 7.1	71 ± 9.9
outcome (GOS score at 6 mos)		
good/moderately disabled	8	7
severely disabled/vegetative	1	3
dead	6	7

(Fig. 1). Additional criteria for distinguishing an infarcted area from edema were the restriction of the hypodense area to a vascular territory, distinct margins, and persistence beyond the acute injury phase. Isolated low attenuation abnormalities in the posterior cerebral artery distribution were regarded as evidence of herniation and not of infarction.

Patient Outcome

Outcome was assessed 6 months after head injury, by means of a clinic visit or telephone interview, according to the Glasgow Outcome Scale[23] (GOS). Patients with a GOS score of "good" or "moderately disabled" are independent for all their needs and participate in a normal social life; for statistical comparison, these patients were classified as having a favorable outcome. Unfavorable outcome was assigned to those patients who died or were not capable of an independent existence.

Statistical Analysis

Data are expressed as the mean ± standard deviation or, in situations in which samples depart substantially from normal distributions, they are summarized as the median. A two-sample significance of data that departed from a normal distribution was tested using the Mann–Whitney U-test. Student's t-test was used to assess differences between groups when the samples were normally distributed. When appropriate, Pearson's chi-square test was used to test for sample differences on categorical variables. Fisher's exact test was substituted when one or more cells had expected frequencies less than five. Simple regression analysis or Pearson's correlation was used to relate continuous variables to one another. In the case of multiple associations, Bonferronian inequality was used. Statistical significance is assumed for comparisons in which probability is less than 0.01. All statistical analyses

were performed using a commercially available software package (StatView II, 1987; Abacus Concepts, Berkeley, CA).

Results

Patient Characteristics

The clinical characteristics of the patients are summarized in Table 1. The majority of patients (25) were injured in motor vehicle accidents; four patients were injured in a fall, and three suffered blunt trauma. Fifteen patients underwent craniotomy for mass lesions (Group A), whereas 17 patients received intravenous administration of mannitol for elevated ICP (Group B). Overall, the mean ICP following craniotomy or mannitol administration was 17.8 ± 7.8 mm Hg (Table 1). The CPP was greater than 70 mm Hg in 27 patients, between 60 and 70 mm Hg in four Group B patients, and less than 60 mm Hg in one Group B patient. The mean CPP was greater in Group A than Group B patients; overall, the mean posttreatment CPP was 75 ± 9.8 mm Hg (Table 1).

Cerebral Arteriovenous Oxygen Difference

Cerebral AVDO$_2$ was elevated before craniotomy or mannitol administration; the mean AVDO$_2$ for all patients before treatment was 8.6 ± 1.8 vol%. Following craniotomy or mannitol administration, the AVDO$_2$ decreased in 27 patients and increased in five; overall, the mean posttreatment AVDO$_2$ was 6.2 ± 2.1 vol% (Group A, 6 ± 1.9 vol%; Group B, 6.4 ± 2.4 vol%). The calculated AVDO$_2$ demonstrated a significant inverse relationship to SjVO$_2$ both before (r = −0.7, p = 0.001) and after treatment (r = −0.8, p < 0.001). Group B results represent only values obtained before and after the first mannitol treatment. When all values obtained for a given patient receiving multiple mannitol infusions were averaged similar findings were observed. There were no complications related to the use of jugular bulb catheters.

Delayed Cerebral Infarction and Arteriovenous Oxygen Difference

Radiographic evidence of delayed cerebral infarction was identified in six Group A patients and eight Group B patients. The relationship between AVDO$_2$ and delayed cerebral infarction is illustrated in Fig. 2. The mean AVDO$_2$ before craniotomy or mannitol infusion was similar in patients who subsequently did or did not develop radiographic evidence of delayed cerebral infarction. By contrast, after treatment both an elevated AVDO$_2$ (p < 0.001) and a limited improvement (reduction) in an elevated AVDO$_2$ (p < 0.001) were significantly associated with the development of delayed cerebral infarction. All five patients who demonstrated an increase in AVDO$_2$ and all six patients who demonstrated a decrease in AVDO$_2$ that was less than 1 vol% following treatment developed delayed cerebral infarction. By contrast, among the 22 patients in whom the AVDO$_2$ decreased greater than 1 vol%, delayed cerebral infarction was observed in only four (19%).

Outcome and Arteriovenous Oxygen Difference
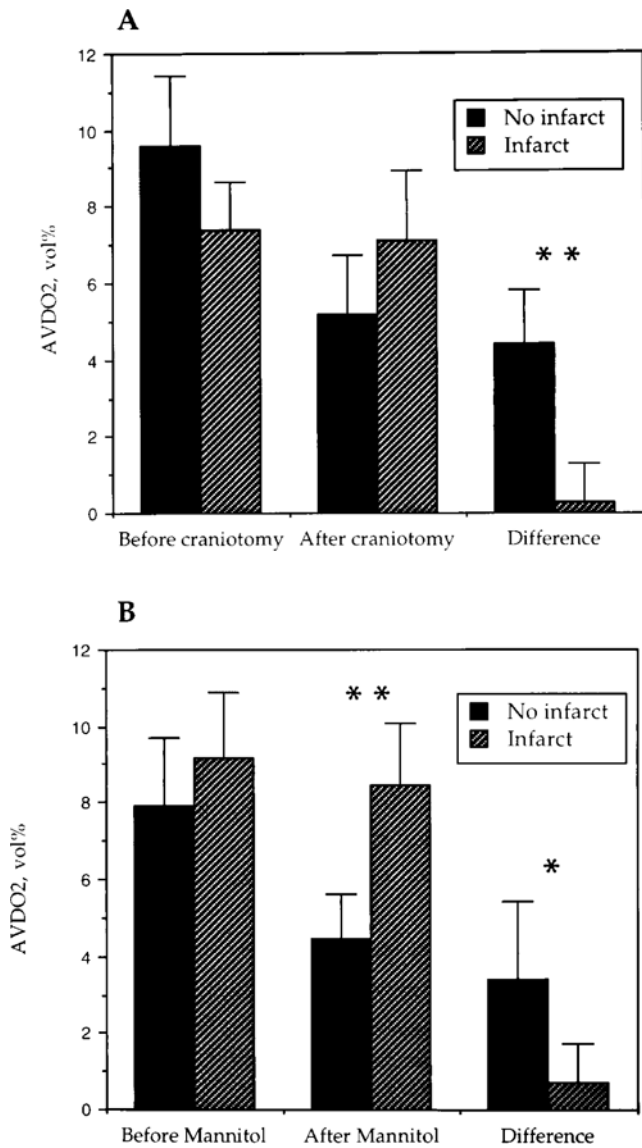
Outcome was assessed at 6 months: 13 patients had

A

B

FIG. 2. Histograms showing the relationship between cerebral AVDO$_2$ and delayed cerebral infarction. Values represent the mean AVDO$_2$ ($\pm$ standard deviation) in patients undergoing craniotomy for traumatic mass lesions (A) or mannitol administration for intracranial hypertension (B). Whereas AVDO$_2$ prior to craniotomy (A) or mannitol administration (B) was not associated with radiographic evidence of cerebral infarction, limited improvement in elevated AVDO$_2$ after treatment was significantly associated with delayed cerebral infarction. *p < 0.01; **p < 0.001.

A
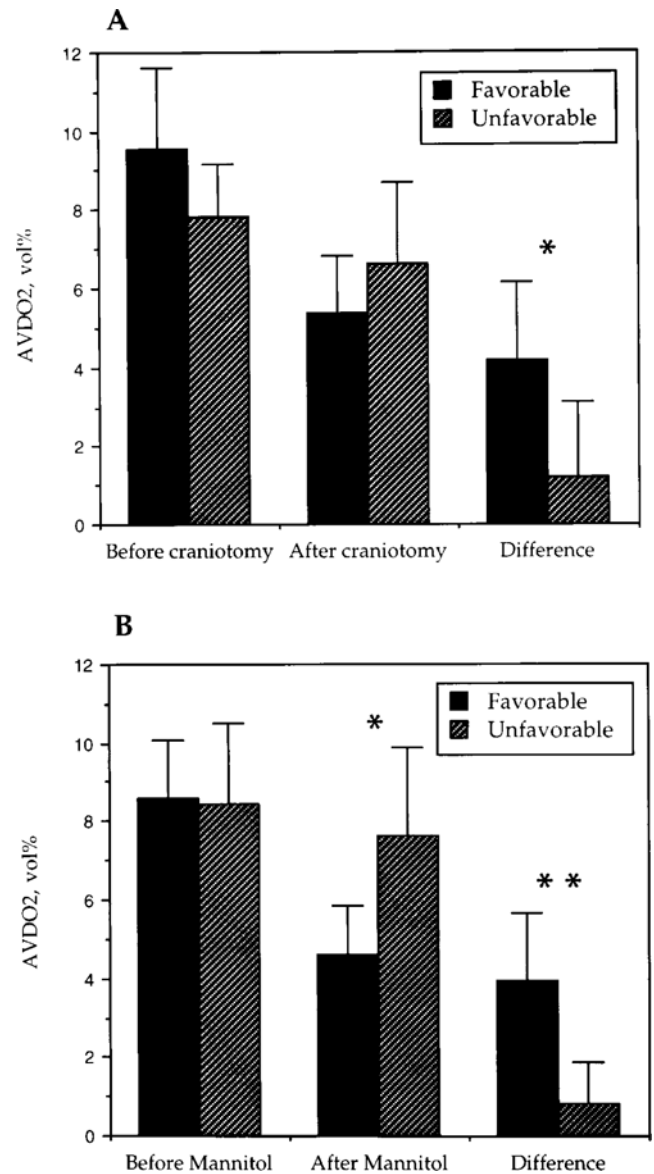

B

FIG. 3. Histograms showing the relationship between cerebral AVDO$_2$ and GOS score at 6 months posttreatment. Values represent the mean AVDO$_2$ ($\pm$ standard deviation) in patients undergoing craniotomy for traumatic mass lesions (A) or mannitol administration for intracranial hypertension (B). Before treatment the AVDO$_2$ was not associated with outcome. By contrast, limited improvement in elevated AVDO$_2$ after treatment was significantly associated with an unfavorable outcome. *p < 0.01, **p < 0.001.

died, four remained in a persistent vegetative state or were severely disabled, and 15 had made a good recovery (Table 1). Delayed cerebral infarction was identified in 85% of patients who experienced an unfavorable outcome, whereas only 13% of patients who experienced a favorable outcome demonstrated radiographic evidence for delayed cerebral infarction (p < 0.01). The relationship between AVDO$_2$ and outcome is summarized in Fig. 3. Whereas the AVDO$_2$ before treatment was similar, an elevated posttreatment AVDO$_2$ (p = 0.002) and a limited improvement in an elevated AVDO$_2$ after treatment (p <

0.001) were significantly associated with an unfavorable outcome. Unfavorable outcomes were observed in all five patients who demonstrated an increase in AVDO$_2$ and in five (83%) of the six patients in whom the AVDO$_2$ decreased less than 1 vol%. When posttreatment AVDO$_2$ decreased more than 1 vol% (21 patients), seven patients (33%) experienced an unfavorable outcome.

Other Variables

An important point in the interpretation of our results is

TABLE 2
Factors associated with radiographic evidence for delayed cerebral infarction in 32 patients with severe head injury*

Factor	All Patients (32 patients)	Group A (15 patients)	Group B (17 patients)
age	+	−	+
admission GCS score	−	−	−
ICP (posttreatment)	−	−	+
CPP (posttreatment)	−	−	−
AVDO$_2$ (pretreatment)	−	−	−
AVDO$_2$ (posttreatment)	+ +	−	+ +
AVDO$_2$ (change)	+ +	+ +	+

* + = $p < 0.01$; + + = $p < 0.001$; − = no significance.

TABLE 3
Factors associated with outcome 6 months after treatment in 32 patients with severe head injury*

Factor	All Patients (32 patients)	Group A (15 patients)	Group B (17 patients)
age	−	+	−
admission GCS score	+	−	−
ICP (posttreatment)	−	−	−
CPP (posttreatment)	−	−	−
AVDO$_2$ (pretreatment)	−	−	−
AVDO$_2$ (posttreatment)	+	−	+
AVDO$_2$ (change)	+ +	+	+ +

* + = $p < 0.01$; + + = $p < 0.001$; − = no significance.

the relationship between AVDO$_2$ and variables such as age, admission GCS score, ICP, and CPP. Before treatment no relationship was observed. After treatment, a moderate relationship between AVDO$_2$ and age (r = 0.4, p = 0.01) and between AVDO$_2$ and ICP (r = 0.5, p = 0.003), particularly in mannitol-treated patients, was observed. No relationship between posttreatment AVDO$_2$ and admission GCS score or posttreatment CPP was observed.

The association between delayed infarction or outcome and age, admission GCS score, ICP, or CPP was examined using bivariate analysis; the results are listed in Tables 2 and 3. Advanced age was significantly associated with delayed cerebral infarction (p = 0.002) and older patients undergoing craniotomy were more likely to experience an unfavorable outcome (p = 0.004). The admission GCS score did not predict delayed cerebral infarction, but a low admission GCS score was associated with unfavorable outcome (p = 0.006). In patients treated with mannitol there was a significant association between elevated posttreatment, but not pretreatment, ICP and delayed cerebral infarction (p = 0.004). An association between CPP and delayed infarction or outcome was not observed.

Discussion

In the present report we describe our experience using jugular bulb monitoring in 32 severely head injured patients. The results demonstrate that AVDO$_2$ is elevated in patients suffering traumatic mass lesions or intracranial hypertension. When measured before craniotomy or mannitol administration, the AVDO$_2$ was not predictive of delayed cerebral infarction or outcome. By contrast, limited improvement in an elevated AVDO$_2$ after either craniotomy or mannitol administration was significantly associated with both delayed cerebral infarction and unfavorable outcome. In addition, a relationship between CPP and AVDO$_2$ was not observed. These findings emphasize the complex pathophysiology leading to delayed cerebral infarction and the need for repeated or continuous observations in patients suffering severe traumatic brain injury.

Methodological Considerations

There are several important points to bear in mind when interpreting jugular bulb oxygen monitoring results. First,

focusing on blood samples from one jugular bulb may lead one to overlook ischemia or infarction in the other hemisphere because differences in oxygen saturation between the two hemispheres can occur. These differences, however, are of potential clinical significance in individuals with unilateral lesions.[15,16,47,48] The likelihood of missing contralateral abnormalities was reduced in this study by placing the catheter ipsilateral to mass lesions because experimental and clinical studies demonstrate that ischemia is generally identified adjacent to traumatic lesions.[25,30,45] In Group B patients (who had no mass lesion) the catheter was placed on the dominant side of jugular flow, usually the right side, by evaluating the size of the jugular foramen on CT scanning.[12] The ICP monitor was placed ipsilateral to the jugular catheter. Second, AVDO$_2$ samples may lead one to miss regional ischemia. We cannot rule out this possibility but we believe that it is unlikely because radiographic evidence of infarction, which always correlated with a defined vascular territory, was only observed in patients in our study whose posttreatment AVDO$_2$ was greater than 6 vol%. By contrast, when posttreatment AVDO$_2$ was less than 6 vol%, no evidence for cerebral infarction was observed. Third, extracerebral contamination may be associated with sample withdrawal, particularly when CBF is low. Dye injection studies, however, demonstrate that jugular bulb samples contain insignificant amounts of extracerebral blood, provided the catheter is within the jugular bulb.[47] We were careful, therefore, to obtain radiographic confirmation of the catheter position in all patients. Finally, there is the question as to whether venous obstruction in the neck can elevate ICP. We think this problem is unlikely because we did not observe an ICP increase during catheter insertion. Studies by Goetting and Preston[17] have similarly demonstrated no evidence of jugular vein obstruction that is sufficient to elevate ICP in the catheterized vessel. Bearing these caveats in mind, when used carefully, jugular bulb oxygen saturation monitoring may provide a reliable estimate of cerebral oxygenation.

Arteriovenous Oxygen Difference and Cerebral Ischemia

Our results demonstrate that before treatment an elevated AVDO$_2$ cannot be used to predict delayed cerebral infarction. By contrast, limited improvement in an elevated AVDO$_2$ after treatment, despite adequate CPP, is significantly associated with delayed cerebral infarction. In

studies comparing $AVDO_2$ and CBF, the highest $AVDO_2$ values correlate with reduced CBF, whereas low $AVDO_2$ values are observed in hyperemic patients.[4,36–38,43] Similarly, therapeutic manipulations that decrease or increase CBF are associated with an increase and decrease in $AVDO_2$, respectively.[35,43] The initial pretreatment $AVDO_2$ value, therefore, indicates that the brain is compensating for reduced flow by extracting more oxygen. Where sufficient aerobic reserve existed, the $AVDO_2$ improved after treatment, but in those patients with an exhausted reserve, no improvement in $AVDO_2$ was observed and delayed infarction occurred. The extent of aerobic reserve may partly explain the association of advanced age, $AVDO_2$, and infarction because older patients are more likely to demonstrate atherosclerosis and vascular disease and thus have limited compensatory reserve. The lack of $AVDO_2$ improvement, however, represents a preinfarction state because the posttreatment $AVDO_2$ remained elevated. By contrast, cerebral infarction is associated with a significant reduction in $AVDO_2$ because the cerebral metabolic rate of oxygen decreases when tissue dies.[37,43] In patients with cerebral infarction, knowledge of cerebral lactate may be useful;[42] however, the compensated but hypoperfused state is important to recognize because the deleterious effects of ischemia and hypoxia may still be ameliorated.

Cerebral Perfusion Pressure and Cerebral Infarction

We did not observe a correlation between $AVDO_2$ and CPP, whereas a relationship between ICP and $AVDO_2$ was observed. Experimental studies using magnetic resonance spectroscopy have demonstrated that ICP and $AVDO_2$ correlate with brain energy failure, as identified by changes in phosphocreatine. By contrast, brain energy failure occurs over a wide range of CPPs.[49,50] Similarly, clinical studies have demonstrated that baseline CBF values may not correlate with CPP or ICP.[30] Other studies, however, have demonstrated a significant linear correlation among CPP (but not ICP) and $SjVO_2$ and $AVDO_2$, provided the CPP is less than 70 mm Hg.[7,8] The majority of patients in our series, however, demonstrated CPPs greater than 70 mm Hg, which in part may explain the poor correlation between $AVDO_2$ and CPP. It is also conceivable that increased ICP may reflect the irreversible end result of biochemical and cellular events, rather than act as the cause of neuron damage, and thus may demonstrate a relationship with $AVDO_2$.

An important finding in this series was the radiographic evidence of delayed cerebral infarction despite an adequate CPP. This finding is consistent with experimental studies in which an ischemic zone has been shown adjacent to subdural hematomas in rats with an adequate CPP.[32] Therapies based on CPP maintenance[44] or determination of an ideal CPP by calculation of a transcranial Doppler pulsatility index and $SjVO_2$ for individual patients[7,8] have been demonstrated to be feasible management strategies for head-injured patients. We believe that an adequate CPP is important in head injury management. However, our results indicate that an adequate CPP alone is insufficient to prevent cerebral infarction in all patients. The progression to infarction despite adequate CPP may be explained by altered autoregulation, direct toxicity

from blood, or neurochemical alterations. For example, experimental models of traumatic hematoma[6] or diffuse axonal injury[13] and clinical studies[1] demonstrate that levels of excitatory amino acids, such as glutamate, which in high concentrations appear integral to the pathophysiological mechanism of neuron injury and death in cerebral ischemia,[27] are increased after head injury and may alter membrane permeability through activation of ligand-gated channels. Similarly, following injury, direct mechanical stimulation can cause ionic fluxes and neuron firing. This ionic destabilization places enormous energy demands on the cells to activate pumping mechanisms to restore the ionic balance in the first few hours after trauma.[20] Microdialysis studies in head-injured patients demonstrate elevated glutamate levels during episodes of jugular oxygen desaturation.[41] Whether the failure of $AVDO_2$ to improve after treatment reflects a continued demand for oxygen to restore membrane stability affected by sustained excitotoxicity or mechanical disruption is not clear from our study. However, the failure of $AVDO_2$ to improve after treatment does define a subgroup of patients who, after treatment, can progress to cerebral infarction despite adequate CPP.

Arteriovenous Oxygen Difference and Outcome

The results in this series demonstrate that a limited improvement in elevated $AVDO_2$ following craniotomy or mannitol administration is associated with an unfavorable outcome and supports a role for $AVDO_2$ monitoring as a predictive tool in head injury. By contrast, posttreatment ICP and CPP in this group of severely head injured patients were not reliable outcome predictors. Several investigators using continuous jugular oxygen monitors have observed a significant association between episodes of jugular oxygen desaturation and poor outcome following head injury.[10,11,40,41,46] For example, Robertson, et al.,[41] observed a 21% mortality rate in patients with no desaturation, 37% after a single episode, and 69% after multiple episodes. Poor outcome may also be associated with a reduced $AVDO_2$,[21,40] because cerebral metabolism is significantly depressed once cerebral infarction has occurred.

Outcome after head injury depends on many variables; although not conclusive, the observations in this report lead us to suggest that posttreatment levels of $AVDO_2$ may provide reliable and, perhaps, independent outcome prediction. In other studies evaluating continuous jugular oxygen saturation after head injury, multivariate analysis has indicated that after adjustment for outcome determinants such as age, ICP, and GCS score, the number of desaturations continues to demonstrate a significant association with outcome: one episode of desaturation doubled the risk of a poor outcome, whereas multiple desaturations were associated with a 14-fold increase in the risk of poor outcome.[18] Whether the predictive information provided by $AVDO_2$ monitoring is a useful management tool is not addressed in this study. The ability to predict outcome, however, is important because when outcome can be accurately predicted, management can be directed at potentially avoidable deleterious factors. In addition, physiological categorization, based on $AVDO_2$ values, of patients at risk for delayed cerebral infarction before CT evidence for ischemia is observed, may help distinguish different

causes of intracranial hypertension or cerebral ischemia early in the patient's clinical course when specific targeted therapies are ideally started.

Applications for Jugular Oxygen Monitoring

The observations described in this report demonstrate that repeated AVDO$_2$ measurements are more reliable than a single pretreatment measurement. In addition, posttreatment AVDO$_2$ values are best interpreted by comparing them with pretreatment values. Intermittent CBF measurements may similarly miss episodes of reversible ischemia.[43] Therefore, continuous SjVO$_2$ monitors, which use oximetric techniques, have been developed. The relationship between AVDO$_2$ and SjVO$_2$ is reciprocal. Although interpretation of SjVO$_2$ is based on several assumptions, a good correlation between SjVO$_2$ measured fiberoptically and via catheter has been observed.[46] Unfortunately, jugular saturation monitors require frequent recalibration and a high percentage of readings are erroneous because of catheter movement, displacement, intimal impaction, or clot formation.[14,46] Despite these limitations, jugular saturation monitoring can help guide therapy, optimize CPP, and measure the effects of therapeutic interventions, such as ventilation or mannitol administration, to ensure adequate CBF to meet metabolic demands.[8,10,11,35,49] Jugular saturation monitors may also detect transient episodes of cerebral hypoxia from potentially preventable systemic causes such as hypotension, hypoxia, fever, or seizures.[11,18,40]

The identification of inadequate cerebral oxygenation is important in the management of cases of head injury. The validity of using CPP as a measure of cerebral oxygenation becomes limited when autoregulatory mechanisms are disturbed and it also leads one to ignore other potential causes of cerebral ischemia after head injury. Results obtained in cerebral blood flow studies are disappointing in identifying which patient is at risk for ischemia because reduced, normal, and increased flow can be associated with a poor outcome.[5,28,30,34,36–40] These discrepancies may result, in part, from methodological differences. However, quantification of CBF alone cannot define the relationship between oxygen supply and consumption because the adequacy of oxygenation is also determined by variables such as autoregulation, CO$_2$ reactivity, and coupling of CBF and cerebral metabolism that are disturbed in a significant number of head-injured patients.[2,3,9,14,26,34,36] Furthermore, confounding variables such as vasospasm, anemia, hypoxia, and seizures may reduce the oxygen carrying capacity. A measure of the balance between cerebral oxygen delivery and consumption, such as AVDO$_2$, may therefore be useful and, when combined with multimodality monitoring, may provide a reasonable means to identify patients in which secondary ischemic damage can be ameliorated by therapeutic intervention directed at its pathophysiological mechanism.

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