Cerebral blood flow and vasoresponsivity within and around cerebral contusions

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There is increasing evidence that regional ischemia plays a major role in secondary brain injury. Although the cortex underlying subdural hematomas seems particularly vulnerable to ischemia, little is known about the adequacy of cerebral blood flow (CBF) or the vasoresponsivity within the vascular bed of contusions. The authors used the xenon-enhanced computerized tomography (CT) CBF technique to define the CBF and vasoresponsivity of contusions, pericontusional parenchyma, and the remainder of the brain 24 to 48 hours after severe closed head injury in 10 patients: six patients with one contusion and four with two contusions, defined as mixed or high-density lesions on CT scanning. The CBF within the contusions (29.3 ± 16.4 ml/100 g/minute, mean ± standard deviation) was significantly lower than both that found in the adjacent 1-cm perimeter of normal-appearing tissue (42.5 ± 15.8 ml/100 g/minute) and the mean global CBF (52.5 ± 17.5 ml/100 g/minute) (p < 0.004, repeated-measures analysis of variance). A subset of seven patients (10 contusions) also underwent a second Xe-CT CBF study during mild hyperventilation (a PaCO₂ of 24–32 mm Hg). In only two of these 10 contusions was vasoresponsivity less than 1% (range 0%–7.6%); in the rim of normal-appearing pericontusional tissue, it was 0.4% to 9.1%. The authors conclude that CBF within intracerebral contusions is highly variable and is often above 18 ml/100 g/minute, the reported threshold for irreversible ischemia. Intracontusional CBF is significantly reduced relative to surrounding brain parenchyma, and CO₂ vasoresponsivity is usually present. In the contusion and the surrounding parenchyma, vasoresponsivity may be nearly three times normal, suggesting hypersensitivity to hyperventilation therapy. Given this possible hypersensitivity and relative hypoperfusion within and around cerebral contusions, these lesions are particularly vulnerable to secondary injury such as that which may be caused by hypotension or aggressive hyperventilation.

KEY WORDS • contusion • carbon dioxide reactivity • head injury • hyperventilation • regional cerebral blood flow • xenon-enhanced computerized tomography
We used the stable xenon-enhanced CT (Xe-CT) CBF method to measure CBF because it provides images of regional blood flow with a higher resolution than other CBF measuring techniques. In addition, using this technique one can select with reliable accuracy regions of interest that are much smaller than those possible using other CBF techniques. Stable xenon has been proven to be safe and does not significantly alter intracranial pressure (ICP) when administered over a 4.5-minute period with a constant PaCO$_2$.

**Materials and Methods**

**Retrospective Selection of Patients**

We reviewed the records of all patients admitted to our neurosurgical service with a severe TBI (Glasgow Coma Scale score of 8 or less) between 1991 and 1994. This study included all patients who had contusions that were defined as heterogeneous mixed or high-density lesions on CT scanning and who underwent Xe-CT CBF studies within 48 hours of injury. Patients who had purely homogeneous high density lesions on CT scanning that were more consistent with intracerebral hematoma were not included in the study. The selection criteria used to determine which patients underwent Xe-CT CBF studies were predetermined by our TBI protocol.

Our study sample was composed of 10 patients (nine men and one woman) with a total of 14 contusions that were sustained largely from motor vehicle accidents and falls. Two patients were found unconscious and the cause of their contusions was not known. The average age of the study sample was 43 years (median 37.5 years). Four patients had bilateral focal areas of contusion. Six patients eventually required craniotomies for uncontrolled intracranial pressure (ICP) or severe mass effect. In accordance with our TBI protocol, all patients were intubated, mechanically ventilated, pharmacologically paralyzed and sedated, and subjected to placement of a ventriculostomy catheter for ICP monitoring. A radial artery catheter was also placed in all patients for continuous blood-pressure monitoring. Patients who had an ICP above 20 mm Hg for more than 15 minutes were treated using a stepwise intervention consisting of intermittent ventricular drainage and a course of diuretic medication. No patients in this study were treated with barbiturate medications prior to obtaining CBF measurements. One patient had an ICP of 22 mm Hg during the CBF study; the others had ICPs that ranged from 8 to 20 mm Hg. Because previous studies have documented significant changes in CBF during the first 24 hours after TBI, all CBF examinations reported here were obtained between 24 and 48 hours after injury.

**Cerebral Blood Flow Measurement Studies**

The CBF studies were performed using a CT scanner (model 9800; GE Medical Systems, Milwaukee, WI) equipped for Xe-CT CBF imaging. Technical details of these studies have been described elsewhere. While the patients inhaled a mixture of 33% Xe/67% O$_2$ (XeScan stable xenon in oxygen USP; Praxair Pharmaceutical Gases, Danbury, CT) for 4.5 minutes, CT scans were obtained at three levels, 2 cm apart. A radial artery catheter was also placed in all patients for continuous blood-pressure monitoring. Patients who had an ICP above 20 mm Hg for more than 15 minutes were treated using a stepwise intervention consisting of intermittent ventricular drainage and a course of diuretic medication. No patients in this study were treated with barbiturate medications prior to obtaining CBF measurements. One patient had an ICP of 22 mm Hg during the CBF study; the others had ICPs that ranged from 8 to 20 mm Hg. Because previous studies have documented significant changes in CBF during the first 24 hours after TBI, all CBF examinations reported here were obtained between 24 and 48 hours after injury.

Direct measurements of CBF were obtained in three regions of interest: within the CT-defined contusion, in a 1-cm rim of normal-appearing brain tissue surrounding the contusion, and in the rest of the brain excluding the contusion and pericontusional area ("global") (Figs. 1 and 2). Mean arterial blood pressures were maintained at 100 ± 10 mm Hg, and baseline PaCO$_2$ values were kept between 31 and 39 mm Hg during these CBF studies. After a 20-minute washout period, a subset of seven patients underwent a second Xe-CT CBF study to evaluate CBF response to a hyperventilation challenge. In these patients, the PaCO$_2$ was reduced by 6 to 10 mm Hg before the Xe-CT CBF study was repeated.

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**Fig. 1.** A: Axial computerized tomography (CT) scan showing a right temporal area of hyperdensity and a peripher-
al area of mixed density, which represent contusion. B: Xenon-enhanced color-flow CT cerebral blood flow (CBF) examination scan of the same level shown in A at a PaCO$_2$ of 38 mm Hg displaying markedly ischemic intracontusional CBF, but relatively normal pericontusional CBF. The global CBF appears slightly hyperemic at this PaCO$_2$ level. C: Xenon-enhanced color-flow CT CBF examination scan of the regions shown in A and B after mild hyperventilation. At a PaCO$_2$ of 32 mm Hg, the CBF within the contusion continues to be ischemic; however, the pericontusional CBF is markedly diminished and shows marginal ischemia. The global CBF is also markedly reduced after hyperventilation.
The mean, median, and standard deviations of CBF in the areas of interest were determined for the 14 lesions at baseline CO$_2$ levels of 32 to 39 mm Hg. A repeated-measures analysis of variance was used to evaluate the relationship of blood flows within the contusions and their adjacent normal-appearing hemispheres. In the subset of patients who underwent double PaCO$_2$-level CT CBF studies (hyperventilation challenge), CO$_2$ vasoresponsivity in each of the three regions of interest was calculated as the percentage change in CBF per millimeter of mercury change in PaCO$_2$, using the standard equation reported in previous studies.

**Results**

Table 1 shows the location of each contusion, the PaCO$_2$ level at the time of the study, and the CBF values in the areas of interest for each patient. The volumes of the contusions ranged from 20.7 ml to 100 ml with a mean volume of 47.8 ml, and were well within the resolution capabilities of the Xe-CT CBF method. The CBF within contusions was highly variable and ranged from 9.6 to 70.1 ml/100 g/minute. Only three contusions had blood flows consistent with severe ischemia (< 18 ml/100 g/minute) at baseline CO$_2$ levels. The CBF within the 14 contusions was 29.3 ± 16.4 ml/100 g/minute (mean ± SD) and was significantly lower than the mean CBF of 42.5 ± 15.8 ml/100 g/minute in the adjacent 1-cm perimeter of normal-appearing tissue (p = 0.004). The mean CBF within contusions also was significantly lower than the mean global CBF of 52.5 ± 17.5 ml/100 g/minute (p = 0.001).

In the seven patients (10 lesions) who underwent double Xe-CT studies, the CBF in all three regions decreased significantly with mild hyperventilation (a PaCO$_2$ of 24–32 mm Hg) (p = 0.001). The CO$_2$ vasoresponsivity (normally a 3% change in CBF per millimeter of mercury change in PaCO$_2$) was less than 1% in only two of 10 contusions, and the range was 0% to 7.6%. In the pericontusional rim of normal-appearing tissue, it was 0.4% to 9.1%. A scatterplot of CBF values demonstrates a direct relationship between CBF and PaCO$_2$ (Fig. 3).

**Discussion**

Miller has suggested that cerebral ischemia is the principal cause of secondary brain injury after severe head trauma, and postmortem studies of the brains of patients who died of severe head injuries support this theory. In addition, the regional reduction of CBF typically seen after a severe head injury has been correlated with a poor outcome. Therapy used for patients with severe TBI often includes interventions such as hyperventilation or osmotic diuresis, both of which directly affect CBF. Characterizing the CBF and vascular sequelae of various posttraumatic lesions would thus help in avoiding iatrogenic ischemia.
Blood flow measurements using Xenon-133 show that the usual response to hyperventilation in patients with severe TBI is a global decrease in CBF, although a regional inverse steal phenomenon has been documented in rare cases. Recent studies using the stable Xe-CT CBF technique have found that global CBF virtually always falls to levels that are at least 50% below normal values during the first few hours after a severe head injury. Marion, et al., found that CBF typically increases after the first 24 hours in these patients but that global CBF values vary widely depending on the type of TBI.

In addition to the global CBF changes caused by trauma, several investigators have described significant regional variations in CBF, most commonly in patients with subdural hematomas. Bouma and associates found regional reductions in CBF as well as regional ischemia in the hemisphere ipsilateral to acute intracerebral hematomas without an impairment in brainstem blood flow. Obrist and colleagues reported that a large proportion of patients with unilateral mass lesions had significantly decreased CBF adjacent to the mass. Salvant and Muizelaar noted significant regional CBF reductions in brain tissue underlying acute subdural hematomas within the first 48 hours of injury, even after evacuation of the lesion. In addition, they documented a 9% incidence of CBF values below 18 ml/100 g/minute in this group of patients during the first 24 hours after injury. Our data support the findings of Schröder, et al., but differ in some respects. All patients in the current study had CBF measurements between 24 and 48 hours, whereas their time of study postinjury ranged from 2 to 204 hours. In addition, these authors defined pericontusional tissue as all contiguous low-density zones adjacent to the contusion, whereas we defined the pericontusional tissue sampled in our population as a 1-cm rim of normally appearing parenchyma. Such differences in studies may account for the markedly profound hypoperfusion found within contusions and pericontusional tissue in their study compared to only the relative hypoperfusion found in the adjacent parenchyma of our patients.

Although some have advocated the use of aggressive hyperventilation for ICP control and normalization of cerebral glucose uptake, research has shown that hyperventilation reduces CBF more consistently than ICP. Obrist and colleagues demonstrated that PaCO₂ reduction from 35 to 25 mm Hg led to significant reductions in CBF in 29 of 30 TBI patients, whereas an associated reduction in ICP was observed in only 15 of the 30 patients. Moreover, the greatest reductions in ICP in this study appeared to occur when the PaCO₂ was lowered to only 35 mm Hg. Reductions below this level have a diminishing effect on ICP.

In patients with severe head injuries, cerebral contusions are some of the most common lesions identified on CT scans obtained on arrival at the hospital. The contusions appear as discrete hypodense or mixed-density lesions and are usually located in the temporal or frontal lobes. These lesions generally are believed to represent irreversibly damaged tissue and their aggressive surgical resection is advocated if ICP is elevated or if the location raises concern about herniation. To our knowledge, how-

**TABLE 1**

<table>
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<tr>
<th>Case No.</th>
<th>Age (yrs), Sex, Mechanism of Injury</th>
<th>GCS Score</th>
<th>Area of Contusion</th>
<th>Volume (ml)</th>
<th>PaCO₂ (mm Hg)</th>
<th>CBF (ml/100 g/min)</th>
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<td>1</td>
<td>17, M MVA, fall rt frontoparietal</td>
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* Dual readings for PaCO₂ and CBF are presented for seven patients who underwent two xenon-enhanced computerized tomography CBF studies. Abbreviations: CBF = cerebral blood flow; GCS = Glasgow Coma Scale; MVA = motor vehicle accident.
ever, no prior study has investigated the CBF or vasoresponsivity in and around these lesions to validate the theory that the CT-defined abnormality is irreversibly ischemic. Only three of the 14 contusions in the present study had a CBF value below 18 ml/100 g/minute, the threshold for irreversible ischemia. This finding indicates that portions of posttraumatic contusions may, in fact, be viable. The pericontusional CBF, although significantly lower than the global CBF, was below the threshold for irreversible ischemia in only one of the patients studied. Moreover, vasoresponsivity was usually present within and around these lesions and is highly variable. Within the contusion and in the pericontusional parenchyma, vasoresponsivity may be as high as three times normal. Given the relative hyperperfusion of these lesions and the possible hypersensitivity to changes in PaCO$_2$, significant hypocarbia may convert marginally ischemic zones into frank ischemic zones.

One of the seven patients who underwent two Xe-CT CBF studies showed evidence of an “inverse steal” phenomenon. The cause of inverse steal has been postulated to be due to loss of autoregulation in the vascular bed of ischemic brain parenchyma.  Thus, when hyperventilation causes vasoconstriction in normal areas of parenchyma with intact vasoresponsivity, blood is shunted into the low-resistance vessels of the adjacent ischemic tissue. Although Lassen has suggested that shunting may improve CBF in areas of ischemia, others have proposed that inverse steal may exacerbate brain edema.

The significantly lower CBF in and around the contusions compared to the global CBF indicates that these areas are particularly vulnerable to ischemia and secondary injury. Our results suggest that the treatment of patients with postrumatic cerebral contusions should be aimed at enhancing blood flow to these vulnerable regions. Therapeutic strategies to control ICP should avoid interventions that could reduce CBF even further, such as aggressive hyperventilation. Moreover, optimum perfusion pressure and avoidance of hypotension are critical in minimizing ischemia in these vulnerable regions.

Conclusions

Cerebral blood flow within intracerebral contusions is highly variable after a severe head injury and often is above 18 ml/100 g/minute, the reported threshold of irreversible ischemia. Vasoresponsivity within and around contusions is also highly variable. The CBF within the contusions is significantly reduced relative to surrounding brain parenchyma. Given the relative hyperperfusion within and around cerebral contusions and the possible hypersensitivity to PaCO$_2$ manipulation, these lesions are particularly vulnerable to secondary injury such as that which may be caused by hypotension or aggressive hyperventilation.

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References


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