

Midline Shift after Severe Head Injury: Pathophysiologic Implications

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Objective: To investigate the mechanism of the adverse effect of midline shift after severe traumatic brain injury.

Methods: This study compared averaged cerebral metabolic parameters of patients with midline shift > 5 mm (S) on initial computerized tomography scan to those of patients with shift ≤ 5 mm (NS). The effect of an acute subdural hematoma (SDH) was determined by separating patients into those with and those without SDH and then re-examining the effect of shift in these subgroups.

Results: Four hundred fifty-four pa-

tients were studied. Cerebral metabolic rate of oxygen ($CMRO_2$, in $mL/100$ g per min) was always lower with shift: 1.74 for SDH-S versus 2.21 for SDH-NS ($p < 0.001$), and 1.80 for non-SDH-S versus 2.24 for non-SDH-NS ($p < 0.001$). No other major effects of shift were seen in SDH patients. Among non-SDH patients, shift was associated with higher intracranial pressure (ICP): 23.1 mm Hg versus 16.3 mm Hg ($p < 0.001$). Other differences between shift and nonshift patients in the non-SDH group were due at least in part to interventions to treat the elevated ICP.

Conclusion: Midline shift after severe traumatic brain injury is associated with reduced $CMRO_2$, regardless of whether or not SDH is present. The deleterious effects of subdural blood may be related more to the mass effect of large SDHs than to the biochemical abnormalities caused by small amounts of blood in the subdural space.

Key Words: Cerebral blood flow, Cerebral metabolic rate of oxygen, Head injury, Intracranial pressure, Midline shift, Subdural hematoma, Traumatic brain injury.

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Midline shift after traumatic brain injury (TBI) is widely recognized as an important marker of severe injury. Numerous reports describe the association of a large amount of midline shift on computed tomographic (CT) scan (usually described as > 5 mm) with poor outcome or other adverse sequelae of TBI.^{1–24} This same association of midline shift with poor outcome has been reported for other pathologic entities, such as embolic stroke,²⁵ spontaneous intracerebral hemorrhage,^{26–28} and neonatal hemorrhagic infarction.²⁹ The presence of midline shift > 5 mm is a commonly used indication for emergency evacuation of an acute intracranial hematoma, whether traumatic or nontraumatic.^{30–32}

Despite the size of this body of literature, the pathophysiologic basis of the deleterious effect of midline shift after TBI remains obscure. Analysis of this issue is complicated by the fact that posttraumatic midline shift is usually caused by an acute subdural hematoma (SDH)¹⁵ (74% in the current report), making it difficult to choose between the blood clot or the midline shift as the more important factor associated with adverse posttraumatic pathophysiologic events. By using a rodent model of SDH, Miller and colleagues have

reported that the presence of blood overlying the cortex is more important than globally raised intracranial pressure (ICP) in terms of causing ischemic damage to the underlying tissue,³³ perhaps because of the release of substances from the overlying hematoma.^{33,34} A different conclusion was reached by Duhaime et al., who also used a rodent model, to demonstrate significantly more histologic damage from subdural blood when this blood was injected into a closed subdural space under pressure than when it was simply layered over exposed cortex without pressure.³⁵ In a model of intracerebral hematoma, Jenkins and colleagues invoked both local tissue pressure and vasoactive substances as playing a role in the immediate reduction in blood flow after intracranial hemorrhage, but they proposed tissue pressure as the more important factor in later ischemic neuronal damage.³⁶

Salvant and Muizelaar examined cerebral blood flow (CBF) and metabolism in 54 patients with severe head injury with SDH and compared these data with those from 76 patients with severe head injury without mass lesions or midline shift.³⁷ They concluded that, in patients with SDH, the reduction in CBF during the first 48 hours after severe head injury is most likely due to a decrease in cerebral metabolism, energy utilization, or both. Although these authors report that nine of their patients did not undergo surgery because the SDH was small and caused little or no shift, they did not investigate the effect of midline shift on their data.

The purpose of this investigation was to examine the relationship between sizable midline shift and disturbances in cerebral physiology after severe head injury. In addition, the influence of an acute SDH was investigated by classifying patients according to whether a SDH was present or absent

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and then analyzing these subgroups according to the presence or absence of midline shift.

MATERIALS AND METHODS

This report is based on prospectively collected data from 454 patients with severe head injury admitted to the Neurosurgical Intensive Care Unit of Ben Taub General Hospital, Houston, Texas. Patients were included if they were not obeying commands (Glasgow motor score ≤ 5) upon postresuscitation neurologic examination or if they deteriorated to this level within 48 hours of admission. Rarely, patients with head injury were not enrolled if consent could not be obtained from family members or if patients were so neurologically devastated that they were admitted to the intensive care unit only for stabilization and evaluation for possible organ donation, e.g., gunshot wound through the diencephalon with nonreactive pupils and Glasgow Coma Scale score of 3.³⁸ Except for such cases, these patients were all enrolled consecutively.

All patients were managed by standardized protocols that emphasize immediate evacuation of large mass lesions and prevention and rapid treatment of secondary insults. All patients underwent monitoring of core temperature and aggressive treatment of fever.

CT scans of the head were obtained in all patients as soon as possible after arrival in the emergency center, or immediately upon worsening of the neurologic examination for those patients who entered the study after neurologic deterioration. A neurosurgeon used the Traumatic Coma Data Bank classification scheme³⁹ to analyze each CT scan so that this information could be entered into a computerized database. One hundred twenty-five patients demonstrated midline shift > 5 mm on their initial CT scans. Three hundred twenty-nine patients had either no midline shift or ≤ 5 mm of shift.

The 454 patients were also divided into groups based on whether or not subdural blood was present. One hundred ninety patients had a detectable amount of acute blood in the

subdural space as visualized by CT scan. Ninety-two of these had shift > 5 mm (SDH-S), and 98 had no shift or shift ≤ 5 mm (SDH-NS). Two hundred sixty-four patients did not have a subdural hematoma. Thirty-three of these were shift patients (non-SDH-S). The remaining 231 non-SDH patients had midline shift ≤ 5 mm (non-SDH-NS). All protocols were approved by the Baylor Affiliates Review Board for Human Subject Research.

Physiologic Measurements and Data Collection

ICP was monitored continuously in all patients. In the vast majority of cases, ventriculostomy catheters were used to monitor ICP. When compressed ventricles or other factors precluded insertion of a ventriculostomy catheter, ICP was monitored with a miniaturized strain gauge or fiberoptic catheter. Cerebral perfusion pressure (CPP) was obtained by subtracting ICP from a simultaneous recording of mean arterial blood pressure (MAP) measured with an indwelling radial artery catheter. Hourly recordings of ICP, CPP, and MAP were used for the analyses in this report. For each patient, all measurements were averaged to calculate a mean value for the entire monitoring period.

Global CBF was determined by the Kety-Schmidt technique,⁴⁰ with N₂O as a tracer. This technique is inexpensive, can be performed at the bedside as often as necessary, and has little effect on cerebral hemodynamics at the low concentrations of nitrous oxide used. Because the same blood sample from the jugular bulb is used to measure jugular venous oxygen content, determinations of cerebral metabolic rate with this technique may be more accurate than those obtained by other methods.⁴¹ Despite these advantages, this technique is limited in that it measures only global CBF and cannot provide information about possible regional heterogeneity of cerebral metabolism.

Cerebral metabolic rate of oxygen (CMRO₂) was calculated from the product of CBF and the difference in oxygen content of arterial and jugular venous blood samples obtained at the time of measurement of CBF. Cerebrovascular resis-

Table 1 Demographic Data

Group	Median Age ^a (yr)	Male (%)	GSHW ^b (%)	Emergency Craniotomy (%)
All patients				
With shift (n = 125)	31.0 (26.0, 41.0)	87.9	16.0	74/79 (93.7)
Without shift (n = 329)	30.0 (22.0, 41.0)	86.0	10.0	107/233 (45.9)
<i>p</i>	0.089	0.71	0.11	<0.001
SDH patients				
With shift (n = 92)	32.0 (26.0, 45.8)	85.9	10.9	68/71 (95.8)
Without shift (n = 98)	30.5 (22.0, 43.0)	91.8	2.0	54/72 (75.0)
<i>p</i>	0.29	0.28	0.028	0.001
Non-SDH patients				
With shift (n = 33)	29.0 (25.8, 35.0)	90.9	30.3	6/8 (75.0)
Without shift (n = 231)	29.0 (22.0, 38.0)	83.6	13.9	53/161 (32.9)
<i>p</i>	0.82	0.40	0.031	0.040

SDH, subdural hematoma; non-SDH, no subdural hematoma.

^a Data presented as median with interquartile range in parentheses.

^b GSHW, gunshot wound to the head.

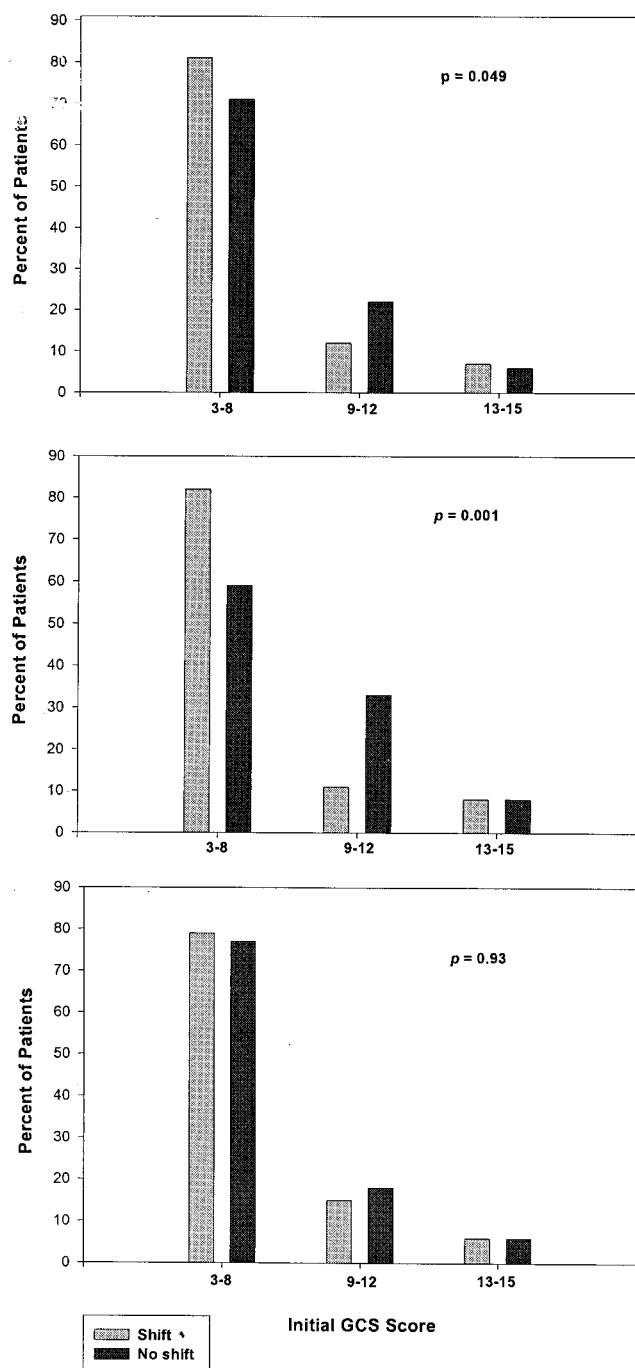


Fig. 1. Distribution of initial GCS scores according to presence or absence of shift: top, entire series of patients; middle, SDH patients; bottom, non-SDH patients.

tance (CVR) was obtained by dividing CPP by CBF; simultaneously obtained values for CPP and CBF were used for these calculations. For each patient, a mean value for each of these parameters was calculated by taking the average of all measurements during the monitoring period.

Jugular venous oxygen saturation ($Sjvo_2$) was measured with an indwelling fiberoptic oxygen saturation catheter (4

French Opticath umbilical artery catheter or 5 French Opticath P540 catheter, Abbott Laboratories, North Chicago, IL, or 4 French regional oxygen saturation catheter, Baxter Healthcare Corporation, Edwards-Critical Care, Irvine, CA). This catheter was placed in the jugular bulb, and its position was verified by a lateral skull radiograph.⁴² $Sjvo_2$ was measured continuously and recorded every 30 seconds by a computerized data collection system. These catheters were calibrated at least every 8 to 24 hours and whenever a jugular venous desaturation to below 50% occurred.⁴³ For each patient, the mean $Sjvo_2$ for the entire monitoring period was recorded.

Outcome was assessed at 1, 3, and 6 months with a three-tiered modification of the Glasgow Outcome Scale:⁴⁴ death, poor outcome (persistent vegetative state or severe disability), or good outcome (moderate disability or good recovery).

Statistical Analyses

Results are reported as the mean \pm SD for normally distributed data or as the median followed in parentheses by the interquartile range for data that were not normally distributed. Data from different groups were compared with the *t* test for normally distributed data, the Mann-Whitney rank sum test for data that were not normally distributed, or the χ^2 test for proportions.

RESULTS

Demographics

Demographic data from the 454 patients are summarized in Table 1. Most of the patients in each group were young men. Gunshot wounds to the head were associated with midline shift in both the SDH and non-SDH groups. Data about whether surgery was performed were not available for patients studied early in this series. When available, such data indicated that patients with shift were more likely to undergo emergency craniotomy in both the SDH and non-SDH groups.

Neurologic Status

For the entire series of patients, the presence of midline shift was associated with a lower initial GCS score (Fig. 1, top). This association was more evident when only SDH patients were analyzed (Fig. 1, middle). In the absence of SDH, GCS scores were distributed similarly in the shift and nonshift groups (Fig. 1, bottom).

Physiologic Data

For the entire series of patients, detailed neurologic monitoring was carried out for a median of 108 hours (67, 190) in shift patients and 93 hours (61, 178) in nonshift patients ($p = 0.44$). Among SDH patients, monitoring was performed for 96.0 hours (62.8, 166) in those with shift versus 115 hours (70.0, 215) in those without shift ($p = 0.12$). Among patients without SDH, monitoring was per-

Table 2 Cerebral Metabolic Data for all Patients^a

Parameter	Patients with Shift	Patients without Shift	p Value
Mean ICP	20.1 (16.2, 23.6)	17.0 (12.4, 20.7)	<0.001
Mean MAP	90.2 ± 9.3	90.9 ± 8.4	0.46
Mean CPP	69.1 (57.2, 78.5)	75.2 (67.2, 80.8)	<0.001
Mean CBF	49.4 (41.7, 58.0)	54.0 (43.8, 67.3)	0.004
Mean CVR	1.47 (1.12, 2.12)	1.44 (1.17, 1.80)	0.16
Mean CMRO ₂	1.75 (1.48, 2.24)	2.22 (1.86, 2.76)	<0.001
Mean Paco ₂	32.6 (29.6, 35.0)	33.3 (30.5, 36.5)	0.032
Mean Sjvo ₂	73.0 (69.4, 76.9)	70.8 (66.9, 74.7)	0.004

ICP, intracranial pressure; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; CBF, cerebral blood flow; CVR, cerebrovascular resistance; CMRO₂, cerebral metabolic rate of oxygen; Sjvo₂, jugular venous oxygen saturation.

^a ICP, MAP, CPP, and Paco₂ in mm Hg; CBF in mL/100 g per min; CVR in mm Hg × min × 100 g/mL; CMRO₂ in mL/100 g per min; Sjvo₂ in percentage. Data presented as mean ± SD or as median with interquartile range in parentheses.

formed for 188 hours (85.0, 248) if shift was present versus 84.0 hours (60.0, 154) if shift was absent, a difference that was significant ($p = 0.016$).

Data about ICP, MAP, CBF, and Sjvo₂ were available for 85 of 92 SDH-S patients (92.4%), 96 of 98 SDH-NS patients (98.0%), 21 of 33 non-SDH-S patients (63.6%), and 209 of 231 non-SDH-NS patients (90.5%). Patients for whom these data are missing were studied early in this series, when data storage and retrieval were not as comprehensive as they later became. Data about CBF, CMRO₂, and CVR were available for all patients.

Cerebral metabolic data are listed in Tables 2 through 4. MAP was comparable in all groups. CPP was consistently lower whenever shift was present. Midline shift was associated with a higher ICP when SDH was absent; when SDH was present, there was a trend toward higher ICP among patients with shift, but this trend did not reach statistical significance.

CBF and CVR were not affected by midline shift when SDH was present. However, when no subdural blood was present, shift was associated with significantly lower CBF and significantly higher CVR. Shift was associated with a

Table 3 Cerebral Metabolic Data for Patients with SDH^a

Parameter	Patients with Shift	Patients without Shift	p Value
Mean ICP	19.5 (15.4, 23.4)	18.3 (13.2, 21.1)	0.074
Mean MAP	90.5 ± 9.4	91.5 ± 7.74	0.44
Mean CPP	70.5 (60.5, 79.8)	75.1 (67.6, 79.6)	0.015
Mean CBF	51.4 (44.9, 60.3)	52.1 (45.2, 63.7)	0.39
Mean CVR	1.39 (1.11, 1.81)	1.53 (1.18, 1.74)	0.86
Mean CMRO ₂	1.74 (1.42, 2.21)	2.21 (1.84, 2.69)	<0.001
Mean Paco ₂	33.0 (30.3, 35.6)	33.5 (30.7, 36.5)	0.44
Mean Sjvo ₂	73.4 ± 7.5	71.3 ± 5.5	0.040

SDH, subdural hematoma; ICP, intracranial pressure; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; CBF, cerebral blood flow; CVR, cerebrovascular resistance; CMRO₂, cerebral metabolic rate of oxygen; Sjvo₂, jugular venous oxygen saturation.

^a ICP, MAP, CPP, and Paco₂ in mm Hg; CBF in mL/100 g per min; CVR in mm Hg × min × 100 g/mL; CMRO₂ in mL/100 g per min; Sjvo₂ in percentage. Data presented as mean ± SD or as median with interquartile range in parentheses.

Table 4 Cerebral Metabolic Data for Patients without SDH^a

Parameter	Patients with Shift	Patients without Shift	p Value
Mean ICP	23.1 (20.1, 32.3)	16.3 (12.1, 20.6)	<0.001
Mean MAP	89.2 ± 9.3	90.7 ± 8.7	0.46
Mean CPP	67.8 (49.8, 75.1)	74.9 (67.1, 82.0)	0.008
Mean CBF	46.4 (35.6, 49.4)	54.4 (43.4, 68.2)	<0.001
Mean CVR	2.08 (1.36, 3.03)	1.43 (1.16, 1.90)	0.002
Mean CMRO ₂	1.80 (1.55, 2.25)	2.24 (1.90, 2.82)	<0.001
Mean Paco ₂	29.8 ± 3.5	33.5 ± 4.2	<0.001
Mean Sjvo ₂	71.8 ± 6.6	70.9 ± 6.1	0.57

SDH, subdural hematoma; ICP, intracranial pressure; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; CBF, cerebral blood flow; CVR, cerebrovascular resistance; CMRO₂, cerebral metabolic rate of oxygen; Sjvo₂, jugular venous oxygen saturation.

^a ICP, MAP, CPP, and Paco₂ in mm Hg; CBF in mL/100 g per min; CVR in mm Hg × min × 100 g/mL; CMRO₂ in mL/100 g per min; Sjvo₂ in percentage. Data presented as mean ± SD or as median with interquartile range in parentheses.

Table 5 Cerebral Metabolic Data for Patients without SDH and without Barbiturate-Induced Coma^a

Parameter	Patients with Shift	Patients without Shift	p Value
Mean ICP	21.2 (17.4, 29.4)	15.3 (11.3, 18.7)	<0.001
Mean MAP	90.2 ± 8.6	91.0 ± 8.6	0.76
Mean CPP	70.5 (58.3, 76.7)	76.6 (69.0, 82.4)	0.073
Mean CBF	45.8 (34.5, 48.5)	56.3 (43.8, 69.9)	<0.001
Mean CVR	2.16 (1.66, 2.90)	1.44 (1.16, 1.94)	0.001
Mean CMRO ₂	1.65 (1.47, 2.24)	2.36 (1.96, 2.91)	<0.001
Mean Paco ₂	30.4 ± 3.9	34.0 ± 4.1	0.005
Mean Sjvo ₂	71.4 ± 7.7	70.6 ± 6.2	0.70

SDH, subdural hematoma; ICP, intracranial pressure; MAP, mean arterial pressure; CPP, cerebral perfusion pressure; CBF, cerebral blood flow; CVR, cerebrovascular resistance; CMRO₂, cerebral metabolic rate of oxygen; Sjvo₂, jugular venous oxygen saturation.

^a ICP, MAP, CPP, and Paco₂ in mm Hg; CBF in mL/100 g per min; CVR in mm Hg × min × 100 g/mL; CMRO₂ in mL/100 g per min; Sjvo₂ in percentage. Data presented as mean ± SD or as median with interquartile range in parentheses.

significantly lower CMRO₂ in both SDH and non-SDH patients.

As a basis for comparison, experimental work has identified 18 mL/100 g per min as the threshold below which irreversible cerebral damage develops after permanent cessation of blood flow.⁴⁵ Normal CBF measured with the nitrous oxide technique in healthy individuals has been reported to be 54 mL/100 g per min,⁴⁰ and normal CMRO₂ in healthy persons has been reported as 3.2 mL/100 g per min.⁴⁰ In previous work, our institution has described groups of patients with severe head injury with a mean CBF of approximately 25 mL/100 g per min as having reduced blood flow, groups with a mean CBF of 42 mL/100 g per min as having normal blood flow, and groups with a mean CBF above 53 mL/100 g per min as having elevated blood flow.^{46,47} Mean CMRO₂ values in such groups were found to be 1.4 mL/100 g per min, 1.7 mL/100 g per min, and 2.2 mL/100 g per min, respectively.⁴⁶

Mean Paco₂ in SDH patients was not influenced by the presence of shift, but among non-SDH patients, it was significantly lower in the group with shift. Sjvo₂ is a marker of cerebral extraction of oxygen from blood, with a low Sjvo₂ suggesting increased oxygen extraction (and, therefore, less oxygen remaining in jugular venous blood). Among SDH patients, a significantly higher mean Sjvo₂ was seen in patients with shift. In the non-SDH patients, mean Sjvo₂ did not vary with the presence or absence of shift.

The average rectal temperature during the course of monitoring did not differ significantly when all shift patients were compared with those without shift, when SDH patients with shift were compared with those without shift, or when non-SDH patients with shift were compared with those without shift.

Barbiturate Coma

The possibility that the physiologic data may have been distorted by differences in the use of barbiturate-induced coma in the groups being compared was investigated by determining the frequency with which this therapy was used. Among SDH patients, barbiturate coma was used in 23 of 92

patients with shift (25.0%) versus 24 of 98 patients without shift (24.5%) ($p = 0.93$).

Among patients without SDH, barbiturate coma was used in 10 of 33 patients with shift (30.3%) versus 36 of 231 patients without shift (15.6%) ($p = 0.066$). Because of the size of this difference (even though it did not quite attain statistical significance), the parameters listed in Tables 2 and 4 were recalculated by using only data from those patients in whom barbiturate coma was not used. The results of this analysis are reported in Table 5. Elimination of the barbiturate coma patients had minimal effect on the association of midline shift with a more ominous status of cerebral metabolism in non-SDH patients.

Outcome

Three-month outcome data were available for 78 SDH patients with shift (84.8% follow-up) and for 77 SDH patients without shift (78.6%). Among non-SDH patients, 3-month outcome data were available for 22 patients with shift (66.7%) and for 182 patients without shift (78.8%). These data are shown in Figure 2. Within both the SDH and non-SDH groups, outcome was worse for patients with shift.

Although an increasing duration of follow-up may result in a more accurate assessment of ultimate neurologic outcome, the proportion of patients lost to follow-up inevitably increases with time. Despite this limitation, the association between shift and poor outcome remained constant in both SDH and non-SDH groups regardless of whether the Glasgow Outcome Scale score was determined 1, 3, or 6 months after injury.

DISCUSSION

The physiologic basis of the association of significant midline shift with poor outcome after head injury has not been defined. Possibilities include a primary reduction of cerebral metabolic rate as a direct sequela of the injury; reduction of CBF from distortion and consequent injury to the cerebral vascular bed, causing increased cerebrovascular resistance; or metabolic effects of substances released from the large SDHs that are frequently the cause of pronounced

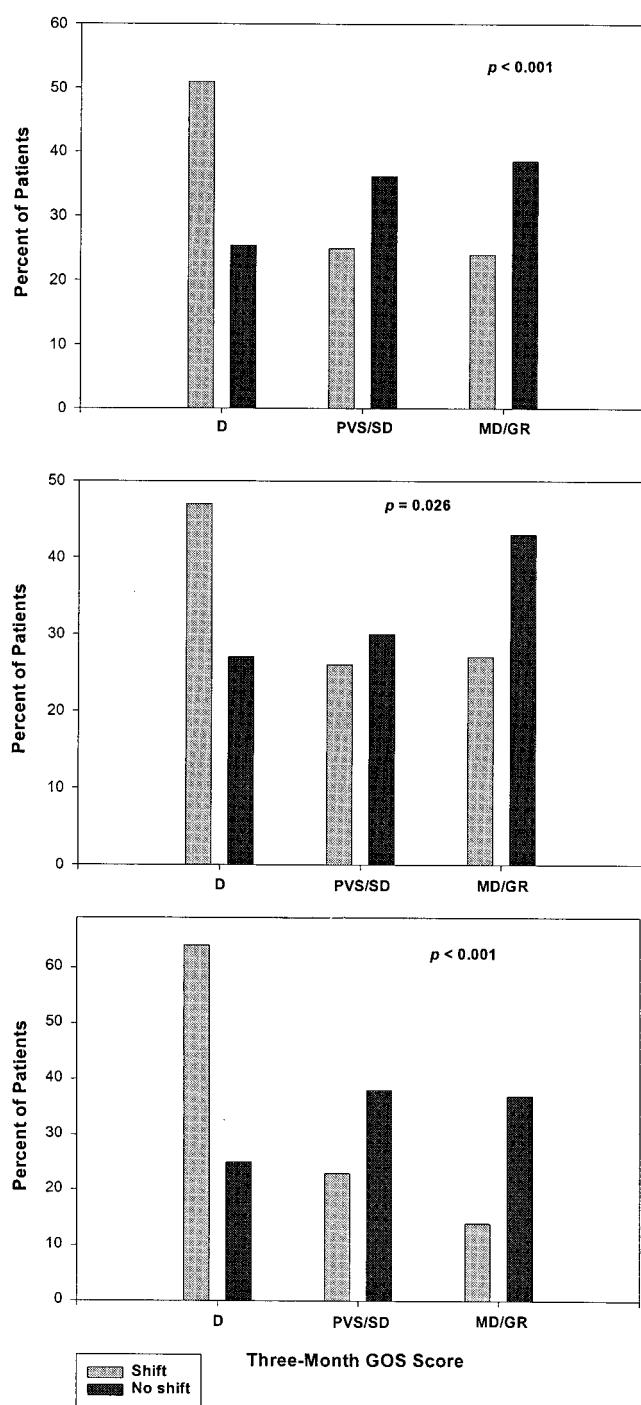


Fig. 2. Distribution of 3-month outcomes according to presence or absence of shift: top, entire series of patients; middle, SDH patients; bottom, non-SDH patients. GOS, Glasgow Outcome Scale; D, dead; PVS, persistent vegetative state; SD, severe disability; MD, moderate disability; GR, good recovery.

midline shift. Our data suggest that depression of CMRO₂ is the most important metabolic abnormality associated with midline shift > 5 mm on the initial CT scan, regardless of whether the shift is associated with SDH.

Patients with SDH

As seen in Table 3, the most important difference between SDH-S and SDH-NS patients is the much lower CMRO₂ among patients with shift. The decreased cerebral metabolic rate of these patients results in less oxygen being extracted from blood. This unconsumed oxygen appears as the slightly but significantly increased Sjvo₂ of this group.

The fact that the large reduction in CMRO₂ in the SDH-S group occurs without other differences between SDH-S and SDH-NS patients supports the concept that a depression of cerebral metabolism is the primary physiologic disturbance associated with midline shift. The importance of cerebral parenchymal damage in patients with traumatic SDH was emphasized by Massaro et al., who suggested that the extent of primary brain injury underlying the SDH was the most important factor affecting outcome.³¹ Table 3 suggests that a relatively small amount of subdural blood is not as deleterious as a SDH large enough to cause > 5 mm of midline shift. This observation argues against the importance of small amounts of subdural blood in explaining the metabolic derangements that occur after TBI. Instead, either the mass effect of a large SDH is necessary to cause the impairment of cerebral metabolism after TBI in these patients, or the development of a large SDH and the occurrence of a significant depression of CMRO₂ are separate phenomena that occur concurrently as sequelae of the traumatic event. It is also possible that, in many cases, both these processes occur.

Patients without SDH

As in SDH patients, CMRO₂ is also significantly lower in patients without subdural blood when shift is present (Table 4). The other metabolic differences between shift and non-shift patients without subdural blood can be explained by the much higher ICP of the shift patients. The higher ICP results in a lower CPP, which contributes to the lower CBF in the shift group. The lower Paco₂ of this group reflects the greater aggressiveness with which hyperventilation was used to treat the higher ICP. Patients with intact pH autoregulation would respond to hyperventilation by decreasing the caliber of the cerebral resistance vessels, thus raising CVR, which would have a negative effect on CBF. CBF may also have been decreased by an increase in CVR as a normal autoregulatory response to an injury-induced decrease in CMRO₂.

The higher ICP of this group suggests the presence of significant cerebral edema. More serious and more prolonged brain swelling would explain the longer duration of cerebral monitoring in these patients. This finding is consistent with the higher percentage of gunshot patients in this group, for we have observed markedly elevated ICP and other diffuse effects on cerebral metabolism (comparable to those seen in patients with closed head injury) in those patients with gunshot wounds to the head in whom we were able to perform physiologic monitoring.³⁸ Unlike the situation in SDH patients with shift, in whom prompt evacuation of the large

extra-axial mass lesion is often effective in lowering ICP, intracranial hypertension from unilateral brain swelling that is severe enough to cause midline shift would be expected to be much more difficult to control in these relatively uncommon patients.

Initial Neurologic Status

For the entire series of patients, the association of a lower GCS score with shift on initial CT scan was of borderline significance (Fig. 1, *top*). However, this association was much stronger when only the SDH group was investigated (Fig. 1, *middle*). This finding is best explained by considering the relatively high percentage of SDH patients without shift who had an initial GCS score of 9 to 12. Presumably, many patients with small SDHs were initially treated nonsurgically because they had good initial neurologic examinations and minimal amounts of shift on their initial CT scans. Subsequent neurologic deterioration from enlargement of the SDH resulted in these patients being brought to the operating room for evacuation of the clot.^{13,14,48}

Among non-SDH patients, GCS score was not related to the presence of midline shift (Fig. 1, *bottom*). According to the hypothesis put forth above, these data suggest that, in the absence of SDH, severe neurologic dysfunction in this series of patients was more likely to be present upon admission, as opposed to developing subsequent to admission.

Outcome

As has been described by other authors,^{10,15} we found that patients with severe TBI and shift fared worse than those without shift (Fig. 2). The association of shift with poor outcome was somewhat stronger in non-SDH patients than in SDH patients. A similar result was reported by Athiappan et al.² This finding is a reversal of the pattern of distribution of the initial GCS scores of our patients, which suggested that shift in non-SDH patients is unrelated to initial neurologic status. This apparent contradiction is best explained by the fact that non-SDH-S patients developed a significantly higher ICP than non-SDH-NS patients, suggesting the development of cerebral edema and other devastating and often fatal sequelae after admission. Given the similarity of initial GCS scores between non-SDH-S and non-SDH-NS patients, it seems that these subsequent problems with ICP, combined with lower CMRO₂, may have contributed to the poorer outcomes of non-SDH-S patients. On the other hand, aggressive care may have been more efficacious in non-SDH-NS patients, perhaps in part because they harbored a less severe parenchymal injury (as indicated by their higher CMRO₂), which made them inherently more salvageable.

Although outcomes for SDH patients were still significantly worse when shift was present, the disparity in outcome between SDH-S and SDH-NS patients was not as great as that seen in their admission GCS scores. Perhaps neurosurgical intervention was helpful in minimizing secondary cerebral insults after these patients arrived at the hospital. Despite the

lower CMRO₂ values in the patients with subdural blood and shift, our emphasis on rapid evacuation of extra-axial mass lesions and aggressive intensive care unit management may have facilitated at least some recovery of function of the underlying brain. As discussed above, the exact opposite situation may have occurred in many non-SDH-S patients, perhaps because the convergence of low CMRO₂ and high ICP in the absence of a readily treatable extra-axial lesion was a combination that was much more refractory to successful management.

SUMMARY

Midline shift after severe TBI is associated with a significant reduction in cerebral metabolic rate. In patients with SDH, this shift-associated decrease in CMRO₂ was the only major difference between shift and nonshift groups. A decrease in CMRO₂ was also seen in non-SDH patients with shift, and other cerebral metabolic differences between non-SDH patients with and without shift were most likely due to the higher ICP in the shift group and to the measures used to treat this elevated ICP. These data suggest that the mass effect of large SDHs may be more important in adversely affecting outcome after TBI than biochemical changes induced by the presence of a small amount of acute blood in the subdural space.

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DISCUSSION

Dr. Lawrence H. Pitts (San Francisco, California): This paper restates a number of issues that we know historically to be true, and examines them with more detailed data than we have had in the past.

A midline shift is an ominous finding. Clearly a 5-mm subdural hematoma without a shift is a very different phenomenon than is a brain injury sufficient to give a midline shift with or without a subdural hematoma. So the degree of

brain injury here remains critically important, more so than the size of the given mass in one space or another. The study's demographics are pretty common: 85 to 90% of each group were men and included 10 to 15% gunshot wounds except for the one group that was particularly ominous in this series. That worst group was nonsubdural shift patients in whom about a third of the patients had gunshot wounds. Outcome was worse with shift, and worse with a mass lesion. Two lesions were worse than one.

Other interesting data report extensive brain metabolic data or brain metabolic rate for oxygen (CMRO₂) which was most abnormal in the two groups with midline shift. In fact, reduced CMRO₂ was the only substantial abnormality in the subdural hematoma group with shift.

In the group without an extracerebral mass lesion but still brain swelling and a midline shift, not only was the CMRO₂ abnormal, but also the cerebrovascular resistance and amount of brain resuscitation or treatment such as hyperventilation that was required. Given the number of features that were abnormal in the nonmass brain swelling group, it seems that this particular injury was worst.

The data summarized a prolonged period of time and were averaged over different periods for different patients. Might the authors not have found more striking abnormalities, particularly in the subdural group, if the data had been limited to 24 hours or 48 hours after injury. All of the patients who survived would have ultimately had normal ICPs, which might have made initially abnormal data average toward more normal values.

The authors found that any brain abnormality great enough to cause a shift is adverse, such as lowering CMRO₂, but is this really a causal relationship or merely a correlation? That is, if you have a sufficiently severe brain injury you may have a bad outcome and a lowered CMRO₂. Conversely, if we were able to improve the CMRO₂, we might not necessarily improve outcome.

The gunshot wounds that produced unilateral brain injuries are an interesting patient group, but conceivably might contaminate the data in the patient group with a midline shift without an extracerebral hematoma. I look forward to seeing the gunshot wound paper from these authors suggesting that there is not a major difference between head injury with or without a gunshot wound. That certainly argues against my impression about the particularly severe injuries caused by gunshot wounds.

This is an interesting paper with an enormous amount of metabolic information. Certainly when the CT shows a severe injury, it is not surprising that brain metabolism is adversely affected. Even if we do not know if lowered CMRO₂ causes a poor outcome, nonetheless we should try to optimize brain metabolism to preserve as much functioning brain as possible. Thanks for the opportunity to discuss the paper.

Dr. Michael D. Pasquale (Allentown, Pennsylvania): I enjoyed the paper. A question: Did you make any attempt to look at different treatment strategies amongst the groups, and

in particular the use of pentobarbital, since that would dramatically affect your cerebral metabolic rate?

Dr. Howard Belzberg (Los Angeles, California): I would like to commend both the author and the discussant. It comes back to the question of, is it the amount of blood in the brain or brain in the blood that we have to contend with?

In particular, what I would like to know from the authors is did you try and quantify the volume of subdural hematoma relative to the volume of the shift? Because that would then correlate with the degree of underlying brain trauma and swelling directly from the brain, rather than caused by the mechanical compression of the subdural blood.

Dr. Alex B. Valadka (closing): Thank you all for those comments. Dr. Pitts was wondering if we perhaps should have cut off our data collection after only 48 hours or so. That certainly was an alternative way to go about doing this. However, similar analyses have been done in terms of the time course of some of these events. I think the problem there, as you have seen, Dr. Pitts, is that some of these patients may not get into severe problems with intracranial pressure until several days after injury.

The way we usually do our monitoring is that we remove our monitors when a patient wakes up and starts obeying commands, or after 5 or 6 days, whichever comes first. On occasion, we have left things in longer for patients who are very unstable, who have a late ICP rise or are being monitored in barbiturate coma or things like that. So I understand your comment. I guess it was just a difference in philosophy about how to go about doing that.

I think you brought up the key point about whether this low CMRO₂ is a cause or just a correlation. I wish I could answer that. This study, the way it was designed, is not able to go about answering that question. And you are right. It is entirely possible that there may be other things going on. You may have an injury that causes a lot of shift, depresses the CMRO₂ and causes something else that is the real culprit behind the worse outcomes.

I know that perhaps in the future we may have some answers. Paul Muizelaar has investigated mitochondrial dysfunction. Geoff Manley presented some interesting data about brain Po₂ monitoring. But I think the ultimate answer to that question is going to have to wait.

In terms of the gunshot wounds, I know that is a very contentious point, and I know time is tight, but let me briefly address that concern. For years, we have been criticized in our group for including gunshot wounds in our series of closed head injury patients, and one of the reasons I undertook that project was to try to look at that practice and see whether we were right or not. So we submitted that data to a neurosurgical journal, and the paper was rejected. They said, "Well, of course, we know that patients with gunshot wounds are going to behave the same as patients with closed head injuries. What is the big surprise here?"

So these same critics who were criticizing us all along have suddenly changed their minds. I was happy to see that

the reviewers for the *Journal of Trauma* are a little more open-minded about these things.

There was a question about barbiturate coma. That is a very good point. We did look at that, but I did not have time to go into it in detail in my talk. When ICP gets to be uncontrollable, we put all our patients in barbiturate coma. There was no difference in the incidence of that among the subdural patients. In the nonsubdural patients, there was a trend for the shift patients to be put in barbiturate coma more

frequently, but when I discarded all the patients who were in barbiturate coma and repeated the analysis, the results did not change. So we understand your concern, but I do not think it was an issue.

And finally, Dr. Belzberg, no, we did not try to measure the thickness or the volume of the subdural and correlate with the degree of shift. That may have given us some more information, but again, those data were not available in the database that we had available for this study. Thank you very much.

G. WHITAKER INTERNATIONAL BURNS PRIZE

The 2000 G. Whitaker International Prize in burn medicine has been awarded to Basil A. Pruitt, Jr., MD, who was the Commander and Director of the United States Army Institute of Surgical Research (Army Burn Center), for 27 years. Dr. Pruitt, who graduated from Harvard College in 1952 and Tufts University School of Medicine in 1957, began his surgical residency at the Boston City Hospital and was drafted into the Army Medical Corps in 1959 to begin a 35-year military career in burn and trauma care. Through his direction and guidance, the Army Burn Center has become the internationally recognized center of excellence in burn care. An analysis of his many publications as author and coauthor (over 415 published papers, 145 textbook chapters, and 12 books) reveals that he has shown deep interest and brought scientific contributions to all aspects of burn care. Dr. Pruitt is a member of 38 professional societies and has held elected or appointed office in many of those societies, including the American Burn Association, the American Association for the Surgery of Trauma, the Surgical Infection Society, the International Society for Burn Injuries, and the American Trauma Society. He is the Immediate Past President of the American Surgical Association and the Editor of *The Journal of Trauma*. Since retiring from the Army he has continued his teaching and operating activity as Clinical Professor of Surgery at the University of Texas Health Sciences Center at San Antonio.

Nominations for the 2001 award are being accepted until **January 31, 2001**. Send a detailed curriculum vitae to Michele Masellis, MD, Secretary-Member, Scientific Committee of G. Whitaker Foundation, Via Dante 167, 90141 Palermo, Italy. The prize is worth 20 million Italian Lire.