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Long-term outcomes and prognostic factors in pediatric patients with severe traumatic brain injury and elevated intracranial pressure

Clinical article

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Object. The management strategies and outcomes in pediatric patients with elevated intracranial pressure (ICP) following severe traumatic brain injury (TBI) are examined in this study.

Methods. This study was a retrospective review of a prospectively acquired pediatric trauma database. More than 750 pediatric patients with brain injury were seen over a 10-year period. Records were retrospectively reviewed to determine interventions for correcting ICP, and surviving patients were contacted prospectively to determine functional status and quality of life. Only patients with 2 years of follow-up were included in the study.

Results. Ninety-six pediatric patients (age range 3–18 years) were identified with a Glasgow Coma Scale score < 8 and elevated ICP > 20 mm Hg on presentation. The mean injury severity score was 65 (range 30–100). All patients were treated using a standardized head injury protocol. The mean time course until peak ICP was 69 hours postinjury (range 2–196 hours). Intracranial pressure control was achieved in 82 patients (85%). Methods employed to achieve ICP control included maximal medical therapy (sedation, hyperosmolar therapy, and paralysis) in 34 patients (35%), ventriculostomy in 23 patients (24%), and surgery in 39 patients (41%). Fourteen patients (15%) had refractory ICP despite all interventions, and all of these patients died. Seventy-two patients (75%) were discharged from the hospital, whereas 24 (25%) died during hospitalization. Univariate and multivariate analysis revealed that the presence of vascular injury, refractory ICP, and cisternal effacement at presentation had the highest correlation with subsequent death ($p < 0.05$). Mean follow-up was 53 months (range 11–126 months). Three patients died during the follow-up period (2 due to infections and 1 committed suicide). The mean 2-year Glasgow Outcome Scale score was 4 (median 4, range 1–5). The mean patient competency rating at follow-up was 4.13 out of 5 (median 4.5, range 1–4.8). Univariate analysis revealed that the extent of intracranial and systemic injuries had the highest correlation with long-term quality of life ($p < 0.05$).

Conclusions. Controlling elevated ICP is an important factor in patient survival following severe pediatric TBI. The modality used for ICP control appears to be less important. Long-term follow-up is essential to determine neurocognitive sequelae associated with TBI. *(DOI: 10.3171.PED.2008.2.10.240)*

Key Words • intracranial pressure • management strategy • outcomes • traumatic brain injury

Management of refractory ICP can be a significant challenge in pediatric patients with TBI. The rationale behind treating elevated intracranial hypertension is to permit adequate cerebral perfusion and cerebral blood flow.[34] Patients who attain ICP control following head injury have been demonstrated to have better short- and long-term prognoses.[22,25]

In addition to the primary injury related to trauma, secondary events such as edema, inflammation, and vascular injury can also play a significant role in the pathophysiology of ICP elevation, complicating its management.[4,37] Although the underlying pathology in malignant cerebral edema is believed to be related to a combination of impaired cerebral autoregulation changes in vascular permeability

Abbreviations used in this paper: CPP = cerebral perfusion pressure; CSF = cerebrospinal fluid; GCS = Glasgow Coma Scale; GOS = Glasgow Outcome Scale; ICP = intracranial pressure; IVH = intraventricular hemorrhage; PCRS = patient competency rating scale; QOL = quality of life; TBI = traumatic brain injury.

and alterations in brain compliance, to date no drug has been able to prevent these sequelae.[30] Because of this, most treatment strategies for raised ICP rely on balancing volumes of blood and CSF in accordance with the principles of the Monroe–Kellie doctrine. This balance can be achieved using medications (such as paralytics and sedatives), diverting CSF flow (using ventriculostomy), or expanding the volume available for the brain (via a decompressive craniectomy).[24,37]

In an earlier study, we demonstrated that a decompressive craniectomy is associated with favorable outcomes in pediatric patients with severe TBI.[22] However, few studies have examined the differences between ICP control modalities in pediatric TBI. Furthermore, it is unclear whether there are different long-term sequelae in pediatric patients with TBI who are medically and surgically treated. This study describes our experience with medical and surgical management of pediatric TBI, as well as long-term outcomes in pediatric patients with severe TBI and refractory ICP.

Methods

Patient Selection

A retrospective review was conducted from a prospectively acquired database containing the records of 750 pediatric patients with head injury who were admitted to the University of Virginia Health System between January 1995 and April 2006. Only patients who sustained accidental trauma with abnormal CT imaging results at presentation and refractory raised ICP (sustained elevation $>$ 20 mm Hg during the 1st hour after the placement of an ICP monitor) were included in this study. Patients who presented to the hospital with no brain activity (determined by the examining neurosurgeon) were excluded from this study.[21]

Patient records were retrospectively reviewed to determine the extent of intracranial injury (classified by Marshall grade[31] and determined by a blinded independent observer), mechanism of injury, time to presentation, systemic injuries, presenting GCS score, indications for intervention, complications, and hospital course.

Trauma Evaluation for Head-Injured Patients

The patient GCS score at presentation was assigned by the examining neurosurgeon in all cases at the patient's arrival in the trauma bay. All patients received a comprehensive trauma evaluation by a dedicated pediatric trauma and neurosurgical team. Following the primary examination, fluid resuscitation, and neurosurgical evaluation, a CT scan of the brain and cervical spine (in patients $>$ 8 years of age) along with a full set of laboratory tests (complete blood cell count, urinalysis, electrolyte tests, coagulation tests, blood type and cross-match, and serum transaminase, amylase, and lipase levels) were assessed for any child with a GCS score $<$ 8 or a mechanism of injury suggestive of head trauma. Remaining radiographic and clinical studies were generally performed at the discretion of the trauma team. Based on the radiographic and systemic injuries, an injury severity score (range 0–100) was calculated based on the criteria described by Baker and colleagues.[6]

Decision to Use ICP Monitoring

Evaluation and management of severe pediatric TBI adhered to an institutional protocol developed by a multidisciplinary team, which has been previously described.[22] Intraparenchymal ICP monitoring is performed on all patients: 1) with a GCS score $<$ 8 and abnormalities noted on their presenting CT scan; or 2) when a trauma patient cannot undergo a reliable clinical examination secondary to systemic injury, hemodynamic instability, or the need for sedative medications, even with a normal head CT scan. None of these patients in the second category met the inclusion criteria for the study.

Medical Management

Patients with elevated ICP and without a mass lesion are admitted to a dedicated pediatric intensive care unit at the University of Virginia Health System. Initial management consists of adequate sedation (in many cases with a neuromuscular blockade), mild hyperventilation therapy (with a PCO_2 goal of 35 mm Hg), and use of osmotic diuretics such as mannitol as needed. Hyperosmolar therapy is typically begun concomitantly with the aforementioned treatments, although we view this as a second-line approach. Because of the known side effects of inducing a barbiturate coma in pediatric patients with head injury, we typically view this treatment as a last resort, following failure of other medical and surgical strategies.[7,27,35]

Ventricular Drain Placement

Ventricular drain placement is typically reserved for patients who are not candidates for surgery, either due to hemodynamic instability or systemic injuries, or for patients with significant IVH and concomitant hydrocephalus. All ventriculostomy procedures for trauma were performed at the patient's bedside. The ideal ventricular drain position in all cases was considered to be the anterior horn of the lateral ventricle.

Following sterilization of the field, we typically made a bur hole by drilling at the Kocher point on the right side (in 14 patients in this study). When drilling at this site was not possible, a left-sided bur hole was placed. The insertion depth goal was 5 cm whenever possible, with a trajectory toward the ipsilateral medial canthus and contralateral external auditory canal.

Decompressive Craniectomy

Patients with mass lesions were taken to the operating room for cranial evacuation. Decompressive craniectomy was performed in patients with refractory ICP ($>$ 20 mm Hg) despite maximal medical management. Our overall strategy is to always identify patients with elevated ICP early in their hospital course, prior to the loss of autoregulation.

The objective of the craniectomy procedure is to perform a wide decompression. All operations were performed by 1 of the 2 senior authors (J.A.J. Sr. or J.A.J. Jr.). When mass lesions caused a midline brain shift, decompression was performed on the side of the injury. In patients in whom no predominant mass lesion was present or in whom there was diffuse cerebral edema, a bifrontal craniectomy was performed. In these cases, the anterior-most superior sagittal sinus is sutured and ligated, and the falx at the anterior skull base is sectioned to allow further decompression. The craniectomy bone flaps are sent to the hospital bone bank, and

all patients are postoperatively transferred to a dedicated pediatric intensive care unit.

Follow-Up Course

Patients were followed-up postoperatively by an interdisciplinary team, with other consultant services used if needed. To accurately evaluate and compare different management strategies for TBI, all deceased patients, and only those surviving patients with ≥ 2 years of follow-up, were included in this study.

Each patient's functional status as assessed by an interdisciplinary team was used to determine a 2-year GOS score. When a 2-year follow-up examination was not available because a patient died during the follow-up period, the most recent clinical evaluation was used to determine the final GOS score.

To investigate more subtle changes in neurocognitive function, patients were also contacted by the authors to assess their individual levels of functioning in activities of daily living, behavioral functions, emotional functions, cognitive abilities, and physical functions using the PCRS. The PCRS consists of a 30-part questionnaire in which the patient or guardian was asked to use a 5-point scale to evaluate the patient's ability to perform a variety of tasks (Table 1).[41] To evaluate self-awareness, when possible, each patient's score was compared with the score given by the caregiver. When the scores were different, the mean value was used. An independent observer conducted all interviews with the patient and/or primary caregiver.

Statistical Analysis

The accumulated data were statistically evaluated using the 2-sided t-test, Student t-test, or Mann–Whitney test, with a confidence interval of 95%. A probability value of 0.05 was considered the limit of statistical significance.

Results

Patient Characteristics

According to the criteria outlined above, 96 patients were considered eligible to be evaluated. Seventy-one patients (74%) were male and 25 patients (26%) were female. The mean age of the patients at presentation was 15.1 years (range 3–18 years). Mechanisms of injury included: motor vehicle/all-terrain vehicle injury as a driver (42 patients, 44%); motor vehicle accident as a pedestrian or passenger (30 patients, 31%); blunt trauma (15 patients, 16%); and falls (9 patients, 9%). The mean presenting GCS score was 5.3 (median 5, range 3–8). Eighty-five patients (89%) were intubated prior to arrival at the University of Virginia, whereas 11 patients (11%) required emergency intubation upon arrival at the trauma bay. Table 2 provides a summary of the characteristics of the patient population.

TABLE 1

Scoring system used in the PCRS for follow-up assessment of QOL

Likert Score	Cognitive Ability
1	cannot perform task
2	very difficult to perform task
3	can perform task, although it is difficult
4	fairly easy to perform task
5	can perform task w/ ease

TABLE 2

*Summary of patient population characteristics**

Criteria	All Patients	ICP Management Group		
		Medical	Ventriculostomy	Craniectomy
age (yrs)	15.1	15.4	14.2	15.4
GCS score at presentation	5.3	6.6	4.6	4.3
Marshall grade	4	3	4	4
injury severity score	65	62	66	63

* All scores are means.

Radiographic Abnormalities

A summary of radiographic abnormalities is provided in Table 3. Subarachnoid hemorrhage was the most common presenting abnormality, and was present in 65 initial CT scans (68%). Diffuse axonal injury was observed on 48 images (50%). Forty-four patients had contusions (46%) and 44 patients had skull fractures (46%). Twenty-two patients (23%) had evidence of subdural hemorrhage and 5 patients (5%) had evidence of an epidural hematoma. Forty patients (42%) had evidence of midline shift on their presenting CT scan, 25 patients (26%) had evidence of cisternal effacement, and 4 (4%) had an area of infarction. Eleven patients (11%) had only 1 radiographic abnormality on their presenting CT scan; 84 patients (88%) had ≥ 2 radiographic abnormalities and 70 patients (73%) had ≥ 3 radiographic abnormalities.

To objectively quantify the extent of radiographic injury, the presenting head CT scans were evaluated retrospectively by a blind observer, and graded using the Marshall grading system (Table 2). The mean Marshall grade for the overall cohort was 4 (range 2–4). The Marshall grades were also reevaluated after the postintervention CT scan (performed after either ventriculostomy or surgery), and the postprocedural changes are summarized in Table 4.

Systemic Injuries

Patient systemic injuries are summarized in Table 5. Or-

TABLE 3

Abnormalities present at the initial head CT scan

Abnormality/No. of Injuries	No. of Patients (%)
subarachnoid hemorrhage	65 (68)
diffuse axonal injury	48 (50)
contusion	44 (46)
skull fracture	44 (46)
subdural hematoma	22 (23)
IVH	20 (21)
epidural hematoma	5 (5)
vascular injury	5 (5)
cisternal effacement	25 (26)
midline shift	40 (42)
infarction	4 (4)
1 injury	11 (11)
≥2 injuries	84 (88)
≥3 injuries	70 (73)

TABLE 4

Changes in Marshall grade following intervention for elevated ICP

Marshall Grade at Presentation	% of Patients w/ Improvement After Ventriculostomy	% of Patients w/ Improvement After Craniectomy
1	0	0
2	15	0
3	0	71
4	0	62

TABLE 5

Summary of patient systemic injuries at presentation

Injury/No. of Injuries	No. of Patients (%)
orthopedic	48 (50)
abdominal	26 (27)
thoracic	19 (20)
facial	19 (20)
coagulopathic	4 (4)
pregnancy (abruption)	1 (1)
vascular (systemic)	1 (1)
none	19 (20)
1 injury	2 (2)
≥2 injuries	73 (76)
≥3 injuries	46 (48)

thopedic injuries were the most common noncranial injury and were present in 48 patients (50%). Seventy-three patients (76%) had ≥ 2 systemic injuries, and 46 patients (48%) had ≥ 3 systemic injuries. Nineteen patients (20%) had isolated (nonsystemic) head injuries. The mean injury severity score of the patient cohort was 65 (range 30–100). There appeared to be a slightly higher injury severity score in the ventriculostomy group compared with the patients who underwent craniectomy or medical ICP management, but this difference was not statistically significant ($p > 0.05$, Student t-test).

Emergency noncranial operations were required for 18 patients (19%). Twelve of these patients required emergency laparotomies and 4 patients required emergency orthopedic fixation of fractures. Two of these 18 patients had open chest wounds, which required emergency thoracotomies. In cases in which patients required emergency stabilizing operations, ICP monitors were placed prior to surgery. One patient had a ventricular drain placed during his laparotomy because of elevated ICP and significant IVH. This patient eventually underwent a craniectomy after he had stabilized from his systemic injuries. There were 2 intraoperative deaths during the stabilizing (noncranial) operation. Both of these patients had elevated ICP at the time of death despite receiving paralytics and ventricular drain placement.

Management Strategies

A summary of management strategies for elevated ICP in this patient population is shown in Fig. 1. The mean time course until peak ICP was 69 hours postinjury (range 2–196 hours). Of the 96 total patients with refractory ICP, 34 patients (35%) were able to achieve ICP control using medical management alone, 23 patients (24%) required ventricular drain placement, and 40 patients (42%) required operative decompression (39 patients who had unsuccessful medical management, and 1 with an unsuccessful ventriculostomy). Despite the fact that patients with a worse injury (as noted on radiographs) had higher peak ICP values (Table 6), univariate and multivariate analyses revealed that radiographic grade of the presenting injury, modality of ICP control, and peak ICP were all unrelated to ICP control or ultimate patient survival ($p > 0.05$, Mann–Whitney test and Cox regression modeling).

Medical Management. As previously outlined, all patients, with the exception of those harboring mass lesions, underwent initial medical treatment for refractory ICP. In 34 cases (35%), medical management was successful in controlling ICP. The mean presenting GCS score as well as the mean Marshall grade was higher in this group compared with the patients undergoing a ventriculostomy or operative treatment. In 14 (41%) of these cases, sedatives without paralytics were administered. A neuromuscular blockade was performed in 20 patients (59%). Twelve patients, all of whom also received a neuromuscular blockade, received hyperosmolar therapy in addition to sedatives. The mean duration to peak ICP in the group with successful medical ICP management was 5 hours following the initial evaluation (range 1–17 hours).

Ventriculostomy Procedure. Twenty-three patients required ventricular drain placement. In 22 patients, this procedure was performed for elevated ICP in spite of medical management, whereas another patient required a ventriculostomy for significant IVH and associated hydrocephalus. The mean duration to ventricular drain placement was 7 hours after the initial evaluation at our institution (range 1–32 hours). The mean duration of ventriculostomy treatment was 102 hours (range 12–133 hours). Successful ICP control was obtained in 20 patients (87%) after the ventriculostomy procedure, whereas 3 patients had refractory ICP after CSF diversion. All 3 patients with refractory ICP despite ventricular drain placement died during their hospital course (the mean duration until death was 2–40 hours following the ventriculotomy). Decompressive craniectomy was considered in all 3 of these patients, but 2 were unable to tolerate an operation because of systemic injuries and hemodynamic instability. The third patient was taken to the operating room for decompression following an isolated spike in ICP to 60 mm Hg, and returned from the operating room without brainstem reflexes and with examination results consistent with brain death.

Operative Management. A total of 39 patients required operative management for refractory elevated ICP. Fourteen of these patients presented with a mass lesion that was believed to be surgically accessible. In 5 (36%) of these 14 cases this lesion could not be removed immediately on admission because of hemodynamic instability. Five of these patients had epidural hematomas and 9 had acute subdural hematomas. In 9 cases (64%) the lesion was small on presenting radiographic imaging, and the decision was made to follow the patient serially with medical management. Operative removal was performed because of lesion growth in 5 (56%) of these 9 cases and because of increasing ICP in 4 cases (44%). The mean duration to operative decompression in this group was 11 hours postinjury (range 4–22 hours).

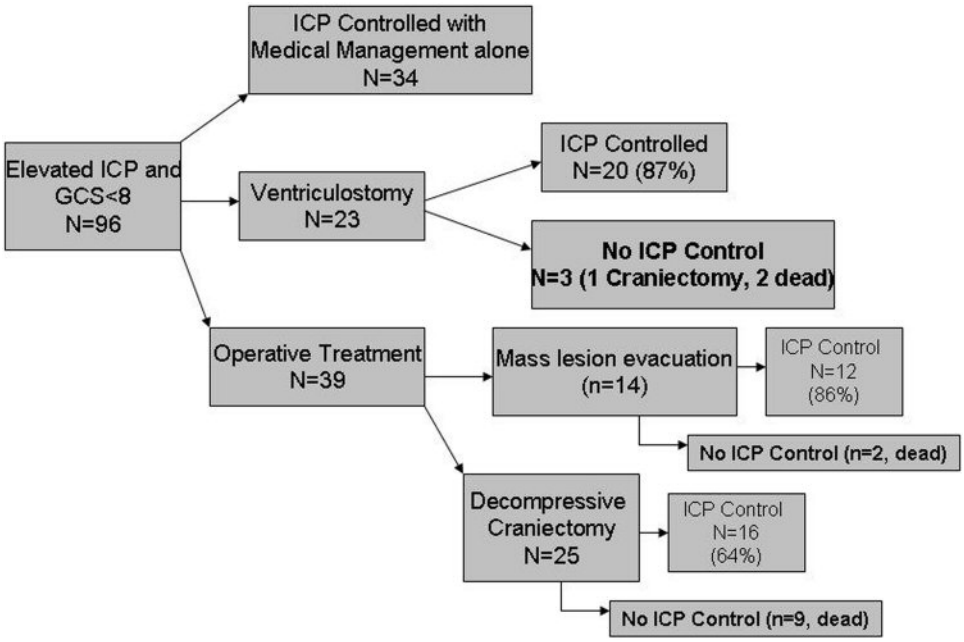

FIG. 1. Flow chart summarizing the management strategies and outcomes in the study population.

Twenty-five patients required a decompressive craniectomy for elevated ICP, which included 23 patients described in our previous report[22] as well as 2 other patients who met the criteria for eligibility in this study. All of these patients failed maximal medical intervention. The mean time course to craniectomy in these patients was 26 hours postinjury. Similar to patients who underwent evacuation of mass lesions, craniectomy patients who had later operations tended to have more severe systemic injuries (Fig. 2).

In addition to refractory ICP, 3 patients (12%) required decompression due to deteriorating neurological examination results showing deterioration. These patients began showing signs of pupillary dilation, and a follow-up head CT scan showed worsening midline shift and cisternal effacement. None of these patients achieved ICP control following craniectomy, and all 3 died.

Five patients had refractory ICP and worsened neurological function after craniectomy. All of these patients were subsequently declared to have suffered brain death. Two patients in this group had transient improvement in ICP following craniectomy, and then had a late abrupt deterioration (75 and 85 hours postoperatively), with evidence of evolving infarcts on follow-up neuroimaging. The mean duration until declaration of brain death in patients who failed craniectomy was 25 hours postoperatively (range 0–85 hours).

One patient experienced intraoperative cardiac arrest. This patient had other systemic injuries, and attempted resuscitation on the operating room table was unsuccessful.

TABLE 6

*Relationship between radiographic head injury and peak ICP at presentation**

Peak ICP Range (mm Hg)	Marshall Grade			
	I	II	III	IV
20–30	0	5	5	10
30–40	0	2	6	51
40–50	0	0	0	10
50–60	0	0	0	4
≥60	0	0	0	3

* All values are number of patients.

Short-Term Outcomes

In addition to the 14 deaths related to refractory ICP described above, 10 patients (10%) were able to achieve successful ICP control, but died during their hospital course. In 3 cases this result was related to systemic injuries, which led

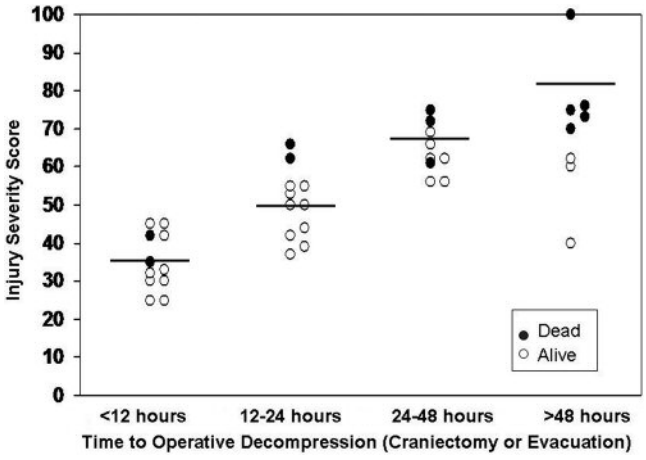

FIG. 2. Histogram demonstrating the relationship between injury severity scores and the time to operative decompression in patients who underwent operative treatment for elevated ICP. The mean injury severity scores *(bars)* were higher in patients who underwent later operative decompression. Patients who died *(black circles)* had higher injury severity scores than survivors *(open circles)*.

to multiorgan system failure. Four patients had concomitant vascular injuries (diagnosed using CT angiography, MR angiography, or conventional angiography), which resulted in large hemispheric infarcts and subsequent brain death. Three other families elected to withdraw care because of the patient's poor medical and neurological condition.

Complications that occurred during the hospital stay included ventilator-associated pneumonia (16 patients, 17%), meningitis (8 patients, 8%), and urosepsis (2 patients, 2%). All of these conditions were successfully treated using antibiotics. One patient had a postoperative subdural hematoma after craniectomy, which required reexploration. There was a statistically significantly higher rate of meningitis ($p < 0.05$, Student t-test) among patients who received ventricular drain placement (5 [22%] of 23 patients) compared with those who underwent operative decompression (3 [7%] of 40 patients).

Seventy-two patients (75%) were discharged from the hospital. Of these 72 patients, feeding tubes were required in 26 patients (36%) and endotracheal tubes were placed in 29 patients (40%) at the time of discharge. Ten (14%) of these 72 patients required shunt placement for posttraumatic hydrocephalus. The mean duration to discharge was 18.3 days (range 4–126 days). Sixty-six (92%) of these 72 patients were discharged to rehabilitation facilities, whereas 6 (8%) were discharged home. All surviving patients who underwent a craniectomy or ventriculostomy for ICP management were discharged to rehabilitation facilities.

Long-Term Outcomes

Posthospital Course. The mean clinical follow-up duration was 53 months (range 11–126 months). Three patients died during the follow-up period, at 11, 13, and 34 months follow-up. Two of these patients died from sepsis. Both patients were shunt dependent and had repeated hospitalizations for recurrent infections. Both of these patients were fully dependent on caregivers at the time of death, and died 11 and 13 months postinjury, respectively. The third patient had a 2-year GOS score of 4, but was noted to have severe delays in behavioral and social adjustment postoperatively. This patient was receiving multiple psychiatric medications, and ultimately committed suicide 34 months after his injury.

Thirty-two (46%) of the 69 patients who survived during follow-up had residual neurological deficits at the most recent follow-up visit. These deficits included hemiparesis (23 patients), visual deficits (7 patients), and speech disturbances (4 patients). Patients who underwent medical management of ICP appeared to have a lower incidence of postoperative neurological deficit compared with those who underwent surgery and/or ventriculostomy (Fig. 3). Twenty-six (38%) of the 69 patients were receiving medications at the time of the most recent follow-up, including anticonvulsants (24 patients), antidepressants (18 patients), antispasmodics (9 patients), and antihypertensives (4 patients). Additionally, 6 patients were receiving medical treatment for obesity. Medications summarized by treatment group are presented in Table 7.

Two-Year GOS Score. The mean 2-year GOS score was 4 (median 4, range 1–5). There was no difference in the mean or median 2-year GOS scores among the different treatment groups. All of the patients with a GOS score ≤ 2 (3 patients), however, belonged to the surgical (2 patients) or ventriculostomy (1 patient) treatment groups. The GOS score at 2 years appeared to be statistically significantly related to the presenting GCS score ($p < 0.05$, chi-square test); those patients who had lower GCS scores at presentation had lower GOS scores at the 2-year follow-up (Fig. 4).

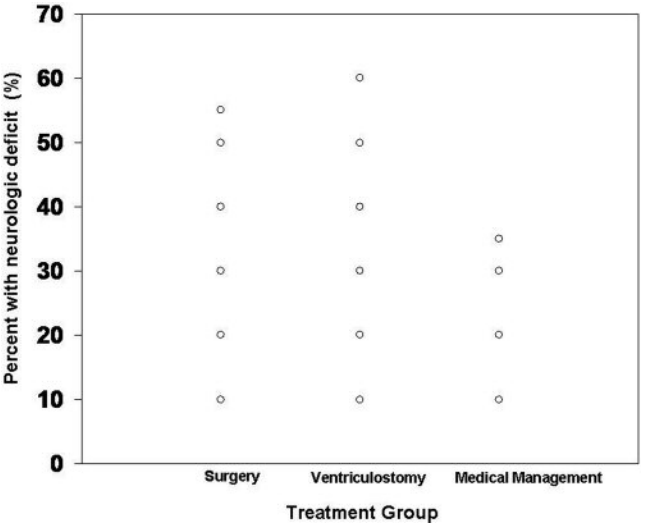

FIG. 3. Graph showing that postoperative neurological deficit was lowest in patients who had medical treatment alone when compared with those who underwent surgery or ventriculostomy. *Data points* represent the percentage of patients in each treatment group who had neurological deficits at follow-up.

Neurocognitive Function at Follow-Up. The mean overall patient competency rating at follow-up was 4.13 out of 5 (median 4.5, range 1–4.8). Overall neurocognitive function among the 3 groups is summarized in Fig. 5. Patients who underwent surgery or a ventriculostomy tended to have lower overall scores in all 4 areas of functioning (daily living, general cognition, interpersonal behavior, and emotional behavior), when compared with the group that underwent medical management of ICP. This difference was statistically significant in the areas of daily living and general cognition ($p < 0.05$, Mann–Whitney test), but not in the areas of interpersonal or emotional behavior.

At the most recent follow-up, 55 survivors had resumed school, and 10 survivors graduated high school and matriculated to college. Thirty-five (74%) of 47 patients > 18 years of age were living independently at follow-up. Eleven patients (16%) were dependent to some extent on caregivers, but only 3 of these patients were fully dependent.

TABLE 7

Summary of patient medication use at most recent follow-up according to treatment group

Medication	ICP Management Group (% of patients)		
	Op	Ventriculostomy	Medical
antiepileptics	37	30	9
antispasmodics	31	10	3
antihypertensives	10	33	0
obesity medications/diet modifications	10	20	5
antidepressants	37	20	31

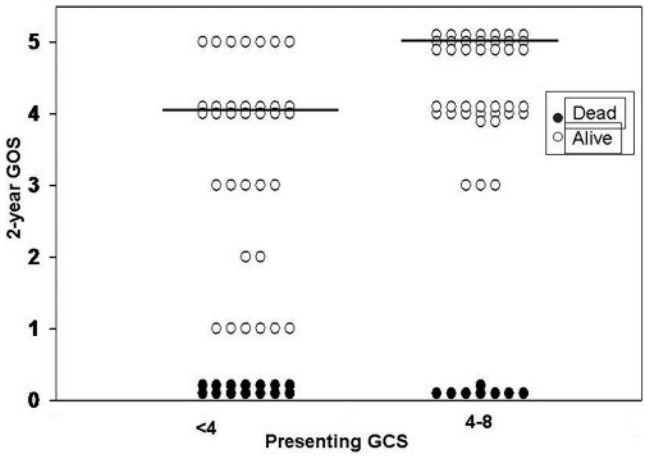

FIG. 4. Histogram showing the relationship between the presenting GCS score and the 2-year GOS score. The median 2-year GOS scores *(bars)* were higher in patients with a GCS score > 4 at presentation (mean 4.7, median 5) compared with patients whose presenting GCS score was ≤ 4 (mean 4.2, median 5). More deaths occurred in patients with lower GCS scores at presentation as well.

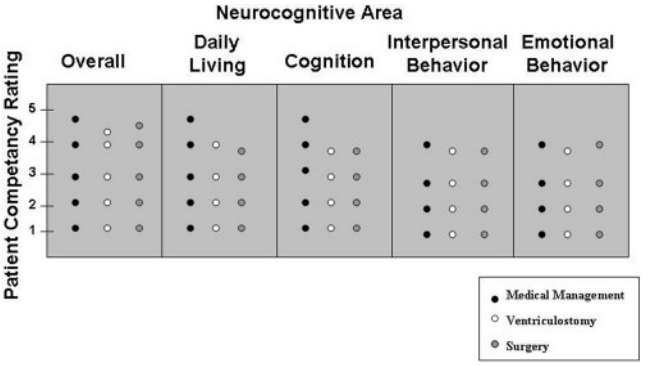

FIG. 5. Graph showing the results of neurocognitive assessment revealing that patients who underwent medical management *(black circles)* had higher neurocognitive outcomes when compared with patients who underwent surgery *(grey circles)* or a ventriculostomy *(open circles)*. The differences in ratings for daily living and cognition were statistically significant between the medical and nonmedical groups. *Data points* represent the average PCRS score for each treatment group according to the neurocognitive area tested.

Predictors of Outcome

Postoperative death was most significantly correlated with the presence of refractory raised ICP on univariate and multivariate analysis (p = 0.0001, Mann–Whitney test). The method used to control ICP appeared to have no correlation with death. Other factors associated with death included concomitant vascular injury (p = 0.04, Student t-test), cisternal effacement (p = 0.02), and greater injury severity (p = 0.04). The duration until intervention, patient age at presentation, peak ICP, presenting GCS score, and Marshall grade were not statistically associated with death.

Improved QOL measures were statistically significantly related to medical management of elevated ICP (p = 0.04, Mann–Whitney test). The presence of a mass lesion on the head CT scan at presentation was also associated with lower neurocognitive abilities on follow-up (p = 0.03, Mann–Whitney test). Long-term outcomes were not correlated with time to intervention, peak ICP, systemic injury, length of hospital stay, patient age, or Marshall grade of the presenting neuroimage.

Discussion

Intracranial Pressure Elevation and Management in Pediatric TBI

There is little in the way of definitive evidence to support ICP monitoring and aggressive treatment of intracranial hypertension in children. In spite of this lack of evidence, ICP monitoring has become the standard of care in the treatment of pediatric patients with severe TBI who are at risk for intracranial hypertension.[8,43,44] This standard of care can be attributed to the fact that the placement of an ICP monitor is associated with relatively low risks[38,39] and because normalization of ICP is believed to play a role in maintaining CPP, optimizing oxygen delivery, and preventing cerebral herniation.[16,19,42,46]

The question of when to treat elevated ICP in pediatric patients is equally controversial. Brief increases in ICP that return to normal in < 5 minutes are probably insignificant. However, sustained increases of > 20 mm Hg for > 5 minutes are likely significant and warrant treatment because global cerebral ischemia can precipitate secondary brain injury.[32]

Our study demonstrates that medical therapy can be highly effective when used initially in the management of elevated ICP in select pediatric patients with head injury; more than one-third of all patients in this series achieved and maintained normalization of ICP using medical management alone. The fact that the neurocognitive outcomes were higher in this group of patients is likely related to the fact that the majority of patients who had unsuccessful medical management of their ICP had a more severe brain injury (radiographically and pathophysiologically).

Although CPP has also been postulated to play an important role in TBI outcomes in adult patients, we typically favor treating ICP versus CPP in pediatric patients when a tradeoff is required.[33,40] For this reason we did not focus on CPP management parameters in this study. Because the mechanics of autoregulation in the injured brain are often impaired, the acceptable CPP threshold in pediatric patients is found on a continuum depending on patient age, weight, and condition.[12,23] Chambers and colleagues[12] suggested approximate CPP thresholds of 48 mm Hg in children between 2 and 6 years of age, 54 mm Hg in children between 7 and 10 years, and 58 mm Hg in children > 10 years of age. These general guidelines are similar to those suggested by the consensus committee on pediatric head injury.[2]

Efficacy and Limitations of ICP Management Strategies Following Pediatric TBI

The critical point that we have attempted to emphasize in this study is that ICP management is a highly individualized process in pediatric patients, and ICP control must be tailored to the patients' specific needs based on their neurological and general medical conditions. In our experience, when ICP control is achieved in pediatric patients, survival and discharge from the hospital can be reasonably expected.

We favor ICP monitoring in any pediatric patient with brain injury in whom it is not possible to monitor neurological status because of sedation, distracting injuries, or other medical conditions. Although an external ventricular drain is probably the best mechanism of transducing ICP, with the potential to correct elevated pressure, the relatively higher risk of meningitis associated with ventricular drainage compared with intraparenchymal ICP monitoring has led us to use external ventricular drains only in cases of refractory ICP.

We use medical therapy as the first-tier modality in TBI management, especially in the absence of a mass lesion. This medical therapy includes hyperosmolar therapy with 3% saline or mannitol, as well as mild hyperventilation. In some centers, jugular venous bulb oximetry has been used either alone or as an adjuvant treatment to ICP monitoring to determine if cerebral oxygenation is adequate.[47,48] Following the initial failure of medical therapy, however, the decision can be more complex. Some investigative groups have suggested that ventricular drain placement is effective in controlling ICP while sparing the patient an operation.[5] Fortune and associates[18] examined the outcomes in 22 patients (including pediatric patients) with a mean age of 24 years and demonstrated that CSF drainage, hyperventilation therapy, and intermittent mannitol administration were all effective in reducing ICP.

Our study also demonstrates that a ventriculostomy can be effective in reducing ICP and has QOL outcomes comparable to that of craniectomy. We tend to select our patients who receive a ventriculostomy extremely carefully and limit the ventriculostomy procedure to patients with IVH or hydrocephalus, but favor early decompressive craniectomy in most cases.

The rationale for more aggressive surgical treatment in pediatric patients is that the underlying pathophysiology in pediatric TBI is significantly different from adults. Lang et al.[26] found as much as 5 times more edema in pediatric patients following TBI when compared with adults. This greater cerebral edema is likely a result of a compensatory hyperemic response that has been demonstrated to be exaggerated in pediatric patients following trauma. In these situations, simply draining spinal fluid may not be enough to allow brain perfusion. By performing a decompressive craniectomy, we believe we can better compensate for cerebral edema, and the short- and long-term benefits have been well demonstrated in both this and previous studies.[22]

Factors Predicting Favorable and Unfavorable Outcomes

Predicting outcomes in pediatric patients with elevated ICP can be difficult. This study demonstrates that ICP control appears to have an extremely strong relationship to patient survival; none of the patients with refractory elevated ICP survived. Hypoxia and hypotension have also been demonstrated to be related to increased morbidity and death, with an increase in both of these factors by as much as 85%.[2,36] Because these factors are also related to ICP control, this data provides another reason for ICP control (a relationship to increasing the development of cytotoxic edema).

Another significant point of this study is the fact that patients with concomitant vascular injury are at a higher risk for infarction and death following TBI. We had previously observed this phenomenon in patients undergoing a craniectomy.[22] This study confirms that vascular injury carries a significant risk of brain death even in patients with less severe TBI (those patients who were treated nonoperatively), and that sudden ICP increases in these patients can be an ominous sign of impending herniation, requiring emergency treatment.

The favorable 2-year GOS scores, even in patients with poor presenting GCS scores, indicate that TBI survivors may only attain maximal recovery many months after injury. This course is in contrast to that of adult patients, in whom Levin and colleagues[28] demonstrated that ICP elevation had little effect on memory and behavioral function at 1 year after trauma. Our data appear to be more consistent with other pediatric studies in demonstrating that young patients have delays in neurocognitive function that may take longer to completely manifest and resolve.[3,17] Other testing modalities such as somatosensory evoked potentials may be helpful in defining poor outcome in patients with TBI, and the possibility of the bilateral absence of somatosensory evoked potentials associated with death or severe disability.[9–11,20]

Patterns of Head-Injury Recovery and Measurement of Long-Term Neurocognitive Sequelae

One of the senior authors (J.A.J. Sr.) worked closely with data from the National Institutes of Health Traumatic Coma Data Bank, which demonstrated that the lowest patient GCS score on admission was especially predictive of neuropsychological performance 1 year postinjury in trauma patients following resuscitation, and that early injury severity was correlated with improved motor outcomes but not with neuropsychiatric outcomes.[29] Those results indicated a pattern of neurobehavioral recovery from severe head injury that we have only begun to elucidate in pediatric patients.

It is important to be cognizant of the fact that pediatric TBI management varies when compared with that in adults, with respect to both the initial management and the recovery period. Because children are at greater risk for primary and secondary injury due to biomechanical vulnerabilities and physiological sensitivity to trauma,[1] they are more likely to develop significant brain injury, even when the presenting CT scan appears normal.

Unlike in adult patients, recovery from pediatric brain injury lacks a clear line of demarcation that allows the development of prognostic scales. The pediatric brain is continuously undergoing arborization and myelination, and disrupting this process at critical points in development may be responsible for some of the neurocognitive delays and disabilities observed in patients in this series. This developmental immaturity may also contribute to the favorable outcome that has been observed following pediatric TBI compared with adult TBI. Normal synaptogenesis and brain growth continues through childhood, allowing the potential for adaptive structural and functional changes after injury.[13,14]

Given these factors, the correct tool and the appropriate time for outcome measurement is unknown. During the acute phase of TBI, the primary concern is patient survival, and outcomes can be measured based on stabilization and resuscitation. Following this period is an intermediate phase, which is a dynamic period in which patients can undergo dramatic changes in neurological function as recov-

ery and neuroplasticity occurs. During this period, it is likely that comorbid injuries and medications may affect the rate of recovery.[49]

The "late phase" of brain injury begins when the child plateaus. During this phase, neuronal regeneration and compensation has ended, and functional improvements result from normal development superimposed on adaptation to physical and cognitive impairments. We chose to study the late effects of TBI using long-term outcome measures to obtain an accurate depiction of patient status at this latter phase, which may provide the most accurate measure of the child's ability to reintegrate into society. In reality, however, clear boundaries for the phases of recovery are arbitrary, and longitudinal care and serial outcome assessment is essential.

The decision on what scale to use in assessing TBI outcomes is a major challenge in the pediatric population. The GOS score and the King's Outcome Scale for Childhood Head Injury (KOSHI) are well-described scales that stratify outcomes as death, persistent vegetative state, severe disability, moderate disability, or good recovery.[15] These scales are limited in their ability to truly predict neurocognitive delays, a factor that is underscored in patients with high GOS scores but clear neuropsychiatric delays upon closer examination (such as the patient who committed suicide, or the multiple patients with obesity). The scale that we used was a global scale that assessed functional morbidity and psychological impairment, and appeared to clearly underscore the limitations in conventional outcome measures.[45] As survival rates for pediatric TBI increase, the focus will have to shift to developing better instruments to assess outcomes that are dedicated to pediatric patients.

Conclusions

Controlling elevated ICP is an important factor in patient survival following severe pediatric TBI. Refractory intracranial hypertension in spite of maximal medical and surgical management is almost always correlated with death in our experience. The modality (medical or surgical) used for ICP control should be tailored to the individual patient. Long-term follow-up is essential to determine neurocognitive sequelae associated with TBI.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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