Intensive insulin therapy for postoperative neurosurgery is associated with reduced infection rate and shortened ICU length of stay.

**Background:** Hyperglycemia is common in neurosurgical patients due to stress and steroids. Reports have suggested that controlling stress-induced hyperglycemia is associated with improved outcome.

**Objective:** To compare the safety and efficacy of intensive insulin therapy with conventional insulin therapy in postoperative neurosurgical patients in an ICU setting.

**Design:** Single-institution prospective blinded randomized controlled study.

**Methods:** Patients expected to spend 3 postoperative days in the ICU following neurosurgical procedures were randomized to receive insulin to maintain a glucose level in the 4.44 to 6.11 mM range (intensive insulin therapy) versus <11.94 mM (conventional insulin therapy). Blood glucose was measured at least every 4 hours, and insulin dose was adjusted accordingly. Safety outcomes measured included severe hypoglycemia episodes (<2.78 mM), and efficacy outcomes included infections, ICU length of stay (LOS), neurological outcome at 6 months measured by the Glasgow outcome scale, and mortality rate at 6 months. Power calculations determined that 240 patients would be required in each group to determine an expected 14% incidence in hypoglycemia between groups.

**Results:** 241 patients receiving intensive insulin therapy were compared to 242 patients treated with conventional insulin therapy after surgery for brain tumors, cerebrovascular disorders, severe head trauma, and intracerebral hemorrhage, either electively or emergently. Non-insulin-dependent diabetes mellitus was present in 23 intensive and 25 conventional patients. Of the intensive insulin patients, 94% had hypoglycemic episodes (median, 8 per patient) compared to 63% of conventional patients (median, 3 per patient). ICU LOS was shorter with intensive insulin therapy (6 days) than with conventional therapy (8 days). The infection rate was lower with intensive (25.7%) versus conventional (39.3%) therapy. Neurological outcome measured by the Glasgow outcome scale and mortality were similar between groups.

**Conclusions:** Intensive insulin therapy is associated with shorter ICU LOS and reduced infection rate. The consequences of the increased episodes of hypoglycemia from intensive insulin therapy are unknown.

**Reviewer's Comments:** This study shows that intensive insulin therapy to rigorously control serum glucose levels in patients treated with elective and emergent neurosurgery operations is associated with reduced ICU LOS and reduced infection rates. Even though neurological outcome and mortality were similar, the reduced resource utilization in the intensive insulin group indicates a role for such rigorous control of blood glucose in the ICU setting. However, better characterization of the consequences of hypoglycemic events is needed. Additionally, some caution is necessary before applying these results widely, as the patients included for study had a range of neurological disorders and severity, and glucocorticosteroids were variably used. To summarize, strict blood glucose control appears to be an appropriate critical care goal after neurosurgical operations. (Reviewer-N. Scott Litofsky, MD).

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Keywords: Insulin

Print Tag: Refer to original journal article
Some MCA Aneurysms Can Be Treated by Endovascular Methods

Endovascular Treatment of Middle Cerebral Artery Aneurysms With Detachable Coils: Angiographic and Clinical Outcomes in 115 Consecutive Patients.
Suzuki S, Tateshima S, et al:
Neurosurgery 2009; 64 (May): 876-889

MCA aneurysms included in this series were treated with endovascular means, with morbidity and mortality rates comparable to those with open surgical treatment methods.

Objective: To review the authors' experience in the treatment of middle cerebral artery (MCA) aneurysms via endovascular means. This technique is unique because most of these aneurysms are treated with microsurgical clipping.

Participants/Methods: 115 patients with MCA aneurysms were included in the study from April 1990 to March 2007. Of these aneurysms, 58% were unruptured and 42% were ruptured. Most (46%) were small with a small neck, while 19% were large, and 11% were characterized as giant. A subset of small aneurysms with wide necks (24%) was included.

Results: Complete occlusion immediately after treatment was reported in 46% of aneurysms, while incomplete occlusion was achieved in 3%. A neck remnant was left in 44% of patients. Eight aneurysms were untreatable by endovascular means. Extracranial-intracranial bypass surgery was required in 13 patients. Overall, the complication rate was 9%, with 10% of aneurysms demonstrating recanalization on long-term angiography. All aneurysms were large or giant, and one ruptured 13 months after embolization. The overall morbidity and mortality rate was 9.9%.

Conclusions: MCA aneurysms in this series may be treated with endovascular means, with morbidity and mortality rates comparable to those of open surgical treatment methods. Large or giant aneurysms may require retreatment or open surgical revascularization.

Reviewer's Comments: Treatment of MCA aneurysms remains controversial. Often, they are wide-necked lesions with branches of the distal MCA arising from the aneurysm neck. This article indicates a reasonably high rate of complete obliteration in a large series of MCA aneurysms. However, shortcomings of the study should be noted. First, the selection criteria by which aneurysms in the study were referred to endovascular management is unclear, leaving the study open to selection bias regarding which patients were referred to endovascular therapy. Additionally, while the study is unique in that it includes treatment data on large and giant MCA aneurysms, these aneurysms were reported to demonstrate recanalization or, in one case, rerupture. While the authors report the use of endovascular treatment in concert with open revascularization for giant or fusiform aneurysms, this is generally unnecessary. Such aneurysms, in our experience, are best treated with revascularization followed by clip trapping distally or proximally at a single sitting without requiring a separate procedure. The best results were, as expected, in small aneurysms with small necks. Even so, the overall obliteration rate was only 46%, with a 7% crossover rate in patients ultimately requiring surgical treatment. Such results reinforce the opinion of many cerebrovascular surgeons that optimal therapy involves microsurgical treatment of MCA aneurysms, especially in younger patients in good neurological condition. Nevertheless, as treatment options continue to evolve, studies such as this one will become more important in defining optimal treatment. (Reviewer-Nicholas C. Bambakidis, MD).

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Keywords: Middle Cerebral Artery Aneurysms

Print Tag: Refer to original journal article
Spinal instability is very uncommon following gunshot wounds to the head, neck, or torso.

**Background:** The need for imaging to clear the spine radiographically and/or immobilization of the cervical spine after gunshot wound to the head, neck, or torso is not clearly defined.

**Objective:** To determine (1) the incidence of spinal injuries among asymptomatic patients with gunshot wounds to the head, neck, or torso, and (2) the proportion of these patients who require operative stabilization of the spine.

**Design:** Single-institution retrospective chart review.

**Methods:** All patients suffering gunshot wounds to the head, neck, and torso from 1995 through 2004 were identified. Patients who died within 24 hours were excluded. Patients with physical exam findings suspicious for spinal injury (complete paralysis, motor weakness, lack of anal tone, sensory abnormalities, or paresthesias), paraspinal pain, or incomplete evaluation were assessed by radiographic studies per protocol. Radiographic findings, final diagnoses, and management plans were recorded for analysis.

**Results:** 339 of 4204 patients (8.1%) had radiographic evidence of bony spinal column injury. Records were available for 327 patients (96.4%). Of these, 150 patients (45.8%) had spinal cord injury. Two patients required operative decompression, but not stabilization. No patient with a Glasgow Coma Scale score of 15 and normal neurological exam required operation. Level of the gunshot wound had no correlation to the presence of spinal cord injury. Bony cervical spinal column injury occurred in 34 of 51 (66.7%) gunshot wounds to the head or neck, and 149 of 288 gunshot wounds to the torso (51.7%) had bony injury with concomitant spinal cord injury.

**Conclusions:** Patients who are awake and alert with normal neurological exam and no paraspinal tenderness will not have injuries requiring operative stabilization or immobilization.

**Reviewer's Comments:** Based on its title, I thought this paper would clarify the role of imaging and immobilization/operative stabilization in patients with gunshot wounds to the paraspinal areas. The results do confirm that instability after gunshot wound to the spine is very rare. Therefore, the routine use of strict spinal precautions or a cervical collar appears to be unnecessary. The issue regarding radiographic evaluation, on the other hand, is not addressed satisfactorily. The patients were managed by an imaging protocol that the authors did not choose to delineate. Patient symptoms were also not quantified. Because 8% of patients studied had some bony injury, some form of imaging is necessary in these patients. At this time, I would evaluate patients with such gunshot wounds with a CT scan of the appropriate spinal area with sagittal and coronal reconstructions. Those with evidence of spinal cord injury may need MRI. Additional imaging would be based on results of these studies. (Reviewer-N. Scott Litofsky, MD).

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**Keywords:** Gunshot Wounds

**Print Tag:** Refer to original journal article
Recurrence CSDH and Negative Workup—Consider PAI-1 Deficiency

A Novel Association Between a Chronic Subdural Hematoma and a Fibrinolytic Pathway Defect: Case Report.
Rughani AI, Holmes CE, Penar PL:
Neurosurgery 2009; 64 (June 6): E1192

PAI-1 deficiency can be detected by measuring plasma levels and is treated by oral aminocaproic acid.

Background: Chronic subdural hematoma (CSDH) frequently occurs in elderly patients following mild to moderate head trauma. After treatment, CSDH has a reported recurrence rate of 20%. In this article, the authors report the case of a recurrent CSDH despite 2 craniotomies for evacuation of hematoma, which proved to be due to a deficiency in plasminogen activator inhibitor type I (PAI-1). Case Report: The patient was a 49-year-old man presenting with dizziness and falls of 1-week duration. Two months before presentation, the patient had slipped on ice and fallen. The patient denied any history of easy bruising or bleeding, but his family history was remarkable for bleeding diatheses in several first-degree relatives. The patient was on no anticoagulation at that time. A physical exam revealed mild confusion and a subtle left pronator drift. A head CT showed a chronic right frontal SDH, 2 cm in maximal thickness with a 1.8 cm midline shift. A small right frontal craniotomy was performed with fenestration of the subdural membranes and subdural irrigation. A subdural drain was left in place until postoperative day (POD) 2. A postoperative head CT demonstrated marked improvement, and the patient had resolution of his pronator drift with mental status amelioration. He was discharged home on POD 3. At 1-month follow-up, the patient reported persistent headaches but was neurologically intact. A head CT showed recurrent CSDH with a small acute component. A second craniotomy was performed with hematoma evacuation and subdural drain placement. The drain was removed on POD 2, and a head CT after surgery showed adequate hematoma evacuation. He was discharged on POD 3. At 1-month follow-up, the SDH had recurred on CT. An extensive hematological workup performed at that time revealed decreased PAI-1 activity with normal PAI-1 antigen levels consistent with a diagnosis of PAI-1 deficiency. PAI-1 is a protease inhibitor that inhibits tissue plasminogen activator (tPA). The theory is that PAI-1 deficiency leads to increased fibrinolysis via reduced tPA inhibition and it has been correlated with bleeding diatheses. The patient was then started on oral aminocaproic acid for 1 month, and a head CT after 1 month showed a decreasing SDH. At 5-month follow-up, a head-CT demonstrated complete resolution of the SDH. PAI-1 activity and antigen levels were repeated at that time and confirmed the diagnosis.

Conclusions: PAI-1 deficiency should be part of the differential-diagnosis in patients with recurrent CSDH and negative routine work-up, especially when a family history of bleeding diatheses is present.

Reviewer's Comments: This article sheds light on an unusual bleeding diathesis that may lead to recurrent CSDH. These results, however, should not prompt an extensive assessment of all coagulation pathways in all patients presenting with CSDH. Rather, a thorough hematological workup including evaluation of PAI-1 might be entertained in the event of a recurrence after surgery when another convincing reason is lacking.

(Reviewer-Ziad A. Hage, MD).

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Keywords: Chronic Subdural Hematoma

Print Tag: Refer to original journal article
Severity of initial hemorrhage or prolonged hydrocephalus may be factors contributing to anosmia in aneurysmal SAH patients.

**Background:** Anosmia is commonly encountered following aneurysmal subarachnoid hemorrhage (SAH). It was considered a complication of clipping but it has recently been reported after coiling.

**Objective:** To assess the prevalence and prognosis of anosmia after aneurysmal SAH treated with coiling. The authors also evaluated potential risk factors as a cause.

**Methods:** All patients admitted at the authors' institution with aneurysmal SAH between January 1997 and May 2007 treated with coiling and who were back to independent living after the procedure were included in this study. SAH had to have occurred 6 months before presentation to evaluate recovery of anosmia over time. Patients with pre-existing anosmia and intracranial surgery other than an uncomplicated intraventricular drain insertion were excluded. Data for age, gender, SAH date, World Federation of Neurological Surgeons scale, aneurysm location, and presence of hydrocephalus using the bicaudate index were gathered. A semi-structured questionnaire was used to interview patients in clinic or by telephone. A visual analog scale (VAS) was used to evaluate the impact of anosmia.

**Results:** 197 patients were included. A CT scan within 72 hours after SAH was available in 161 cases; of these, 60% had intraventricular hemorrhage (IVH), 27% had a Hijdra score ≥4 for IVH, 89% demonstrated interhemispheric blood, and 29% had the highest possible score. Anosmia was recorded in 18%. An impact of anosmia on daily life averaging 65 on the VAS was noted in 10% of patients; 43% could not judge the impact. Anosmia was permanent in 26%, partially resolved in 8.5%, and completely resolved in 57%; 8.5% of patients could not express whether the anosmia had resolved. Median duration of anosmia was 6 weeks in those who recovered completely. Time of partial recovery ranged from 8 to 20 months. Univariate analysis demonstrated that IVH correlated with anosmia. Multivariate analysis showed that IVH was the sole factor significantly correlated with anosmia.

**Conclusions:** The authors concluded that anosmia following coiling was noted in 1 of 6 patients with aneurysmal SAH. Nonetheless, anosmia had good prognosis in the majority of patients. While the cause of anosmia after coiling for ruptured aneurysms remained unidentified, the authors speculated that the severity of initial hemorrhage or prolonged hydrocephalus may be associated factors.

**Reviewer’s Comments:** This report has several limitations. First, the authors relied on questionnaires to assess the presence of anosmia. A more accurate and less subjective method such as olfaction tests would have been preferred. It is known that patients can report normal olfaction in the setting of anosmia. Another drawback is the issue of recall bias in which patients were interviewed a minimum of 6 months after SAH and, therefore, might have forgotten a transient anosmia episode. In such a case, the prevalence of anosmia would have been undervalued. Nevertheless, this study provides further insight on a topic that is underreported.

(Reviewer-Ziad A. Hage, MD).

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Keywords: Intracranial Aneurysm

Print Tag: Refer to original journal article
Decompressive Hemicraniectomy Can Be Lifesaving in Severe CVST

Decompressive Hemicraniectomy in Cerebral Sinus Thrombosis: Consecutive Case Series and Review of the Literature.
Coutinho JM, Majoie CBLM, et al:
Stroke 2009; 40 (June): 2233-2235

In patients with severe CVST, decompressive hemicraniectomy can be lifesaving with excellent results.

**Background/Objective:** Of patients with cerebral venous and sinus thrombosis (CVST), about 13% fare poorly. The major cause of mortality is transtentorial herniation. Predictors of poor outcome include coma, intracerebral hemorrhage, and deep vein thrombosis (DVT). While treatment with endovascular thrombolysis might be considered in some patients with CVST, the latter approach in imminent transtentorial herniation due to large infarcts or hemorrhages does not seem efficacious. Consequently, the authors started performing decompressive hemicraniectomy for these cases as of mid-2006. In this series, they report on their first 3 consecutive patients.

**Methods:** As of July 2006, patients with severe CVST and signs of transtentorial herniation were treated with decompressive hemicraniectomy. Indications for surgery included unilateral third nerve dysfunction, decline in Glasgow Coma Scale (GCS) score due to local brain swelling or venous infarction with midline shift, and obliteration of basal cisterns. At time of surgery, a wide hemicraniectomy was done to maximize decompression. High-dose nadroparin was administered subcutaneously when the diagnosis of CVST was made; a prophylactic dose was continued postoperatively for 24 hours, followed by a dosage increase to reach therapeutic levels. Follow-up occurred at 6 and 12 months after discharge, and outcome was measured using the modified Rankin Scale (mRS).

**Results:** Patient A was a 39-year-old man who was known to be protein C deficient after left leg DVT. He presented with severe headache, nausea, disorientation, and $E_4M_6V_5$. CT demonstrated a left temporal hemorrhagic stroke, and magnetic resonance venography (MRV) showed left transverse/sigmoid thrombosis. Despite nadroparin, the hemorrhage increased with a 12-mm midline shift, and the patient worsened to $E_1M_5V_1$. He underwent a hemicraniectomy and markedly improved to $E_3M_5V_4$ perioperatively. Patient B was a 36-year-old woman presenting with a generalized seizure and $E_4M_6V_5$. MRV demonstrated superior sagittal sinus thrombosis along with a right-sided parieto-occipital hemorrhagic stroke. Despite nadroparin, the patient worsened to $E_3M_5V_4$ and developed a dilated right pupil. CT demonstrated an expanding hemorrhage with 9-mm midline-shift. A hemicraniectomy was performed, after which the pupils became symmetrical and GCS improved. At 6- and 12-month follow-up, the patient's only deficit was a quadrant anopia. Patient C was a 55-year-old woman who was found comatose at home with $E_1M_5V_1$, a fixed/dilated left pupil, and no bilateral corneal reflexes on exam. CT showed a sizeable left temporal hemorrhage with uncal-herniation and 15-mm midline-shift. Contrast-enhanced CT showed left transverse/sigmoid sinus thrombosis. Despite decompressive hemicraniectomy, she continued to deteriorate, and treatment was withdrawn. She died on day 8.

**Conclusions:** In patients with severe CVST, decompressive hemicraniectomy can be lifesaving with excellent results.

**Reviewer’s Comments:** This small series suggests a benefit of decompressive hemicraniectomy in patients with severe CVST and impending transtentorial herniation. In fact, hemicraniectomy has been proven effective in malignant middle cerebral artery infarction and imminent herniation. (Reviewer-Ziad A. Hage, MD).

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Keywords: Sinus Thrombosis

Print Tag: Refer to original journal article
Microsurgical management of previously coiled aneurysms are best managed by direct clipping, however, other methods must be deployed if direct clipping is not feasible.

**Background:** Endovascular treatment of intracranial aneurysms has grown significantly; however, this therapy can be associated with recurrence. Options for recurrent aneurysms after coiling include recoiling or microsurgical approaches including clipping. Clipping a recurrent previously coiled aneurysm presents many challenges.

**Objective:** The authors report on their microsurgical experience at the University of California, San Francisco, with patients with incompletely coiled and recurrent aneurysms to demonstrate recent trends, surgical techniques, morphological features that predict clippability, and observations on coil extrusion.

**Methods:** The records of patients seen between December 1997 and December 2007 were analyzed; 1459 patients with 1847 intracranial aneurysms had surgery, 43 of whom underwent surgical management of incompletely coiled or recurrent aneurysms. There were 34 women and 9 men, with a mean age of 51 years. Anterior communicating artery aneurysms were the most common in these patients. The mean diameter was 14 mm, including 12 large and 6 giant aneurysms. The Glasgow Outcome Scale was used to grade outcomes.

**Results:** A spike in the number of aneurysms treated microsurgically after coiling was noted in the last year of the study. Twenty-one patients had incompletely coiled aneurysms; 19 of these patients were referred for coiling, while 2 were referred after recurrent hemorrhage. The remaining 22 patients had recurrent aneurysms. Extrusion of coils into the subarachnoid space was noted in 1 of the 21 incompletely coiled aneurysms and in 12 of the 22 recurrent aneurysms. In the 43 patients, 33 aneurysms were clipped directly, 7 non-clippable aneurysms required a bypass, and 3 were wrapped. Three patients died, and 1 patient experienced permanent neurological morbidity; the remaining 39 patients had good outcomes. Interestingly, angiography failed to show coil extrusion in the recurrent aneurysm. Four mechanisms are hypothesized for coil extrusion by the authors: iatrogenic extrusion of coils during initial coiling, initial coiling of a pseudoaneurysm, forcible coil compaction leading to extrusion, and degradation of the distal aneurysm.

**Conclusions:** The authors demonstrate the utility, efficacy, and safety of microsurgical techniques in the management of both incompletely coiled and recurrent aneurysms after coiling.

**Reviewer's Comments:** Recent data emphasize complete aneurysm obliteration as the goal of aneurysm treatment in most cases. This is particularly true for a ruptured aneurysm. When this cannot be achieved endovascularly, microsurgery should be considered. Surveillance imaging is needed to rule out recurrence after coiling. Recurrence should usually be treated interventionally or microsurgically depending on many factors, including morphology and mass effect issues. Of particular concern is recurrence of large and giant aneurysms after coiling. Such recurrences can be associated with significant mass effect issues as well as formidable microsurgical challenges. For aneurysms that pose a high recurrence risk from an interventional perspective, microsurgical repair should be carefully considered. This study emphasizes the continued importance of microsurgical skills in aneurysm management. (Reviewer-Bernard R. Bendok, MD).

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Keywords: Aneurysm Recurrence

Print Tag: Refer to original journal article
Cerebral Hyperperfusion Predicted by MRA

Prediction of Cerebral Hyperperfusion After Carotid Endarterectomy Using Middle Cerebral Artery Signal Intensity in Preoperative Single-Slab 3-Dimensional Time-of-Flight Magnetic Resonance Angiography.

Kuroda H, Ogasawara K, et al:

Neurosurgery 2009; 64 (June): 1065-1072

Preoperative 3D time-of-flight MRA images may be able to predict post-CEA hyperperfusion.

**Objective:** To determine the role of magnetic resonance angiography (MRA) in predicting cerebral hyperperfusion after carotid endarterectomy (CEA).

**Design:** Prospective case series.

**Methods:** 81 consecutive patients with carotid stenosis and good Rankin scores were enrolled. Axial single-slab 3D time-of-flight (TOF) images were obtained from the carotid bifurcation to the terminal middle cerebral artery (MCA) branches using a 3-T MR scanner. Patients were stratified based on the ability to visualize the branches of the ipsilateral MCA: grade A, visualization of all M3 branches at the cortical surface; grade B, lack of visualization of 1 or more M3 branches; grade C, lack of visualization of an M2 branch; and grade D, lack of visualization of the M1 branch. Cerebral blood flow (CBF) was calculated using single-photon emission computed tomography (SPECT) with N-isopropyl[123I]-p-iodoamphetamine. Hyperperfusion was characterized as CBF 2 times greater than the preoperative value. The incidence of hyperperfusion was calculated for each patient category. The relationship between any single variable and the development of hyperperfusion was determined by univariate analysis.

**Results:** 10 patients developed radiographic hyperperfusion. Both internal carotid artery stenosis and loss of signal in the MCA were independently associated with post-CEA hyperperfusion ($P=0.0006$ and 0.0001, respectively). Grade C and D patients were significantly more likely to develop hyperperfusion than grade A patients ($P=0.0002$ for grade C and 0.0082 for grade D). When the decrease in MCA signal intensity was described as an alteration in cerebral hemodynamics, this finding was 100% sensitive and 63% specific for the development of post-CEA hyperperfusion. Of the 10 patients with radiographic hyperperfusion, 8 regained normal perfusion values by postoperative day 3. The other 2 patients progressed to symptomatic hyperperfusion.

**Conclusions:** A decrease in MCA signal intensity on MRA may identify patients who are more likely to develop hyperperfusion.

**Reviewer's Comments:** Cerebral hyperperfusion is a rare but important complication of CEA and is marked by headache, seizure, and focal neurological symptoms. The pathophysiology involves loss of CBF autoregulation secondary to chronic ischemia. In this study, Kuroda and colleagues investigate the role of MCA imaging in identifying patients at risk for hyperperfusion. The study is well designed and proposes a role for MRA in identifying at-risk patients. Clinicians should recognize that hyperperfusion, as defined here, is usually clinically silent. Only 2 of the 12 cases of radiographic hyperperfusion had symptoms. Other techniques for predicting hyperperfusion exist. These techniques (SPECT with acetazolamide challenge or perfusion-weighted MRI) have disadvantages preventing their generalized use. However, they have higher specificity than MRA. A more quantitative phase-contrast MR might prove useful in future studies. Also, larger studies may be needed to establish the utility of MRA in predicting clinically relevant hyperperfusion after CEA.

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Keywords: Carotid Endarterectomy

Print Tag: Refer to original journal article
Civilian gunshot wounds to the head are sometimes survivable and require judicious management decisions based on consideration of clinical and radiographic parameters.

**Background:** Gunshot wounds to the head are fairly common and are associated with poor outcome.  
**Objective:** To identify prognostic factors of gunshot wounds to the head in a civilian setting.  
**Design:** Single-institution retrospective chart review.  
**Methods:** The records of all patients with isolated gunshot wounds to the head from 1999 to 2005 were reviewed. Operative interventions included craniotomy for debridement of necrotic tissue debridement, foreign body (missile and bone fragments) removal, hematoma evacuation, and dura, bone, and soft-tissue reconstruction; bone flaps were replaced except in cases of severe contamination or edema. Most patients with a Glasgow Coma Scale (GCS) score ≤8 had intracranial pressure monitoring. Aggressive removal of all intracranial fragments was not attempted.  
**Results:** 72 patients suffered isolated gunshot wounds to the head. Mortality was significantly greater at 81% with a GCS ≤8 compared to 14.3% with a GCS >8. Overall mortality was 58% (42 patients); most deaths occurred early—10 upon arrival, 9 within 24 hours, 19 within 5 days, and only 4 after 5 days. Mortality (79%) was significantly greater in the 75% of patients intubated prior to hospital arrival compared to 25% in non-intubated patients. Pupillary abnormalities were not associated with significant mortality differences (78% with abnormalities, 53% with none). Mean arterial lactate was significantly lower in surviving patients (2.7 vs 6.65). Missile trajectory crossed midline in 23 of 36 patients; the 69% mortality rate in bi-hemispheric injury was not significantly different than the 46% rate in uni-hemispheric injury. Twenty-two patients with dural-penetrating injuries survived, 19 with a Glasgow Outcome Scale (GOS) score of 3 and 3 with a GOS of 4. Craniotomies were performed in 24 patients; 14 cranial complications occurred.  
**Conclusions:** Indicators of outcome in civilian gunshot wounds to the head include mechanism of injury, presenting GCS, pupillary abnormalities, and CT assessment of severity of injury. Triaging patients on the basis of GCS and pupillary findings is acceptable when resources are limited.  
**Reviewer’s Comments:** In attempting to define prognostic factors, this paper describes the management and outcome of patients with civilian gunshot wounds to the head. However, the authors’ conclusion of triaging patients on the basis of GCS and pupillary function is not substantiated by their data because pupillary abnormality was not associated with statistically significant differences in mortality. In addition, GCS was not stratified in a manner to make triage decisions. Several data are of interest. The low number of craniotomies suggests biased management that likely affects survival. Increased lactate levels in non-surviving patients suggest that systemic perfusion and/or oxygenation deficits are poor prognostic features. Bi-hemispheric injuries are not necessary fatal, as 31% of these patients survived. Lastly, since most deaths occur early after injury, once an aggressive care pathway is initiated, it should be continued because the patient is likely to survive. (Reviewer—N. Scott Litofsky, MD).

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Keywords: Gunshot Wounds

Print Tag: Refer to original journal article
Exclusion of intracerebral hemorrhage patients with very poor prognosis and earlier treatment with recombinant activated factor VII may have resulted in improved functional outcome in the FAST trial.

**Background:** The Factor Seven for Acute Hemorrhagic Stroke (FAST) trial showed that 80 μg/kg of recombinant activated factor VII (rFVIIa) significantly reduced intracerebral hemorrhage (ICH) expansion when given within 4 hours of onset but did not improve survival or functional outcome.

**Objective:** To determine whether earlier treatment and exclusion of patients with poor prognosis at baseline would enhance the benefit of rFVIIa treatment.

**Design:** Subgroup analysis of a randomized, controlled clinical trial.

**Participants:** A subgroup of 114 patients (55 treated with rFVIIa, 59 with placebo) who had treatment within 150 minutes of onset, were aged ≤70 years, and had an intraventricular hemorrhage (IVH) volume <5 cc and ICH volume <60 cc.

**Methods:** The FAST data were analyzed for the impact of onset to treatment time, age, ICH and IVH volume, Glasgow Coma Scale scores, and infratentorial ICH on poor outcome (modified Rankin score of 5 or 6) at 90 days. The effect of treatment on outcome was assessed for the target subgroup using all patients who met criteria from the FAST dataset and then was externally validated using similar patients from the phase II study.

**Results:** The subgroup identified from the sensitivity analysis optimizing treatment effect and sample size (n=160 patients from FAST) included the following: age ≤70 years, ICH volume <60 mL, IVH volume <5 mL, and onset to treatment time ≤2.5 hours. The adjusted odds ratio was 0.28 for poor outcome with rFVIIa treatment. This was not statistically different from that of placebo. The absolute difference in ICH volume growth at 24 hours was 7.3 mL in the target subgroup versus 3.8 mL in the entire FAST population (P =0.02). External validation with phase 2 patients confirmed the improved outcome.

**Conclusions:** It is rational to explore potential benefits of rFVIIa for ICH in younger patients without extensive bleeding who are treated within 2.5 hours of symptom onset.

**Reviewer's Comments:** This study provides further insight into possible reasons for the failure of the FAST trial to replicate the findings of the phase 2b study. Many baseline variables contribute to the prognosis of patients with ICH. The FAST trial did not exclude patients with several poor prognostic indicators, especially age and large IVH. It is reasonable that rFVIIa may benefit some patients more than others—the subgroup identification was rigorous, and the criteria identified must now be validated with another prospective trial. In limiting the time window for rFVIIa to 150 minutes, clearly the percentage of patients with ICH who would be eligible for treatment will decrease. (Reviewer-Wendy C. Ziai, MD).

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IVH Score--Practical Tool to Estimate IVH Volume

Hallevi H, Dar NS, et al:

Crit Care Med 2009; 37 (March): 969-974

Using both intracerebral hemorrhage (ICH) and intraventricular hemorrhage volume improves mortality prediction in spontaneous nontraumatic ICH.

**Background:** Intraventricular hemorrhage (IVH) volume is an independent predictor of poor outcome in patients with intracerebral hemorrhage (ICH).

**Objective:** To develop a useful tool to rapidly assess IVH volume and to establish the relationship between IVH volume or total volume (TV) of both ICH and IVH with clinical outcome.

**Design:** Retrospective study.

**Participants:** 175 patients with spontaneous non-traumatic ICH and IVH on CT within 24 hours of onset; 92 patients were in the derivation group and 83 were in the validation group.

**Methods:** IVH was graded using a simple classification scheme called the IVH score (IVHS), which accounts for the amount of blood in each ventricle and the presence/absence of hydrocephalus. IVH volume was also measured by computerized volumetric analysis for comparison. ICH volume was measured by the ABC/2 method. Poor outcome was defined as modified Rankin score of 4 to 6.

**Results:** The derived IVHS ranged from 0 to 23 and can be converted to IVH volume using a logarithmic transformation: IVH volume (mL) = eIVHS/5. The IVH estimation formula was verified with the validation group, which yielded high accuracy (R2 of 0.8). Correlation of volumes with poor clinical outcome at discharge found TV (=ICH+IVH) to be a better predictor than ICH volume alone. In logistic regression models, Glasgow Coma Scale score and TV were independently associated with outcome after controlling for age, infratentorial location, and hydrocephalus.

**Conclusions:** The IVHS readily estimates IVH volume, and the addition of IVH volume to ICH volume significantly increases the predictive power for poor outcome and mortality.

**Reviewer’s Comments:** The IVHS is relatively easy to use and is superior to prior IVH scoring systems in its ability to estimate IVH volume. The clinical significance of specific IVH volumes at this point is unclear. The IVHS requires prospective validation as this study was entirely retrospective, and development and validation cohorts had significant differences: more patients in the index group were treated with ventricular drainage and intraventricular recombinant tissue plasminogen activator compared with the validation group. The logistic regression model failed to include important potential outcome predictors, namely surgical treatments for ICH such as clot evacuation and intraventricular thrombolysis. If the accuracy of the IVHS is validated, it may become a useful tool for prognostication and clinical decision-making. (Reviewer-Wendy C. Ziai, MD).

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Keywords: Intraventricular Hemorrhage

Print Tag: Refer to original journal article
Intensive Insulin Therapy May Impair Brain Glucose Metabolism

Impact of Tight Glycemic Control on Cerebral Glucose Metabolism After Severe Brain Injury: A Microdialysis Study.

Oddo M, Schmidt JM, et al:

Crit Care Med 2008; 36 (December): 3233-3238

Tight systemic glucose control may impair cerebral glucose availability and aggravate neuronal injury.

Background: Excessive reduction in glucose availability in brain-injured patients may compromise brain energy metabolism.

Objective: To analyze the effect of tight glycemic control with intensive insulin therapy on cerebral glucose metabolism in patients with severe brain injury.

Design: Retrospective analysis of a prospective observational cohort.

Participants: 20 patients with a Glasgow Coma Scale (GCS) score <9 who were monitored with cerebral microdialysis (CMD).

Methods: Samples were collected every hour and analyzed for glucose, lactate, and pyruvate along with simultaneous serum glucose concentration. Systemic glucose was maintained between 80 and 120 mg/dL using an IV insulin infusion. CMD glucose <0.7 mmol/L was considered low; a lactate pyruvate (L/P) ratio >40 indicated "brain energy failure." Brain energy crisis was defined as a microdialysis glucose level <0.7 mmol/L and L/P ratio >40.

Results: In all patients, CMD glucose and CMD/systemic glucose were reduced compared with normal, and L/P ratios were increased. Systemic glucose in the tight range (80 to 120 mg/dL) was associated with lower CMD glucose and higher L/P ratios compared with systemic glucose in the intermediate range (121 to 180 mg/dL). Tight control of systemic glucose was associated with a higher prevalence of low CMD glucose (65% vs 36%) and brain energy crisis (25% vs 17%) compared with the intermediate range. Lower systemic glucose and higher insulin dose were both independent predictors of brain energy crisis after adjusting for intracranial pressure (ICP) and cerebral perfusion pressure (CPP). Brain energy crisis was an independent predictor of increased hospital mortality after adjustment for hourly ICP, CPP, and GCS.

Conclusions: Intensive insulin therapy may significantly impair cerebral glucose metabolism in patients with severe brain injury.

Reviewer's Comments: This paper suggests that insulin therapy and systemic glucose targets may require different goals in patients with severe neurologic injury than in those with other disorders. CMD may be useful either as a prognostic indicator or a target for therapy. However, it is apparent that tight glucose control is difficult to implement in many patients with severe brain injury. It is significant that reductions of CMD glucose were not blinded during insulin therapy and may have influenced systemic glucose target levels. It is also not clear whether brain glucose metabolites are markers of disease severity or contribute to neuronal injury, as the models were not adjusted for a multitude of factors known to affect mortality in these patient subgroups. This study should be viewed as preliminary evidence, and we await larger prospective studies to determine how predefined levels of metabolic crisis translate into neurologic outcome. (Reviewer-Wendy C. Ziai, MD).

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