Intraventricular tPA After Aneurysmal SAH May Prevent Hydrocephalus

Intraventricular Tissue Plasminogen Activator for the Prevention of Vasospasm and Hydrocephalus After Aneurysmal Subarachnoid Hemorrhage.

Ramakrishna R, Sekhar LN, et al:

Neurosurgery 2010; 67 (July): 110-117

Intraventricular tissue plasminogen activator administration after aneurysmal subarachnoid hemorrhage reduces the need for angioplasty and cerebrospinal fluid shunting.

Background: Despite modern advances, aneurysmal subarachnoid hemorrhage (SAH) is still associated with high morbidity and mortality rates in part due to vasospasm and hydrocephalus-related complications.

Objective: To analyze the impact of administration of intraventricular tissue plasminogen activator (tPA) with or without concurrent lumbar drainage, on the rate of cerebrospinal fluid shunt placement and on the incidence and severity of vasospasm.

Participants/Methods: This study compares 41 patients who received intraventricular tPA from June 2007 to October 2008, to 35 controls admitted between 2006 and 2007. Data were collected retrospectively. All patients had suffered from aneurysmal SAH, and had an admission Hunt and Hess grade ≥3. The treatment received by both groups was protocol-based and similar except for tPA administration. In total, 5 mg of tPA were given 12 hours after surgical or endovascular aneurysm occlusion via an antibiotic impregnated ventriculostomy catheter.

Results: There were no significant demographic differences between the 2 groups. Aneurysm locations were similar. Patients in the tPA treatment arm had significantly lower Hunt and Hess grades but significantly higher presenting Fisher grades compared to controls. Overall, 74% of the tPA group had a lumbar drain versus none in the control group. The average number of tPA doses administered was 6. A ventricular shunt was needed in 17.5% of cases in the tPA group versus 42.8% in the control group. Similarly, tPA patients had a 15% angioplasty rate versus 40% in the control group, and spent fewer days in severe transcranial doppler-defined spasm. When an intervention was needed, the number of vessels angioplastied was 2.1 in tPA patients versus 3.5 in control patients. The 10 patients who received tPA and did not have a lumbar drain showed reduced angioplasty and shunt rates, suggesting an independent protective effect of tPA.

Conclusions: In patients suffering from aneurysmal SAH with Hunt and Hess grades ≥3, intraventricular injection of tPA with or without lumbar drainage reduces the need for angioplasty, as well as the number of vessels requiring treatment if angioplasty is deemed necessary. It also minimizes the duration of severe vasospasm and the need for cerebrospinal fluid shunting within 3 months after the hemorrhage.

Reviewer's Comments: Advances in the management and prevention of SAH-related complications have been slow to materialize. This paper revisits the idea that reducing the clot burden in the ventricles may improve outcomes after aneurysmal SAH. The study design is by no means flawless. Still, the results reported here are encouraging. A prospective blinded randomized trial is warranted though before recommendations can be made. (Reviewer-Bernard R. Bendok, MD).

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Keywords: Hydrocephalus, SAH, Thrombolysis, Tissue Plasminogen Activator, Vasospasm

Print Tag: Refer to original journal article
Correction of hematocrit to >28% does not appear to improve or worsen outcome after severe traumatic brain injury.

**Background:** Secondary injury caused by hypoxia and hypotension after severe traumatic brain injury (TBI) can be ameliorated in part by transfusing red blood cells (RBC). Because blood transfusions can be associated with complications, optimal hematocrit is poorly defined.

**Objective:** To evaluate the influence of different hematocrit levels reached at the end of the initial operating department phase on in-hospital mortality and morbidity.

**Design:** Single institution retrospective case series.

**Methods:** Patients with severe TBI surviving >24 hours and not taking oral anticoagulants or antiplatelet agents were resuscitated by ATLS guidelines. Intracranial pressure (ICP) was monitored if Glasgow Coma Scale (GCS) score <9. Treatment included continuous sedation with fentanyl and midazolam and intermittent muscle paralysis. Blood products were transfused to maintain hematocrit >28%, platelets >80,000, and international normalized ratio (INR) <2. Hypothermia was corrected if temperature was <34°C and coagulopathy was present. Elevated ICP treatment included increased sedation, mannitol, adjusting PaCO₂, and craniectomy. Outcome measures of pulmonary complications, ICU length of stay (LOS), in-hospital mortality, and neuropsychological recovery at 6 months (assessed by extended GCS [eGOS]) were assessed.

**Results:** 60 of 139 patients (GCS mean of 6) received RBC transfusions. Injury severity score was higher in patients receiving RBC transfusions (35) than those not (25); survival was similar. Survival was less in patients requiring craniectomy, pleural drainage, or laparotomy, independent of hematocrit. Hematocrit of >28% at the end of operating department phase was reached in 45% of patients requiring transfusion. Coagulopathy was more common in RBC transfused patients. Mortality was lowest in patients with hematocrit between 28% and 30% at the end of operating department phase, unrelated to RBC transfusion. Trends (not statistically significant) toward lower survival probability if hematocrit was <28% and higher survival probability if hematocrit was >28% were observed. eGOS was unrelated to hematocrit or transfusion, but was associated with highest ICP measured during initial operating department phase. Pulmonary complications and ICU LOS were unrelated to hematocrit or transfusion.

**Conclusions:** Correction of hematocrit to >28% during the initial OR phase following severe TBI does not appear mandatory. The lowest acceptable hematocrit must still be determined.

**Reviewer's Comments:** Neurosurgeons and trauma surgeons frequently disagree about hematocrit level necessitating RBC transfusion. Neurosurgeons typically desire transfusion to optimize brain perfusion, while trauma surgeons focus on concerns about transfusion complications. This study suggests that hematocrit >28% may have some benefit to patients with severe TBI. Unfortunately, the study was not powered a priori; perhaps more patients studied would have increased confidence in the statistical analysis. Patients not requiring transfusions differ from those with acute blood loss anemia, and grouping these patients together clouds results. (Reviewer-N. Scott Litofsky, MD).

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Keywords: Critical Care, Intracranial Pressure, Transfusion, Secondary Brain Injury

Print Tag: Refer to original journal article
Salvage surgery of “inoperable” pediatric brain tumors may often be associated with positive outcomes.

**Background:** Multidisciplinary teams (MDT) are often used to provide comprehensive care to pediatric brain tumor patients. The results of approaches contrary to the group are unknown.

**Objective:** To review pediatric patients with brain and spinal cord tumors managed surgically in contrast to MDT recommendations against surgery.

**Design:** Single-institution retrospective case series.

**Methods:** Medical records of pediatric brain and spinal cord tumor patients evaluated between 1999 and 2010 were reviewed to determine those operated on despite recommendations against surgery by MDT. Data considered included preoperative treatment, preoperative diagnosis, clinical status, postoperative diagnosis, early and late outcomes, progression-free survival, overall survival, and parental satisfaction.

**Results:** 47 of 256 (18%) surgical patients had been advised against surgery by an MDT for “inoperable” tumors or terminal disease. Thirty (64.0%) had previous surgery, 19 (40.0%) had previous radiation therapy, and 20 (42.5%) had previous chemotherapy. Twenty-two (47%) presented in extremis. Tumor types included the range of pediatric brain tumors, including 22 (47.0%) low-grade astrocytoma, 12 (25.5%) high-grade astrocytoma, and 5 (10.5%) craniopharyngioma. Most tumors were in brainstem (22; 47.0%) or sellar/suprasellar (13; 27.5%) locations. Mean follow-up after surgery was 46 months (1 week to 10 years). Fourteen patients (30%) died (mean survival, 21 months). Nineteen of 33 living patients had clinical improvement, 6 were unchanged, 3 transiently worsened and then completely recovered, and 4 had permanent neurological sequelae. Progression-free survival and overall survival were 78.0% and 85.0% at 6 months, 75.5% and 75.5% at 12 months, 65.0% and 72.5% at 24 months, 47.0% and 61.0% at 36 months, and 43.0% and 57.0% at 60 months. No parents regretted their decision to proceed with surgery.

**Conclusions:** Sometimes dramatic and favorable short- and long-term outcomes may be achieved with salvage surgery of so-called “inoperable” pediatric brain tumors, even in the face of recommendations against surgery by an MDT.

**Reviewer's Comments:** This study illustrates potential difficulties in MDT approaches to neuro-oncological care. The reasons why MDTs recommended against surgery are not explored. For instance, were the MDTs swayed by highly vocal conservative views or by timid neurosurgeons wishing to avoid potential poor surgical results? The high percentage of brainstem tumors reflects the authors’ own aggressive surgical stance. Also unstated was the number of patients evaluated by the authors deemed not to be candidates for surgery in agreement with an MDT. Why was surgery offered for this reported group of patients? Some selection biases are likely. Neurosurgeons must include a broad differential diagnosis for lesions identified on imaging studies, as some presumed “malignant” lesions are actually surgically curable. Neurosurgeons must also candidly consider their own technical skills in the context of these challenging patients, keeping in mind that desperate patients and families may often agree to any treatment offered. (Reviewer-N. Scott Litofsky, MD).
En bloc resection is the preferred surgical option for single brain metastases <9.7 cm3.

Background: The risk of local recurrence (LR) following resection of a single brain metastasis is 23% to 46%. This decreases with whole-brain radiation therapy (WBRT) to 10.0% to 12.5%. Two possible surgical options to resect single brain metastases are en bloc resection (EBR) and piecemeal resection (PMR).

Objective: To directly compare LR in patients undergoing either EBR or PMR.

Design/Methods: The authors performed a retrospective review of 570 patients who underwent resection of a single brain metastasis from 1993 until 2006. All patients either had tumors considered to be radioresistant or declined postoperative radiation therapy. Median patient age was 58 years, 55% were male, and Karnofsky Performance Scale Score ≥80%. Primary outcome was radiological recurrence of local tumor at routine follow-up appointments until patients either succumbed or stopped following up.

Results: PMR was performed in 201 patients (35%) and EBR in 369 patients (65%). Local recurrence developed in 84 patients (15%). Two factors were identified that led to higher rates of local recurrence. Tumor volume >9.7 cm3 led to an increase in local recurrence, irrespective of resection method used. PMR led to a 1.7 times higher rate of recurrence than EBR.

Conclusions: The LR risk of a single brain metastasis is influenced by biological factors such as tumor volume and resection method. Early administration of postoperative WBRT may be particularly warranted when such negative tumor-related prognostic factors are noted or when treatment related ones such as piecemeal resection are unavoidable.

Reviewer's Comments: This interesting study is limited by a number of factors. By design, only patients who did not receive any radiation therapy were included, thus the effect of radiation therapy on local recurrence rates after different surgical resection methods is not known. The study population is biased toward traditionally radio-resistant tumors (melanoma, renal cell carcinoma, and sarcoma). In some tumors, location, morphology, and invasion of critical structures dictated resection method. However, this study shows solid evidence for making clinical decisions. In single brain metastasis <9.7 cm3, the surgeon should aim for en bloc resection.

(Reviewer-Richard D. Murray, MD).

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Keywords: Brain Metastasis, Surgery, Local Tumor Recurrence, Resection Method

Print Tag: Refer to original journal article
Regarding surgical treatment of intracerebral hemorrhage, clot removal is recommended with cerebellar hemorrhage and neurological decompensation from brainstem compression/hydrocephalus.

**Background:** Spontaneous, nontraumatic intracerebral hemorrhage (ICH) causes considerable morbidity and mortality worldwide. The last ICH guidelines were published in 2007 and this article is an updated version of these guidelines.

**Objective:** To present the latest recommendations for diagnosing and treating acute spontaneous ICH.

**Methods:** The authors met by teleconference and established the following subcategories to evaluate: emergency diagnosis/assessment of ICH and its causes, hemostasis, blood-pressure (BP), intracranial pressure (ICP), fever/glucose/seizures/hydrocephalus, iron, ICP monitors/tissue oxygenation, clot removal, intraventricular hemorrhage (IVH), withdrawal of technological support, preventing recurrent ICH, nursing care, rehab/recovery, and future considerations. MEDLINE literature searches were performed of all English articles pertinent to this disease entity. Summaries and recommendations were drafted and finalized/approved by the entire committee. The AHA Stroke Council’s Levels of Evidence grading algorithm was used to classify each recommendation. These guidelines will be updated in 3 years.

**Results:** Recommendations for hemostasis/antiplatelet therapy/deep vein thrombosis (DVT) prophylaxis were:

1. Severe coagulation factor deficiency and thrombocytopenia should be replaced/treated with appropriate blood components (new);
2. ICH patients with elevated international normalized ratio due to warfarin should be reversed by stopping warfarin, receiving fresh frozen plasma (FFP)/prothrombin complex concentrates (PCCs), and recombinant FVIIa as needed (revised);
3. Due to elevated thromboembolic risk, rFVIIa is only recommended in selected patients (new);
4. Benefit of platelet transfusions in the setting of ICH and antiplatelet use remains to be determined (new);
5. Low-dose subcutaneous heparin for DVT prevention may be used at 1 to 4 days post-ictus if hemorrhage is stable (revised). In case of IVH, safety/efficacy of intraventricular recombinant tissue plasminogen activator remains to be determined. Regarding clot removal, recommendations were as follows:

   1. Usefulness of surgery remains doubtful (new) except with:
   2. Cerebellar-hemorrhage and neurological decompensation from brainstem compression/hydrocephalus (new);
   3. Lobar-hemorrhages >30 mL/within 1cm from surface (revised);
   4. Efficacy of stereotactic/endoscopic clot aspiration with/without thrombolytics remains to be defined (new);
   5. No benefit has been shown from early clot evacuation for supratentorial ICH (revised). In terms of withdrawal of life support, aggressive full care early on after ICH and delaying DNR status until the second hospital day may be warranted. In regard to preventing ICH recurrence:

   1. Risk factors include lobar location, older age, ongoing anticoagulation, apolipoprotein E ε2/ε4 alleles, and more microbleeds on MRI (new);
   2. Goal BP<140/90 mm Hg is recommended (new); and
   3. Stop heavy alcohol consumption (new).

**Conclusions:** As a rule, early aggressive patient management can favorably affect outcomes, and treatment should be tailored on a case-by-case basis.

**Reviewer’s Comments:** Patients with ICH can be critically ill and prompt recognition of the disease process as well as aggressive management is key. Several comorbidities/ongoing treatments can render management more challenging such as when patients have a mechanical heart valve on long-term anticoagulation. Therefore balancing risks and benefits as well as careful planning in a multidisciplinary setting is warranted. (Reviewer-Ziad A. Hage, MD).

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Keywords: AHA Scientific Statements, ICH, Treatment, Diagnosis, ICP, Hydrocephalus, Surgery
Print Tag: Refer to original journal article
The overall morbidity and mortality rates in this study are comparable to other published mixed case series.

**Background:** Brain tumors are the second most common malignancy to occur during childhood. Surgical resection remains the mainstay of treatment. Analysis of outcomes for single tumor entities has been widely reported but rarely for mixed tumor case series.

**Objective:** To perform an internal quality control of the authors’ experience and to contribute to the accumulating data concerning outcome in pediatric neurosurgery.

**Design/Methods:** This was a retrospective review of surgical mortality and morbidity of 121 patients, aged 0 to 18 years, who were surgically treated for a brain tumor from January 1999 to August 2007.

**Results:** Mean age at first surgery was 8.2 years. Male-to-female ratio was 1.4:1. Overall, 66% were total resections, 26% subtotal resections, and 8% partial resections. Reasons for partial removal included unfavorable pathology/anatomy in 9 and technical reasons in 1. Reasons for subtotal removal were unfavorable anatomy/pathology of the tumor. The tumor locations were divided into 8 categories: supratentorial hemisphere/ventricle (47); cerebellum (21); brain stem (18); fourth ventricle (16); sellar/suprasellar/third ventricle (10); thalamus/basal nuclei (7); cerebellopontine angle (1); and pineal gland (1). Fourteen patients had a second surgery, and 2 underwent a third surgery. Overall surgical morbidity rate was 69% after first surgery, 50% after second surgery, and 1 out of 2 after third surgery. The surgical mortality rate was 0.8%: 1 patient (4 days old) with an astrocytoma WHO grade IV suffered from a sudden cardiac arrest during surgery not related to blood loss. For 83 patients (69%), the distribution of complications was as follows: 53 (44%) neurological complications; 27 (22%) endocrinologic disturbances; 25 (21%) infectious complications; 21 (17%) cerebrospinal fluid (CSF) disturbances; 5 (4%) postoperative hematomas; and 21 (17%) other complications. The endocrinologic complications were seen in 3 tumor locations: sellar/suprasellar/third ventricle, brain stem, and supratentorial/right or left hemisphere/ventricle. Of all 21 CSF disturbances, only 4 (19%) patients turned out to be shunt-dependent. Surgical infection complications consisted of meningitis, urinary tract infections, and wound infections and were all short-term. In 5 cases, a postoperative hematoma occurred. After second surgery (50%), complications were as follows: 11 of 14 (79%) neurological complications, 1 of 14 (7%) endocrinologic disturbances, 1 of 14 (7%) CSF disturbances, and 1 of 14 (7%) other complications.

**Conclusions:** The overall morbidity and mortality rates are comparable to other published mixed case series.

**Reviewer’s Comments:** The article reminds us of the high morbidity, especially neurological complications, after tumor removal in children. Tumor location, pathology, age at surgery, and surgeon’s expertise are all dependent variables that carry a different rate and type of morbidity and that is why mixed case series’ morbidity and mortality have no significant clinical application that can be translated to all cases. (Reviewer-Amir Kershenovich, MD).

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Keywords: Brain Tumors, Pediatric Neurosurgery, Outcomes

Print Tag: Refer to original journal article
The results of this study reflected positively on patients’ awake and outpatient surgery experience. These insights can lead to better delivery of care and improved outcomes.

**Background:** Awake craniotomies are likely becoming more common as a way to localize function during lesion resection. The authors contend that the avoidance of general anesthesia lessens risk and reduces resource use by decreasing length of stay.

**Objective:** To explore patients’ perceptions about awake and outpatient craniotomy.

**Participants/Methods:** The authors interviewed 27 participants who underwent craniotomy between October 2008 and April 2009 about their experiences with awake and outpatient craniotomy. These patients were discharged 6 hours after the procedure. Six of 27 had grade III or IV primary tumors with the remainder having either low grade or benign tumors, or brain metastases. Of inpatients, 7 had general anesthesia and 4 had awake procedures; of outpatients, 1 had general anesthesia and 15 had an awake procedure. The majority of awake patients were cared for as outpatients. Interviews were conducted within a week prior to surgery and 1 to 2 weeks postoperatively. None of these patients had cognitive deficits either from their brain tumors or for other reasons.

**Results:** Patients did understand the rationale for having an awake operation and they were surprised that it could be done on an outpatient basis. Patients generally had a positive experience with an awake craniotomy, with minimal pain. The process made them believe that the procedure was not a significant one. Patient satisfaction with outpatient surgery was quite high and half of the patients believed they would recover faster and be more comfortable at home. Trust in the surgeon was important, with the assumption that the surgeon would not do such a procedure if it was not safe. Recollection of intraoperative events was incomplete. The most painful parts were applying cranial fixation and removing it.

**Conclusions:** The results reflected positively on the patients’ awake and outpatient surgery experience. Some areas required improvement, specifically perioperative pain control and postoperative care. These insights can lead to better delivery of care and improved outcomes.

**Reviewer’s Comments:** Awake craniotomy certainly seems well accepted by patients, and is done with little discomfort. The fact that the patients believed that craniotomy was not a significant procedure seems to have a beneficial psychological effect -- if they were being sent home there was little to worry about. Although these patients had no cognitive deficits, there is no mention as to what the frequency of other neurological deficits was in this group. Further, there is no mention about how they would deal with the onset of postoperative neurological deficits while at home. I was surprised that patients did not raise issues about the risks of a lack of postoperative monitoring. Despite some literature regarding these risks, it is still not clear that safety is equivalent in these settings, or that the patients knew the difference. They simply trusted the surgeon to make these judgments. Would this practice have the same acceptance in a more questioning environment? The decision about doing outpatient surgery hinges more on risk assessment than patient perception of safety and comfort. (Reviewer-Paul L. Penar, MD).

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Keywords: Awake Craniotomy, Outpatient Craniotomy, Patient Perception, Qualitative Research

Print Tag: Refer to original journal article
Does Fever Affect Outcome of Patients With Subarachnoid Hemorrhage?

Impact of Induced Normothermia on Outcome After Subarachnoid Hemorrhage: A Case-Control Study.
Badjatia N, Fernandez L, et al:

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Elimination of fever with advanced fever control (AFC) methods may be associated with improved outcome after subarachnoid hemorrhage. A prospective randomized trial of AFC versus conventional fever control is warranted.

Background: Up to 70% of patients who suffer from subarachnoid hemorrhage (SAH) develop a fever in the first week. Fever can either be secondary to injury or it can be an independent factor influencing outcome or both.

Objective: To assess the impact of induced normothermia using advanced fever control (AFC) methods on outcome after SAH.

Participants/Methods: The authors studied 40 consecutive febrile patients between 2003 and 2005 who underwent advanced fever control with a surface-cooling device during the first 14 days after SAH. A historic group of 80 SAH patients treated between 1996 and 2003 with conventional fever control served as the comparative group randomly matched by age, Hunt and Hess grade, and SAH sum score to the study group. Average daily fever was calculated based on the time and extent above 37°C. Modified Rankin Scale score of ≥4 and death were considered poor outcome. Factors associated with poor outcome 12 months after SAH were identified. In-hospital complications were categorized into medical, infectious, and neurologic. Neurologic complications included neurologic deficit with angiographic vasospasm or presence of cerebral infarction.

Results: The advanced fever control patients had a lower fever burden as compared with the patients receiving conventional fever control; however, they had higher rates of hyperglycemia and arrhythmias. AFC was associated with a reduced risk for poor outcome at 12 months in contrast to higher admission Hunt and Hess grade and the development of pneumonia.

Conclusions: Elimination of fever with advanced fever control may be associated with improved outcome after SAH. A prospective randomized trial of advanced fever control versus conventional fever control is warranted.

Reviewer’s Comments: Fever may affect outcome of patients with subarachnoid hemorrhage. This study was designed with a historic comparison group. The fact that the management of subarachnoid hemorrhage patients has evolved significantly and a lot of outcome modifying paradigms have been introduced, it is hard to conclude from this study if advanced fever control methods affect outcome. (Reviewer-Joseph Adel, MD).

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Keywords: Neurointensive Care, Induced Normothermia, Advanced Fever Control

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In spine surgery there is no clear consensus as to what constitutes a complication and an adverse event. As such, it is extremely difficult to compare different studies with one another.

**Background:** In spine surgery, the overall incidence of complications and adverse events is not known. Multiple studies and differing methodologies exist. Authors usually focus on complications relevant to health care providers -- medical versus surgical complications and perioperative complications to perioperative events.

**Objective:** To review the spine surgery literature and to address the effect of study design on reported complication incidence and to compare thoracolumbar to cervical regions.

**Methods:** The MEDLINE database was queried using the keywords "spine surgery" and "complications". The results of this search were then analyzed and limited by an exclusion process. In total, 105 articles were finally selected, of which 25 concerned cervical spine surgery and 80 thoracolumbar spine surgery. Among these 105 articles were 84 retrospective and 21 prospective studies. These were then analyzed according to cervical versus thoracolumbar surgery, prospective versus retrospective design, date of publication, duration of follow-up, etc.

**Results:** In the 105 articles that were reviewed, a total of 79,471 patients with 13,067 complications were included. This yielded a complication rate of 16.4% per patient. Complications were more common in the thoracolumbar group (17.8%) than in the cervical group (8.9%; $P<0.0001$; OR, 2.23). Prospective studies had a higher incidence of complications (19.9%) than retrospective studies (16.1%; $P<0.0001$; OR, 1.3). Increased duration of follow-up correlated with increased complication incidence (0.001). A very wide range of complications was reported. The average for cervical procedures was 8.9% with a range of 3% to 61% and for thoracolumbar 1% to 70%.

**Conclusions:** Retrospective studies significantly underestimate the overall incidence of complications in spine surgery.

**Reviewer's Comments:** On the basis of this article, 2 conclusions can be made: (1) retrospective studies in the spine literature underestimate the incidence of complications, and (2) as noted by the authors, there is no clear definition as to what constitutes a complication in the spine literature. There is a very wide variation in rates of complications that are being reported. As such, it is very difficult to compare different institutions, techniques and procedures, and even surgeons. Only once clear guidelines and definitions are established will it become possible to accurately measure and compare outcomes. (Reviewer-Richard D. Murray, MD).

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Keywords: Spine Surgery, Complication, Outcomes Reporting, Study Methodology

Print Tag: Refer to original journal article
Cerebral Oxygenation and Perfusion Can Be Optimized By Assessing Cerebrovascular PRx

Effects of Cerebrovascular Pressure Reactivity-Guided Optimization of Cerebral Perfusion Pressure on Brain Tissue Oxygenation After Traumatic Brain Injury.

Jaeger M, Dengl M, et al:

Crit Care Med 2010; February 11 (): epub ahead of print

| Individual traumatic brain injury patients have unique optimal cerebral perfusion pressure levels ranging from 60 to 100 mm Hg that achieve optimization of cerebral vasomotor reactivity. |

**Background:** The method of optimizing the cerebral perfusion pressure (CPP) based on continuous monitoring of the cerebrovascular pressure reactivity (PRx) to spontaneous fluctuations in mean arterial pressure (MAP) in traumatic brain injury (TBI) patients may be associated with improved neurologic outcome. **Objective:** To analyze the relationship between optimal CPP and partial pressure of brain tissue oxygen ($P_{br}O_2$).

**Design:** Prospective observational cohort study.

**Participants:** 38 patients with TBI with Glasgow Coma Scale score 3 to 13 and requiring neuromonitoring of intracranial pressure (ICP) and $P_{br}O_2$ using intraparenchymal probes inserted into frontal white matter of the more severely injured hemisphere.

**Methods:** PRx was calculated as a moving linear correlation coefficient between 30 consecutive samples of MAP and ICP. The optimal CPP ($CPP_{OPT}$) was the CPP group (range, 5 mm Hg) in which average PRx was lowest. The CPP level was identified at which $P_{br}O_2$ reached a plateau and was not pressure-dependent on CPP (called the $P_{br}O_2$ "change point").

**Results:** $CPP_{OPT}$ could be identified in 32 of 38 patients and ranged from 60 to 65 mmHg to 95 to 100 mm Hg (median, 70 to 75 mm Hg). CPP at the $P_{br}O_2$"change point" could be determined in 30 patients. This CPP ranged from 50 to 55 mm Hg to 95 to 100 mm Hg (median, 70 to 75 mm Hg). There was a significant correlation between $CPP_{OPT}$ and the CPP at the $P_{br}O_2$ "change point" (deviation <5 mm Hg in 67% of patients; <10 mm Hg in 93%). At $CPP_{OPT}$, PRx was -0.04 and $P_{br}O_2$ was 24.5 mm Hg. The $P_{br}O_2$ decreased in parallel with CPP at levels of CPP below $CPP_{OPT}$ and did not improve further at levels of CPP above $CPP_{OPT}$.

**Conclusions:** A relationship exists between CPP and $P_{br}O_2$. $P_{br}O_2$ reaches a plateau above $CPP_{OPT}$ and exhibits relative pressure passive behavior below $CPP_{OPT}$. Pushing CPP above $CPP_{OPT}$ does not improve brain oxygenation or perfusion and having a CPP below $CPP_{OPT}$ results in a decrease in autoregulatory vasomotor reactivity, pressure passive cerebral blood flow, and possible ischemia.

**Reviewer's Comments:** This is a conceptually appealing study that suggests that titrating CPP to individual physiology represents an improvement over using the same goal for all TBI patients. The methodology assumes that $P_{br}O_2$ is a surrogate for cerebral blood flow. This has been demonstrated, but does not take into account the impact of arteriovenous oxygen tension difference. Blood gas alterations, especially hypocapnia, may influence the PRx. $CPP_{OPT}$ cannot be identified in all patients (16%) and may occur because $CPP_{OPT}$ is outside the range studied or the patient has complete absence of autoregulatory function. In these patients, $P_{br}O_2$ may add important information about $CPP_{OPT}$. Whether this technology improves patient outcomes is not known. (Reviewer-Wendy C. Ziai, MD).

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Keywords: Brain Injury, Brain Tissue Oxygen, Cerebrovascular Pressure Reactivity, Cerebral Perfusion Pressure, Neuromonitoring, Cerebral Autoregulation

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