Posterior Fossa Syndrome Can Be Predicted

Posterior Fossa Syndrome After Posterior Fossa Surgery in Children With Brain Tumors.

Küpeli S, Yalçin B, et al:

Pediatr Blood Cancer 2010; October 25 (): epub ahead of print

Posterior fossa syndrome is more likely to occur in pediatric patients after surgery for medulloblastoma or midline tumors or in patients with lower family socioeconomic status.

Background: Posterior fossa syndrome (cerebellar mutism) occurs relatively commonly in children after surgery for cerebellar tumors. Risk factors for its development are not well defined.

Objective: To define risk factors for posterior fossa syndrome and determine accompanying neurobehavioral and psychological problems.

Design: Single-institution retrospective study.

Methods: Patients aged <16 years with newly diagnosed posterior fossa tumors treated with surgery, excluding those with known mental retardation or neurobehavioral or psychological problems, were evaluated preoperatively and postoperatively for neurological and emotional findings. Preoperative status precluded mental status evaluation. Demographics, tumor characteristics, and treatments were detailed. Postoperative changes in speech (mutism and dysarticulation), emotion, and motor function, as well as surgical complications were recorded. Duration of new findings was determined. Postoperative neuropsychological and behavioral changes were assessed using Denver II Developmental Screening Test (DDST) for ages 0 to 6 years or Wechsler Intelligence Scale for Children-Revisited for those aged >6 years.

Results: 9 of 36 children (25%) developed posterior fossa syndrome. Mutism occured immediately after surgery in 4 patients and between 1 and 4 days in 5 patients. Mutism lasted between 1 and 14 days in 8 and last 120 days in 1 patient. Medulloblastoma tumor type, midline cerebellar tumor location, and low family socioeconomic status were independent risk factors for development of posterior fossa syndrome. DDST was not different between patients with mutism and those without. Wechsler Intelligence Scale could only be administered to 11 of 20 children aged >6 years and showed no difference between groups. Hydrocephalus, tumor size, patient age, spinal seeding, extent of resection, edema, and shunting had no statistical relationship to development of posterior fossa syndrome.

Conclusions: Medulloblastoma, midline tumor location, and low family socioeconomic status are significant risk factors for development of posterior fossa syndrome in children who have surgery for posterior fossa brain tumors. Transient ischemia and edema due to manipulation of dentate nuclei and superior cerebellar peduncles may contribute to its development.

Reviewer's Comments: The occurrence of posterior fossa syndrome in this study is consistent with previous reports. Neurosurgeons should be aware of the risk factors identified in this study – medulloblastoma tumor type, midline tumor location, and low family socioeconomic status – as anticipation of the occurrence of posterior fossa when ≥1 risk factors are present. This knowledge can be helpful in counseling families that the postoperative situation is not unexpected and is likely to resolve within a few days to weeks. The study does not support a specific mechanism of development of posterior fossa syndrome. If edema or transient ischemia of the dentate nuclei or superior cerebellar peduncles is involved, care in minimizing retraction, maintaining perfusion, and reducing vascular compromise should lead to reduction in incidence. (Reviewer-N. Scott Litofsky, MD).

Keywords: Children, Mutism, Posterior Fossa Syndrome, Posterior Fossa Tumors, Risk Factors

Print Tag: Refer to original journal article

Driving Restrictions Confound Physicians, Patients

Current Practices of Driving Restriction Implementation for Patients With Brain Tumors.

Thomas S, Mehta MP, et al:

J Neurooncol 2010; October 23 (): Epub ahead of print

National guidelines for driving restrictions in brain tumor patients are greatly needed.

Background: Primary benign and malignant brain tumors and metastatic brain tumors may compromise patients' neurocognitive functions or cause seizures, impairing driving ability. Only state-based restrictions are present in the United States; no national driving restrictions are available, unlike in other countries.

Objective: To identify trends and variations in recommended driving restrictions for patients with brain tumors to increase awareness of practitioners about the importance of this issue.

Design: E-mail survey.

Methods: A 24-question survey was distributed by e-mail (3 attempts) to members of the Society of Neuro-Oncology and Radiation Therapy Oncology Group brain tumor committee. Questions were designed to assess respondent demographics, individual practice patterns, knowledge of state laws, and practitioner opinions regarding appropriate driving restrictions.

Results: 251 responses (mostly neurosurgeons, medical oncologists, and radiation oncologists) from 39 states were received from 1157 queries (21.7%). In total, 71.2% of respondents recommended driving restrictions for brain tumor patients; 39% of respondents from states requiring reporting of seizure activity indicated they are not required to report or were unsure. Overall, 81.7% base restriction recommendations on seizure activity and 87.5% issue driving restrictions on guidelines provided by motor vehicle licensing authority. A total of 24.8% utilize formal, standardized testing to determine driving eligibility. Of respondents, 56.9% felt that a 5-to 6-month seizure-free period while on therapeutic anti-convulsant medications should occur before re-evaluation for patients who had seizure. Longer periods of driving restriction were selected for malignant tumors relative to benign tumors, and 45.4% intensify restrictions for commercial drivers. Overall, 86.6% did not restrict driving for posterior fossa tumor patients without seizure, but 24.4% restricted driving during radiation therapy. Only 31.0% addressed driving restrictions with every patient, and 67.6% addressed driving restrictions on an as-needed basis. Regarding guidelines, 49.8% stated that no guidelines exist for modifying driving restrictions and 46.5% were unaware of any guidelines.

Conclusions: This survey highlights the lack of uniformity with which brain tumor patients are being evaluated and advised on driving restrictions. National guidelines should be developed.

Reviewer's Comments: Brain tumor patients are significantly troubled by driving restrictions. These restrictions increase patient dependency on others and likely reduce quality of life and sense of self (at least my patients indicate as much). Patient requests to return to driving and continued restrictions also create conflict between patients, families, and physicians. Resources for evaluating patients for driving safety are sparse in many locales. I agree that this study shows great variability in how physicians address driving restrictions in brain tumor patients. Unfortunately, the 21.7% response rate does not positively reflect the importance of this issue. A national set of guidelines would be a highly worthwhile contribution. In the meantime, physicians should be aware of their state's issued restrictions to have a starting point for decisions regarding brain tumor patients' driving. (Reviewer-N. Scott Litofsky, MD).

Keywords: Brain Tumor, Driving Restrictions, Driving Impairment, Seizure

Print Tag: Refer to original journal article

Spinal Cord Stimulation for Parkinson Disease? The Jury Is Out

Spinal Cord Stimulation Failed to Relieve Akinesia or Restore Locomotion in Parkinson Disease.

Thevathasan W, Mazzone P, et al:

Neurology 2010; 74 (April 20): 1325-1327

Ongoing studies show that spinal cord stimulation improves motor functions in a non-human primate model of Parkinson disease, but this is not yet true in humans.

Background: Spinal cord stimulation (SCS) in dopamine-depleted rats and mice reverses akinesia and improves locomotion (Fuentes et al, *Science* 2009). Because this therapy is much less invasive than deep brain stimulation, it is worth testing in Parkinson patients.

Objective: To determine if SCS would improve motor function in patients with Parkinson disease.

Design: Prospective study in 2 patients.

Participants/Methods: Patients were formally tested 10 days post-implantation of the electrode at the upper cervical level dorsal epidural space on the midline. The stimulation parameters were: 30 to 300 Hz; 0 to 4 volts; 240 µs pulse width. The testing was done during the off period 12 hours after withdrawal from dopaminergic agonists. SCS was either off, subthreshold, or suprathreshold for feeling paresthesiae. Patients rated the paresthesiae on a scale of 1 to 10. Two neurologists, blind to the patient's stimulator settings, scored the motor behavior using the unified Parkinson disease rating scale (UPDRS). Secondary measures included alternating movements and time to walk. Scores were obtained 20 minutes after new settings were programmed in the stimulator.

Results: Only suprathreshold stimulation was felt. The motor symptoms were not improved by SCS. The primary and secondary outcome measures were the same regardless of the stimulator settings. Patient #2 remained incapable of walking regardless of the settings. The 2 neurologists had similar scores for both patients.

Conclusions: There is no evidence that SCS improves the motor symptoms of Parkinson disease.

Reviewer's Comments: Given that thousands of chronic pain patients use spinal cord stimulators, it's surprising that there is no report in the literature of an improvement of motor symptoms in those patients that also have Parkinson disease. Different explanations for a lack of effect of SCS in the 2 patients of the present report include that the stimulating electrodes were different from those used in rats, that the patients did not exhibit a startle reflex as rats did, and that the electrodes were placed at the upper cervical level rather than at the upper thoracic level as they were in the rodents. Yet, the negative results observed in these 2 patients are likely to limit the enthusiasm for further testing in humans. However, there are new data that might change all this. Ongoing studies also show that SCS improves motor functions in a non-human primate model of Parkinson disease (Fuentes, Petersson, Nicolelis, E*ur J Neurosci*, 2010). We are waiting with agitation for these results, which are likely to pave the way to further trials in humans. (Reviewer-Luc Jasmin, MD).

Keywords: Motor Function, Electrical Stimulation, Spinal Cord Stimulation, Parkinson Disease

Print Tag: Refer to original journal article

Is Cerebellar Mutism Permanent?

Postoperative Cerebellar Mutism Syndrome Following Treatment of Medulloblastoma: Neuroradiographic Features and Origin.

Wells EM, Khademian ZP, et al:

J Neurosurg Pediatr 2010; 5 (April): 329-334

Cerebellar mutism syndrome after resection of a cerebellar medulloblastoma in children can occur in over 25% of cases; is associated with atrophy of cerebellum, vermis, and brainstem; and can be permanent and severe.

Background: Cerebellar mutism syndrome (CMS) consists of diminished speech, hypotonia, ataxia, and emotional lability following resection of a posterior fossa tumor; it has been reported to affect approximately 25% of patients undergoing resection for medulloblastoma and it was initially believed to be transient, but recent studies revealed persistent neurological and neurocognitive impairment. Neuroimaging studies have been limited, and no study has examined whether longitudinal MR imaging shows lasting brain damage associated with CMS.

Objective: To determine factors associated with development of CMS.

Participants/Methods: 28 children who either underwent operations or were referred after surgery between 1990 and 2005 were included. The presence and severity of CMS were determined and MRI images analyzed.

Results: 11(39%) patients had CMS; on preoperative MRI they had more brainstem tumor invasion than patients without CMS (89% vs 44%), and a trend for more involvement of the cerebellar medullary angle (66% vs 31%). Postoperatively, CMS patients had trends for more middle and superior cerebellar peduncle edema compared with those without. Complete resection was not shown to be a significant factor on developing CMS. A review of MR imaging performed 1 year after resection revealed significantly more atrophy of total cerebellum, vermis, and brainstem atrophy in patients with CMS compared to those without. Since few patients had diffusion-weighted imaging series, this was not analyzed in the study. Mutism, hypotonia, and irritability were each found to be severe in approximately half of the patients with CMS. The amount of vermis split and the development of CMS were not found to be associated.

Conclusions: This study not only replicates the chronic effects found in the large prospective COG study, but also demonstrates radiographic evidence of lasting cerebellar and brainstem damage. Postoperative diffusion-weighted imaging may help clarify the type of neurological damage in CMS and predict which patients will develop the syndrome.

Reviewer's Comments: The overall treatment of patients with medulloblastoma has changed dramatically in the last 2 decades with most patients now achieving long-term survival. A permanent deficit after surgical resection in the face of such a good prognosis in a young patient with so many years of life ahead can be regretful. The reviewed article found similar long-term outcomes to the larger COG study on mutism supporting this relatively new knowledge on the chronic state of this neurological deficit. Despite the fact that the authors found some evidence that damage to the middle and superior cerebellar peduncles could be associated with the syndrome, they did not or could not suggest specific ways to improve damage to these areas. More so, I was disappointed that once again diffusion-weighted images on MRI were not analyzed. (Reviewer-Amir Kershenovich, MD).

Keywords: Postoperative Cerebellar Mutism Syndrome

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Botox Is Not for All Migraines

OnabotulinumtoxinA for Treatment of Chronic Migraine: Results From the Double-Blind, Randomized, Placebo-Controlled Phase of the PREEMPT 2 Trial.

Diener HC, Dodick DW, et al:

Cephalalgia 2010; 30 (July): 804-814

Botox reduces the incidence of migraine attacks in chronic migraine, but is not useful in the treatment of episodic migraines.

Background: Chronic migraine (CM) is a subtype of migraine, which is defined by ≥15 headache days per month with ≥8 migraine days for at least 3 months. Botox® acts by blocking cholinergic innervation of muscles. "Botoxing" neck and scalp muscles would prevent the muscle spasms associated with migraine and the feed forward effect on pain neurotransmission.

Objective: To assess the safety and efficacy of onabotulinumtoxinA (Botox) in adults with CM.

Design: Double-blind randomized placebo-controlled multicenter clinic trial.

Participants/Methods: Patients with established CM were recruited in 66 sites (50 in North America, 16 in Europe). Overall, 347 received Botox and 358 received placebo. The double-blind phase lasted 24 weeks, which was followed by an open-label period of 32 weeks. Botox was injected every 12 weeks. The primary end point was the incidence of headache days.

Results: While there was a decrease in the number of headache days in both groups, it was significantly greater in the Botox group over placebo at week 24. Secondary outcomes were also better in the Botox group, except for the frequency of usage of acute medication with the exception of triptans. Adverse events were more common in the Botox (65.1%) versus placebo group (56.4%). Muscle weakness (5.2%) and neck pain (7.5%) were seen only in the Botox group. The only serious event was a migraine requiring hospitalization in the Botox group. The dropout rate was 3.5% in the Botox and 1.4% in the placebo group.

Conclusions: Botox reduces the incidence of migraine attacks in CM.

Reviewer's Comments: Botox has received FDA approval in October of this year for the treatment of chronic migraine, despite not being useful in the treatment of episodic migraines. The data from the studies funded by Allergan (the maker of Botox) show only a moderate improvement of number migraines similar to what is obtained with topiramate, which has also been extensively studied. This small margin of efficacy is somewhat of a concern. In the PREEMPT 1 study, Botox was not more effective than placebo at 24 weeks. Patient selection might have been the problem. For instance, Kim (*Arch Dermatol*, 2010) suggested that only "imploding" types of migraines respond to Botox. It is possible that Botox produces a positive placebo effect. The addition of a behavioral re-enforcement such as muscle weakness to the actual intervention (here an injection) can make the difference. For instance, in a recent trial of a β-blocker migraine, only the combination of the drug with behavioral therapy led to a reduction in migraine episodes. Despite all these concerns, Botox has been used for many years by migraine specialists, which might be a sign that it works, we are just not sure how. (Reviewer-Luc Jasmin, MD).

Keywords: OnabotulinumtoxinA, Botox®, Chronic Migraines

Print Tag: Refer to original journal article

CAE Reduces 10-Year Stroke Risk in Asymptomatic Patients With Severe Stenosis

10-Year Stroke Prevention After Successful Carotid Endarterectomy for Asymptomatic Stenosis (ACST-1): A Multicentre Randomised Trial.

Halliday A, Harrison M, et al:

Lancet 2010; 376 (September 25): 1074-1084

Benefits from carotid endarterectomy will be determined by the efficacy of medical treatment, upcoming surgical risks, and the patient's life expectancy.

Background: Carotid artery disease is a major risk factor for stroke. Patients with a stenosis of >60% are 3 times more likely to experience debilitating embolic and ischemic events compared to the general population. Although preventive surgery for asymptomatic patients has been debated, it is likely to benefit previously healthy and independent individuals. While the Asymptomatic Carotid Atherosclerosis study and the 5-year follow-up of the Asymptomatic Carotid Surgery Trial (ACST) showed significant reductions in stroke rates after endarterectomy, the longer-term efficacy of successful surgical intervention has yet to be determined.

Objective: To provide a 10-year follow up to the ACST trial.

Methods: Between 1993 and 2003, 3120 patients from 126 international centers were randomized to either carotid endarterectomy (CAE) with medical management or medical management alone. The inclusion criteria comprised: severe unilateral or bilateral carotid stenosis with a lumen reduction of ≥60%, the absence of stroke or stroke-related symptoms during the previous 6 months, and the indecision of both patients and physicians on whether to initiate or defer surgery. The degree of stenosis was assessed by duplex Doppler ultrasound. The primary outcome consisted of perioperative morbidity and mortality, and the non-perioperative long-term event of stroke.

Results: 3120 patients were equally randomized between CEA and surgical deferral groups. The characteristics of patients were similar, including the degree of stenosis and the use of antihypertensive, antiplatelet, anticoagulant, and lipid-lowering drugs. At the 10-year mark, 92.5% of patients in the CEA group actually underwent surgery compared to 26.0% of those who were initially allocated deferral. Non-perioperative stroke rates at 5 years were 4.0% in the CEA group compared to 10.0% in the deferral group, with a net reduction of 5.9%. At the 10-year interval, stroke rates increased to 10.8% in the CEA group versus16.9% in the deferral group, with a net reduction of 6.9% after surgery. A total of 50% of risk reduction was in disabling or fatal strokes. While significant benefits were observed in patients undergoing surgery independently from the administration of lipid-lowering agents, little or no gain was reported in individuals aged >75 years.

Conclusions: Despite some perioperative morbidity and mortality, surgery provides asymptomatic patients with severe carotid artery stenosis with a substantial benefit. This gain was found to be independent from age up to 75 years, sex, cholesterol levels, blood pressure, ultrasound characteristics of plaque, or the extent of stenosis >60%. The use of lipid-lowering agents seemed to be the only factor affecting stroke rates.

Reviewer's Comments: This paper lends further support to carotid endarterectomy for patients with asymptomatic stenosis. One has to be careful though, to consider high-risk factors for surgery as well as life expectancy in the decision making. (Reviewer-Bernard R. Bendok, MD).

Keywords: ACST, Endarterectomy, Asymptomatic, Stroke Reduction

Print Tag: Refer to original journal article

Subdural Evacuation Port System Is Effective in Tx of Chronic Subdural Hematoma

Analysis of the Subdural Evacuating Port System for the Treatment of Subacute and Chronic Subdural Hematomas.

Kenning TJ, Dalfino JC, et al:

J Neurosurg 2010; 113 (November): 1004-1010

The subdural evacuation port system is effective in the treatment of chronic subdural fluid collections in selected patients and has a lasting effect when effective.

Background: Chronic and subacute subdural hematomas commonly occur in patients with multiple medical comorbidities who are poor surgical candidates. As such, less invasive techniques have been developed, that can effectively drain these collections under local anesthesia. The subdural evacuation port system (SEPS; Medtronic, Inc.) is one such minimally invasive technique: a hollow cranial screw is connected via a 1-way valve to a suction bulb, thereby draining the subdural fluid collection.

Objective: To evaluate a single institution's results with the use of this system.

Design/Methods: A single-institution retrospective chart review was conducted on all patients who underwent this procedure during a 53-month period. The treating neurosurgeon decided which patients would undergo this procedure. Pre- and post-procedure CT scans were evaluated and fluid collections classified according to fluid density (hypo, iso, and mixed-density). Complications were noted and procedures classified into a success or failure group. These 2 groups were then compared to one another in an attempt to identify predictors of success.

Results: 85 collections were treated in 74 patients, of which 63 were unilateral and 11 bilateral. In total, 63 collections (74%) were successfully drained. No statistical significance was found between these 2 groups in regard to age, Glasgow Coma Scale score, presenting symptoms, underlying coagulopathy, or use of anticoagulation or antiplatelet drugs. The only statistically significant difference between the groups was found to be the radiographic appearance (P <0.05). More hypodense collections were successfully treated (32 of 63 collections) and mixed-density collections were more likely to fail (14 of 22 collections). Isodense collections did not demonstrate a statistically significant trend. Effects of successful treatment were lasting in the subgroup of patients that had follow-up scans >30 days after the procedure (mean duration of follow-up, 108 days). At time of surgery for failed SEPS procedures, dense membranes were usually found. Two acute hemorrhages were reported post-SEPS placement, of which one patient needed to undergo urgent surgical evacuation of this bleed.

Conclusions: This system is a safe and effective treatment option. It can be inserted under local anesthesia, which makes it suitable for patients who are poor surgical candidates. Hypodense collections are more likely to be drained successfully with this procedure, while mixed-density collections are more likely to fail. Some hypodense collections still failed treatment, while some mixed-density collections were successfully treated.

Reviewer's Comments: This study is hampered by significant selection bias, its retrospective nature, and lack of a control group. A number of conclusions can still be made. This procedure has a low rate of complications, is generally effective in hypodense collections, and might be effective in mixed-density collections. Due to its low morbidity, it is worth considering as a first-line treatment for chronic subdural fluid collections. (Reviewer-Richard D. Murray, MD).

Keywords: Subdural Hematoma, Minimally Invasive Technique, Subdural Evacuation Port System

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What Are Poor Prognostic Factors Identified for Spontaneous ICH With IVH?

Spontaneous Intracerebral Hemorrhage With Ventricular Extension and the Grading of Obstructive Hydrocephalus: The Prediction of Outcome of a Special Life-Threatening Entity.

Stein M, Luecke M, et al:

Neurosurgery 2010; 67 (November): 1243-1251

Age >70 years, Glasgow coma scale score ≤8, intracerebral hemorrhage volume of >60 cm3, and severe hydrocephalus are all predictors of poor prognosis after intracerebral hemorrhage with ventricular extension.

Background: Spontaneous intracerebral hemorrhage (SICH) occurs in 10% to 15% of all strokes and intraventricular hemorrhage (IVH) in about 40% of these cases. The 30-day mortality for SICH with IVH is the highest amongst all SICH patients. Hydrocephalus is seen in 20% to 40% of IVH patients. Some studies have shown that the presence of hydrocephalus on initial CT was predictive of poor outcome, while others argue that since hydrocephalus is easily treated via external ventricular drain (EVD) it should not alter outcome.

Objective: To evaluate predictive variables in SICH with IVH.

Design/Methods: A retrospective chart review of 104 patients with a mean age of 63 years was conducted. Inclusion criteria were SICH with IVH, all patients had an EVD, age >18 years. Exclusion criteria included IVH due to trauma, aneurysm, arteriovenous malformation, and tumor. Clinical and demographic data, ICH volume, and presence of mild, moderate, or severe hydrocephalus was evaluated. Multivariate logistic regression analysis was applied to identify predictors of mortality and outcome. The authors also developed an IVH score that was applied to a retrospective cohort of 51 patients.

Results: An initial SICH volume of >60 cm3, severe hydrocephalus, Glasgow Coma Scale (GCS) score of ≤8, and age >70 years were all identified as independent predictors of 30-day mortality. At 6 months after the initial hemorrhage, 50% of patients were still alive, with a favorable outcome in 34%. An IVH score was created based on these variables and is calculated as follows: GCS ≥13, 9 to 12, and ≤8 are given 0, 1, and 2 points, respectively. Intracerebral hemorrhage (ICH) volume <30, 30 to 60, and >60 are given 0, 1, and 2 points, respectively. Hydrocephalus is scored with absent, moderate, and severe hydrocephalus receiving 0, 1, and 2 points, respectively. Age is divided into <70 years and >70 years, with 0 and 1 points, respectively, being allocated. This is then calculated to a score of 0 to 7. When this score was applied to this cohort, it yielded the following: 30-day mortality for IVH scores 2, 3, 4, 5, and 6 were 9%, 14%, 46%, 75%, and 100%, respectively. No patient with an IVH score ≥6 survived. Six-month functional outcome, defined as modified Rankin Scale score 0 to 3, was seen in 50%, 67%, 22%, and 17% of patients with IVH scores of 0, 1, 2, and 3, respectively.

Conclusions: Severe hydrocephalus, age >70 years, ICH volume, and admission GCS were independent predictors of mortality and outcome. The authors applied this to a retrospective cohort, where it served to predict 30-day mortality and functional outcome accurately.

Reviewer's Comments: This is a well-designed, but retrospective study. The IVH scoring system is simple to use and while not validated as of yet, will give some useful predictive information. (Reviewer-Richard D. Murray, MD).

Keywords: Hydrocephalus, Intracerebral Hemorrhage, Intraventricular Hemorrhage

Print Tag: Refer to original journal article

For Seizures After TBI, Try Keppra

Prospective, Randomized, Single-Blinded Comparative Trial of Intravenous Levetiracetam Versus Phenytoin for Seizure Prophylaxis.

Szaflarski JP, Sangha KS, et al:

Neurocrit Care 2010; 12 (April): 165-172

Keppra is as good as phenytoin for seizure prophylaxis after severe traumatic brain injury.

Background: Antiepileptic drugs are commonly used for seizure prophylaxis after neurological injury. In this study, neurological injury was defined as either subarachnoid hemorrhage (SAH) or severe traumatic brain injury (TBI). The authors state that 25% to 50% of patients with SAH or severe TBI have seizures.

Objective: To compare intravenous levetiracetam (Keppra®) to intravenous phenytoin (Dilantin®) for safety, seizure prophylaxis, and long-term outcome after neurological injury.

Design/Methods: This is a prospective single-center randomized single-blinded comparative trial of Keppra versus phenytoin. Patients enrolled received an IV load with either Keppra or phenytoin followed by standard IV doses. Doses were adjusted to maintain therapeutic serum phenytoin concentrations. Continuous EEG monitoring was performed for the initial 72 hours. Outcome data were collected in the form of Glasgow Outcomes Scale (GOS) and the Disability Rating Scale.

Results: 52 patients were randomized; 89% suffered a severe TBI. When controlling for baseline severity, Keppra patients experienced better long-term outcomes than those on phenytoin; the Disability Rating Scale score was significantly more favorable at 3 months and the GOS score was significantly more favorable at 6 months. There were no differences between groups in seizure frequency or mortality. There were no differences in side effects between groups except for less gastrointestinal problems in the Keppra-treated group.

Conclusions: Currently, the American Academy of Neurology supports phenytoin for seizure prophylaxis in severe TBI. This study exploring the use of Keppra versus phenytoin for seizure prevention showed improved long-term outcomes of Keppra-treated patients. Keppra appears to be a valid alternative to phenytoin for seizure prophylaxis in this setting.

Reviewer's Comments: This trial answers an important question but has design flaws that may introduce bias. First, the authors should not have changed their initial proposal to enroll 52 patients with SAH and 52 patients with severe TBI, but instead they combined both disease groups. SAH and TBI have a different pathophysiology and combining those decreases the external validity. What makes this even more problematic is that we do not know the Hunt and Hess grade of the SAH patient. The authors report that the GCS ranged from 3 to 15, from which I deduce that SAH patients with GCS >8 were enrolled but only severe TBI patients were included. Secondly, continuous EEG was only recorded for the first 72 hours. This number seems to be arbitrarily chosen. It would have been preferable to continue it up to 7 days as long as antiepileptic medication was given. This study demonstrated that Keppra, as a single agent, is as effective as phenytoin for seizure prophylaxis in severe TBI and may even be neuroprotective. I don't think the data can be extrapolated to SAH patients, because only 11% of patients enrolled fall into this group. (Reviewer-Martina Stippler, MD).

Keywords: Seizure Control

Print Tag: Refer to original journal article

Lumbar Decompression 5 Years Later

Five-Year Outcome of Surgical Decompression of the Lumbar Spine Without Fusion.

Mannion AF, Denzler R, et al:

Eur Spine J 2010; 19 (November): 1883-1891

Over 5 years, the benefit of lumbar decompression did not deteriorate and patients experienced low levels of back and leg pain and moderate disability.

Background: Degenerative spine surgery, like surgical decompression of the lumbar spine, is being performed with increasing frequency as the population ages. Right now it represents the most common type of lumbar spinal surgery in older patients. Current literature reports that as far as decompression surgery is concerned, good outcomes decreased from 67% to 88% success in the initial year to approximately 52% to 70% after 5 to 8 years.

Objective: To examine the 5-year outcome of lumbar decompression surgery without fusion to ascertain whether results deteriorate or improve over time.

Design: Prospective study.

Participants/Methods: The group comprised 159 patients who underwent lumbar decompression for degenerative spinal disorders. These patients were initially enrolled in a randomized controlled trial of 2 different postoperative rehabilitation programs that had shown no difference at 2 years. Outcome measures were leg pain and back pain, self-rated disability, global outcome of surgery, and reoperation rates. Questionnaires were completed before surgery, and at 2 months, 5 months, 1 year, 2 years, and 5 years after surgery.

Results: 10 patients died before the 5-year follow-up. Of the remaining 149 patients, 143 returned a 5-year follow-up questionnaire. Their mean age was 64 years and 64% were men. In the 5-year follow-up period, 34 of 143 patients (24%) had a reoperation. Half of them needed further decompressions and half of them underwent fusions. In total, 88% of reoperations involved the same segment as in the initial surgery. Overall, patients without a reoperation had significantly decreased leg pain compared to before surgery at 2-month follow-up, after which there was no significant change up to 5 years. Low back pain also decreased significantly by 2-month follow-up and increased a small, statistically significant, but clinically non-relevant amount at 5 years. Disability decreased significantly after the surgery and remained stable up to the 5-year follow-up. Patients who were reoperated had significantly worse final outcomes for leg pain and disability.

Conclusions: Over 5 years, the benefit of lumbar decompression did not deteriorate and patients experienced low levels of back and leg pain and moderate disability. The reoperation rate was high at 24% and reoperation resulted in worse final outcomes.

Reviewer's Comments: Long-term outcome studies are extremely helpful in evaluating the effectiveness of any intervention and procedure, especially in degenerative spine surgery where surgery cannot halt the ongoing degenerative process. The effective return rate excluding deaths was 96%, which adds to the validity of this study. About 12% of patients had to undergo a fusion procedure, but the authors failed to report the risk factors associated with this outcome. The knowledge of this long-term outcome study should be incorporated into the preoperative patient information process. (Reviewer-Martina Stippler, MD).

Keywords: Degenerative Disease, Long-Term Outcome, Reoperation Rate

Print Tag: Refer to original journal article

Beware Disappearing Lesions Before Brain Biopsy

Identification of Disappearing Brain Lesions With Intraoperative Magnetic Resonance Imaging Prevents Surgery.

Sutherland CS, Kelly JJ, et al:

Neurosurgery 2010; 67 (October): 1061-1065

Always make sure there is a recent MRI scan (<4 weeks) before starting a brain biopsy.

Background: Negative brain biopsies are known to occur and may result from disappearing brain lesions.

Objective: To evaluate the frequency of non-tumor diagnoses at a single institution.

Design: A prospective database retrospectively reported.

Participants: 982 patients treated from December 1997 to January 2009.

Methods: Patients were identified for surgical treatment using intraoperative MRI. Of 982 total patients, 624 had suspected brain tumors and were scheduled for surgery with 6 unexpected diagnoses and 5 disappearing brain lesions.

Results: Approximately 2% of patients had a non-tumor diagnosis in this series. Of the 6 patients who had a biopsy, 2 had hemorrhagic infarct, 2 had demyelination, and 1 each had radiation necrosis and abscess. Five patients had a disappearing lesion. It was suspected that of the 5, 2 had radiographic changes due to seizures, 2 had probably sarcoidosis, and 1 had demyelinating disease. The time from last scan to disappearance ranged from 4 weeks to 13 weeks. None of the lesions in these 5 patients have progressed.

Conclusions: An MRI scan must be done close to the time of surgery to account for the small chance that the lesion has disappeared. Long-term follow-up indicates that these lesions do not progress.

Reviewer's Comments: This study raises a very important patient safety issue, which is making sure the proper imaging is available before surgery and that the imaging is recent. While it may seem that intraoperative imaging is ideal for avoiding this possibility, in fact, the patients in this study were induced with anesthesia and had to be reversed. Ideally, the patients would not be subjected to this risk. The most common non-tumor diagnoses were demyelinating, infarct, and sarcoidosis, which is what would be expected. The authors raise an important point that seizures were likely the culprit in 2 cases. Although rare, this finding has been reported and should always be considered, particularly in patients with status epilepticus. It's not unusual for patients to have their surgery delayed for a variety of reasons, and in those situations, a system should be put in place to ensure that if significant time has elapsed since the last scan, then a new MRI needs to be ordered. The length of that time frame is subject to debate, but I suggest that no more than 4 weeks be allowed to elapse. (Reviewer-Lawrence S. Chin, MD).

Keywords: Brain Tumor, Disappearing Lesion, Biopsy

Print Tag: Refer to original journal article

Wrong-Site Craniotomy Is Almost Always Preventable

Wrong-Site Craniotomy: Analysis of 35 Cases and Systems for Prevention.

Cohen FL, Mendelsohn D, Bernstein M:

J Neurosurg 2010; 113 (September): 461-473

Inadequate preoperative checks and communication breakdowns are the most common causes of wrong-site surgery.

Background: Wrong-site surgery is a devastating error and often with disastrous complications in the brain. In addition to lawsuits, these cases result in public reporting and occasional unwanted media publicity. Neurosurgery is the third most vulnerable specialty behind orthopedics and general surgery.

Objective: To identify cases of wrong-site craniotomy (WSC) and determine preventable causes.

Methods: WSC cases were searched from MedLine, LexisNexis, and WestLaw databases, media search, and licensing boards.

Results: 35 cases were identified and analyzed. Four primary categories were identified: (1) Communication breakdown in 11 cases - Medical records were sometimes not reviewed before surgery and incorrect assumptions were made. In 1 case, a concern was raised by an operating department team member who was ignored. In 2 cases, patients were scanned in different orientation resulting in right-left confusion. (2) Inadequate preoperative checks - Although preoperative checklists are now commonplace and required, this was not standard in the past. Failure to mark the incision preoperatively was noted in at least 5 cases. Identical name confusion has occurred and confusion over correct films or films hung backwards has also occurred. (3) Technical factors - Mislabeled reports and images may be out of the surgeon's control. Absence of equipment or changing a room orientation has been cited as a factor in 3 cases. (4) Human error - This was a common factor in all cases. Time pressure and different team members preparing the patient can cause errors.

Conclusions: WSC can still occur despite checklists and preoperative protocols. Maintaining open communication and vigilant adherence to checklists are critical.

Reviewer's Comments: This excellent review highlights a critical topic that concerns all neurosurgeons. Many have some experience with a "near-miss" or know a colleague who had a WSC experience. In all cases, it seems that a chain of events occurred that could have been broken at any point with proper vigilance. Strict adherence to a preoperative checklist, even in an emergency situation, is absolutely key to protecting both the patient and the surgeon from liability. These established protocols need to be followed without fail. I think it is critical to have a review of the procedure just before incision. Much of the preoperative timeout is done with the patient awake before anesthesia and positioning. Once the patient is draped, it can be very difficult to determine sidedness. A review of the patient’s preoperative films with the preoperative note to make sure that the images correlate with the x-ray findings can pick up errors related to imaging and mislabeling. It's also helpful to have the patient state what their procedure is and the side or level of their pain or deficit. We should strive to reduce the incidence of wrong-site surgery in neurosurgery to zero and this article is a step in that direction. (Reviewer-Lawrence S. Chin, MD).

Keywords: Wrong-Site Craniotomy, Prevention

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Staged Correction of Transsphenoidal Encephalocele Improves Outcome

Successful Staged Correction of Transsphenoidal Encephaloceles.

Kohan E, Lazareff J, et al:

Plast Reconstr Surg 2010; 1 (July): 197-204

In patients with transsphenoidal encephalocele, staged correction improves both function and appearance.

Background: Incomplete closure of the cranial base can result in transsphenoidal encephaloceles, wherein the meninges, cerebrospinal fluid (CSF), brain matter, or some combination of these, forms cystic herniations. Transsphenoidal encephaloceles are associated with midface anomalies, problems with brain development, and aberrations of the endocrine system.

Objective: To discuss an approach to staged operative repair that is mindful of avoiding complications such as recurrent meningitis and progressive neurologic decline.

Design: Retrospective review.

Participants/Methods: 4 patients with symptomatic transsphenoidal encephaloceles who underwent staged operative repair (intracranial and transpalatal cyst correction, facial bipartition, and cleft palate repair) were studied. Data on perioperative complications, recurrence, interdacyron distance comparison, speech, and development were aggregated and analyzed.

Results: All 4 patients studied had successful staged repairs, with no recurrence of meningitis, CSF leakage, or encephalocele relapse reported. All patients also experienced alleviation of headaches and esthetic improvement. Interdacyron distance was improved, with a mean 22-mm reduction (56%), according to CT analysis. Mean speech scores improved after cleft palate repair and speech therapy to 1.4 (borderline competent), despite initial postoperative declines. Developmental tests demonstrated normal global memory and attention skill evaluations in 3 patients; the fourth had deficiencies in preoperative evaluations as well.

Conclusions: Staged correction of transsphenoidal encephaloceles improves not only facial morphology but also functional symptoms such as recurrent meningitis, CSF leakage, encephalocele relapse, speech, and development.

Reviewer's Comments: This article is a case series of 4 patients with transsphenoidal encephaloceles who underwent staged operative repairs with extremely successful outcomes. Not only do the authors demonstrate improved morphology and esthetics with interdacyron distance, but they also demonstrate improvement in symptoms such as meningitis, headaches, and relapse of encephaloceles. Data for speech and development show that these are not worsened, and are perhaps improved by this approach. Although the case series is small for this rare cystic herniation syndrome, with only 4 patients, it is a compelling presentation of a staged successful approach. (Reviewer-Robert T. Grant, MD).

Keywords: Transsphenoidal Encephaloceles, Operative Technique, Staged Repair

Print Tag: Refer to original journal article

Prolonged Hypocapnia Often Harmful, Rarely Beneficial

Hypocapnia and the Injured Brain: More Harm Than Benefit.

Curley G, Kavanagh BP, Laffey JG:

Crit Care Med 2010; 38 (May): 1348-1359

Hyperventilation is the most effective means for acutely lowering intracranial pressure, so brief use of hypocapnia can be useful in patients with acute brain injury. However, prolonged hypocapnia is frequently harmful.

Background: In patients with acute brain injury, prophylactic hyperventilation has been widely used to induce hypocapnia and acutely reduce intracranial pressure (ICP). Extremes of hypocapnia for prolonged periods have been advocated for treatment of acute brain injury.

Objective: To determine the prevalence of hypocapnia in the management of acute brain injury and to determine the outcomes associated with this treatment strategy.

Design: Review of the literature published between 1966 and 2009. **Prevalence:** Prophylactic hyperventilation to induce hypocapnia is widely used in adults and children with acute brain injury. For example, 36% of board-certified neurosurgeons in the United States routinely use prophylactic hyperventilation in patients with severe traumatic brain injury. **Deleterious Effects:** A serious concern associated with hypocapnia is that it may cause adverse neuronal oxygen supply and demand through various mechanisms, resulting in brain ischemia. During prolonged hypocapnia, the pH of cerebrospinal fluid (CSF) is buffered toward normal and cerebral blood flow normalizes by 6 hours. This CSF buffering ablates the effectiveness of ongoing hypocapnia. Also during prolonged hypocapnia, further reductions in carbon dioxide are difficult to achieve, making it difficult to acutely reduce ICP any further without causing lung damage. Finally, when normocapnia eventually is restored, a rebound elevation in ICP may occur, potentially resulting in brain stem herniation or intracranial hemorrhage (premature infants). Some other adverse outcomes associated with hypocapnia include decreased perfusion to the heart and other organs, and acute lung injury or acute respiratory distress syndrome due to high tidal volumes used to achieve hypocapnia. **Benefits:** Hyperventilation is the most effective means for acutely lowering ICP, so brief use of hypocapnia can be useful while definitive measures to manage ICP are being instituted. Normocapnia should be restored as soon as feasible because hypocapnia becomes ineffective within hours.

Conclusions: Prophylactic hyperventilation in brain injury is increasingly recognized as being frequently harmful and rarely, if ever, beneficial. Prolonged hypocapnia does not improve neurologic outcomes in patients with brain injury, and its use is associated with worsening cerebral ischemia, worse outcomes, and injury to other organs. Therefore, use of hypocapnia should be brief and limited to emergency management of life-threatening ICP or to acutely reduce brain bulk in the operating room while definitive measures to manage ICP are being instituted. Further prospective trials of prophylactic hyperventilation in brain injury are difficult to justify.

Reviewer's Comments: This paper dispels almost 3 decades of thought about hyperventilation in brain injury patients. As it turns out, the reduced cerebral blood flow is more detrimental than the change in ICP at least after 6 hours of therapy. (Reviewer-Eric Howard Gluck, MD, JD).

Keywords: Acute Brain Injury, Therapeutic Hypocapnia, Outcomes

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CT Very Sensitive for Subarachnoid Hemorrhage

Determining the Sensitivity of Computed Tomography Scanning in Early Detection of Subarachnoid Hemorrhage.

Cortnum S, Sorensen P, et al:

Neurosurgery 2010; 66 (May): 900-903

Newer CT scanners appear to have a higher sensitivity for identifying subarachnoid hemorrhage.

Background: Early detection of subarachnoid hemorrhage (SAH) leads to improved outcomes. Previous guidelines, based on studies from the 1980s and 1990s, suggest that lumbar puncture is needed to rule out this entity if the CT scan is negative. Previous sensitivity of CT scanning ranged from 93% to 95% in the first 24 hours, 85% at 3 days after symptom onset, and 50% after 1 week.

Objective: To test the sensitivity of CT scanning using newer high-resolution multidetector CT scanners and to reevaluate the need for lumbar puncture.

Design: Retrospective study.

Participants: All patients referred to the neurosurgical unit for suspected SAH from 2000 to 2005.

Methods: Medical records were reviewed, as well as the CT scan, angiography, and results of the lumbar puncture. All patients had a CT scan of the head and, if it was positive for SAH, they also had an angiogram. Those with a negative CT scan had a lumbar puncture with cerebrospinal fluid (CSF) sent to the lab for cell counts and analyzed for xanthochromia by spectrophotometry. These were done no earlier than 12 hours after onset of symptoms.

Results: Of 510 patients admitted, 8 were excluded because there was no clinical suspicion of SAH, and 2 were excluded because their CT scan showed a capillary hemangioblastoma. A patient with a spinal hemorrhage on MRI with no vascular abnormality on angiography was also excluded. Of the remaining 499 patients, 203 had the diagnosis excluded by CT scan and negative lumbar puncture, and 296 had a SAH. SAH was diagnosed on positive CT scan in 295 of 296 patients. The remaining patient with SAH was diagnosed by lumbar puncture on day 6. From day 1 to day 5, CT scanning had 100% specificity and 100% sensitivity. Overall, CT scanning had 99.7% sensitivity and 100% specificity. In those who underwent a lumbar puncture, 4 had viral meningitis and 15 had a post-spinal headache.

Conclusions: CT scanning is excellent for diagnosing SAH and appears sufficient to exclude this entity in the first few days after ictus.

Reviewer's Comments: This study is very encouraging because many patients with sudden, severe headache presently undergo only a CT scan without lumbar puncture. I would like to see further studies confirming this finding before changing my present diagnostic approach. (Reviewer-John Schwankhaus, MD).

Keywords: Subarachnoid Hemorrhage, Detection, CT Scanning, Lumbar Puncture

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Evidence Continues to Accumulate on Negative Effects of Prolonged ED Stays

Impact of Delayed Transfer of Critically Ill Stroke Patients From the Emergency Department to the Neuro-ICU.

Rincon F, Mayer SA, et al:

Neurocrit Care 2010; 13 (August): 75-81

Patients with intracerebral hemorrhage, ischemic stroke, and transient ischemic attack awaiting admission from the emergency department fare worse the longer they wait, but the specific reason continues to elude identification.

Objective: To determine the effect of emergency department (ED) length of stay (LOS) on outcomes in stroke patients awaiting admission to a neurological ICU (NICU).

Design/Methods: Retrospective review of data from patients presenting to a single ED at a single center over a 26-month period with acute ischemic stroke (AIS), intracerebral hemorrhage (ICH), or transient ischemic attack (TIA) within 12 hours of symptom onset. The authors evaluated demographics, National Institutes of Health Stroke Scale (NIHSS) on admission and discharge, modified Rankin score (mRS) on discharge, and total ED length of stay. The primary outcome measure was poor outcome, defined as mRS ≥4 at discharge, indicating death or severe disability. The effect of ED-LOS on these measures was assessed by logistic regression.

Results: Of 519 patients presenting to the ED, 75 (15%) were critically ill and admitted to the NICU (mean age, 65 years; 31% men; 37% Hispanic). Admission diagnosis included AIS (49%), ICH (47%), TIA (1%), and others (3%). Median ED-LOS was 5 hours (interquartile range [IQR], 3 to 8 hours) and median hospital LOS was 7 days (IQR, 3 to 15 days). In both the univariate and multivariate analysis, a poor outcome was predicted by ICH, admission NIHSS of ≥6, and an ED-LOS of ≥5 hours. Odd ratios for a poor outcome in the multivariate analysis were 2.1 for ICH, 6.4 for elevated NIHSS, and 3.8 for an extended ED-LOS. There was no association between ED-LOS and discharge NIHSS among survivors, and no association with total hospital LOS. Patients from both the delayed and non-delayed groups were comparable in terms of age, comorbidities, physiological variables, or NIHSS on admission, suggesting that neither triage decisions, therapeutic interventions, nor need for further testing were likely to have biased these results.

Conclusions: Among critically ill stroke patients, an extended ED-LOS of ≥5 hours before transfer to the NICU is independently associated with poor outcome at hospital discharge.

Reviewer's Comments: I know why this happens. The ED environment is inherently unsuited for maintenance and surveillance of aggressive therapies we can otherwise very easily initiate before we walk away. We pull the trigger, but we don't really aim the gun, and for sure we don't reload as necessary. Patients do better in homogenous care environments where everyone is geared to the subtleties and details that accrue from continual implementation of the same course of care to selected patients. The fundamental problem is quantifying this in a study. Stephan Mayer is a big name in thrombolysis and a gentleman, undeniably a respectful colleague toward physicians in emergency medicine. I've met him and heard him speak numerous times. This paper offers important data for policy discussion. (Reviewer-Steven B. Abrams, MD).

Keywords: Emergency Department Overcrowding, Transient Ischemic Attack, Cerebrovascular Accident

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