A summary of some of the recently published seminal papers in Neuroscience

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The authors attempted to determine the role of cerebrospinal fluid (CSF) in platelet-dependent hemostasis during neurosurgery. Their observation was that sodium bicarbonate facilitates hemostasis through amplification of platelet aggregation function. The existence of CSF and irrigation with artificial CSF solution provides better conditions for physiological hemostasis and has the potential of improving hemostasis by bipolar coagulation or with irrigation during neuroendoscopic procedures.

Oh SK, et al. A phase III clinical trial showing limited efficacy of autologous mesenchymal stem cell therapy for spinal cord injury. Neurosurgery October 08, 2015; DOI: 10.1227/NEU.0000000000001056

The authors report on the results of a phase III clinical trial of autologous mesenchymal stem cell (MSC) therapy. Patients were selected based on the following criteria: Chronic American Spinal Injury Association B status patients who had more than 12 months of cervical injury, and no neurological changes during the recent 3 months of vigorous rehabilitation. They injected 1.6 × 10⁷ autologous MSCs into the intramedullary area at the injured level and 3.2 × 10⁷ autologous MSCs into the subdural space. Outcome data were collected over 6 months regarding neurological examination, magnetic resonance imaging with diffusion tensor imaging, and electrophysiological analyses. Among the 16 patients, only 2 showed improvement in neurological status. Both patients with neurological improvement showed the appearance of continuity in the spinal cord tracts by diffusion tensor imaging. There were no adverse effects associated with MSC injections. The authors concluded that a single MSC application to the intramedullary and intradural space is safe but had a very weak therapeutic effect compared with multiple MSC injections, and that further clinical trials to enhance the effect of MSC injections are necessary.


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The aim of this study was to determine the natural progression of spinal schwannomas and establish the risk of tumor growth. This study retrospectively analyzed data from 23 patients (12 men and 11 women, 40–89 years old) with schwannomas detected by magnetic resonance imaging (MRI). The mean follow-up period was 5 years (range: 2–10 years). The absolute and relative growth rates of the tumors were calculated. Tumors were classified into three groups based on their enhancement patterns: Isointense/hyperintense (iso/high; 11 cases), rim enhancement when enhancement was peripheral (high/rim; 5 cases), and heterogeneous/heterogeneous (hetero/hetero; 7 cases) based on gadolinium (Gd)-enhanced T2-weighted MRI. Although the tumors classified as iso/high and high/rim on T2-weighted Gd-enhanced MR images were small and grew very little, most tumors with hetero/hetero classification increased in size. The latter tumors should be followed up closely and may require surgery.


Demonstrating the value of spine care requires adequate outcome assessment. Long-term outcomes are best measured as overall improvement in quality of life (QOL) after surgical intervention. Present registries often require parallel data entry, introducing inefficiencies and limiting compliance. The authors detail the methodology of constructing an integrated electronic health record (EHR) system to collect QOL metrics and demonstrate the effect of data collection on routine clinical workflow. A streamlined approach to collecting QOL data can capture patient data without requiring dual data entry and without increasing clinic visit times. Through extensive literature review, a combination of QOL assessments was selected, consisting of the Patient Health Questionnaire-2 and 9, Oswestry Disability Index, Neck Disability Index, and visual analog scale for pain. These metrics were used to provide assessment of QOL following spine surgery and were incorporated into the standard clinic workflow by a multidisciplinary team of surgeons, advanced practice providers, and health care information technology specialists. A clinical dashboard tracking more than 25 patient variables was developed. Clinic flow was assessed, and opportunities for improvement were reviewed. The duration of clinic visits before and after initiation of QOL measure capture was recorded, with assessment of mean clinic visit times for the 12 months before and the 12 months after implementation. A systematic approach to collecting spine-related QOL data within an EHR system is possible and offers distinct advantages over registries that require dual data entry. The process of data collection does not impact patients’ clinical visit or providers’ clinical workflow. This method of data collection may be the basis for a decentralized outcome registry network.


The optimal timing for surgery for poor-grade aneurysmal subarachnoid hemorrhage has still not been determined. Poor-grade aneurysmal subarachnoid hemorrhage was defined as World Federation of Neurosurgical Societies grade of IV or V after resuscitation. Early surgery was defined as surgery performed within 72 hours of ictus, and delayed surgery was defined as surgery after 72 hours. Outcomes were assessed by modified Rankin score. The mean time of follow-up was 12.5 ± 3.4 months. Of the 118 patients included in the study, 80 (68%) underwent early surgery and 38 (32%) underwent delayed surgery. Patients with brain herniation (P < 0.001) and a better Fisher grade (P = 0.02) more often underwent early surgery. Patients in the early group more often underwent decompressive craniectomy (P < 0.001). Multivariate analysis showed a slight trend towards an excellent outcome in the early surgery group. Younger age, World Federation of Neurosurgical Societies grade IV after resuscitation, and middle cerebral artery aneurysms were independent predictors of an excellent outcome.


Although generally considered as being safe and effective, surgery for the treatment of cervical spondylotic myelopathy (CSM) is associated with complications in 11–38% of patients. Several predictors of postoperative complications have been proposed, but few are used to detect high-risk patients. A standard approach that is aimed at identifying “at-risk” patients would improve the surgeons’ ability to prevent and manage these complications. The authors attempted to compare the complication rates between various surgical procedures utilized in treating CSM and to identify patient-specific, clinical, imaging, and surgical predictors of complications. The authors conducted
a systematic review of the literature and searched MEDLINE, MEDLINE in Process, EMBASE, and Cochrane Central Register of Controlled Trials from 1948 to September 2013. Cohort studies designed to evaluate predictors of complications, and intervention studies conducted to compare different surgical approaches, were included. Each article was critically appraised independently by two reviewers, and the evidence was synthesized according to the principles outlined by the Grading of Recommendation Assessment, Development and Evaluation (GRADE) Working Group. A total of 5472 citations were retrieved. Of those, 60 studies met the inclusion criteria and were included in the review. These studies included 36 prognostic cohort studies and 28 comparative intervention studies. Evidence suggested that older patients are at a greater risk of perioperative complications. Other clinical factors such as body mass index, smoking status, duration of symptoms, and baseline severity score were not predictive of complications. With respect to the surgical factors, the estimated blood loss, surgical approach, and number of levels did not affect rates of complications. A longer operative duration (moderate evidence), however, was predictive of perioperative complications, and a two-stage surgery was related to an increased risk of major complications (high evidence). In terms of the surgical techniques, higher rates of neck pain were found in patients undergoing laminoplasty compared with anterior spinal fusion. In addition, with respect to the laminoplasty techniques, there was a lower incidence of C5 palsy in laminoplasty with concurrent foraminotomy compared with nonforaminotomy.


Early management of traumatic intracerebral hemorrhage (TICH) is not harmonized across the world. The authors conducted an international, multicenter, randomized trial comparing early surgery (hematoma evacuation within 12 hours of randomization) with initial conservative treatment (subsequent evacuation allowed if deemed necessary) to find out whether the former would improve outcomes in patients with supratentorial TICH. Only 170 of the initially planned 840 patients were recruited (trial halted by the UK funding agency owing to failure to recruit patients) from 31 centers in 13 countries between December 2009 and September 2012 and randomly assigned to either group within 48 hours of traumatic brain injury. Only TICH patients for whom the treating neurosurgeon was in equipoise about the benefits of early surgical evacuation, compared with initial conservative treatment, were eligible for the trial. Several other strict inclusion and exclusion criteria have been detailed. The primary outcome measure was the Glasgow Outcome Scale at 6 months. Of the 82 patients randomized to early surgery, 37% had an unfavorable outcome. Of the 85 patients randomized to initial conservative treatment, 47% had an unfavorable outcome, with an absolute benefit of 10.5%. There were significantly more deaths in the first 6 months in the initial conservative treatment group (33% vs. 15%; P = 0.006). There were crossovers from initial conservative treatment to early surgery and vice versa, as occurs in all surgical trials. Despite these crossovers, the absolute benefit of early surgery exceeded 10% and was almost statistically significant. While a larger trial is needed to confirm this potentially beneficial effect of earlier surgery, the authors showed a statistically significant survival advantage (85% vs. 67%) and a nonsignificant benefit on GOS, both associated with early surgery.


Traumatic brain injury (TBI) is a leading cause of death in pediatric patients. A physician may be faced with complex medical and ethical challenges in the care of the most severely injured TBI patients. In this retrospective study, from a database of 1636 children admitted with TBI from 1988 to 2004, 67 (4%) patients with a GCS score of 3 or 4 were identified. The outcomes of all patients at the time of death or discharge and at 1-year and long-term follow-up were measured with a modified Glasgow Outcome Scale (GOS). Three of the presenting factors differed between the GCS 3 patients (n = 44) and the GCS 4 patients (n = 23): Presence of hypoxia, single seizure, and open basilar cisterns on CT scan. The clinical outcomes were statistically similar between the 2 groups. In total, 72% patients died, remained vegetative, or were severely disabled by 1 year. Eight patients (12%) were normal at 1 year. Of the 22 patients with a long-term follow-up, 10 were either normal or had a GOS score of 5. The authors concluded that 15% of patients had a good outcome at 10 or more years. The pupillary response was the factor most predictive of both survival and outcome. This study helps to make decisions in the acute phase of treatment, by providing long-term data on the outcomes of these critically ill patients. The chances of meaningful survival in a patient with an abnormal pupillary response and hypothermia are extremely low. The clinician may decide that aggressive therapy in these patients is not warranted. Conversely, children with normal pupillary responses who were injured
by a mechanism other than abuse may have a good or even normal outcome despite the GCS score being 3 or 4.

**Jug M, et al. Neurological recovery after traumatic cervical spinal cord injury is superior if surgical decompression and instrumented fusion are performed within 8 hours versus 8 to 24 hours after injury: A single center experience. J Neurotrauma 2015;32:1385-92**

The effect of surgical decompression (SD) of the injured spinal cord on neurological recovery within different time windows during the first 24 hours after injury remains poorly investigated. The authors conducted this prospective study (n = 42) to evaluate the impact of SD and instrumented fusion within 8 hours (n = 22) versus 8–24 hours (n = 20) after injury on neurological recovery after subaxial cervical traumatic spinal cord injury (tSCI) from January 2007 to December 2012. Only patients with the ASIA Impairment Scale (AIS) grades of A through C and with MRI-confirmed spinal cord compression were enrolled. The primary outcome was the change in AIS grade at the 6-month follow-up. At admission, there was no statistically significant difference in AIS grades between the study groups. At the 6-month follow-up, an improvement of at least two AIS grades was found in 45% of patients in the 8-hour group and 10% of patients in 8–24-hour group (P = 0.017). The median improvement in the ASIA motor score was 38.5 motor points in the 8-hour group and 15.0 motor points in the 8–24-hour group (P = 0.0468). In a multivariate analysis, adjusted for the preoperative AIS grade and the degree of spinal canal compromise, the odds of a minimum of two-grade AIS improvement were at least 106% higher for patients in the 8-hour group than for patients in the 8–24-hour group (odds ratio = 11.08, P = 0.004). No statistically significant difference was found in the rate of perioperative complications, pneumonia, and the number of ventilator-dependent days or the mortality between the groups. The authors concluded that patients with tSCI who undergo SD within 8 hours after injury have superior neurological outcomes than patients who undergo SD 8–24 hours after injury, without any increase in the rate of adverse effects. To define which additional factors affect neurological recovery after tSCI, further studies are necessary.


The authors conducted a randomized, prospective, open-cohort study to investigate the significance of prophylactic use of levetiracetam (LEV), in comparison with phenytoin (PHT), for patients with supratentorial tumors in the perioperative period. A total of 146 patients were randomized to receive LEV (n = 73) or PHT (n = 73) from the start of surgery until the seventh postoperative day. The history of seizures prior to surgery was not considered but patients were excluded if they had a history of seizures and their seizures remained after medication with LEV or PHT. The primary end point was the occurrence of seizures, and secondary end points included the occurrence of hematological and nonhematological adverse events. The incidence of postoperative seizures was significantly less in the LEV group (1.4%) compared with the PHT group (15.1%, P = 0.005). The observed odds ratio for being seizure free in the LEV prophylaxis group relative to the PHT group was 12.77 (P = 0.001). In a subgroup analysis of patients who did not have seizures before craniotomy, similar results were demonstrated: The incidence of seizures was 1.9% (LEV) and 13.8% (PHT, P = 0.034). History of seizures before surgery was not associated with postsurgical seizures. The course of LEV was completed in all cases, while PHT was withdrawn in five patients owing to liver dysfunction (1), skin eruption (2), and atrial fibrillation (2). The authors concluded that prophylactic LEV in the perioperative period significantly reduced the risk of seizures and recommended it for treatment of patients with supratentorial tumors. However, this was a single-institution trial. Multi-institutional, double-blind studies are required to validate these results and confirm the efficacy of LEV for seizure prophylaxis during and after craniotomy in patients with brain tumors.


Patients with high-grade gliomas have been noted to be at particularly high risk for venous thromboembolism (VTE). The authors conducted this prospective, multicenter study (n = 107) between June 2005 and April 2008 to determine the hazard rate of first symptomatic VTE in newly diagnosed, histologically confirmed grade III and IV glioma patients and identify the clinical and laboratory risk factors. Adult patients with a mean KPS score of at least 60 were included. The study end point was objectively documented symptomatic VTE. The median age was 57 years. Ninety-one (85%) patients had a glioblastoma multiforme. During an average survival of 17.7 months, 26 patients (24%) developed VTE (hazard rate, 0.15 per person-year) and 94 patients (88%) died. The median time to VTE was 14.2 weeks after operation (range, 3–126). Patients who underwent an initial tumor biopsy were 3.0-fold more likely to develop VTE (P = 0.02). Patients with an elevated factor
VIII activity were 2.1-fold more likely to develop VTE. The ABO blood group, the D dimer levels, and thrombin generation were not associated with VTE. Surprisingly, no fatal VTE occurred. The authors concluded that VTE is a common complication in patients with newly diagnosed high-grade gliomas, particularly in the first 6 months after diagnosis. Therefore, clinicians should maintain a high index of suspicion for DVT and PE when patients report symptoms (e.g., leg swelling or cramping, dyspnea, fatigue) that could indicate the occurrence of VTE. Patients who underwent an initial tumor biopsy and elevated factor VIII levels are at increased risk. However, VTE was not judged to be primarily responsible for any patient deaths. Therefore, outpatient primary VTE prophylaxis remains investigational until more effective primary prophylaxis strategies and therapies for glioma are identified.


Endoscopic pituitary surgery has been on the rise in the past two decades. In this first, multicenter, prospective cohort study (n = 218), the authors compared sinonasal morbidity and patient-reported quality of life (QOL) in patients who have undergone direct microscopic transsphenoidal surgery (n = 111) with patients who have undergone endoscopic trans-sphenoidal surgery for pituitary lesions (n = 107). Adult patients with sellar pathology who underwent a planned trans-sphenoidal surgery at four US pituitary centers between October 2011 and August 2013 were included. The primary end point of the study was postoperative patient-reported sinonasal QOL as measured by the Anterior Skull Base Nasal Inventory–12 (ASK Nasal-12). Supplementary end points included patient-reported health status estimated by the 8-Item Short Form Health Survey (SF-8) and EuroQol (EQ)-5D-5L instruments, and sinonasal complications. Patients were followed up for 6 months after surgery. The most common complication in both the groups was sinusitis (7% in the microsurgery group, 13% in the endoscopic surgery group; P = 0.15). Patients treated with the endoscopic technique were more likely to have postoperative nasal debridements (P < 0.001). The ASK Nasal-12 and SF-8 scores worsened substantially for both the groups at 2 weeks after surgery, but then returned to baseline at 3 months. At 3 months after surgery, patients treated with endoscopy reported statistically better sinonasal QOL compared with patients treated using the microscopic technique (P = 0.02), but there were no significant difference at 6 months, suggesting that the difference seen at 3 months was not clinically significant. The study showed that surgical technique did not significantly impact these patient-reported measures when performed at high-volume centers. Because of its design as a QOL study, the protocol does not address some very intriguing questions of interest to pituitary surgeons, such as endocrine outcomes, extent of resection, and biochemical remission rates between the two cohorts, and hence is unable to address which surgical technique has overall superiority.


Cervical spondylotic myelopathy (CSM) is a progressive degenerative spinal condition and the most common cause of spinal cord impairment in adults worldwide. The authors conducted a prospective, multicenter, international study to evaluate outcomes of surgical decompression for CSM at a global level. Between October 2007 and January 2011, 479 symptomatic patients with evidence of CSM on radiological imaging were enrolled from 16 global sites. Preoperative and postoperative clinical status, functional impairment, and quality of life were evaluated. Outcomes were evaluated at 12 and 24 months. There were significant differences in age, etiology, and surgical approaches between the regions. At 24 months postoperatively, the mean modified Japanese Orthopedic Association (mJOA) score significantly improved from 12.5 to 14.9 and the Nurick Grade from 3.3 to 1.7; the Neck Disability Index improved from 36.4 to 23.2; and the SF 36v2 Physical Component Score and Mental Composite Score improved from 34.3 to 40.8 and 39.5 to 46.2, respectively. There were also significant improvements across all 8-health dimensions of the SF-36v2. The improvements after surgical decompression were sustained between follow-up examinations at 1 year and 2 years after surgery. There were no deaths within 30 days of surgery. Fifteen patients (3.13%) experienced postoperative neurological injury. The rate of postoperative infection was 3.34%. The authors concluded that surgical decompression for CSM is safe and resulted in improved functional status and quality of life in patients around the world, irrespective of the differences in medical systems and sociocultural determinants of health.


The authors conducted a prospective, randomized, multicenter study in Sweden to ascertain factors that
Evidence is growing that lumbar spinal decompressive surgery offers an advantage over nonsurgical management for selected patients with persistent severe symptoms. The authors conducted this study between October 2006 and December 2011 to investigate the frequency and predictors of deterioration after decompressive surgery for a single-level and two-level lumbar spinal stenosis. Prospective data were retrieved from the Norwegian Registry for Spine Surgery. Clinically significant deterioration was defined as an 8-point increase in the Oswestry disability index (ODI) between the baseline status and the index at a 12-month follow-up. Patients with the diagnosis of central lumbar spinal stenosis who underwent an operation at less than or equal to two lumbar levels with either open laminectomy or microdecompression were included. Patients who underwent discectomy as part of the decompression or spinal instrumentation were excluded. The mean age was 65.5 years. Of the 1735 patients with complete 12-month follow-up, 9% reported deterioration. A clinically significant improvement was seen in 66% and clinically unchanged state in 25% of patients. The variables significantly associated with deterioration at a 12-month follow-up period were decreasing age, tobacco smoking, American Society of Anesthesiologists grade ≥3, decreasing preoperative ODI, previous surgery at the same level, and previous surgery at other lumbar levels (p < 0.05). As the incidence of spinal stenosis increases, offering treatment to patients most likely to respond and avoiding unnecessary procedures when there is a high risk of deterioration are important because resources in the health care services frequently are limited. The findings in the present study may be used to provide more accurate information to the patients with lumbar spinal stenosis before surgery about the risk of deterioration.


The authors conducted this study to compare the clinical outcomes and complications of all ruptured anterior communicating artery (ACoA) aneurysms treated by clipping or coiling as a cohort of the large-scale, prospective, randomized Barrow Ruptured Aneurysm Trial (BRAT) conducted between March 2003 and January 2007. This subgroup included 130 patients with a mean age of 52.5 years and a mean aneurysm size of 5.8 mm. After randomization and crossover, 70% of ACoA aneurysms were clipped and 30% were coiled. While 17% of patients initially randomized to clipping crossed over to clipping after evaluation, no patients crossed over from clipping to coiling. Characteristics that prevented the aneurysms from being coiled included an unfavorable dome-to-neck ratio, lesions difficult to access by a catheter, and a branch vessel involvement. The aneurysm size and dome projection were not significantly associated with the treatment group, clinical outcome, or retreatment. There were no significant differences in the clinical outcome by modified Rankin scale (mRS) score between the clipping and coiling groups at discharge or at 1-year or 3-year follow-up. There were no aneurysmal rebleeds during the follow-up period in this cohort. Rates of re-treatment were not significantly different between the clipped patients (n = 3) and coiled patients (n = 3), and re-treatment was not significantly associated with aneurysm size or dome projection. Clinical outcomes and stroke rates did not differ significantly in as-treated or intention-to-treat analyses. The authors concluded that ruptured ACoA aneurysms were safely

treated by either microsurgical clipping or endovascular coiling in this study. This study has allowed us to better characterize modern paradigms for the management of ruptured ACoA aneurysms.


The authors aimed to quantitatively analyze the timing and volumetric changes of adverse radiation effects (AREs) in a series of arteriovenous malformation (AVM) patients treated with Gamma Knife radiosurgery (GKRS). From a prospective institutional review board–approved database, the authors identified 105 AVM patients with a minimum of 2 years of follow-up and thin-slice T2-weighted MRI sequences for volumetric analysis. The median clinical and MRI follow-up was 4.5 and 3 years, respectively. AVMs with a Spetzler-Martin grade ≥III were observed in 48% of patients. The median administered margin and maximum doses were 22 and 40 Gy, respectively. The average nidus volume was 4.7 ± 4.3 ml. The overall obliteration rate was 70%. Of patients who showed complete obliteration, 75% developed AREs within 4–6 months after GKRS. Late-onset AREs (i.e., >12 months) correlated with a failure to obliterate the nidus. Complete nidus obliteration was performed in 58% of patients who developed appreciable AREs (defined as ARE index >8). Appreciable AREs were found to be influenced by AVM nidus volume >3 ml, lobar location, number of draining veins and feeding arteries, prior embolization, and higher margin dose. On the other hand, a minimum ARE index >8 predicted obliteration (P = 0.043). The authors concluded that ARE development after radiosurgery follows a temporal pattern peaking at 7–12 months after stereotactic radiosurgery. The ARE index (volume on T2-weighted or FLAIR changes/irradiated volume) serves as an important adjunct tool in patient follow-up and outcome prediction, as it relates to the probability of nidal obliteration.


The Pipeline for Uncoilable or Failed Aneurysms (PUFS) trial was an international, multicenter, prospective trial evaluating the safety and efficacy of the Pipeline Embolization Device (PED) for the treatment of unruptured large and giant aneurysms of the ICA (petrous to the superior hypophyseal segments and proximal to the posterior communicating segment) that measured at least 10 mm in maximum diameter and also had an aneurysm neck of at least 4 mm in one dimension. The average age of the patients was 56.4 years. In total, 108 patients were treated in the PUFS trial, 98 of whom had complete neuro-ophthalmological follow-up at 6 months. As expected, a higher proportion of patients with cavernous segment aneurysms exhibited neuro-ophthalmological deficits (57%) when compared with those with aneurysms of the petrous (0%), superior hypophyseal (22%), paraophthalmic (27%), or supraclinoidal (25%) segments. At the 6-month follow-up, 82% of the aneurysms showed angiographic occlusion. Of the patients with complete follow-up, 40% presented with a...
neuro-ophthalmological baseline deficit that was presumed to be attributable to the aneurysm, and patients with these baseline deficits had significantly larger aneurysms. In 64% of these patients, the baseline deficit showed at least some improvement, whereas in 1 patient, the deficits worsened. In 5% of the entire cohort, new deficits had developed, while in another 6%, deficits that were not originally assumed to be related to the aneurysm had improved by that time. A history of diabetes was associated with failure of the baseline deficits to improve after the treatment. This study is the first to report the neuro-ophthalmological findings from endovascular stent-only reconstruction of large and giant ICA aneurysms. However, the relatively brief period of follow-up is a limitation of the study.


There is no strong evidence regarding the predictors of seizure outcome after resective epilepsy surgery in children with tuberous sclerosis (TS). The authors performed a multicenter (six institutions between 2005 and 2013) observational study to identify preoperative factors associated with seizure outcome in children with TS undergoing resective epilepsy surgery. Seizure outcome was ascertained using a time-to-event measure, that is, time to first seizure after surgery. Seventy-four patients were included, with a median age of 120 months (range, 3–216 months). The median time to seizure recurrence was 24.0 ± 12.7 months. Engel Class I outcome was achieved in 65% and 50% of patients at 1- and 2-year follow-up, respectively. On univariate analyses, a younger age at seizure onset, larger size of the predominant tuber, and resection larger than a tuberectomy were associated with a longer duration of seizure freedom. In multivariate analyses, only resection larger than a tuberectomy (P = 0.022) was independently associated with a longer duration of seizure freedom. The authors concluded that a greater extent of resection (more than just the tuber) is associated with a greater probability of seizure freedom. They suggested that that the malformed cortex surrounding the tuber may contribute more to the epileptogenicity as opposed to the tuber itself. This is the largest multi-institutional cohort study in TS and epilepsy surgery till date.


The authors had shown the significant benefit of riluzole after 8 weeks in their previous study in patients with cerebellar ataxias of different causes. In this article, they aimed to confirm these results in patients with spinocerebellar ataxia or Friedreich’s ataxia in a 1-year trial. Patients with spinocerebellar ataxia or Friedreich’s ataxia (2:1 ratio) from three Italian neurogenetic units were enrolled in this multicenter, double-blind, placebo-controlled trial, and randomly assigned to riluzole (50 mg orally, twice daily) or placebo for 12 months. The randomization list was computer-generated, and a centralized randomization system was implemented. Participants and assessing neurologists were masked to treatment allocation. The primary end point was the proportion of patients with improved Scale for the Assessment and Rating of Ataxia (SARA) score (a drop of at least one point) at 12 months. Between May 22, 2010 and February 25, 2013, 60 patients were enrolled. The proportion with decreased SARA score was 14 (50%) of 28 patients in the riluzole group versus 3 (11%) of 27 in the placebo group (OR: 8.00, 95% CI: 1.95–32.83; P = 0.002). Their findings lend support to the idea that riluzole could be used in the treatment protocol for cerebellar ataxia. Further studies that are longer and disease specific would confirm these findings and assess whether these can be applied in clinical practice.


Major depressive disorder (MDD) is a highly prevalent and disabling condition associated with significant morbidity and mortality. The authors conducted a double-blind, randomized, placebo-controlled, multicenter (20 centers) trial to investigate the efficacy and safety of deep transcranial magnetic stimulation (dTMS) applied daily as monotherapy in subjects with MDD who had either failed one to four antidepressant trials or not tolerated at least two antidepressant treatments in the current episode. Patients (n = 212) were randomly assigned to either active dTMS or sham TMS in a 1:1 ratio. Primary and secondary efficacy end points were the change in the Hamilton Depression Rating Scale (HDRS-21) score and response/remission rates at week 5, respectively. dTMS induced a 6.39-point improvement in HDRS-21 scores, while a 3.28-point improvement was observed in the sham group (P = 0.008), resulting in a 0.76 effect size. Response and remission rates were higher in the dTMS than in the sham group (response: 38.4% vs. 21.4%, P = 0.013; remission: 32.6% vs. 14.6%, P = 0.005). These differences between active and sham treatment were stable during the 12-week maintenance phase. dTMS was associated with few and minor side effects apart from one seizure in a patient in whom a protocol violation occurred. The authors suggest that dTMS constitutes a novel intervention in MDD, which is efficacious

Alternating hemiplegia of childhood is caused by mutation in the ATP1A3 gene expressed in neurons and cardiomyocytes and is characterized by episodes of alternating hemiplegia starting early in life along with seizures or nonparoxysmal neurologic events. Premature mortality due to cardiac arrest is well known in this condition. In this study, the authors analyzed electrocardiographic (ECG) recordings of 52 such patients from 9 countries, and all of these patients underwent a whole-genome, whole-exome, or Sanger sequencing of ATP1A3. Data regarding autonomic function testing, medicines taken, family history of cardiac disease, and sudden deaths were collected. Electrocardiograms were analyzed for cardiac axis, cardiac interval, repolarization pattern, and J-point analysis. Half of the patients had ECG abnormalities in the form of T wave abnormalities; and interventricular conduction abnormalities, a shorter corrected QT interval, and J-point abnormalities were also seen more in the patient group. The authors concluded that electrocardiogram abnormalities were common in alternating hemiplegia, showing the characteristics of inherited cardiac channelopathies and most likely amounted to an impaired repolarization reserve. Cardiac dysfunction may account for some of the unexplained premature mortality of alternating hemiplegia. As cardiac arrhythmias are preventable, systematic cardiac evaluation is warranted in such patients.


The authors used the database of SWIFT and STAR trials to identify patients who were treated with solitaire stent retriever and achieved substantial reperfusion. They further analyzed data in terms of ordinal number outcome instead of dichotomous disability outcome, which had been used previously. The authors' apprehension was that there could have been under-representation of good outcome with dichotomous analysis used earlier. Among 202 patients treated with endovascular therapy with TICI 2b to 3 perfusion, the day 90 modified Rankin scale (mRS) outcomes for onset to reperfusion (OTR) time intervals ranging from 180 to 480 minutes had shown substantial time-related reductions in disability across the entire score range. Shorter OTR was associated with improved mean 90-day mRS (1.4 vs. 2.4 vs. 3.3, for OTR groups of 124–240 vs. 241–360 vs. 361–660 minutes, respectively; $P < 0.001$.) For every 15-minute acceleration of OTR, 34 per 1000 treated patients had improved disability outcome. Authors concluded that the analysis of disability across the whole range of mRS demonstrated better disability outcome, and that every 5-minute delay in achieving reperfusion was associated with worse disability outcome in 1 in 100 patients.


Thirty-one patients having Charcot-Marie–Tooth (CMT) disease of predominantly common phenotypes 1A, 1B, and TX1 type were subjected to skin biopsy to examine dermal nerve fibers. Axonal loss was assessed by quantification of Meissner’s corpuscles and intrapapillary myelinated endings along with morphometric changes of dermal nerve fiber endings. Results showed reduction in both Meissner’s corpuscles and intrapapillary myelinated endings in all genotypes of CMT disease. A wider nodal gap, an abnormal connection between axon and glia, and a shorter internodal length were common features in all but were more pronounced in CMT1A. Mutations in both myelin and axonal genes probably were responsible for the universally shorter internodal length and wide nodal gaps, which in turn are responsible for the conduction abnormality seen on neurophysiological studies. The authors concluded that these changes on nerve biopsy shed light on the pathogenetic mechanism of axonal and demyelinating forms of CMT.


The authors studied the incidence and early predictors of generalized tonic–clonic (GTC) seizures in children with childhood absence epilepsy (CAE) in a cohort of patients who participated in a trial comparing ethosuximide, lamotrigine, and sodium valproate as the initial therapy, 94% showed a GTC seizure. The authors concluded that GTC seizure occurrence appears lower in CAE as has been previously reported. An older age at onset, the duration of shortest burst on electroencephalography (EEG), and failure to respond to the initial monotherapy were associated with a higher risk of having a GTC seizure. Of those who failed on ethosuximide therapy, 94% showed a GTC seizure. The authors concluded that GTC seizure occurrence appears lower in CAE as has been previously reported. An older age is a risk factor of GTC seizure occurrence, and responders to ethosuximide have a lower risk.

This was a systematic review and meta-analysis aimed at studying the risk of an intracerebral bleed in patients who have cerebral microbleeds (CMBs) on MRI and are undergoing a thrombolytic therapy for acute ischemic stroke. PubMed database was searched for relevant studies, and pooled odds ratios were calculated using the Mantel-Haenszel fixed-effects method, among individuals with or without CMBs on pretreatment MRI scans. Data of the patients having received only intravenous thrombolytic therapy were used to avoid a potential bias. Data were pooled from 2028 patients from 10 eligible studies. The results showed that the prevalence of CMBs was 23.3%, and 8.5% of patients with CMBs had symptomatic intracerebral hemorrhage (ICH) as compared with 3.9% of patients without CMBs. The odds ratio for the presence of CMBs and symptomatic ICH was 2.87 (95% CI: 1.76–4.69; P < 0.0001). The authors concluded that although the results from this meta-analysis suggest an increased risk of symptomatic ICH in patient with CMBs going for intravenous thrombolysis, potential bias makes interpretation of these results hypothesis-generating rather than a message to avoid administering thrombolytic therapy in all eligible candidates suitable for thrombolysis. There is a need for further exploration of these findings in terms of the number and location of microbleeds.


Mannitol is often used to reduce cerebral edema in acute intracerebral hemorrhage but without any supporting evidence of benefit. The authors planned to study its impact on the clinical outcome among participants of the Intensive Blood Pressure Reduction in Acute Intracerebral Hemorrhage Trial (INTERACT2). INTERACT2 was an international open-label randomized control trial conducted on 2839 patients to compare intensive blood pressure control versus guideline-recommended blood pressure control in spontaneous intracerebral hemorrhage within a 6-hour duration. The authors did a propensity score and multivariate analysis to investigate the relationship between mannitol treatment in acute stage (7 days) and poor outcome defined as death or a modified Rankin scale score of 3–6 at 90 days. The results showed no significant difference between the mannitol and nonmannitol groups on the propensity score and multivariable analyses (propensity analysis, OR: 0.90, 95% CI: 0.75–1.09; multivariable analysis, OR: 0.87, 95% CI: 0.71–1.07). Mannitol was not associated with excess side effects. The conclusion was that mannitol does not improve outcome but is safe to use.


The authors planned to study the epidemiological characteristics of epilepsy surgery, which is the most effective treatment that may be offered to selected patients suffering from refractory epilepsy. Data were collected on the clinical, radiological, and histopathological information of patients who underwent epilepsy surgery at nine major epilepsy centers in the United States, Germany, and Australia from 1991 to 2011. It was found that there was a gradual shift from surgery for mesial temporal sclerosis (MTS) to nonlesional surgeries at these centers. There was a yearly increase of 0.6 ± 0.07% in the performance of invasive electroencephalography in five of nine centers. Overall, MTS surgery ranging from 33.3% to 70.2% during 1991 to 2001 dropped to 33.6% of all surgical resections at these centers in 2011. The significance of this study was to highlight the trends in the evolution of epilepsy surgery in the past two decades in well-established epilepsy centers of the world. It was evident from this study that more complicated evaluations and procedures were being initiated with the passage of time.


As seizures are common during and after treatment of brain tumors, the authors aimed to study the incidence of, and the risk factors for seizures in long-term survivors of pediatric brain tumors. In children with brain tumors, data regarding seizure semiology, seizure frequency, imaging characteristics, electroencephalographic findings, and antiepileptic drugs were collected retrospectively from the records. A cohort of 298 patients with an average follow-up duration of 7.6 years underwent total resection (109), subtotal resection (143), only biopsy (29), or no surgical intervention (17). Low-grade gliomas, medulloblastomas, and ependymomas were the most frequent diagnoses. Seizure was observed in 24% of patients. Tumor location (cortical versus subcortical), their histology (low grade
versus high grade), their recurrence rate, and the incidence of incomplete resection were factors associated with a higher seizure risk. The identification of patients at a higher risk of having a seizure may help in the management, as potential treatment trials with antiepileptic drugs may be prophylactically instituted in them for a limited period.


This was a single-center retrospective study aimed at identifying demographic characteristics and clinical features of pregnant women presenting with acute headache. Data of a 5-year period were collected. Patients usually presented in the third trimester with headache. Primary headaches were diagnosed in 65% of patients, while secondary headaches were diagnosed in 35% of patients. Migraine as the cause of primary headache was observed in 92.2% of patients; among secondary headaches, hypertension was the commonest reason, found in 51% of patients. Univariate analysis showed factors such as lack of prior headache history, fever, seizure, elevated blood pressure, and abnormal neurologic examination were associated with the possibility of secondary headache, Elevated blood pressure (odds ratio [OR]: 17.0, 95% confidence interval [CI]: 4.2–56.0) and a lack of headache history (OR: 4.9, 95% CI: 1.7–14.5) had an increased association with secondary headache, while psychiatric comorbidity (OR: 0.13, 95% CI: 0.021–0.78) and phonophobia (OR: 0.29, 95% CI: 0.09–0.91) had a reduced association with secondary headache in the multivariate analysis. The authors concluded that more than one-third pregnant female patients with headache may have a secondary headache that may not be distinguishable from the primary headache based on the severity of headache; however, certain factors may point toward secondary headache like the lack of previous history of headache, presence of hypertension, or an abnormal neurologic examination. We must have a low threshold for neuroimaging investigations for these patients.