A summary of some of the recently published, seminal papers in neuroscience

K. Sridhar, Manjul Tripathi, Ravi Yadav, Aastha Takkar, Mazda K. Turel, Kuntal Kanti Das, Anant Mehrotra

Department of Neuro and Spine Surgery, Global Hospitals and Health City, Chennai, Tamil Nadu, Departments of Neurosurgery and Neurology Postgraduate Institute of Medical Education and Research, Chandigarh, Department of Neurology, National Institute of Mental Health and Neurosciences, Bangalore, Karnataka, Department of Neurosurgery, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, Department of Neurosurgery, Rush University Medical Centre, Chicago, Illinois, US


Even in the time of increasing insurance covers, cancer therapies cost financial distress to the patients. It involves significant out of pocket expenditure leading to a status now termed “Financial Toxicity”. In this thoughtful article, Ramsey et al., have analyzed the bankruptcy data of patients suffering from different cancers recorded in Western Washington Cancer Surveillance System (CSS) from 1995-2009. After the consideration of various confounding variables such as the organ involved, stage of the disease, the insurance status and the economic status of the patient, the mortality rate of patients who filed for bankruptcy is compared to the ones who did not. For different cancers, the hazard ratio of mortality was greater by 1.5-2.5 times among the bankrupt patients than the non-bankrupt individuals. Young, female, non-white patients with local or early stage of cancer, who had earlier received treatment, were more likely to file for bankruptcy. Financial toxicity has multifaceted implications such as non-adherence to the treatment, financial distress to the family, or refusal for treatment. This study highlights a debatable issue of whether or not an oncology practitioner should consider his treatment plan according to the possible financial implications. In a country like India, where majority of population still does not have any insurance cover for health, such possibility of financial distress should be more prevalent. The high cost of treatment also warrants new policies for the effectual financial support for cancer patients to curb such circumstances, which drag them towards the path of poorer survival.


The advent of newer and refined treatment modalities such as stereotactic radiosurgery (SRS) has caused a paradigm shift in the management of various benign and malignant intracranial
pathologies over the last few decades. However, the literature has been skeptical about the risk profile for the development of secondary malignancies after the earlier reports of radiation-induced meningiomas developing in children suffering from tenia capitis in Israel. Radiation induced neoplasia (RIN) or malignant transformation of a benign lesion is a devastating collateral condition, if it happens to occur. The common RINs are meningiomas, gliomas or triton tumors. The Cahan’s criterion is the commonly followed guideline for the diagnosis of RIN. In this study, authors have analyzed a large number of patient data from “Surveillance, Epidemiology and End Result (SEER)” database for patients having an unilateral vestibular schwannoma (VS). With the conventional dosing schemes, the risk of development of RIN or malignant transformation of VS remains 0.8% at five year follow up regardless of the treatment modality, and the risk of acquiring secondary malignancy, 1 per 1000 cases, testifying the safety of SRS for non-neurofibromatosis VS. Interestingly, the short and intermediate term risk of development of another malignancy after SRS is not greater than after microsurgery or observation. Since the previous reports have been single center experience, more such analysis with longer follow up period are required to gain an insight into factors responsible for tumor genesis in a patient with pre-existing malignancy.

Contributed by Dr. Manjul Tripathi


Obesity is the new epidemic of the world population. It not only increases the chances of other metabolic problems such as hypertension, diabetes etc., but also the development of deep venous system thromboembolism (VTE). In this study, conducted over nearly a decade long period, obesity has been analyzed as a risk factor for central venous thrombosis (CVT). The risk of CVT has been found to be especially high in obese females of the reproductive age group who are taking oral contraceptive pills (OCP). Strikingly, this association has been found to be gender specific as there was no statistically significant correlation between obesity and CVT in men or in females not taking OCP. This study raises significant concerns as a sizeable population of sexually active female is prescribed OCP as a measure for birth control. The risk of CVT is increased in a dose dependent manner. This interesting study highlights the value of body mass index (BMI) in the evaluation of patients with idiopathic intracranial hypertension (IHH) and CVT. Physicians should consider alternate birth control measures in this specific cohort of population.

Contributed by Dr. Manjul Tripathi


An increased incidence of traumatic brain injury (TBI) is the bane of modern civilization. TBI has been attributed to also be responsible for an increased incidence of neurodegenerative disorders such as dementia, Parkinson’s disorder (PD) or Alzheimer’s disease (AD) in later life. Similarly, various studies have determined a causal association between concussion injury as well as sports-related head injuries and progressive neurodegeneration, especially amongst boxers, where this entity is described as ‘punch drunk syndrome’. This study analyzes the late effects of TBI with the critical evaluation of clinical (n = 7130) and autopsy (n = 1589) findings of patients with a history of trauma and loss of consciousness (LOC). Neurofibrillary tangles, neuritic plaques, microinfarcts, cystic infarcts, Lewy bodies, and hippocampal sclerosis are the neuropathological markers of TBI. This pooled analysis of three prospective cohort studies denies the role of TBI as a causative factor for dementia and AD, which is contrary to the current concepts. However, it clearly states that a statistically significant association exists between TBI and the progression of Parkinsonism and PD.

Contributed by Dr. Manjul Tripathi


Baharoglu et al., in this trial (PATCH) have sought to answer the question on whether or not the platelet transfusion therapy has an effect on death and dependence in patients with spontaneous primary intracerebral haemorrhage who are already being administered antiplatelet therapy. They compared the outcome of platelet transfusion with standard care, and standard care alone. This was a multicentre, open-label, masked-endpoint, randomised trial at 60 hospitals in the Netherlands, UK, and France. Adult patients who arrived within 6h of the occurrence of spontaneous supratentorial intracerebral haemorrhage symptoms with a positive history of antiplatelet therapy in the last 7 days and a Glasgow Coma Scale score of at least 8 were enrolled. The primary outcome was a shift towards death or dependence, rated on the modified Rankin

Contributed by Dr. Manjul Tripathi

Neurology India / September 2016 / Volume 64 / Issue 5

DOI: 10.1001/jamaneurol.2016.1948

An increased incidence of traumatic brain injury (TBI) is the bane of modern civilization. TBI has been attributed to also be responsible for an increased incidence of neurodegenerative disorders such as dementia, Parkinson’s disorder (PD) or Alzheimer’s disease (AD) in later life. Similarly, various studies have determined a causal association between concussion injury as well as sports-related head injuries and progressive neurodegeneration, especially amongst boxers, where this entity is described as ‘punch drunk syndrome’. This study analyzes the late effects of TBI with the critical evaluation of clinical (n = 7130) and autopsy (n = 1589) findings of patients with a history of trauma and loss of consciousness (LOC). Neurofibrillary tangles, neuritic plaques, microinfarcts, cystic infarcts, Lewy bodies, and hippocampal sclerosis are the neuropathological markers of TBI. This pooled analysis of three prospective cohort studies denies the role of TBI as a causative factor for dementia and AD, which is contrary to the current concepts. However, it clearly states that a statistically significant association exists between TBI and the progression of Parkinsonism and PD.
Sridhar, et al.: The fourth dimension

Scale (mRS) at 3 months. The study recruited 190 patients during the study period of which 97 patients received platelet transfusion and 93 received standard care. There were higher odds of death or dependence at 3 months in the platelet transfusion group than in the standard care group (adjusted common odds ratio 2.03, 95% CI 1.18–3.56; P = 0.0114).

There was a significantly higher occurrence of serious adverse events in the platelet transfusion group as compared to the standard care alone group. There was a significantly higher mortality in the platelet transfusion therapy group (24% versus 17%) during the hospital stay. This study shows that platelet transfusion is inferior to standard care in patients with antiplatelet therapy before intracerebral haemorrhage. Although this study shows disappointing results, it has been able to answer the question regarding the benefit of platelet transfusion in intracranial haemorrhage.

Contributed by Dr. Ravi Yadav


The hyperkinetic disorders like Huntington’s disease, levodopa-induced dyskinesia and dystonia are unable to reverse the changes in synaptic plasticity and associated increase in the excitatory neuronal inputs to the various parts of the brain, thus increasing peripheral movements. In this review, Calabresi et al., have reviewed the dysfunctional mechanisms in patients with hyperkinetic disorders. The defect can occur at different levels and is associated with underlying genetic and molecular mechanisms. The article is an interesting read on the mechanisms and suggests that the loss of synaptic downscaling may be working both at the level of cortex as well as the basal ganglionic structures.

Contributed by Dr. Ravi Yadav


There are very few tests available in the antemortem stage, to diagnose a patient suspected of having sporadic Creutzfeldt-Jakob disease (CJD). The reliability and low sensitivity and specificity of cerebrospinal fluid test of protein 14-3-3 is also well known. McGuire et al., in this study, have evaluated real-time quaking-induced conversion (RT-QuIC) as a sensitive diagnostic test for sporadic CJD. Once validated, this could have an important bearing on the diagnosis of CJD.

In this study, two international ring trials were undertaken in which a set of 25 cerebrospinal fluid samples were analysed by a total of 11 different centres using a range of recombinant prion protein substrates and instrumentation. This study showed that there was almost complete concordance between the centres and demonstrate that RT-QuIC was a reliable technique for the diagnosis of CJD in clinical practice.

Contributed by Dr. Ravi Yadav


This study presents data from a Global Burden of Disease study 2013 to measure the population-attributable fraction (PAF) of stroke-related disability-adjusted life-years (DALYs) associated with the potentially modifiable environmental, occupational, behavioural, physiological, and metabolic risk factors, in different age and sex groups worldwide, in high-income, low-income and middle-income countries, from 1990 to 2013. The investigators found that 90.5% of the global stroke burden was due to the modifiable risk factors. Of these, 74% stroke burden was due to the behavioural factors (smoking, poor diet and low physical exercise). Metabolic factors (hypertension, dyslipidemia and diabetes) and environmental factors (air pollution and lead exposure) were the 2nd and 3rd largest contributors to DALYs. Overall, 29.2% of the burden of stroke was attributed to air pollution. As expected, the behavioural cluster was more common in males. There was an increase in the PAF of all the factors from 1990 to 2013. The important finding of this large study was that more than 90% of the stroke burden was due to modifiable risk factors, and that air pollution has emerged as an important contributor to the global burden.

Contributed by Dr. Ravi Yadav


Bray et al., have studied the phenomenon of weekend effect based on the literature evidence that the patients of stroke who are admitted on weekends than during the week are administered poor-quality health care. They hypothesized that variations in the quality was not only dependent on the day but also the time of admission. This was a registry based, prospective

Rothwell et al., in this paper, have tested the hypothesis that the short-term benefits of early aspirin have been underestimated. The authors pooled the data of all randomised control trials of aspirin versus control in secondary prevention after TIA or ischaemic stroke and studied the effects of aspirin on the risk and severity of recurrent stroke, stratified by the following time periods: Less than 6 weeks, 6–12 weeks, and more than 12 weeks after randomisation. The pooled data from 15778 participants from 12 trials showed that aspirin reduced the 6-week risk of recurrent ischemic stroke by about 60% and disabling or fatal ischemic stroke by about 70%. Maximum benefit was noted in patients presenting with TIA or minor stroke. They report that these benefits were independent of the dose, patient characteristics, or aetiology of TIA or stroke.

They found that the medical treatment substantially reduces the risk of early recurrent stroke after TIA and minor stroke, and that aspirin was the key intervention. They suggest this significant benefit from aspirin warrants public education about the benefits of its self-administration after a possible attack of TIA.

Contributed by Dr. Ravi Yadav


This is a nice review by Alberto Espay and colleagues on the challenges of treating neurogenic orthostatic hypotension and supine hypertension in patients with Parkinson’s disease, as both the conditions are present in synucleinopathies and can cause opposite changes in the blood pressure. Also, the treatment of one condition may worsen the other. Because of this, the treatment requires a detailed assessment of the patients with coexistent neurogenic orthostatic hypotension and supine hypertension. The patients with orthostatic hypotension are more likely to develop falls and cognitive impairment, while supine hypertension can be associated with stroke and myocardial infarction in the long term. There are few studies that have addressed this topic. The authors suggest that the future studies should focus on finding the therapeutic window during which neurogenic orthostatic hypotension should be treated. This treatment should primarily be administered under the presence of supine hypertension.

Contributed by Dr. Ravi Yadav


China and India account for 38% of the population of the world. This study by Charlson et al., aimed at providing estimates of the burden of mental, neurological, and substance use disorders for China and India from the Global Burden of Disease Study 2013 (GBD 2013). The authors conducted systematic reviews as per the PRISMA guidelines. Using various statistical methods, they found around 1/3rd of global disability-adjusted life years (DALYs) attributable to mental, neurological and substance use disorders in China and India, which was greater than the combined incidence in all the developed countries. Around 50% of the DALYs in India were due to non-communicable diseases as compared to 80% in China. The overall population growth in India explains a greater proportion of the increase in mental, neurological, and substance use disorder burden from 1990 to 2013 (44%) than in China (20%). The burden of mental, neurological, and substance use disorders is estimated to increase by 10% in China and 23% in India between 2013 and 2025. The authors suggested that, based on this data, both China and India should urgently prioritize the programmes focused on targeted prevention, early identification, and effective treatment of these disorders.

Contributed by Dr. Ravi Yadav
who want to understand the scientific and physiological aspects of “Free will” as compared with the philosophical standpoint. Dr Hallet explains the physiology of will based on the experiments. The origin of the processes pertaining to any voluntary activity begins much before the initiation of the conscious effort required to perform the act. Therefore, even before the Bereitschaftspotential (measure of activity in the motor cortex and supplementary motor area of the brain leading up to voluntary muscle movement) in electroencephalogram (EEG) is detected, there is evidence to show in fMRI (Functional Magnetic Resonance Imaging) that the processes regarding the movement have begun in the parietal lobes. There is evidence to show that free will occurs only when the brain is free from any strong external stimulus or neurological abnormality (seizure). This article explores the contemporary and scientific explanations of the free will.

*Contributed by Dr. Ravi Yadav*


The SOCRATES trial by Johnston et al., evaluated whether ticagrelor is more effective as an antiplatelet agent than aspirin for the prevention of recurrent stroke and cardiovascular events in patients with acute cerebral ischemia. This was an international double-blinded, controlled trial in 674 centres in 33 countries, in which 13,199 patients were recruited. These patients had an ischemic stroke that was not severe; or, had a high-risk transient ischemic attack. In addition, they had not received intravenous or intra arterial thrombolysis. They were randomly assigned within 24 hours after symptom onset, in a 1:1 ratio, to receive either ticagrelor (180 mg loading dose on day 1, followed by 90 mg twice daily from day 2nd to 90th) or aspirin (300 mg on day 1 followed by 100 mg daily from day 2nd to 90th). The primary end point was the time to the occurrence of stroke, myocardial infarction, or death within 90 days.

The number of patients in whom the primary endpoint occurred in the ticagrelor group were 442 of 6589 patients; and, in the aspirin group, 497 of 6610 patients (hazard ratio of 0.89) during the 90 days of treatment. In this trial, ischemic stroke occurred in 385 (5.8%) patients in the ticagrelor group and 441 (6.7%) patients in the aspirin group (hazard ratio: 0.87). Major hemorrhagic complications occurred in 0.5% of patients treated with ticagrelor and in 0.6% of patients treated with aspirin, and death due to bleeding was 0.1% in both groups. Thus, this trial did not find ticagrelor superior to aspirin in the treatment of patients with acute ischemic stroke or transient ischemic attack, in reducing the rate of stroke, myocardial infarction, or death at 90 days.

*Contributed by Dr. Ravi Yadav and Dr. Aastha Takkar*


The mainstay of treatment available for myasthenia gravis include disease-modifying agents: Corticosteroids alone or in combination with immunosuppressive drugs. The only immunosuppressive drugs shown to be effective for MG in randomized placebo-controlled studies are azathioprine and cyclosporine. Methotrexate (MTX) is an immunosuppressant used in many autoimmune diseases. The potential advantages of MTX include its oral weekly dosing, a moderate side effect profile, and the inexpensive generic preparations available, making it an important medication to consider in a resource poor settings. Prior uncontrolled studies of MTX in MG suggested that MTX reduced symptoms or decreased the corticosteroid dose in 38%–87% of patients; and, one single-blind uncontrolled study also showed that its efficacy was similar to that of azathioprine at 10 months.

Pasnoor et al., performed a 12-month multi-center randomized, double blind, placebo- controlled trial of MTX in MG, attempting to determine the steroid-sparing effect of methotrexate (MTX) in patients with symptomatic generalized myasthenia gravis. MTX, 20 mg orally once a week regimen, was compared with a placebo arm in 50 acetylcholine receptor antibody–positive patients with MG between April 2009 and August 2014. The primary outcome measure was the prednisone area under the dose-time curve (AUDTC) from months 4 to 12. This outcome was chosen as the authors presumed that it closely mimicked the clinician’s experience in treating MG, where the prednisone dosing varies by the patient’s visits based on his/her symptoms. Secondary outcome measures included 12-monthly changes in the Quantitative Myasthenia Gravis Score, the Myasthenia Gravis Composite Score, the Manual Muscle Testing, the Myasthenia Gravis Quality of Life, and the Myasthenia Gravis Activities of Daily Living. 50 out of 58 patients screened were enrolled in the study.

MTX was not seen to reduce the month 4–12 prednisone AUDTC when compared to the placebo (difference MTX 2 placebo: 2488.0 mg, 95% confidence interval -22,443.4 to 1,467.3, \( P = 0.26 \)); however, the average daily prednisone dose decreased in both the groups. MTX did not improve secondary
The optic canal size is associated with non-specific pain (19%). The primary endpoint of our study, month 4–12 prednisone AUDTC, was not significantly different between the MTX and placebo groups, so no steroid-sparing benefit of MTX in MG was demonstrated.

This study was funded by Food and Drug Administration Orphan Products Division. It had some definite disadvantages with a seemingly smaller study population appearing to make it underpowered. It included older average participants, which may have enriched the study population with late-onset MG cases. Also, patients with comparatively milder disease were included (Myasthenia Gravis Foundation of America score of Class 2 \( \text{n(%) patient group 23 (92); and, placebo group 20 (80).} \) The study claims to have provided Class I evidence that, for patients with generalized MG, administration of MTX does not significantly reduce the prednisone AUDTC over 12 months of therapy. This study also demonstrated the challenges encountered during the conduction of clinical trials related to MG, including the difficulties arising during recruitment of subjects, and participants improving on prednisone alone, as well as the need for a better understanding of the outcome measure variability for future clinical trials.

Contributed by Dr. Aastha Takkar


Myasthenia gravis is an autoimmune disease of the neuromuscular junction, commonly affecting the ocular muscles. Cigarette smoking has been shown to influence many autoimmune diseases, including multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus and Graves’ disease. Cigarette smoking and other forms of chronic nicotine use have also been shown to alter acetylcholine receptors on neuronal receptors in the brain. Few case reports/series have found a higher prevalence of MG among cigarette smokers as compared with the general population and little is known about whether or not cigarette smoking plays a causal role, influences the disease activity, or exacerbates the symptoms and quality of life in MG.

The authors in this prospective, cross-sectional study sought to determine whether cigarette smoking influenced disease-related symptoms in ocular myasthenia gravis (OMG).

A clinic-based, cross-sectional study was performed in a single academic neuro-ophthalmology setting. 44 patients diagnosed with OMG between November 2006 and April 2014 were included. A prospective telephone survey was administered to determine the smoking status and myasthenia gravis-related symptom severity. The main outcome measure was the myasthenia gravis-specific activities of daily living (MG-ADL) score, a well-validated marker of symptoms and quality of life in myasthenia gravis. Comparison of MG-ADL total scores between current smokers (3.4 ± 2.6), former smokers (1.8 ± 2.1), and never smokers (1.1 ± 1.5) revealed a statistically significant relationship \( (P = 0.031) \), where current smokers had the highest MG-ADL total scores, and never smokers, the lowest. Comparison of MG-ADL total scores revealed the same relationship (current 5.6 ± 4.5, former 2.9 ± 3.1, never 1.4 ± 2.5, \( P = 0.003) \). There were borderline significant correlations of pack years with MG-ADL total score \( (r = 0.27, P = 0.074) \) and MG-ADL total score \( (r = 0.30, P = 0.051) \). This association suggests that smoking cessation in OMG patients may lead to an improved symptom-related quality of life.


Idiopathic intracranial hypertension (IIH) has long been mesmerizing neurologists with varied presentations, varied risk factors and varied response to treatment. High-grade papilledema remains a risk factor for irreversible visual loss in IIH but factors contributing to the severity of papilledema remain unclear. Variability of the optic disc response to raised cerebrospinal fluid (CSF) pressure may be a plausible explanation. Other factors, such as the magnitude of the CSF pressure elevation, the intraocular pressure, and structural changes in the lamina cribrosa or the optic nerve sheath, have been inconsistently associated with the degree of papilledema, suggesting that additional factors may interfere with the development of papilledema.

This interesting study by Bidot et al., was aimed to determine whether the size of the bony optic canal is associated with the severity of papilledema and poor visual function in IIH. This was a retrospective review of patients with definite IIH with requisite brain magnetic resonance imaging allowing for optic canal measurement. The clinical characteristics and automated (Humphrey) visual field results were reviewed;
Sridhar, et al.: The fourth dimension

papilledema was graded according to the modified Frisén scale. Cross-sectional area of the optic canals was measured independently by 2 readers and averaged for each canal. Logistic regression modelling was applied. Sixty-nine patients with IIH were included (mean age: 33; 91% women; 65% black). Controlling for age, sex, body mass index, race, and cerebrospinal fluid (CSF) opening pressure, each square mm increase in the canal size was associated with a 0.50 dB reduction in the Humphrey visual field mean deviation ($P = 0.006$); this was likely mediated by the increased odds of developing Grade 4–5 papilledema or optic atrophy in patients with larger canals (odds ratio: 1.30 [95% CI: 1.10–1.55; $P = 0.003$]). It was, therefore, concluded that poor visual function and severe papilledema or optic atrophy were associated with a larger optic canal. Potential mechanisms include alteration in local CSF flow or bony remodelling at the optic canals.

Contributed by Dr. Aastha Takkar


A subset of patients with myasthenia gravis (MG) does not respond to conventional treatment and has severe or life-threatening symptoms. Alternate and emerging therapies have not yet proven to be consistently or durably effective. Autologous hematopoietic stem cell transplantation (HSCT) has been effective in treating other severe autoimmune neurological conditions. The authors in this cohort study presumed the possibility of similar application of HSCT in MG. In the current study, the authors report on seven cases suffering from severe MG treated with autologous HSCT in whom consistent, durable, symptom-free, and treatment-free remission was achieved. These were retrospective cohort study reports from The Ottawa Hospital, a large, Canadian, tertiary care referral center with expertise in neurology and HSCT (from January 1, 2001 to December 31, 2014), with a median follow-up of 40 months (range, 29-149 months). Data collection and analysis were performed from February 1 to August 31, 2015. All patients with MG treated with autologous HSCT were included. All had persistent severe or life-threatening MG-related symptoms despite continued use of intensive immunosuppressive therapies.

Autologous hematopoietic stem cell grafts were mobilized with cyclophosphamide and granulocyte colony-stimulating factor, collected by peripheral blood leukapheresis, and purified away from contaminating lymphocytes using CD34 immuno-magnetic selection. The patients were treated with intensive conditioning chemotherapy regimens to destroy the auto-reactive immune system followed by graft reinfusion for blood and immune reconstitution. The primary outcome considered was MG disease activity after administration of autologous HSCT measured by the frequency of emergency department visits and hospitalizations and Myasthenia Gravis Foundation of America (MGFA) clinical classification, MGFA therapy status, and MGFA post-intervention status. Safety outcomes included all severe autologous HSCT-related complications.

Seven patients underwent autologous HSCT, 6 for MG and 1 for follicular lymphoma with coincident active MG. The mean (standard deviation) ages at MG diagnosis and at autologous HSCT were 37 (11) and 44 (10) years, respectively. Five patients (71%) had concurrent autoimmune or lympho-proliferative illnesses related to immune dysregulation. All patients had distinct clinical and electro-myographic evidence of MG (MGFA clinical classification IIb-V). All patients achieved durable MGFA complete stable remission with no residual MG symptoms and freedom from any ongoing MG therapy (MGFA post-intervention status of complete stable remission). Three patients (43%) experienced transient viral reactivations, and 1 (14%) developed a secondary autoimmune disease after autologous HSCT, all of which resolved or stabilized with treatment. There were no treatment or MG-related deaths. The authors concluded that autologous HSCT may result in a long term symptom and treatment-free remission in patients with severe MG. The application of autologous HSCT for this and other autoimmune neurologic conditions warrants further prospective studies.

Contributed by Dr. Aastha Takkar


The authors conducted this study to compare the safety and effectiveness of minimally invasive sacroiliac joint fusion (SIJF) using triangular titanium implants vs conservative management (CM) in patients with chronic sacroiliac joint (SIJ) pain. One hundred and three adults with chronic SIJ pain at nine sites in four European countries were randomly assigned to and underwent either minimally invasive SIJF using triangular titanium implants ($N = 52$) or CM ($N = 51$). CM was performed according to the European guidelines for the diagnosis and management of pelvic girdle pain and consisted...
of optimization of medical therapy, individualized physical therapy (PT) and adequate information and reassurance as part of a multifactorial treatment. The primary outcome was the difference in change in self-rated low back pain (LBP) at 6 months. Additional endpoints included quality of life using EQ-5D-3L, disability using Oswestry Disability Index (ODI), SIJ function using active straight leg raise (ASLR) test and adverse events. At 6 months, the mean LBP improved by 43.3 points in the SIJF group and 5.7 points in the CM group (difference of 38.1 points, \( P < 0.0001 \)). The mean ODI improved by 26 points in the SIJF group and by 6 points in the CM group (\( P < 0.0001 \)). ASLR, EQ-5D-3L, walking distance and satisfaction were statistically superior in the SIJF group. The frequency of adverse events did not differ between the groups. The authors concluded that in patients with chronic SIJ pain, minimally invasive SIJF was safe and more effective than CM in relieving pain, reducing disability and improving patient function and quality of life. This study gives more credence to the fact that the sacroiliac joint is now considered as a proven pain generator and that this entity should be looked for in patients whose back pain does not have the classical symptomatology of other commonly treated lumbar spine pathologies.

**Contributed by Dr. Mazda K. Turel**


The aims of this study were to evaluate the laminectomy width as a risk factor for C5 palsy and to assess its correlation with the severity of palsy. The patient population included all patients with cervical spondylotic myelopathy who underwent cervical laminectomy and fusion (CLFI) between 2007 and 2014 by a single surgeon. Patients who underwent CLFI for trauma, infection, or tumor, or had undergone previous or circumferential cervical surgery were excluded. All patients with a new C5 palsy received postoperative magnetic resonance imaging. An additional computed tomography (CT) scan was ordered to assess the hardware. All control patients received a CT scan at 6 months postoperatively to evaluate their fusion. Seventeen patients with a C5 nerve palsy and 12 controls were identified. There were no baseline differences in age, sex, diabetes, smoking history, number of surgical levels, or sagittal alignment. The body mass index was significantly higher in the control cohort. There was no significant increase in the C3-C7 laminectomy width in patients with postoperative C5 palsy. There was no correlation between the laminectomy width and the severity of palsy. The authors concluded that this was the largest series where the patients had suffered C5 palsy after a laminectomy that was documented with a CT imaging. The laminectomy width was not associated with an increased risk of postoperative C5 palsy at any level. A reduction in the laminectomy width may not reduce the rate of postoperative nerve palsy. This is an interesting study that challenges the dogma that the width of laminectomy influences the development of postoperative C5 palsy. However, the major limitation of the study was the lack of direct magnetic resonance imaging based visualization of the preoperative and postoperative cord and foraminal morphology.

**Contributed by Dr. Mazda K. Turel**

Hoy K, et al. Addition of TLIF does not improve outcome over standard posterior instrumented fusion. 5-10 year long-term follow-up: Results from a RCT. Eur Spine J 2016 May 7. [Epub ahead of print]

The use of inter-body device in lumbar fusions has been difficult to validate as only a few long-term randomized control trials (RCTs) are available. Between 2003 and 2005, 100 patients entered a RCT that investigated the clinical outcome between the transforaminal lumbar inter-body fusion (TLIF) and posterolateral instrumented lumbar fusion (PLF). The patients suffered from low back pain due to segmental instability, disc degeneration, former disc herniation, or spondylolisthesis (Meyerding grade <2). Functional outcome parameters such as Dallas pain questionnaire (DPQ), short form (SF)-36, low back pain questionnaire (LBRS), and Oswestry disability index (ODI) were registered prospectively, and after 5-10 years. Follow-up reached 93 % of the recruited patients (94 %, \( n = 44 \) in the PLF and 92 %, \( n = 44 \) in the TLIF group). The mean follow-up was 8.6 years (range 5-10 years). The mean age at follow-up was 59 years. The reoperation rate when considered in the long-term perspective was equal among the groups, being 14 % each. The mean scores on a scale of 0-10 were as follows: Back pain 3.8 (mean), TLIF (3.65) and PLF (3.97); and, leg pain 2.68 (mean), TLIF (2.90) and PLF (2.48). There was no difference in the functional outcome between the groups (\( P = 0.93 \)). Overall, global satisfaction with the primary intervention at 8.6 years was 76 % (75 % in the TLIF and 77 % in the PLF group). In the long-term perspective, patients who had undergone TLIF did not experience better outcome scores. With the growing popularity of MIS interbody fusion and now the expandable cage technology, this might be an important study to consider.

**Contributed by Dr. Mazda K. Turel**

This was a multicenter, prospective analysis of consecutive adult spinal deformity (ASD) patients opting for the operative or nonoperative care. Operative and nonoperative patients were propensity matched with the baseline Oswestry Disability Index, Scoliosis Research Society-22r, thoracolumbar/lumbar Cobb angle, pelvic incidence-to-lumbar lordosis mismatch (PI-LL), and leg pain score. Analyses were confined to patients with a minimum of 2 years of follow-up. 286 patients, who underwent an operation, and 403 non-operative patients met the criteria, with their mean ages being 53 and 55 years, with the 2-year follow-up rates being 86% and 55%, and the mean follow-up duration being 24.7 and 24.8 months, respectively. At baseline, the operative patients had a significantly worse health-related quality of life (HRQOL) based on all the measures assessed ($P < 0.001$), and had a worse deformity based on pelvic tilt, pelvic incidence-to-lumbar lordosis mismatch, and sagittal vertical axis ($P \leq 0.002$). At the minimum 2-year follow-up, all HRQOL measures assessed significantly improved for the operative patients ($P < 0.001$), but none improved significantly for the non-operative patients, except for modest improvements in the Scoliosis Research Society-22r pain ($P = 0.04$) and satisfaction ($P < 0.001$) domains. On the basis of matched operative-nonoperative cohorts (97 in each group), operative patients had a significantly better HRQOL at follow-up for all measures assessed ($P < 0.001$), except for the Short Form-36 mental component score ($P = 0.06$). At the minimum 2-year follow-up, 71.5% of operative patients had $\geq 1$ complications. The authors concluded that operative treatment for ASD can provide significant improvement of HRQOL at a minimum 2-year follow-up. In contrast, nonoperative treatment on an average, maintains presenting levels of pain and disability.

Contributed by Dr. Mazda K. Turel


The authors aimed to determine cut-offs between mild, moderate and severe myelopathy on the modified Japanese Orthopedic Association (mJOA) score. Between December 2005 and January 2011, 757 patients with clinically diagnosed degenerative cervical myelopathy (DCM) were enrolled in the prospective AOSpine North America ($n = 278$) or International ($n = 479$) study at 26 sites. Their functional status and quality of life were evaluated at baseline using a variety of outcome measures. Using the Nurick score as an anchor, receiver operating curve (ROC) analysis was conducted to determine the cut-offs between mild, moderate and severe disease. A mJOA score of 14 was determined to be the cut-off between mild and moderate myelopathy and a mJOA score of 11 was the cut-off score between moderate and severe disease. Patients in the severe myelopathy group ($n = 254$) had significantly reduced quality of life and functional status and a greater number of signs and symptoms compared to patients classified as mild ($n = 190$) or moderate ($n = 296$). The authors concluded that mild myelopathy could be defined as mJOA from 15 to 17, moderate as mJOA from 12 to 14 and severe as mJOA from 0 to 11. These categories should be adopted worldwide to standardize clinical assessment of DCM.

Contributed by Dr. Mazda K. Turel


The aim of the study was to compare the outcome of surgery in patients with lumbar canal stenosis (LCS) based on magnetic resonance imaging (MRI) morphology. This was a prospective study of 96 consecutive patients who underwent surgery at 43 levels of LCS (from L3-L4 to L5-S1). Using patterns on T2 axial MRI, the type of stenosis was determined for each patient. The Swiss Spinal Stenosis Score (SSS) was used to evaluate the patients’ functionality and outcomes. The definition of treatment success was based on the criteria developed by Stucki et al. Demographic characteristics and post-operative outcomes were compared between the trefoil, triangular, and pin-hole groups. Finally, correlation between the SSS score and the MRI morphology was assessed. The mean age of the patients was 58.4 ($SD = 8.9$) years. Post-treatment satisfaction was observed in a large portion of the patients (87.5%). The trefoil group ($n = 44$), triangular group ($n = 38$), and pin-hole group ($n = 14$) had similar pre-operative Swiss Spinal Stenosis Score and were not significantly different in age, operative time, blood loss, duration of symptoms, walking distance, symptom severity and physical function (all $P > 0.4$). No correlation between the SSS score and the magnetic resonance imaging (MRI)
morphology was observed. The findings suggest that the type of stenosis based on MRI morphology is not indicative of surgical outcome among patients with lumbar canal stenosis who undergo surgery at a 1-year follow-up.

**Contributed by Dr. Mazda K. Turel**


The aim of this study was to compare rates of postoperative dysphagia, length of stay, infection, and wound complications following short and long anterior cervical discectomy and fusion (ACDF) in patients who received local intraoperative steroids and those who did not. The incidence of dysphagia was significantly lower (9.0% vs. 14.6%, *P* = 0.005) in patients who received local steroids in the long ACDF (3 or more level) group (n = 322) than a control group who did not (n = 45,432). This was not observed (*P* = 0.198) in the short ACDF (1-2 level) group who received steroids (n = 1,770) compared with a control group who did not (n = 198,230). The mean difference in the length of stay was 1 day less for patients who received local steroid in both the short and long ACDF groups (*P* < 0.0001). The combined rate of postoperative infection and wound complications was not significantly different between steroid and control groups (*P* = 0.717). This analysis of a large administrative database suggests that local intraoperative steroid is associated with a significantly reduced rate of postoperative dysphagia after a long segment ACDF and reduced the average length of stay following both long and short ACDF procedures without any increase in the rate of postoperative infection or wound complication.

**Contributed by Dr. Mazda K. Turel**

Loumeau TP, et al. A RCT comparing 7-year clinical outcomes of one level symptomatic cervical disc disease (SCDD) following ProDisc-C total disc arthroplasty (TDA) versus anterior cervical discectomy and fusion (ACDF). Eur Spine J 2016;25:2263-2270

The objective of this trial was to compare the safety and efficacy of TDA using the ProDisc-C implant versus ACDF in patients with a single-level SCDD between C3 and C7. The authors report on the single-site results from a larger multicenter trial of 13 sites using an approved US Food and Drug Administration protocol (prospective, randomized controlled non-inferiority design). The patients were randomized one-to-one to either the ProDisc-C device or ACDF. All enrollees were evaluated pre- and post-operatively at regular intervals through 84 months. Visual Analog Scale (VAS) for neck and arm pain/intensity, Neck Disability Index (NDI), Short-Form 36 (SF-36), and satisfaction were assessed. Twenty-two patients were randomized to each arm of the study. Nineteen additional patients received the ProDisc-C via continued access. The NDI improved with the ProDisc-C more than with ACDF. The total range of motion was maintained with the ProDisc-C, but diminished with the ACDF procedure. Neck and arm pain improved more in the ProDisc-C than in the ACDF group. The patient satisfaction remained higher in the ProDisc-C group at 7 years. SF-36 scores were higher in the TDA group than the ACDF group at 7 years; the difference was not clinically significant. Six additional operations (two at the same level; four at an adjacent level) were performed in the ACDF group, but none in the ProDisc-C group. The authors concluded that the ProDisc-C implant appears to be safe and effective for the treatment of SCDD. Patients with the implant retained motion at the involved segment and had a lower reoperation rate than those who had undergone the ACDF procedure.

**Contributed by Dr. Mazda K. Turel**


Surgical revascularization for adults with moyamoya disease (MD) includes direct, indirect, or combination bypasses. It is unclear which provides the best outcomes. The authors sought to determine the best surgical management for adults with MD by comparing the perioperative complications and long-term outcomes among the three bypass types. Literature databases were searched for articles reporting the revascularization bypass outcomes for adults with MD. A pooled analysis of all qualified studies and meta-analyses using only studies reporting direct comparisons of the two bypass types were performed. Overall odds ratios (ORs) comparing 2 bypass types were computed and the publication bias was assessed. Rates of perioperative and long-term hemorrhage and ischemia and favorable outcomes were compared. Forty-seven studies were analysed; 8 had level 1 or 2 evidence. Pooled analyses showed that perioperative hemorrhage rates were significantly (*P* = 0.02) lower with indirect (0%) compared with direct (3.8%; OR = 0.03) or combined (3.9%; OR = 0.03) bypasses. The meta-analysis showed that direct bypass was better at preventing long-term
hemorrhage (3.6%) than indirect bypass (4.6%; OR = 0.26, \( P = 0.02 \)). Pooled analyses showed that direct bypass (3.9%) is significantly better (\( P < 0.01 \)) than indirect (7.4%; OR = 0.51) and combined (7.9%; OR = 0.47) bypasses in preventing long-term ischemia. The meta-analysis showed that the direct bypass was better than indirect bypass in producing long-term favourable outcomes (OR = 2.62, \( P = 0.02 \)), and the pooled analysis showed that combined bypass was better than indirect bypass in producing long-term favorable outcomes (OR = 1.26, \( P = 0.02 \)). Despite the limitations of the study heterogeneity, Simpson’s paradox of using pooled analysis, and most of the studies analysed being in Japanese, the analyses suggested that the direct bypass with or without indirect augmentation provides the best outcomes for adults with MD. However, the results of this analysis need to be substantiated by a large-scale, well-designed, randomized control trial that involves multiple treatment centres around the world with diverse ethnic backgrounds.

*Contributed by Dr. Mazda K. Turel*


Aneurysmal subarachnoid hemorrhage (aSAH) may be complicated by hydrocephalus in 6.5%-67% of cases. The objectives of this study were to review the published risk factors for shunt dependency in patients with aSAH, determine the level of evidence for each factor, and calculate the magnitude of each risk factor to better guide in patient management. The authors searched PubMed and MEDLINE databases for Level A and Level B articles published through December 31, 2014, that described the factors affecting shunt dependency after aSAH and performed a systematic review and meta-analysis, stratifying the existing data according to the level of evidence. Risk factors for shunt dependency included a high Fisher grade (OR 7.74), acute hydrocephalus (OR 5.67), in-hospital complications (OR 4.91), presence of intraventricular blood (OR 3.93), a high Hunt and Hess Scale score (OR 3.25), rehemorrhage (OR 2.21), posterior circulation location of the aneurysm (OR 1.85), and age ≥60 years (OR 1.81). The only risk factor included in the meta-analysis that did not reach statistical significance was female sex (OR 1.13). Although some of these risk factors are not independent of each other, this information assists clinicians in identifying at-risk patients and in managing their treatment.

*Contributed by Dr. Mazda K. Turel*


Several small trials have inconclusively evaluated the effect of hemicraniectomy in reducing death and disability in acute ischemic stroke patients with large hemispheric infarctions. The authors compared the effects of hemicraniectomy on death and disability, with conservative treatment, in patients with large hemispheric infarctions. They calculated pooled odds ratios (ORs) and 95% confidence intervals (CIs) using random-effects models from 7 randomized trials that compared hemicraniectomy with conservative treatment in acute ischemic stroke patients. The primary end point was a favorable outcome defined by the modified Rankin Scale grades of 0 (no symptoms), 1 (no significant disability), 2 (slight disability), and 3 (moderate disability) at 6-12 month post randomization. Of the 341 total subjects randomized, the proportion of subjects who achieved a favourable outcome was significantly greater among those randomized to the hemicraniectomy group than among those randomized to the conservative treatment group (OR 2.04, \( P = 0.04 \)). Survival was also significantly greater among those randomized to the hemicraniectomy group (OR 5.56, \( P < 0.001 \)) than among those randomized to the conservative treatment group. There was a trend toward higher odds of a favorable outcome among those randomized to the hemicraniectomy group than among those randomized to the conservative treatment group in trials that permitted recruitment of patients aged 60 years or older (303 subjects analysed; OR 1.87, \( P = 0.09 \)). The authors concluded that compared with conservative treatment, the odds of achieving a favourable outcome at 6 months is approximately 2-folds higher with performance of hemicraniectomy in patients with large hemispheric infarctions.

*Contributed by Dr. Mazda K. Turel*


Microvascular decompression (MVD) is a surgical treatment for cranial nerve disorders via a small craniotomy. The postoperative pain of this procedure can be classified as
surgical site somatic pain and postcraniotomy headache similar in nature to a migraine, including its association with photophobia, nausea, and vomiting. This headache can be difficult to treat and can have a significant impact on postoperative recovery. Sumatriptan is used to treat migraine-like headaches in various settings. This single-centre randomized controlled trial investigated if postoperative administration of sumatriptan after MVD surgery impacts the quality of postoperative recovery. Fifty patients who complained of postoperative headache after MVD were randomized to receive a subcutaneous injection of sumatriptan (6 mg) or saline. The primary outcome was quality of recovery as measured by the Quality of Recovery-40 (QoR-40) score at 24 h. The QoR-40 scores were significantly higher in the sumatriptan group (median 184; interquartile range 169-196) than in the placebo group (133; 119-155; P < 0.01), suggesting a higher quality of recovery. The sumatriptan group also had significantly lower headache scores at 4, 12, and 24 h. There were no significant differences in the other secondary outcomes. Use of sumatriptan improved the quality of recovery as measured by the QoR-40, and brought about a reduction in the severity and duration of headache at 24 h after surgery. Sumatriptan is a useful alternative treatment for postcraniotomy headache. The mechanism remains unknown but could be related to stimulation of factors that lead to a reduction in headache or to mood modulation, or both, mediated by the effect of serotonin.

Contributed by Dr. Mazda K. Turel


Despite aggressive standard of care (SOC) treatment, survival of malignant gliomas remains very poor. This phase II, prospective, match-controlled, multicenter trial was conducted to assess the safety and efficacy of agatimogene besadenovec (AdV-tk) plus valacyclovir (gene-mediated cytotoxic immunotherapy [GMCI]) in combination with SOC treatment for newly diagnosed malignant glioma patients. Treatment cohort patients received SOC + GMCI and were enrolled at 4 institutions from 2006 to 2010. The preplanned, match-control cohort included all concurrent patients meeting the protocol criteria and undergoing SOC treatment at a fifth institution. AdV-tk was administered at surgery followed by SOC radiation and temozolomide. Subset analyses were preplanned, based on prognostic factors: pathological diagnosis (glioblastoma vs others) and extent of resection. Forty-eight patients completed SOC treatment + GMCI, and 134 met the control cohort criteria. The median overall survival (OS) was 17.1 months for GMCI + SOC treatment versus 13.5 months for SOC treatment alone (P = 0.04). Survival at 1, 2, and 3 years was 67%, 35%, and 19% versus 57%, 22%, and 8%, respectively. The greatest benefit was observed in patients in whom gross total resection was possible with the median overall survival (OS) being 25 versus 16.9 months (P = 0.04); and, the 1, 2, and 3-year survival being 90%, 53%, and 32% versus 64%, 28% and 6%, respectively. There were no dose-limiting toxicities; fever, fatigue, and headache were the most common GMCI-related symptoms. The authors concluded that GMCI can be safely combined with SOC treatment in newly diagnosed malignant gliomas. Survival outcomes were most notably improved in patients with minimal residual disease after gross total resection. These data should help guide future immunotherapy studies and strongly support further evaluation of GMCI in the treatment of malignant gliomas.

Contributed by Dr. Mazda K. Turel


Patients with a glioblastoma (GBM) often suffer from symptomatic epilepsy. Older antiepileptic drugs (AEDs), which affect the enzyme system cytochrome P450 have been in extensive use, but there is an increasing focus on their interactions with other drugs. This study investigated if newer AEDs with little or no enzyme effect should increasingly be preferred. Previous research has indicated that valproate improves survival in GBM. The authors investigated the impact of AEDs on overall survival in GBM patients. All GBM patients diagnosed in Norway 2004-2010 were included through a linkage of national registries, and follow-up data on malignancy and drug usage were analysed. In a multivariate cox proportional-hazards regression, AEDs were adjusted for each other and for relevant factors. Immortal time bias was eliminated with time-dependent variables. The study population was 1263 patients with histologically confirmed GBM. Carbamazepine was the most frequently prescribed AED to patients diagnosed with a GBM during 2004-2006, while levetiracetam was increasingly prescribed to patients diagnosed later on. Taking AEDs on a reimbursement code of epilepsy was not beneficial for survival. None of the six AEDs valproate, levetiracetam, carbamazepine, oxcarbazepine, lamotrigine or phenytoin significantly altered overall survival. There has been a shift in the prescriptions of AEDs to GBM patients from older to newer AEDs over time. The authors found no significant survival benefit in GBM patients either
randomized clinical trial of P

observational study of hydrocephalus management, the aim of Network (HCRN) conducted a comprehensive prospective unacceptably high. The Hydrocephalus Clinical Research The rate of cerebrospinal fluid (CSF) shunt failure remains

which was to isolate specific risk factors for shunt failure. The study followed all first-time shunt insertions in children younger than 19 years at 6 centers. Shunt failure was defined as shunt revision, subsequent endoscopic third ventriculostomy, or shunt infection. A total of 1036 children underwent initial CSF shunt placement between April 2008 and December 2011. Of these, 344 (33%) patients experienced shunt failure, including 265 malfunctions and 79 infections. The mean length of follow-up for the entire cohort was 400 days. The Cox model found that age younger than 6 months at first shunt placement (hazard ratio [HR] 1.6), a cardiac comorbidity (HR 1.4), and endoscopic placement (HR 1.9) were independently associated with reduced shunt survival. The following had no independent associations with shunt survival: Etiology, payer, center, valve design, valve programmability, the use of ultrasound or stereotactic guidance, surgeon experience and volume of surgeries performed. This was the largest prospective study reporting on children who had undergone a CSF shunt procedure for hydrocephalus. It confirms that a young age and the use of the endoscope during shunt placement are contributing risk factors for the first shunt failure and that the valve type has no impact on shunt failure. A new risk factor, an existing cardiac comorbidity, was also associated with shunt failure.

No evidence-based guideline has been approved for the postoperative management of paediatric patients with tethered cord syndrome (TCS). The purpose of this randomized clinical trial was to evaluate the effectiveness of prone positioning and acetazolamide administration on complication rates following spinal cord untethering surgeries. Patients with a primary diagnosis of TCS were randomly allocated to 1 of 4 intervention modality groups postoperatively: (1) Group A, acetazolamide administration for 10 days; (2) Group B, prone positioning for 10 days; (3) Group C, acetazolamide administration and prone positioning for 10 days; and (4) Group D, no intervention. Cerebrospinal fluid (CSF) leakage, CSF collection, wound dehiscence, operative site infection, and secondary surgical wound repair were considered as failures. A total of 161 patients were enrolled in this study (Group A, n = 39 [24.2%]; Group B, n = 41 [25.5%]; Group C, n = 39 [24.2%]; and Group D, n = 42 [26.1%]). The overall failure rate was 12.42% (20 patients). Complication rates through pooled analyses were as follows: CSF leakage (n = 9, 5.6%), CSF

from treatment with AEDs for epilepsy in general, or from the usage of six separate AEDs.

Contributed by Dr. Mazda K. Turel


The authors aimed to evaluate the biological behaviour of tumor remnants intentionally left behind in the surgical bed following incomplete excision of vestibular schwannomas [VS], and to review the relation between extent of resection and preservation of facial nerve function. A retrospective chart review of 450 patients who underwent surgery for resection of a VS over 23 years [1992-2014] was performed. Of these, 50 (11%) patients had a residual tumor intentionally left on/ around the facial nerve [near-total or subtotal excision] to preserve facial nerve function intra-operatively. 8 NF2 patients were excluded from our analysis. Of the 42 non-NF2 cases, where the tumor was intentionally left incompletely excised, 28 (67%) patients underwent subtotal resection [mean follow up 68.5 ± 39.0 months] and 14 (33%) underwent near total resection [mean follow up 72.9 ± 48.3 months]. Three patients [all in subtotal resection group] showed regrowth. This was not statistically different from the near total resection group (P = 0.31). The mean overall growth for these cases was 0.68mm ± 0.32 mm/year. In the non-NF2 group, poor facial nerve outcomes [House-Brackmann scores of III-VI were seen in 5/14 (33%) of the near total compared to 11/25 (44%) in the subtotal group. Given that the primary surgery for the VS was only for tumors that were relatively large or for those that grew during the period during which they underwent conservative treatment, the low rate of tumor remnant growth [7%] was reassuring. The authors concluded that it might be appropriate to have a lower threshold for leaving tumor on the facial nerve in non-NF2 patients, where complete resection may jeopardize facial nerve function.

Contributed by Dr. Mazda K. Turel


The rate of cerebrospinal fluid (CSF) shunt failure remains unacceptably high. The Hydrocephalus Clinical Research Network (HCRN) conducted a comprehensive prospective observational study of hydrocephalus management, the aim of which was to isolate specific risk factors for shunt failure. The study followed all first-time shunt insertions in children younger than 19 years at 6 centers. Shunt failure was defined as shunt revision, subsequent endoscopic third ventriculostomy, or shunt infection. A total of 1036 children underwent initial CSF shunt placement between April 2008 and December 2011. Of these, 344 (33%) patients experienced shunt failure, including 265 malfunctions and 79 infections. The mean length of follow-up for the entire cohort was 400 days. The Cox model found that age younger than 6 months at first shunt placement (hazard ratio [HR] 1.6), a cardiac comorbidity (HR 1.4), and endoscopic placement (HR 1.9) were independently associated with reduced shunt survival. The following had no independent associations with shunt survival: Etiology, payer, center, valve design, valve programmability, the use of ultrasound or stereotactic guidance, surgeon experience and volume of surgeries performed. This was the largest prospective study reporting on children who had undergone a CSF shunt procedure for hydrocephalus. It confirms that a young age and the use of the endoscope during shunt placement are contributing risk factors for the first shunt failure and that the valve type has no impact on shunt failure. A new risk factor, an existing cardiac comorbidity, was also associated with shunt failure.

Contributed by Dr. Mazda K. Turel


No evidence-based guideline has been approved for the postoperative management of paediatric patients with tethered cord syndrome (TCS). The purpose of this randomized clinical trial was to evaluate the effectiveness of prone positioning and acetazolamide administration on complication rates following spinal cord untethering surgeries. Patients with a primary diagnosis of TCS were randomly allocated to 1 of 4 intervention modality groups postoperatively: (1) Group A, acetazolamide administration for 10 days; (2) Group B, prone positioning for 10 days; (3) Group C, acetazolamide administration and prone positioning for 10 days; and (4) Group D, no intervention. Cerebrospinal fluid (CSF) leakage, CSF collection, wound dehiscence, operative site infection, and secondary surgical wound repair were considered as failures. A total of 161 patients were enrolled in this study (Group A, n = 39 [24.2%]; Group B, n = 41 [25.5%]; Group C, n = 39 [24.2%]; and Group D, n = 42 [26.1%]). The overall failure rate was 12.42% (20 patients). Complication rates through pooled analyses were as follows: CSF leakage (n = 9, 5.6%), CSF
collection (n = 12, 7.5%), wound dehiscence (n = 2, 1.2%), and infection of operation site (n = 3, 1.9%). Two patients (1.2%) required surgical secondary wound repair due to complications. CSF leakage and collection rates were significantly lower in patients who underwent prone positioning (P = 0.042 and 0.036, respectively). The administration of acetazolamide, either in isolation or in combination with prone positioning, not only could not significantly lower the complication rates, but also added to the burden of side effects.

Contributed by Dr. Mazda K. Turel


The authors have analysed 50 patients of residual and/or recurrent atypical meningioma, who received either stereotactic radiosurgery (SRS) or external beam radiation therapy (EBRT), to determine the predictors of progression by using the Cox regression and Kalplan-Meier analyses. Among the 50 patients, 32 patients (64%) received adjuvant radiation after subtotal resection, 12 patients (24%) received salvage radiation after progression following sub-total resection, and 6 patients (12%) received salvage radiation after recurrence following gross total resection. Among the 21 patients who received SRS (median 18 Gy), 7 had tumour progression and similarly, among the 29 patients who received EBRT, 13 had tumour progression. Spontaneous necrosis (hazard ratio [HR] = 82.3, P < 0.001), embolization necrosis (HR = 15.6, P = 0.03), and brain invasion (HR = 3.8, P = 0.008) predicted progression, whereas tumor volume (P = 0.53), SRS vs EBRT (P = 0.45), and adjuvant vs salvage therapy (P = 0.34) were not associated with progression after radiation therapy. The 2 and 5 year actuarial locoregional control rates for tumours treated with SRS/EBRT were 91%/88% and 71%/69%, respectively. Tumors with spontaneous necrosis, embolization necrosis, and no necrosis had 2- and 5-year loco-regional control rates of 76%, 92%, and 100% and 36%, 73%, and 100%, respectively (P < 0.001).

Contributed by Dr. Anant Mehrotra


The authors intended to assess the outcomes in people living for more than 10 years after surviving stroke. The authors collected the data for the population-based South London Stroke Register where an annual follow up until death of the participant was available. Survival, disability, activity, cognitive impairment, quality of life, depression and anxiety were considered as outcomes. Among the 2625 people who had first ever stroke, 262 survived for 15 years. Majority of the long term survivors were male (61%) with a median age of stroke onset of 58 years (interquartile range [IQR] 48–66). Among the 15 year survivors, 33.8% had mild disability, 14.3% had moderate disability, 15% had severe disability, and 87% were living at home. The prevalence of cognitive impairment was 30%, depression 39.1% and anxiety 34.9%. The authors concluded that one in five people survive for at least 15 years after stroke; and, poor functional, cognitive and psychological outcomes affect a substantial proportion of these long-term survivors.

Contributed by Dr. Anant Mehrotra

Murthy SB, et al. Rate of perihaematomal oedema expansion is associated with poor clinical outcomes in intracerebral haemorrhage. J Neurol Neurosurg Psychiatry doi: 10.1136/jnnp-2016-313653

The authors aimed to determine whether or not the perihaematomal edema (PHE) expansion in the first 72 hours after intracerebral haemorrhage (ICH) predicts outcome. The 596 patients included were part of the Virtual International Stroke Trials Archive. The authors calculated the PHE expansion rate using the equation: (PHE at 72 hours − PHE at baseline) (time to 72-hour CT scan − time to baseline CT scan). Mortality and a poor 90-day outcome (modified Rankin Scale score of > 3) were considered as outcomes of interest. The median haematoma volume at baseline was 15 ml with the median PHE volume of 8.7 ml. The median PHE expansion rate was 0.31 ml/hour (IQR 0.12–0.55). The odds of mortality were greater with an increasing PHE expansion rate (OR 2.63, CI 1.10 to 6.25), while the odds of poor outcome also increased with a greater PHE growth (OR 1.67, CI 1.28 to 2.39). The PHE growth had an inverse relationship with female sex but baseline haematoma volume had a direct relation. The authors concluded that the rate of PHE growth over 72 hours was an independent predictor of mortality and poor functional outcome in ICH.

Contributed by Dr. Anant Mehrotra


The authors conducted a randomised, double blind, placebo controlled phase 2/3 trial at 12 hospitals in Japan to assess the safety and efficacy of thalidomide for treatment of
Nonatherosclerotic isolated middle cerebral artery disease may be early manifestation of moyamoya disease. Stroke doi: 10.1161/STROKEAHA.116.012751

The authors prospectively enrolled 81 patients less than 60 years old with transient ischaemic attack or stroke caused by middle cerebral artery steno-occlusive disease (MCAD). The exclusion criteria included patients with a confirmed diagnosis of moyamoya disease, dissection, or vasculitis; with significant steno-occlusion in cerebral arteries other than the MCA; or with a high-risk cardioembolic source. The patients were classified into the atherosclerosis group (45; 55.6%) and into the nonatherosclerosis group (36; 44.4%) by using high-resolution magnetic resonance imaging (MRI). The nonatherosclerosis group was significantly younger ($P = 0.013$), showed a lower homocysteine level ($P < 0.001$), thinner intima-media thickness ($P = 0.006$), had a smaller number of vascular risk factors ($P = 0.001$) than the atherosclerosis group. The authors concluded that moyamoya disease is responsible for a significant portion of non-atherosclerotic lesions of MCA.

Contributed by Anant Mehrotra


Considering the increased use of tractography in visualizing cranial nerves (CNs) in recent years and the drawbacks of currently used technology, the authors hypothesized that a substantial improvement in image resolution could be achieved with high-angle diffusion magnetic resonance imaging and atlas-based fiber tracking. Thus, they aimed to study the CNs in healthy subjects as well as in patients with brain tumors using high-definition fiber tractography. They subjected five neurologically healthy adults and 3 patients with brain tumors to diffusion spectrum imaging that allowed high-angular-resolution fiber tracking. Additionally, an atlas of space fiber tracking of CNs was constructed from the Human Connectome Project data comprising 488-subject diffusion imaging that allowed high-angular-resolution fiber tracking. The entire optic radiation, medial longitudinal fasciculus, spinal trigeminal nucleus/tract, petroclival portion of the abducens nerve, and intra brainstem portion of the facial nerve from the root exit zone to the adjacent abducens nucleus could also be identified. This, according to the authors, suggested that the high-angular-resolution fiber tracking could potentially distinguish the facial nerve from the vestibulocochlear nerve complex. In patients with tumors, tractography showed displacement of CNs which could be confirmed during surgery. The authors concluded that high-angular-resolution fiber tracking and atlas-based fiber tracking, could identify all CNs in unprecedented details and such a tool could be extremely helpful in localization of CNs during surgical planning.

Contributed by Dr. Kuntal Kanti Das


In this study, the authors focused on the patients with medically refractory epilepsy in whom PET studies were deemed normal by visual assessment. They aimed to evaluate the usefulness of statistical parametric mapping (SPM) in improving the sensitivity of [18F] fluorodeoxyglucose–positron emission tomography (18F-FDG-PET) to localize the seizure-onset zone (SOZ) in such dubious cases. They studied 55 patients with medically refractory epilepsy whose 18F-FDG-PET was...
visualized as normal. Twenty of these patients had ultimately undergone surgical intervention. PET images were analyzed by SPM8 using a corrected $P$ value of $P < 0.05$ and three uncorrected $P$ values of $P < 0.0001$, $P < 0.001$, and $P < 0.005$, matched with minimum cluster sizes of $k > 0$, $k > 20$, $k > 100$, and $k > 200$, respectively. They compared SPM-identified potential seizure zone (SZ) to the SOZ. The latter was determined by a consensus during patient management meetings in their epilepsy unit, taking into account all the presurgical tests. Studies in which the SPM-identified potential SZ was concordant with the SOZ were considered “correctly localizing.” The SPM threshold combination with the least restrictive $P$ value and greatest minimum cluster size achieved the highest rate of correctly localizing studies. When $P < 0.005/k > 200$ was used, 40% (22/55) of studies were correctly localizing, and the concordance obtained in the surgically intervened subgroup was substantial ($k = 0.607$, 95% confidence interval [CI] 0.258–0.957). The latter figure, as per the authors, was comparable to the concordance obtained by magnetic resonance imaging [MRI] ($k = 0.783$, 95% CI 0.509–1.000). Thus, the authors concluded that SPM could potentially offer improved SOZ localization in 18F-FDG-PET studies that are negative on visual assessment. They recommended that the statistical parametric maps could be thresholded with liberal $P$ values and restrictive cluster sizes to enhance the sensitivity of 18F-FDG-PET studies.

Contributed by Dr. Kuntal Kanti Das


In this paper, the authors intended to elucidate the different mechanisms underlying chronic pain and altered pain sensitivity seen in patients with traumatic spinal cord injury (SCI). Such an understanding, the authors believe, could lead to better diagnostic capabilities and improved treatments of these patients. The authors included 16 participants with cervical ($n = 14$) and upper thoracic ($n = 2$) injuries with post traumatic pain. Thermal stimulus was applied to the medial palm (C8 dermatome) as a series of repeated brief noxious thermal pulses in these patients. Functional magnetic resonance imaging (fMRI) of the brainstem and spinal cord was used to determine the neuronal activity evoked by the noxious stimulation, and connectivity between regions was characterized with structural equation modelling (SEM). The results showed that the pain ratings, the location and magnitude of blood oxygenation–level dependent fMRI results, and connectivity assessed with SEM varied widely across participants. Their results varied in relation to the perceived pain and the level/severity of injuries, particularly in terms of the hypothalamic connectivity with other regions, and descending modulation via the periaqueductal gray matter-rostral ventromedial medulla-cord pathway. The authors thus concluded that each patient had their individual unique response to pain and the ability to demonstrate pain processing mechanism in individuals with SCI using fMRI was a significant technological advance.

Contributed by Dr. Kuntal Kanti Das


The authors of this study aimed to explore the micro-level structural damage in the motion segments subjected to vibration at subcritical peak loads. The background on which this study was based was related to certain epidemiological evidences that suggested that cumulative whole body vibration could damage the disc and thus play an important role in low back pain. Twenty-nine healthy mature ovine lumbar motion segments were subjected to 7° flexion and vibration loading (1300 ± 500 N) in a sinusoidal waveform at 5 Hz to simulate moderately severe physiologic exposure. The exposure was dichotomized into medium dose (20,000 to 48,000 cycles) or high dose (70,000 to 120,000 cycles). The discs were microstructurally analysed at these doses. The authors observed that there was no large drop in displacement over the duration of both vibration doses, thus ruling out any catastrophic failure in all the tests. The tested discs experienced internal damage in the form of delamination and disruption to the inner and mid-annular layers as well as diffuse tracking of the nucleus material involving both the posterior and anterior regions. Tearing between the inner disc and endplate was also observed, albeit less conspicuously. The anulus fibrosus showed severe changes like intralamellar tearing and buckling with obvious strain distortion involving the bridging elements within its wall. This led the authors to the conclusion that vibration loading could lead to delamination and disruption of the inner and mid-annular layers and limited diffuse tracking of nucleus material. These subtle changes could eventually lead to initiation of the degenerative cascade via micro-level disruption, and finally cell death and altered nutrient pathways.

Contributed by Dr. Kuntal Kanti Das

The authors undertook this study to explore a better imaging tool to visualize the subthalamic nucleus (STN), a well-established target for deep brain stimulation (DBS) for motor symptoms in patients with pharmacoresistant Parkinson’s disease (PD). They mention that the current gold standard, T2-weighted imaging (T2WI) at 1.5 Tesla (T) was unable to allow a thorough visualization of the STN, optimize DBS lead implantation, and enlarge DBS diffusion, factors very much essential for the success of this procedure. The authors first designed a spin-echo three-dimensional (3D) SPACE (sampling perfection with application-optimized contrasts using different flip angle evolutions) fluid attenuated inversion recovery (FLAIR) sequence at 3 T. Then they validated the same histologically in 2 nonhuman primates. Finally, they applied the sequence to 10 patients with PD and the findings were compared in a double-blinded manner with a control group of 10 other patients with PD in whom STN targeting was performed using T2WI. The authors observed that the overlap between the nonhuman primate STNs segmentation on 3D-histological and on 3D-SPACE-FLAIR volumes was high for the 3 most anterior quarters (mean [± SD] Dice scores 0.73 ± 0.11, 0.74 ± 0.06, and 0.60 ± 0.09). The limits of the STN, as determined by the 3D-SPACE-FLAIR sequence, were more consistent with electrophysiological edges than those determined by T2WI (0.9 vs 1.4 mm, respectively), thus rendering the former a definite edge in a physiological treatment like DBS. Additionally, the imaging contrast of the STN on the 3D-SPACE-FLAIR sequence was 4 times higher ($P < 0.05$) than the conventional T2WI. The improvement in the Unified Parkinson’s Disease Rating Scale Part III score (off medication, on stimulation) 12 months after the operation was significantly higher in patients who underwent 3D-SPACE-FLAIR–guided implantation than for those in whom T2WI was used (62.2% vs 43.6%, respectively; $P < 0.05$). The total electrical energy delivered also decreased by 36.3% with the 3D-SPACE-FLAIR sequence ($P < 0.05$). Thus, the authors concluded that 3D-SPACE-FLAIR sequences at 3 T improved STN lead placement under stereotactic conditions, improved the clinical outcome, and increased the benefit/risk ratio of STN-DBS surgery in patients with PD.

Contributed by Dr. Kuntal Kanti Das