COMMENTARY

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

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Conversion disorder is a common somatic symptom disorder characterized by non-specific symptoms not explained by the underlying organic disease. The systemic review of patients with motor symptoms secondary to conversion disorder shows a highly variable recovery rate varying from 10% to 90%. It is not clear whether these patients use hospital care facilities transiently or have repeated admissions. The present study was performed to study the hospital revisits of all the patients discharged with the diagnosis of conversion disorder from all non-federal emergency departments and acute care hospitals in California, Florida and New York from the year January 2005 to December 2011. The revisit rate was compared between the patients diagnosed with conversion reaction to those with seizure disorder and transient global amnesia. The authors found the hospital revisit rate of patients with conversion disorder was significantly higher as compared to patients with transient global amnesia and seizure disorder. The results signify the fact that the conversion disorder is not an acute-stress induced transient event but a manifestation of chronic neuropsychiatric background with a significant hospital based burden of disease.

Contributed by Dr Vimal Paliwal


A change in the eating behaviour is well known in patients with behaviour variant of fronto-temporal dementia (bvFTD). Eating behaviour changes are increasingly recognized in patients with semantic dementia. However, most of the studies have used the care-giver questionnaires to assess the eating behaviour and food preferences of these patients. The present study used more ecological methods to assess the eating behaviour of patients with bvFTD. The present study

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Intermittent head drops (IHD) refer to the episodic flexion-extension movements of head occurring once to several times per day. Usually, these conditions are thought to be epileptic, namely atonic epileptic seizures, infantile spasms or negative myoclonus of neck. The review deals with all other causes of intermittent head drops published from 1980 to February 2015. The authors broadly characterized the differential spectrum. J Neurol Neurosurg Psychiatry 2016;87:414-419

Interruption of head drops refer to the episodic movement disorders, conditions associated with IHD include Huntington chorea, chorea-athetosis, Gilles de la Tourette’s syndrome, benign paroxysmal torticollis of infancy, stereotypes seen in head banging in infants and children. Cataplectic attacks associated with emotions in narcolepsy is another sleep related cause. IHD may be seen in unclassified conditions like head nodding, a type of endemic epileptic encephalopathy extensively described from Sudan especially in the 1960s, Sandifer syndrome may be seen in infants. IHD of unknown origin in infants like benign myoclonus of infancy and benign non-epileptic attacks in infancy may also occur.

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In this study, the authors used transcranial direct current stimulation of the primary motor cortex on the left side (corresponding to the hand area) to assess the improvement in the language function of patients with post-stroke aphasia. Twenty-six patients were included in the study. All 26 patients received intensive naming therapy for 2 weeks. All patients were randomly shown 344 pictures to name. The 60 pictures that were not named correctly for each patient were used to train in subsequent training period and were called trained items. Rest of the 284 items were regarded as ‘untrained’ items and were used to assess the transfer effect. Thirteen patients each were randomly assigned to the treatment arm with transcranial direct current stimulation and the sham transcranial stimulation group. Each patient was immediately assessed following treatment and at a 6-month post-treatment follow up for trained items, transfer effect and everyday communication. The authors found that both the treatment arm and the sham-group did better than the baseline score but the treatment group did better than the sham-group during the immediate post-treatment and at 6 month assessment for naming and routine communication. The authors claim that this is the first randomized study that shows the sustained benefit of anode-transcranial direct current stimulation in patients with chronic aphasia.
Contributed by Dr Vimal Paliwal

Navarro V, et al. Motor cortex and hippocampus are the two main cortical targets in LGI 1-antibody encephalitis. Brain 2016;139:1079-93

LGI 1 antibody associated encephalitis is a recently described autoimmune encephalitis which was initially diagnosed by associated voltage-gated potassium channel antibody (VGKC-antibody). LGI1 antibody and contactin-associated protein antibody (Casp2) are associated within the complex regulating the VGKCs. Since, this is a recently identified entity, the natural history of the LGI1 antibody associated encephalitis is not known. Whether the antibody targets the cortex or the sub-cortical structures is also not known. Therefore, the author described 32 patients of LGI1 antibody encephalitis who were identified retrospectively. The initial symptoms were unilateral tonic-dystonic seizures in 11 patients, and temporal lobe focal seizures in 13 patients. At a later stage, 22 patients displayed tonic-dystonic seizures and 29 presented with frequent seizures including status epilepticus. Cognitive impairment was evident in 30 patients. Initially, 8 patients exhibited hippocampal hyperintensity whereas 17 patients showed hippocampal hyperintensity at a later stage. The authors stated that the origin of tonic-dystonic seizures was cortical as shown by the polymyographic tests; on EEG, these patients show a contralateral, frontal slow-wave preceding the EMG artefact secondary to the tonic-dystonic spell. The also showed a strong contralateral frontal cortical hypermetabolism on fludeoxyglucose (18F) positron emission tomography (FDG-PET) further bolstering their claim of there being cortical targets of the LGI1 antibody.

Contributed by Dr Vimal Paliwal


The authors studied the volumetric assessment of brain in patients with chronic migraine. Twenty four patients with chronic migraine and 24 controls were included in the study. High resolution anatomical magnetic resonance images were acquired that were processed using an automated segmentation method (FreeSurfer). White matter abnormality were also compared between the two groups. Among the different brain areas studied, the authors found that the volume of the cerebellum and brainstem were found to be smaller in chronic migraine patients compared to the healthy controls. The authors did not found any significant correlation between the clinical variables and the volume decrease in these regions. The authors speculated whether the volume decrease was a cause or effect of chronic migraine. Further clarification of this question would require longitudinal volumetric studies in these patients.

Contributed by Dr Vimal Paliwal


There is an ongoing debate of the cause-effect relationship of migraine with patent foramen ovale (PFO) and of the utility of closing the foramen ovale for seeking improvement in migraine. The authors conducted an electronic database search to study the relationship of foramen ovale with migraine and the utility of closure of foramen ovale. The search was performed to study: (1) The prevalence of migraine in patients with a PFO; (2) the prevalence of PFO in migraine; and, (3) the effect of closure of PFO on migraine. Authors found 14 observational studies with 2602 patients with PFO and 20 studies with migraine. They found the prevalence of migraine ranging from 16% to 64% in PFO, and the prevalence of PFO ranging from 15% to 83% in migraine. Twenty observational studies examined the effect of PFO closure on migraine. Migraine resolution was reported in 10% to 83% of patients, with an improvement in 14% to 83%; no change in 1% to 54%, and worsening in 4% to 8% patients. Three randomized trials (234 patients) failed to meet the primary end point of migraine resolution (50% reduction in migraine at 1 year). Therefore, the authors concluded that there is no good quality evidence to support a link between migraine and a PFO and that PFO closure does not prevent migraine attacks.

Contributed by Dr Vimal Paliwal


Natalizumab is an immunomodulating agent used in the treatment of multiple sclerosis. Multifocal leukoencephalopathy is a known complication of natalizumab therapy caused by John Cunningham (JC) virus infection. In this study, the authors have evaluated the effectiveness and tolerability of fingolimod and rituximab in patients who were switched to these agents from natalizumab therapy due to JC virus seropositivity. Authors compared the outcomes for 256 relapsing-remitting multiple sclerosis (RRMS) patients (net usage of fingolimod
in 55% patients), from three Swedish multiple sclerosis centers (Stockholm, n = 156, fingolimod 51%; Gothenburg, n = 64, fingolimod 88%; and, Umeå, n = 36, fingolimod 19%). These patients were on natalizumab therapy and had JC virus positive serology. Within 1.5 years of cessation of natalizumab, 1.8% (rituximab) and 17.6% (fingolimod) of patients experienced a clinical relapse (hazard ratio for rituximab = 0.10, 95% confidence interval [CI] = 0.02-0.43). The hazard ratio (favouring rituximab) for adverse events (5.3% vs 21.1%) and treatment discontinuation (1.8% vs 28.2%) were 0.25 (95% CI = 0.10-0.59) and 0.07 (95% CI = 0.02-0.30), respectively. Contrast-enhancing lesions were found in 1.4% (rituximab) versus 24.2% (fingolimod) on MRI examinations (odds ratio = 0.05, 95% CI = 0.00-0.22). Differences remained significant even after adjusting for possible confounders (age, sex, and disability status, time on natalizumab, washout time, follow-up time, and study center). These findings suggest an improved effectiveness and tolerability of rituximab compared with fingolimod in stable RRMS patients who switch from natalizumab due to JC virus antibody positivity. Although other confounding factors could not be ruled out, the valid reason for shifting from natalizumab to rituximab or fingolimod mitigates these concerns.

Contributed by Dr Abhijeet Kumar Kohat


The revised criteria of international classification of headache disorders (ICHD) – III- beta version was released in 2013. In this revised criteria, ipsilateral sensation of fullness in the ear and ipsilateral forehead/facial flushing were added to the diagnostic criteria of headache. In this cross sectional study, the authors evaluated the possible additional value of these symptoms in the diagnosis of cluster headache. Cluster headache patients, who were not fulfilling the ICHD II but fulfilling the ICHD III criteria were included using a web based questionnaire. The reported response rate was 916/1138 (80.5%). Of all the 573 patients with cluster headache, according to the ICHD-II criteria, 192 (33.5%) reported an ipsilateral ear fullness and 113 (19.7%) reported facial flushing during the attacks. There were no differences in reporting ipsilateral ear fullness and facial flushing between patients who received a diagnosis of cluster headache and patients who did not. None of the patients who did not fulfil the entire ICHD-II criteria could be categorized as having cluster headache, according to the ICHD-III beta criteria. The authors concluded that the results of this study do not support the addition of ear fullness and facial flushing to the new ICHD-III beta criteria.

Contributed by Dr Abhijeet Kumar Kohat


The caregivers’ own health may suffer during the care of critically ill patients. This study was aimed to determine which characteristics of patients or caregivers were associated with caregiver’s health outcomes during the first year after patient discharge from an intensive care unit (ICU). In this study, 280 caregivers of patients who had received 7 or more days of mechanical ventilation in an intensive care unit (ICU) were enrolled. Information regarding the caregiver and patient characteristics were collected using hospital data and self-administered questionnaires that included the caregiver’s depressive symptoms, psychological well-being, health-related quality of life, sense of control over life, and effect of providing care on other activities. Assessments were done after 7 days and at 3, 6, and 12 months after ICU discharge. The caregivers’ mean age was 53 years, 70% were women, and 61% were caring for a spouse. Among the caregivers, 67% initially, and 43% at 1 year, reported high levels of depressive symptoms. Depressive symptoms decreased partially in 84% of the caregivers but did not in 16%. A younger age, a greater effect of patient care on other activities, less social support, less sense of control over life, and less personal growth were associated with worse mental health outcome in caregivers. No patient variables were consistently associated with the caregiver outcomes over time. In this study, most caregivers of critically ill patients reported high levels of depressive symptoms, which commonly persisted for up to 1 year.

Contributed by Dr Abhijeet Kumar Kohat


Patients after subarachnoid hemorrhage (SAH) are at risk of delayed cerebral ischemia and infarct, attributed to the impaired cerebral autoregulation. In contrast, patients with intact autoregulation appear not to experience delayed ischemia after SAH. This study was aimed to understand the physiological basis of impaired cerebral autoregulation in SAH and its relationship to neurologic outcomes. The study was performed in over 121 patients of non-traumatic SAH admitted in the neurointensive critical care unit from March 2010 to May 2015. Vasospasm was confirmed by digital subtraction angiography. Delayed cerebral ischemia (DCI) was defined as the presence of new cerebral infarction on high-resolution CT. Cerebral blood flow and beat-by-beat pressure were...
recorded daily on days 2-4 after admission. Autoregulatory capacity was quantified from pressure flow relation via projection pursuit regression. The main outcome was early alteration in the autoregulatory mechanisms. 43 patients developed only vasospasm, 9 only DCI, and 14 both. Patients who developed DCI had a distinct autoregulatory profile compared to patients who did not develop secondary complications or those who developed only vasospasm. The rate of decrease in the flow was significantly steeper in response to transient reductions in pressure. The rate of increase in flow was markedly lower, suggesting a diminished ability to increase flow despite transient increases in pressure. The authors concluded that the extent and nature of impairment in autoregulation accurately predicted the development of neurological complications on an individual patient level, and suggests potentially differential impairments in the underlying physiologic mechanisms. A better understanding of these impairments can lead to targeted interventions to decrease neurological morbidity.

*Contributed by Dr Abhijeet Kumar Kohat*


The International Panel for NMO Diagnosis (IPND) developed a revised diagnostic criteria using systematic literature reviews and electronic surveys to facilitate consensus. The new nomenclature defines the unifying term NMO spectrum disorders (NMOSD), which is stratified further by serologic testing (NMOSD with or without aquaporin-4 immunoglobulin G antibodies [AQP4-IgG]). This study was aimed to evaluate the application of the 2015 IPND criteria to consecutive cases of NMOSD in 594 patients with CNS inflammatory diseases. Confirmation of the patients’ AQP4-IgG status throughout the disease duration (mean 9.2 ± 5.7 years) using repeated assays, including enzyme linked immunosorbent assay [ELISA] and cell-based assay, was performed. A total of 252 patients fulfilled the IPND criteria (AQP4-IgG positive: 226 [90%], AQP4-IgG negative: 26 [10%]). Of these, 136 (54%) patients met the 2006 NMO criteria. When the authors assumed an unknown AQP4-IgG status in the confirmed NMOSD group with AQP4-IgG, 162 of 226 (72%) patients with AQP4-IgG were classified as having NMOSD by the IPND criteria. The majority of patients were diagnosed with NMOSD within 2 years of onset (73%) or after a second attack (72%). Acute myelitis (83%) and optic neuritis (65%) were the most common clinical features throughout the disease duration. Optic neuritis (42%) was the most common initial manifestation, followed by acute myelitis (38%) and area postrema syndrome (14%). With the above observations, the authors concluded that the IPND criteria reflected the broader clinical spectrum of NMOSD well and provided a markedly improved diagnostic yield compared to the previous criteria, even in patients with an unknown AQP4-IgG status.

*Contributed by Dr Abhijeet Kumar Kohat*

Bathgate CJ, et al. Objective but not subjective short sleep duration associated with increased risk for hypertension in individuals with insomnia. Sleep 2016;39:1037-45

Insomnia is, by far, the most commonly encountered sleep disorder in medical practice. There are paucity of studies that have linked insomnia and hypertension, as has already been carried out with obstructive sleep apnoea. This study was aimed to determine the prevalence of hypertension in individuals with insomnia who have a short total sleep duration (less than 6 hours) compared to those who have insomnia of more than 6 hours sleep duration using both objective and subjective measures of total sleep duration. This was a cross sectional observational study that included 255 adult volunteers (n = 165 women; 64.7%, Mean age = 46.2 years, standard deviation 13.7 years) who were meeting the diagnostic criteria for the presence of an insomnia disorder. Two nights of polysomnography, 2 weeks of sleep diaries, questionnaires focused on sleep, medical, psychological, and health history, including presence/absence of hypertension were recorded. Logistic regressions assessed the odds ratios of hypertension among persons with insomnia with a short sleep duration ≤6 h compared to persons with insomnia with a sleep duration ≥6 h, measured both objectively and subjectively. Using the objective total sleep duration, individuals with insomnia and a short sleep duration ≤6 h were associated with a 3.59 increased risk of reporting hypertension as compared to individuals with insomnia with a sleep duration ≥6 h. Increased risk for hypertension was independent of major confounding factors frequently associated with insomnia or hypertension. No significant risk was observed using subjectively determined total sleep time groups. Receiver operating characteristic curve analysis found that the best balance of sensitivity and specificity using subjective total sleep time was at a 6-h cut-off, but the area under the receiver operating characteristic curve showed a low accuracy and did not have good discriminant value. Authors concluded that the objectively measured short sleep duration increased the odds of reporting hypertension more than threefold. This relationship was not significant for subjectively measured sleep duration.

The association of primary headaches, especially of migraine, with RLS has recently attracted much attention. The prevalence of migraine was reported to be higher in patients with RLS than in the general population. Similarly, a higher severity of restless leg syndrome (RLS) in migraine patients has been reported. The present study was aimed to study the prevalence, severity and correlation between the sleep quality and RLS in a population of well-defined migraine patients. This was a cross sectional observation study. 2385 migraine and RLS patients diagnosed by the International Classification of Headache Disorders (ICHD)-IIb and 332 non-headache controls were recruited. RLS severity (International RLS Study Group severity scale) and sleep quality (Pittsburgh Sleep Quality Index) were assessed. Risk factors for RLS and RLS severity were calculated using multivariable-adjusted regression models. Prevalence of RLS in migraine was higher than in controls (16.9% vs. 8.7%; 95% CI 1.18-2.86; \( P = 0.008 \)) and more severe (adjusted severity score 14.5 ± 0.5 vs. 12.0 ± 1.1; \( P = 0.036 \)). There were more poor sleepers amongst the migraineurs (50.1% vs. 25.6%; \( P < 0.001 \)). Poorer sleep quality was independently associated with RLS occurrence (odds ratio 1.08; \( P < 0.001 \)) and RLS severity (\( P < 0.001 \)) in migraine patients. It was concluded that RLS is not only twice as prevalent but also more severe in patients suffering from migraine, and was associated with decreased sleep quality.

Asuzu D, et al. TURN Score predicts 24-hour cerebral edema after IV thrombolysis. Neurocrit Care 2016;24:381-8

Development of cerebral edema after IV thrombolysis is associated with a poorer outcome. Asuzu D. et al., had recently described the TURN score (Thrombolysis risk Using mRS and NIHSS) which predicts the 90-day outcome in acute ischemic stroke patients after intravenous (IV) thrombolysis. The purpose of the present study was to evaluate the ability of the TURN score to predict the development of 24-h cerebral oedema. Retrospective data were analysed from 303 patients who received IV recombinant tissue plasminogen activator (rt-PA) during the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA trial. Measures of brain swelling included oedema, mass effect and midline shift assessed at baseline, at 24 h and new onset oedema at 24 h. Outcome was assessed using intracerebral haemorrhage (ICH), symptomatic intracerebral haemorrhage (sICH), 90-day severe outcome, and 90-day mortality. Statistical associations were assessed by logistic regression reporting odds ratios (OR) and by areas under the receiver operating characteristic curves (AUROC). Baseline brain swelling did not predict a poor outcome; however, the 24-h brain swelling predicted ICH (OR 5.69, \( P < 0.001 \)), sICH (OR 9.50, \( P = 0.01 \)), 90-day severity outcome (OR 7.10, \( P < 0.001 \)), and 90-day mortality (OR 5.65, \( P = 0.01 \)). Similar results were seen for new brain swelling at 24 h. TURN predicted 24-hour brain swelling (OR 2.5, \( P < 0.001 \)); area under receiver operating characteristic curve [AUROC] 0.69, 95% CI, 0.630-0.75) and new brain swelling at 24 h (OR 2.1, \( P < 0.001 \); AUROC 0.67, 95% CI 0.61-0.73). These findings indicate that cerebral oedema at 24 h is associated with a poor outcome and a higher 90-day mortality. TURN predicts the characteristic of ischemic stroke patients who will develop 24-h cerebral oedema after IV thrombolysis.


Ventriculostomy can cause cerebrospinal fluid infections as contamination of the cerebrospinal fluid, colonization of the shunt tube, or frank ventriculitis may occur. The aim of the present study was to explore the characteristics of ventriculostomy associated infections (VAI) and their effect on the outcome of intracerebral haemorrhage (ICH). This was a retrospective cohort study. ICH patients requiring ventriculostomy with and without VAI were identified from 2002 to 2011 using International Classification of Disease (ICD)-9 codes. The demographics, co- morbidities, hospital characteristics, inpatient outcomes, and resource utilization measures were compared between the two groups. Pearson’s Chi-square and Wilcoxon-Mann-Whitney tests were used for categorical and continuous variables, respectively. Logistic regression was used to analyse the predictors of VAI. There was an increasing rate of ventriculostomy utilization in ICH, which increased from 5.7 % in 2002-2003 to 7.0 % in 2010-2011 (\( P < 0.001 \)), and the rate of VAI also showed a gradual upward trend from 6.1 to 7.0 % across the same interval (\( P < 0.001 \)). The VAI group was associated with higher inpatient mortality (41.2 vs. 36.5 %, \( P < 0.001 \)) and it remained higher despite controlling the confounding factors. The VAI group had a longer length of hospital stay and a higher inflation-adjusted cost of care. The predictors of
VAI were a higher age, the male gender, a higher Charlson’s comorbidity scores, a longer length of stay, and the presence of systemic infections, mainly pneumonia and sepsis. The authors concluded that VAI resulted in a higher inpatient mortality, a more unfavourable discharge disposition, and a higher resource utilization. Steps should be taken to mitigate VAI to improve the management outcome of ICH and to decrease the hospital costs.

Contributed by Dr Abhijeet Kumar Kohat


The authors surveyed literature from the 1980s and 1990s and found the etiology of neuropathy to be idiopathic in 20%-30% of patients despite a thorough investigation. Since then, new etiologies have been recognized, and skin biopsy has been used to confirm small-fibre neuropathy. The authors reviewed the charts of 373 patients with idiopathic neuropathy who were referred to a neuropathy centre between 2002 and 2012. Among the 284 eligible patients, 93 (32.7%) remained idiopathic. The most common cause was impaired glucose metabolism (72 patients, 25.3%), including diabetes in 26 and prediabetes in 46 patients. Other etiologies were chronic inflammatory demyelinating polyneuropathy (CIDP) in 57 (20%) patients and monoclonal gammopathy in 20 (7%) patients. The other causes of neuropathy were toxic injury, impaired glucose metabolism (72 patients, 25.3%), including diabetes in 26 and prediabetes in 46 patients. Other etiologies were chronic inflammatory demyelinating polyneuropathy (CIDP) in 57 (20%) patients and monoclonal gammopathy in 20 (7%) patients. The other causes of neuropathy were toxic injury, impaired glucose metabolism (72 patients, 25.3%), including diabetes in 26 and prediabetes in 46 patients. Other etiologies were chronic inflammatory demyelinating polyneuropathy (CIDP) in 57 (20%) patients and monoclonal gammopathy in 20 (7%) patients. Despite a thorough evaluation, in 32.7% patients, the cause still remained idiopathic.

Contributed by Dr Abhijeet Kumar Kohat


The split-hand phenomenon refers to preferential wasting of the thenar muscles with relative sparing of the hypothenar muscles in amyotrophic lateral sclerosis (ALS). The authors compared the split-hand index (SI) calculated from the compound muscle action potential (CMAP; SICMAP) with that calculated from the motor unit number index (MUNIX; SIMUNIX). MUNIX is a method for assessment of number and size of motor units (MUs) using the compound muscle action potential (CMAP) and surface electromyographic interference pattern (SIP). MUNIX was performed on the abductor pollicis brevis (APB), first dorsal interosseous (FDI), and abductor digiti minimi (ADM) muscles of 39 ALS patients and 40 age-matched, healthy controls. SI is derived by multiplying the CMAP (or MUNIX) recorded over the APB and FDI and dividing by the CMAP (or MUNIX) recorded over the ADM. The authors concluded that SIMUNIX and SICMAP were useful in differentiating ALS patients from healthy controls. SIMUNIX appears to be a better electrophysiological marker than SICMAP for the split-hand sign of ALS.

Contributed by Dr Abhijeet Kumar Kohat


Fisher syndrome (FS), pharyngeal-cervical-brachial variant form of GBS (PCB-GBS), and Bickerstaff brainstem encephalitis (BBE) may present as an isolated entity or in overlap. The aim of this study was to elucidate the frequency of this overlap and the patterns of clinical progression in patients with FS. Sixty patients with a diagnosis of pure FS were studied. FS/PCB-GBS was diagnosed when the patients developed pharyngeal, cervical and/or brachial weakness. Patients with flaccid tetraparesis were diagnosed as having FS/conventional GBS. FS/BBE was defined as the development of disturbances in consciousness. All 60 patients who initially developed FS had the clinical triad alone suggestive of pure FS. Thirty (50%) patients had pure FS throughout their course, whereas the remaining 50% of patients showed an overlap: PCB-GBS occurred in 14 (23%) patients, the conventional GBS occurred in nine (15%) patients and BBE occurred in seven (12%) patients. The median (range) duration from the onset of FS to the progression to FS/PCB-GBS, FS/GBS or FS/BBE were 5 (1-7), 3 (1-4) and 3 (1-5) days, respectively. Patients with overlap syndromes had a more favourable outcome as this group received more frequent immune-modulating treatment. The frequencies of positivity for anti-GQ1b, GT1a, GD1a, GD1b, GalNAc-GD1a and GM1 antibodies were not significantly different amongst the four groups. It can be concluded that pure FS, in 50% patients, may overlap with PCB-GBS, conventional GBS or BBE within the initial 7 days. Thus, physicians should pay attention to the possible development of this overlap.

Contributed by Dr Abhijeet Kumar Kohat

Faster heart rate predicts higher mortality in patients with ischemic heart disease and acute ischemic stroke but in intracerebral hemorrhage (ICH), the role of heart rate is uncertain. The present study was aimed to determine the effect of admission heart rate on clinical and imaging outcomes in patients with ICH. It was a post hoc pooled analysis of the pilot study and the main phases of the Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trial (INTERACT 1 and 2). The clinical outcomes were mortality and modified Rankin Scale score at 90 days; and imaging outcome was the absolute growth in hematoma volume during the initial 24 hours. Patients were divided into 4 categories according to baseline heart rate (<65, 65–74, 75–84, and ≥ 85 bpm), with the lowest heart rate group as the reference. Data was available for 3185 patients. A higher admission heart rate was associated with both mortality and worse modified Rankin Scale score; the adjusted hazard ratio for heart rate (≥85 versus <65 bpm) being 1.50 (95% CI, 1.07–2.11) and the adjusted odds ratio 1.33 (95% CI, 1.08–1.63), respectively (both P < 0.05). There was no significant relationship between the heart rate and absolute growth in hematoma volume (P-trend, 0.196). This analysis shows that a higher admission heart rate is independently associated with death and poor functional outcome after an acute intracerebral haemorrhage.

Contributed by Dr Abhijeet Kumar Kohat


In the natural history of Parkinson’s disease (PD), 60% patients experience psychosis and 80% develop dementia. Antipsychotic (APs) medications are commonly used in the patients with PD. It is unknown whether the use of APs in PD is associated with a higher mortality as occurs in with patients with dementia. The authors carried out a retrospective analysis to examine the risk associated with the AP medication use in a cohort of patients with idiopathic PD and in recent stable physical health. The rates of 180-day mortality were compared in 7877 patients initiating AP therapy and for comparison, 7877 PD patients who did not initiate AP therapy were included (Matched for age ± 2.5 years, sex, race, index year, presence and duration of dementia, PD duration, delirium, hospitalization, Charlson’s Comorbidity Index, and new nonpsychiatric medications). The main outcome was mortality rates at 180 days. Cox proportional hazard regression models were used with intent-to-treat (ITT) and exposure-only analyses. The study population included 7877 matched pairs of patients with PD (65 women [0.8%] and 7812 men [99.2%] in each cohort; the mean [SD] age was 76.3 [7.7] years for those who initiated AP therapy and 76.4 [7.6] years for those who did not). Antipsychotic medication use was associated with more than twice the hazard ratio (HR) of death compared with nonuse (ITT HR, 1.08–1.63), respectively (both P < 0.05). There was no
Advances in autoimmune encephalitis (AE) have been enormous in recent literature with the emergence of a flurry of new antibodies. The management strategies have also witnessed a drastic change. Lee et al., report on the efficacy and safety of rituximab treatment as second-line therapy for AE in a retrospective cohort of adult patients enrolled in the Korea Autoimmune Synaptic and Paraneoplastic Encephalitis Registry (KASPER). They identified 80 patients who met their inclusion criteria and were treated with rituximab after treatment with steroids, intravenous immunoglobulin, or plasma exchange as first-line therapy. 81 controls met the inclusion criteria but were treated only with first-line therapies, and not with rituximab.

Inclusion of the patient was focused on clinical and laboratory findings compatible with diagnosis. Notably, the presence of an autoantibody was not required for diagnosis. However, the patients were grouped according to the detection or type of antibodies. In addition, clinical and laboratory characteristics, first-line immunotherapy, and rituximab treatment profiles were evaluated. Outcomes were defined as improvements on the modified Rankin Scale (mRS) score and achievement of a favorable mRS score (0–2) at the last follow-up.

The study suggested that rituximab treatment as second-line therapy was associated with improved outcomes compared to no rituximab treatment, independent of whether the patients were autoantibody positive or negative. Earlier diagnosis, lesser disability at the time of treatment, and an early initiation of treatment were associated with better outcomes. This study provides Class IV evidence that rituximab improves mRS scores for patients with autoimmune limbic encephalitis who fail the first line therapy. The authors propose using rituximab as a first line agent or as part of the first line combination treatment to further improve outcomes.

Contributed by Dr. Aastha Takkar


Giant cell arteritis has always remained of significant interest to a neurologist/neo-ophtalmologist because of its potentially life threatening neurological complications and sight threatening aftereffects. Simple bedside tests for the diagnosis may prove to be a boon for an early detection. Claudication of the jaw is a specific symptom with a high predictive value for giant cell arteritis. Kuo et al., suggest a “chewing gum test” for jaw claudication based on their observations on two patients of proven giant cell arteritis.

The patients were asked to chew gum at the rate of one chew per second. The appearance of pain on attempted chewing, and its disappearance on cessation of chewing, were noted consistently and repeatedly. This observation comes as a simple and repeatable test for jaw claudication and may allow for a better characterization of this symptom. Further research is warranted to validate the chewing gum test for jaw claudication.

Contributed by Dr. Aastha Takkar


The recently published article by Balestrini S, et al., has been a refreshing approach into a common menace – refractory epilepsy. Retinal nerve fibre layer (RNFL) thickness is related to the axonal anterior visual pathway and is considered a marker of overall white matter ‘integrity’. The authors hypothesised that RNFL changes would occur in patients with epilepsy, independent of anti-epileptic (vigabatrin) exposure, and is related to the clinical characteristics of epilepsy. Three hundred people with epilepsy attending specialist clinics and 90 healthy controls were included in this retrospective cross-sectional cohort study. RNFL imaging was performed using spectral-domain optical coherence tomography (OCT). Drug resistance was defined as failure of adequate trials of two antiepileptic drugs to achieve sustained seizure freedom. Significantly thinner average RNFL thickness with decrease in the thickness of each of the 90° quadrants was noted in the patients with epilepsy than
in the healthy controls (P < 0.001). In a multivariate logistic regression model, drug resistance was the only significant predictor of abnormal RNFL thinning (P = 0.03). The duration of epilepsy (coefficient −0.16, P = 0.004) and presence of intellectual disability (coefficient −4.0, P = 0.044) also showed a significant relationship with RNFL thinning in a multivariate linear regression model. The authors suggest that people with epilepsy with no previous exposure to vigabatrin have a significantly thinner RNFL than healthy participants. Drug resistance was found as a significant independent predictor of RNFL borderline attenuation or abnormal thinning in a logistic regression model. As this is easily assessed by OCT, RNFL thickness might be used to better understand the mechanisms underlying drug resistance, and possibly the severity of epilepsy.

**Contributed by Dr. Aastha Takkar**


Approximately half of recurrent strokes occur within days and weeks of an ischemic stroke. Identifying the patients at imminent risk of recurrent stroke is imperative because recurrent events lead to prolonged hospitalization, worsened functional outcome, and increased mortality.

Recently, a web-based, prognostic score (RRE-90) was proposed. The score integrates clinical and imaging information available in the acute setting to quantify early risk of recurrence of stroke. This hospital-based cohort study was performed at 3 teaching hospitals in the United States, Brazil, and South Korea and comprised adult patients admitted within 72 hours of symptom onset with a magnetic resonance imaging (MRI)—confirmed diagnosis of acute ischemic stroke. The study included 1468 consecutive patients with 59 recurrent ischemic stroke events. The primary outcome was recurrent ischemic strokes defined by a clinical incident that was clearly attributable to a new area of brain infarction occurring within the 90 days of index infarction. An investigator who was masked to the patient’s recurrence status calculated the Recurrence Risk Estimator (RRE) score for each patient based on information available after the initial line of testing in the emergency department. The cumulative 90-day recurrence rate was 4.2%. The mean RRE score was 2.2 (95% CI, 1.9-2.5) in patients with recurrence and 1.0 (95% CI, 1.0-1.1) in patients without recurrence. The risk of recurrence increased with a higher RRE score (log-rank test, P < 0.001). The RRE identified 710 patients (48.4%) in the study population as high risk (>10%) or low risk (<1%). The sensitivity and specificity were 38% and 93% for identifying low-risk subsets and 41% and 90% for identifying high-risk subsets, respectively.

This study confirms the validity of the RRE score in a multicenter cohort of patients with diverse characteristics. The authors suggest that RRE could be useful in identifying high- and low-risk patients for targeted stroke prevention.

**Contributed by Dr. Aastha Takkar**


In the past decade, dramatic progress in the treatment of children with congenital hemiparesis has been noted. One important step was the introduction of intensive rehabilitation approaches based on principles of motor learning and neuroplasticity, such as constraint-induced movement therapy (CIMT) and intensive bimanual training. Often these approaches are implemented in socially stimulating “camp” environments.

Kirton et al., report a treatment study on congenital hemiparesis due to perinatal stroke, comparing camp alone with camp + repetitive transcranial magnetic stimulation (rTMS), camp + CIMT, and camp + rTMS + CIMT. They found that while all groups showed improvement, the patients who received the combination of rTMS and CIMT showed the greatest benefits.

This was a factorial-design, blinded, randomized controlled trial, which assessed rTMS and CIMT effects in hemiparetic children (aged 6–19 years) with MRI-confirmed perinatal stroke. The study aimed at determining whether the addition of rTMS and/or constraint-induced movement therapy (CIMT) to intensive therapy increases motor function in children with perinatal stroke and hemiparesis. All the 45 participants included completed a 2-week, goal-directed, peer-supported motor learning camp randomized to daily rTMS, CIMT, both, or neither. Primary outcomes were the ‘Assisting Hand Assessment’ and the ‘Canadian occupational performance measure’ at baseline, and 1 week, 2 and 6 months post-intervention. Outcome assessors were blinded to treatment. Interim safety analyses occurred after 12 and 24 participants. Intention-to-treat analysis examined treatment effects over time (linear mixed effects model).

Addition of rTMS, CIMT, or both, doubled the chances of clinically significant improvement. Assisting hand
This paper studied the risk of stroke after an attack of transient ischemic attack (TIA). The previous studies were done between 1997-2003 and had estimated a risk of stroke or acute coronary event of 12-20% during the first 3 months after the TIA. This study provides new information in the current scenario with the current health system and treatment by experts of stroke. This study recruited 4789 patients from 2009 to 2011 in 21 countries. The patients included had TIA or minor stroke in the last 7 days. About 78.4% of the patients were evaluated within 24 hours of the onset of symptoms by stroke specialists. The Kaplan Meier estimate of the 1-year event rate of the composite cardiovascular outcome was 6.2%, and of stroke at 2.7, 30, 90 days and at 1 year was 1.5%, 2.1%, 2.8%, 3.7% and 5.1%, respectively. This was found to be much lower than the previously published data where the incidence was found to be 12-20% at 90 days after a TIA. These lowered rates have been proposed by the authors to be due to better and quicker management strategies for secondary prevention of stroke (by starting antiplatelet therapy and anticoagulation therapy in atrial fibrillation, conducting an intervention in carotid artery stenosis, and also by administering statins and antihypertensive drugs). According to some other trials like EXPRESS (Early use of Existing Preventive Strategies for Stroke) study, those who received urgent treatment in clinics had a recurrence rate of only 2%, highlighting the fact that with due attention and intervention, the risk of stroke can be reduced drastically. In the CHANCE (Clopidogrel in High Risk Patients with Acute Non-Disabling Cerebrovascular Events) trial, the best effect of dual antiplatelet therapy was achieved within 8 days after symptom onset.

Contributed by Dr. Aastha Takkar


This position paper on the clinical approach to the diagnosis of autoimmune encephalitis (AE) broadens the definition based on the clinical features and does not rely heavily on the antibody testing. As the diagnosis and treatment of autoimmune encephalitis is delayed in the absence of antibody testing leading to an increased morbidity and mortality in the patients, the authors propose the diagnosis of definite AE based on the subacute onset (<3 months) of working memory deficits, seizures, or psychiatric symptoms (indicating the involvement of the limbic system), bilateral magnetic resonance imaging (MRI) abnormalities in the temporal lobes, cerebrospinal fluid pleocytosis or electroencephalogram abnormality. This diagnosis should be considered after exclusion of mimickers. This article also attempts to propose a diagnostic algorithm for the diagnosis of these disorders. This paper would further enhance the scope of the diagnosis of AE but in the Indian scenario, we need to be more cautious in over-diagnosing this condition, and infectious causes should be excluded adequately before giving immunomodulatory treatment.

Contributed by Dr. Ravi Yadav


There is no approved treatment of primary progressive multiple sclerosis (PPMS). This trial tested the drug fingolimod in patients with PPMS. Previously this drug was shown to be effective in relapsing remitting multiple sclerosis. The “INFORMS” trial was designed in a way to improve the methodological issues of the previous trials in PPMS like “PROMiSe” (glatiramer acetate versus placebo) and OLYMPUS (rituximab versus placebo). “INFORMS” had a novel composite endpoint to increase the sensitivity and specificity to detect the treatment effect and the patients received the study drug for 3 years.

“INFORMS” was a multicentre, double blind, placebo controlled parallel group study, in 148 centres and 18 countries. The patients were randomly allocated to fingolimod or placebo in a dosage of 1.25 mg and 0.5 mg per day. Patients of PPMS included in the study were 25-65 years

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INFORMS "was a multicentre, double blind, placebo controlled parallel group study, in 148 centres and 18 countries. The patients were randomly allocated to fingolimod or placebo in a dosage of 1.25 mg and 0.5 mg per day. Patients of PPMS included in the study were 25-65 years
of age and had 1 year or more of disease progression with a positive magnetic resonance image. A novel primary endpoint was used based on the change from baseline of the ‘Expanded Disability Status Scale (EDSS), 25’ Timed Walk Test, or Nine-Hole Peg Test’ to assess time to 3 month confirmed disability progression in study participants treated for at least 3 years. Out of the 970 patients randomised, the efficacy analysis set of 823 consisted of 336 patients in the fingolimod group and 487 in the placebo group. The risk reduction was 5.05%, hazard ratio 0.95 and 95% CI 0.80-1.12; \( P = 0.544 \). This study was adequately powered to detect a reduction in both the groups considering the dropouts of 10% per year. In this trial, the anti-inflammatory effects of fingolimod failed to show any effect in slowing the disease progression in primary progressive multiple sclerosis. Interestingly in this study, the effect of fingolimod on the disease activity in the form of reduction in gadolinium enhancement, in the appearance of new lesions, or on visualizing enlarging T2 lesions was similar to its effect as seen in relapsing remitting multiple sclerosis. This, however, did not manifest as a reduction in the clinical disease progression. Thus, this trial was unable to demonstrate any benefit in patients with PPMS.

**Contributed by Dr. Ravi Yadav**


Spinal cord sarcoidosis is a rare disease but poses a great challenge in diagnosis for neurologists and neurosurgeons equally. This study showcases the clinical and radiological differences between the two conditions. This retrospective study by Flanagan *et al.*, addresses the differentiating features of long segment myelitis of neuromyelitis optica (NMO) from spinal cord sarcoidosis in a large cohort of patients. It compared longitudinally, extensive myelitis in neuromyelitis optica spectrum disorders (NMOSD) and spinal cord sarcoidosis (SCS). The patient from 1996 to 2015 were evaluated. All NMOSD patients were positive for aquaporin 4 antibodies and all the sarcoidosis cases were pathologically confirmed. Out of the total of 71 cases, patients with NMOSD were 37 and SCS were 34 in number. The delay in the diagnosis was longer in cases of spinal cord sarcoidosis. This study also showed that NMOSD was more common in female patients, who had a history of optic neuritis or intractable vomiting and a relatively faster onset of neurological deficits. Paroxysmal tonic spasms were seen in 49% patients of NMOSD. However, SCS patients had systemic constitutional symptoms, pleocytosis in cerebrospinal fluid (CSF), hilar lymphadenopathy, reduction in CSF sugar, and elevated angiotensin converting enzyme (ACE) levels. Subpial gadolinium enhancement in the dorsal cord extending ≥2 vertebral segments and persistent enhancement >2 months was more common in SCS. The pathological confirmation of sarcoidosis was performed by transbronchial biopsy, spinal cord biopsy, concurrent brain lesion biopsy. They found a ring like enhancement favouring NMOSD. The maximum neurological disability was the same in both the groups. Other groups have also shown that CSF pleocytosis, reduced CSF sugar, enhancing cervical or thoracic cord lesions were more in favour of spinal cord sarcoidosis.

**Contributed by Dr. Ravi Yadav**


and,


These 2 studies further expand the utility of the botulinum toxin A (BoNT A) in patients with neuropathic pain due to spinal cord injury and peripheral neuropathic pain. The mechanism suggested in both the studies is the reduction in neurogenic inflammation and peripheral sensitization of the pain fibres. Han *et al.*, studied the potential use of BoNT A in neuropathic pain in patients with spinal cord injury (SCI). BoNT A has been used in patients with post herpetic neuralgia and chronic migraine in the previous studies. They recruited 40 patients of SCI associated neuropathic pain in the placebo controlled design. This was an 8 week, randomised, double blind, placebo controlled, parallel group study. The injection (200 units of BoNT A) was administered over the maximally affected area. Compared with the placebo group, the BoNT A group had significant reduction in the visual analogue score at 4 and 8 weeks after the injection. About 50% patients in this study showed 20% or greater pain relief for at least 8 weeks after the BoNT A injection. The conflict of interest was that this study was funded by the manufacturers of BoNT A in Korea. BOTNEP study also showed similar results in the form of reduction of severity of pain assessed at the end of 24 weeks.

**Contributed by Dr. Ravi Yadav**

The conversion rate of mild cognitive impairment (MCI) into Alzheimer’s disease (AD) is estimated to be around 10-15% per year. Many patients of MCI remain stable or may become normal while others develop AD. This large systematic review and meta-analysis included many cohort studies to identify the risk factors for progression to AD in patients with MCI. Out of the 3565 articles found in the initial search, they included 60 articles for meta-analysis and 31 for the systematic review. They excluded the factors of interest, if they were not reported by 3 or more studies. Among the demographic features, older age and female gender had a high risk of progression. The presence of one APOe allele had a relative risk (RR) of 1.84. The pooled RR for progression in the presence of the APOe allele was 3.02. No association of higher education level and smoking was found. Depression was found to be associated with an increased risk of conversion to AD but apathy and anxiety were not. A high body mass index had a protective effect in progression. Imaging markers of hippocampal atrophy, medial temporal lobe atrophy and entorhinal atrophy had higher conversion to AD. Among the biomarkers, the ratio of the cerebrospinal fluid tau to Aβ1-42 (CSF tau/Aβ1-42) was a significant predictor of progression of MCI to AD. The patients with APOE4, abnormal CSF tau level, female gender and old age with depression, diabetes, lower scores of mini mental status examination had a higher chance of developing AD. The surprising finding was that the higher educational status did not come out as significant although it has been found to be protective in many studies. Secondly, as pointed by the authors, this review could not estimate the various subtypes of MCI and the associated risk of conversion in them. It is known that amnestic MCI has a higher conversion rate to AD.

Contributed by Dr. Ravi Yadav


There is always this clinical question in the mind of treating neurologists about the effectiveness of pre-stroke aspirin in the patients with acute stroke. This study provides good a insight on this topic. Park et al., studied the severity of stroke, haemorrhagic transformation and functional outcome in patients taking prestroke aspirin. Interestingly, they found that those patients with large artery stroke had a better outcome although there was a slight increase in the haemorrhagic transformation. The functional outcome at discharge as measured by the modified Rankin Scale was also better in patients taking pre-stroke aspirin. However, this was not the case in patients with small vessel occlusion as there was no benefit in them as well as in those patients with a cardioembolic stroke.

Contributed by Dr. Ravi Yadav


Idiopathic Rapid Eye Movement (REM) sleep behaviour disorder is a premotor marker of Parkinson’s disease. The presence of REM sleep behaviour disorder (RBD) can precede the onset of Parkinson’s disease and other alpha synucleinopathies by many years and decades. There is a high rate of development of idiopathic RBD into one of the alpha synucleinopathies like Parkinson’s disease, multiple system atrophy and diffuse Lewy body dementia. Currently, there is increased interest among the researchers in identifying the people with idiopathic RBD so that the clinical, biochemical and imaging biomarkers can be studied and identified. The paper by Ehrminger et al., studied the coeruleus/subcoeruleus complex by neuromelanin sensitive imaging in 21 patients and controls and found that there was reduced signal intensity in patients with idiopathic RBD. The mean sensitivity of visual analysis was 82.5% and specificity was 81%. This analysis was performed by the neuroradiologists. The results show the involvement of this complex in idiopathic RBD and neuromelanin-sensitive imaging provides an important clue in the detection of abnormalities in these patients. This knowledge will generate further interest in studying this disorder.

Contributed by Dr. Ravi Yadav


Previous studies have found an association between the use of statins and the risk of haemorrhagic stroke. This trial investigated the relationship between statin use,
total serum cholesterol levels and haemorrhagic stroke. This was a multicentre study on cerebral haemorrhage in Italy and included 3492 patients and an equal number of controls. A higher total serum cholesterol level was inversely associated with the risk of haemorrhage. The use of statin was associated with an increased risk (OR, 1.54). The risk of haemorrhage was increased more so in the lobar brain regions.

In this article, the authors report a subgroup analysis of the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) to find out if the infarct size modified the intra-arterial treatment in patients with large infarcts. MR CLEAN is a randomized, controlled, open-label, phase 3 trial of intra-arterial treatment in patients (aged ≥18 years from the Netherlands) with proximal arterial occlusion of the anterior circulation in which the intra-arterial treatment is given within 6 h of stroke onset. The authors analysed the effect of the baseline Alberta Stroke Program Early CT Score (ASPECTS) on the safety and efficacy of intra-arterial treatment. Based on the ASPECTS score, the infarct size was divided into large (score 0–4), moderate (score 5–7) and small (score 8–10). Modified Rankin Scale (mRS) score at 3 months was considered as a primary outcome. The authors divided the total number of 496 patients in this study into two comparable groups. 232 (47%) patients were randomized in the intra-arterial treatment plus usual care arm, and 264 (53%) patients were given the usual standard care. They noted no significant difference in the effect of intra-arterial treatment between the ASPECTS subgroups when compared to the standard treatment subgroup, as far as the primary outcome was concerned. The intra-arterial treatment did not cause a significant increase in the proportion of patients with at least one serious adverse event in any of the ASPECTS subgroups. Similarly, perioperative deaths (within 30 days) and hemicraniectomy were also not significantly different between the intra-arterial treatment and usual care versus usual care alone groups in any of the ASPECTS subgroups. A significantly higher proportion of patients, however, had recurrent ischaemic strokes in the intra-arterial treatment plus usual care group than in the usual care alone group in the ASPECTS 8–10 subgroup (eight [5%] vs one [<1%; P = 0.007].

On the basis of their findings, the authors recommended the intra-arterial treatment in patients having a non-contrast CT ASPECTS score 5 or more. Stating that treatment might yield only a marginal absolute benefit, the authors advised further studies before intra-arterial therapy may be considered in patients with ASPECTS 0–4.

The authors intended to look into the details of the synapse loss seen in Alzheimer’s disease (AD) and its correlation with the cognitive decline. They reiterated the existing understanding that the microglia and the compliment system play a prominent role in the later phases of AD secondary to the neuroinflammation that ensues at this point in time. The authors state that C1q, the initiating protein of the classical complement pathway, was increased and was associated with the synapses even before the overt plaque deposition had taken place. They also observed that the inhibition of C1q, C3, or the microglial complement receptor CR3 reduced the number of phagocytic microglia, as well as the extent of early synapse loss, which suggested that compliment activation was an initial event. Also, the authors observed that C1q was necessary for the toxic effects of soluble β-amyloid (Aβ) oligomers, the building blocks of the subsequent Alzheimer’s plaque, on the synapses and long-term potentiation of the hippocampi. Finally, the authors stated that the microglia in adult brains engulfed the synaptic material in a CR3-dependent process when exposed to soluble Aβ oligomers. Hence, the authors concluded that the complement-dependent pathway and microglia were inappropriately activated and mediated an early synapse loss in AD.

Headache is a presenting feature in 37% to 70% of patients with a pituitary tumour. It is not always clear whether the presenting headache is an unrelated primary headache, a lesion-induced aggravation of a pre-existing primary headache, or a separate secondary headache related to the lesion. The authors used a self-administered survey of headache characteristics completed by patients upon presentation and after any pituitary surgical procedure.

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**Contributed by Dr. Ravi Yadav**


**Contributed by Dr. Kuntal Kanti Das**


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One hundred thirty-three participants completed the preoperative questionnaire (response rate of 99%). The overall prevalence of headache was 63%. Compared to patients without headache, the group with headache was more likely to be female ($P = 0.001$), younger ($P = 0.001$), and to have had a prior diagnosis of headache ($P < 0.001$). Seventy-two percent of patients reported headache localized to the anterior region of the head. Fifty-one patients with headache underwent transsphenoidal pituitary surgery. Headache was not associated with increased odds of having surgery (odds ratio, 0.90). At 3 months, 81% of surgically treated patients with headache, who completed the postoperative questionnaire (21/26), reported improvement or resolution of headaches. No patient who completed the postoperative questionnaire (44/84) reported new or worsened headache. The authors concluded that surgery for patients with headache and a pituitary tumour was associated with headache improvement or resolution in the majority and was not found to cause or worsen headaches. Based on these findings, they also suggested a revision in the International Classification of Headache Disorders diagnostic criteria pertaining to pituitary disorders that is supported by these findings. Headache is currently not widely considered to be a major indication for surgery in patients who have pituitary lesions; however, given the possibility for improvement from surgery and the observation that the utility of surgery as a headache management tool in these patients is a commonly occurring clinical question, the role of surgery in the management of pituitary-associated headache still remains controversial and may warrant further investigation.

**Contributed by Mazda K. Turel**


The impact of transsphenoidal surgery for nonfunctional pituitary adenomas (NFAs) on the preoperative hypopituitarism relative to the incidence of new postoperative endocrine deficits remains unclear. The authors investigated the rates of hypopituitarism resolution and development after transsphenoidal surgery. Of the 305 surgeries performed over a 5-year period, patients with preoperative endocrine deficits ($n = 153, 50\%$) were significantly older (mean age 60 vs 54 years; $P = 0.004$), more frequently male (65% vs 44%; $P = 0.0005$), and had larger adenomas (2.4 cm vs 2.1 cm; $P = 0.02$) than patients without preoperative deficits ($n = 152, 50\%$). Of patients with preoperative endocrine deficits, 53% exhibited symptoms. Preoperative deficit rates were 26% for the thyroid axis; 20% and 16% for the male and female reproductive axes, respectively; 13% for the adrenocorticotropic hormone (ACTH)/cortisol axis, and 19% for the growth hormone (GH)/insulin-like growth factor-1 (IGF-1) axis. Laboratory normalization rates 6 months after surgery without hormone replacement were 36% for male and 13% for female reproductive axes; 49% for the thyroid axis; 3% for the cortisol axis; and 22% for the IGF-1 axis ($P < 0.05$). New postoperative endocrine deficits occurred in 42 patients (13.7%). Rates of new deficits by axes were: Male reproductive 3% ($n = 9$), female reproductive 1% ($n = 4$) axis, thyroid axis 3% ($n = 10$), cortisol axis 6% ($n = 19$), and GH/IGF-1 axis 4% ($n = 12$). Patients who failed to exhibit any endocrine normalization had lower preoperative gland volumes than those who did not (0.24 cc vs 0.43 cc, respectively; $P < 0.05$). Multivariate analyses revealed that no variables predicted new postoperative deficits or normalization of the female reproductive, cortisol, and IGF-1 axes. However, increased preoperative gland volume and younger age predicted the chances of a patient with any preoperative deficit experiencing normalization of at least 1 axis. Younger age and less severe preoperative hormonal deficit predicted normalization of the thyroid and male reproductive axes ($P < 0.05$). The authors concluded that after NFA resection, endocrine normalization rates in this study were greater than the incidence of new endocrine deficits. A low preoperative gland volume precluded recovery. The patient’s age and the severity of the deficiency influenced the recovery of the thyroid and male reproductive axes, the most commonly impaired axes and the axes most likely to normalize postoperatively. This information can be of use in counselling patients with hypopituitarism who undergo transsphenoidal surgery for the a NFA.

**Contributed by Mazda K. Turel**


Patients with incomplete surgical resection of medulloblastomas are controversially regarded as having markers of high-risk disease, which leads to these patients being subjected to aggressive surgical resections, the so-called second-look surgeries, and intensified chemoradiotherapy. All previous studies assessing the clinical importance of the extent of resection have not accounted for the molecular
subgrouping of these lesions. The authors analysed the prognostic value of the extent of resection in a subgroup-specific manner. They retrospectively identified patients who had a histological diagnosis of medulloblastoma and complete data about their extent of resection and survival at 35 international institutions. They classified the extent of resection on the basis of postoperative imaging as: Gross total resection (no residual tumour), near-total resection (<1.5 cm tumour remaining), or sub-total resection (≥1.5 cm tumour remaining). They included 787 patients with a medulloblastoma (86 with wingless (WNT) tumors, 242 with sonic hedgehog (SHH) tumours, 163 with group 3 tumours, and 296 with group 4 tumours). A progression-free survival benefit for gross total resection over sub-total resection, but with no overall survival benefit, was noted. They found no progression-free survival or overall survival benefit for gross total resection compared with near-total resection. No significant survival benefit existed for greater extent of resection for patients with WNT, SHH, or group 3 tumours. For patients with group 4 tumours, gross total resection conferred a benefit to progression-free survival compared with sub-total resection, especially for those with metastatic disease. However, gross total resection had no effect on the overall survival compared with sub-total resection in patients with group 4 tumours. They concluded that the prognostic benefit of increased extent of resection for patients with medulloblastoma is attenuated after molecular subgroup affiliation is taken into account. Although maximum safe surgical resection should remain the standard of care, surgical removal of small residual portions of medulloblastoma is not recommended when the likelihood of neurological morbidity is high because there is no definitive benefit in gross total resection compared with near-total resection.

**Contributed by Mazda K. Turel**


Radiological characteristics may reflect the biological features of brain tumours and may be associated with genetic alterations that occur in tumorigenesis. This study aimed to investigate the relationship between radiological features and isocitrate dehydrogenase (IDH) 1 status as well as their predictive value for survival of glioblastoma patients. The clinical information and MRI images of 280 patients with histologically confirmed glioblastoma were retrospectively reviewed. The radiological characteristics of tumours were examined on MR images, and the IDH1 status was determined using deoxyribonucleic acid sequencing for all cases. The Kaplan-Meier method and Cox regression model were used to identify prognostic factors for progression-free and overall survival. The IDH1 mutation was associated with longer progression-free survival (P = 0.022) and overall survival (P = 0.018). In patients with the IDH1 mutation, tumour contrast enhancement and peritumoral oedema indicated worse progression-free survival (P = 0.015 and P = 0.024, respectively) and worse overall survival (P = 0.024 and P = 0.032, respectively). For tumours with contrast enhancement, multifocal contrast enhancement of the tumour lesion was associated with a poor progression-free survival (P = 0.002) and a poor overall survival (P = 0.010) in patients with wild-type IDH1 tumours. The authors concluded that combining the radiological features and IDH1 status of a tumour allowed for a more accurate prediction of survival outcomes in glioblastoma patients. They propose that complementary roles of genetic changes and radiological features of tumours should be considered in future studies.

**Contributed by Mazda K. Turel**


Grade 2 gliomas occur most commonly in young adults and cause progressive neurologic deterioration and premature death. Early results of this trial showed that treatment with procarbazine, lomustine (also called CCNU), and vincristine after radiation therapy at the time of the initial diagnosis resulted in a longer progression-free survival, but not overall survival, than radiation therapy alone. The authors now report the long-term results of this RCT. They included patients with grade 2 astrocytoma, oligoastrocytoma, or oligodendroglioma who were younger than 40 years of age and had undergone subtotal resection or biopsy, or who were 40 years of age or older and had undergone biopsy or resection of any of the tumour. The patients were stratified according to age, histologic findings, Karnofsky performance-status score, and presence or absence of contrast enhancement on preoperative images. They were randomly assigned to radiation therapy alone or to radiation therapy followed by six cycles of combination chemotherapy. A total of 251 eligible patients were enrolled from 1998 through 2002. The median follow-up was 11.9 years; 55% of the patients died. Patients who received radiation therapy plus chemotherapy had longer median overall survival than did those who received radiation therapy alone (13.3 vs. 7.8 years; hazard ratio for death, 0.59; P = 0.003). The rate of progression-free survival at 10 years was 51% in the group that received radiation therapy plus chemotherapy versus 21% in the group that...
received radiation therapy alone; the corresponding rates of overall survival at 10 years were 60% and 40%. A Cox model identified receipt of radiation therapy plus chemotherapy and histologic findings of oligodendroglioma as favorable prognostic variables for both progression-free and overall survival. The authors concluded that in this cohort of patients with a grade 2 glioma, who were younger than 40 years of age and had undergone subtotal tumor resection, or who were 40 years of age or older, progression-free survival and overall survival were longer among those who received combination chemotherapy in addition to radiation therapy than among those who received radiation therapy alone. The magnitude of treatment benefit from combined chemotherapy plus radiation therapy were substantial, but the toxic effects were greater than those observed with radiation therapy alone. Patients and their physicians will have to weigh whether the longer survival justifies the more toxic therapeutic approach.

*Contributed by Mazda K. Turel*


Age was reported to be an effect-modifier in four randomized controlled trials (RCTs) comparing carotid artery stenting (CAS) and carotid endarterectomy (CEA), with better CEA outcomes than CAS outcomes noted in the more elderly patients. The authors aimed to describe the association of age with treatment differences in symptomatic patients and provide age-specific estimates of the risk of stroke and death within narrow (5 year) age groups. In this meta-analysis, they analysed individual patient-level data from four randomised controlled trials (n = 4754) within the Carotid Stenosis Trialists’ Collaboration (CSTC) involving patients with symptomatic carotid stenosis. They included only trials that randomly assigned patients to CAS or CEA and only patients with symptomatic stenosis. 433 events occurred over a median follow-up of 2-7 years. For patients assigned to CAS, the periprocedural hazard ratio (HR) for stroke and death in patients aged 65-69 years compared with patients younger than 60 years was 2.16 (95% CI 1.13-4.13), with HRs of roughly 4.0 for patients aged 70 years or older. They noted no evidence of an increased periprocedural risk by age group in the CEA group (P = 0.34). These changes underpinned a CAS-versus CEA periprocedural HR of 1.61 (95% CI 0.90-2.88) for patients aged 65-69 years and an HR of 2.09 (1.32-3.32) for patients aged 70-74 years. Age was not associated with the postprocedural stroke risk either within the treatment group (P ≥ 0.09 for CAS and 0.83 for CEA), or between the treatment groups (P = 0.84).

The authors concluded that in these RCTs, CEA was clearly superior to CAS in patients aged 70-74 years and older. The difference in older patients was almost wholly attributable to increasing periprocedural stroke risk in patients treated with CAS. Age had little effect on the CEA periprocedural risk or on the postprocedural risk after either procedure.

*Contributed by Mazda K. Turel*


Previous clinical trials have suggested that carotid-artery stenting with a device to capture and remove emboli (“embolic protection”) is an effective alternative to carotid endarterectomy in patients at average or high risk for surgical complications. In this trial, the authors compared carotid-artery stenting with embolic protection and carotid endarterectomy in patients 79 years of age or younger who had severe carotid stenosis and were asymptomatic (i.e., had not had a stroke, transient ischemic attack, or amaurosis fugax in the 180 days before enrollment) and were not considered to be at high risk for surgical complications. The trial was designed to enroll 1658 patients but was halted early, after 1453 patients underwent randomization, because of slow enrollment. Patients were followed for up to 5 years. The primary composite end point of death, stroke, or myocardial infarction within 30 days after the procedure or ipsilateral stroke within 1 year was tested at a noninferiority margin of 3 percentage points. They found that stenting was noninferior to endarterectomy with regard to the primary composite end point (event rate, 3.8% and 3.4%, respectively; P = 0.01 for noninferiority). The rate of stroke or death within 30 days was 2.9% in the stenting group and 1.7% in the endarterectomy group (P = 0.33). From 30 days to 5 years after the procedure, the rate of freedom from ipsilateral stroke was 97.8% in the stenting group and 97.3% in the endarterectomy group (P = 0.51), and the overall survival rates were 87.1% and 89.4%, respectively (P = 0.21). The cumulative 5-year rate of stroke-free survival was 93.1% in the stenting group and 94.7% in the endarterectomy group (P = 0.44). The authors concluded that in this trial involving asymptomatic patients with severe carotid stenosis who were not at high risk for surgical complications, stenting was noninferior to endarterectomy with regard to the rate of the primary composite end point at 1 year. In analyses that included up to 5 years of follow-up, there were no significant differences between the study groups in the rates of non-procedure-related stroke, all stroke, and survival.
Resuming AT following the evacuation of cSDH is a highly variable practice, with scant evidence in the literature for guidance. Here, a retrospective analysis of a cohort of patients (n = 479) from a single institution undergoing surgical drainage of cSDH was performed to evaluate postoperative complications and determine the optimal timing of the resumption of common antithrombotic agents. Among all 479 patients, 71 experienced major hemorrhage (14.8%), 110 experienced minor hemorrhage (23.0%), and 8 experienced thromboembolism (1.67%) postoperatively. Patients on any type of preoperative AT regimen were at a higher risk of major hemorrhage (19.0% vs 10.9%; P = 0.014). The type of AT agent did not affect the frequency of any postoperative complications. Patients on any preoperative AT regimen experienced earlier postoperative major hemorrhages (mean 16.2 vs 26.5 days; P = 0.052) and thromboembolic events (mean 2.7 vs 51.5 days; P = 0.036) than those patients without a history of AT; the type of AT agent did not affect the timing of complications. Patients who were restarted on any AT therapy postoperatively were at decreased risk of major rebleeding following resumption than those patients who were not restarted (P < 0.01). The authors concluded that patients with a history of preoperative AT experienced thromboembolic complications significantly earlier than those patients without AT, which peaked at
3 days postoperatively with no increase in hemorrhage risk when AT was restarted. Cursory evidence is presented that shows resuming AT early following the surgical evacuation of cSDH at 3 days postoperatively may be safe. However, much larger prospective studies are required prior to providing any definitive recommendations regarding the optimal timing and method of resumption of individual agents.

Contributed by Mazda K. Turel


Minimally invasive surgical (MIS) techniques are gaining popularity in the treatment of adult spinal deformity (ASD). The premise is that MIS techniques will lead to equivalent outcomes and a reduction in the perioperative complications when compared with open techniques. Potential issues with MIS techniques are their limited capacity to correct lumbar lordosis, their unknown long-term efficacy, and the potential need for revision surgery. This study compares the reoperation rates and the reasons for reoperations following MIS, hybrid, and open surgery for ASD through a multicenter database analysis. The authors retrospectively analyzed a prospective multicenter ASD database comparing open and MIS correction techniques. The inclusion criteria were: Age >18 years with minimum 20° coronal lumbar Cobb angle, a minimum of three levels fused, and a minimum of 2-year follow-up. The patients were propensity matched for preoperative sagittal vertebral axis (SVA), pelvic incidence-lumbar lordosis (PI-LL), and number of levels fused. The study included 189 patients from three propensity-matched subgroups of 63 patients each: (1) MIS: Lateral or transforaminal lumbar interbody fusion (LIF) and percutaneous pedicle instrumentation, (2) Hybrid: MIS LIF with open posterior segmental fixation (PSF), and (3) OPEN: Open posterior fixation ± osteotomies. With propensity matching, there were significant differences between the groups in the pre-operative SVA or PI-LL (P > 0.05). The MIS group had significantly fewer levels fused (5.4) [0-14] than the OPEN group (7.4) [P = 0.002, 0-17]. The rate of revision surgery was significantly different between the groups with a higher rate of revision (27%) amongst the HYB group versus MIS = 11.1%, and OPEN = 12.0%. The most common reason for reoperation in the OPEN and HYB groups was a postoperative neurological deficit (7.9 and 11.1%), respectively. The most common reason for reoperation in the MIS group was pseudoarthrosis (7.9%).

The authors concluded that reoperation rates were not statistically different among the MIS, and OPEN surgical groups, but differed significantly on multivariate analysis with the HYB group. The incidence of reoperations was twice as high in the HYB group compared to OPEN and MIS groups.

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Traditional surgical options for the treatment of symptomatic lumbar spinal stenosis include decompression alone vs decompression and fusion; both options have potential limitations.

The authors reported the 36-month follow-up analysis of the coflex interlaminar stabilization after decompression, which is intended to preserve normal segmental motion at the treated level. The coflex trial was a prospective, randomized investigational device exemption study conducted at 21 clinical sites in the United States. Composite clinical success at 36 months was achieved by 62.2% among 196 coflex interlaminar stabilization patients and by 48.9% among 94 fusion patients (difference = 13.3%, P = 0.03). Bayesian posterior probabilities for noninferiority (margin = -10%) and superiority of coflex interlaminar stabilization versus fusion were >0.999 and 0.984, respectively. Substantial and comparable improvements were observed in both the groups for patient-reported outcomes, although the percentage with a clinically significant improvement (≥15) in the Oswestry Disability Index seemed larger for the coflex interlaminar stabilization group relative to the fusion group (P = 0.008). Radiographic measurements maintained index level and adjacent level range of motion in the coflex interlaminar stabilization patients, although range of motion at the level superior to the fusion was significantly increased (P = 0.005).

The authors concluded that coflex interlaminar stabilization for stenosis has proven to be effective and durable at improving the overall composite clinical success without altering the normal spinal kinematic motion at the index level of decompression or at adjacent levels.

Contributed by Mazda K. Turel


This meta-analysis aimed to evaluate the efficacy of motion-preservation procedures to prevent the adjacent
segment degeneration (ASDeg) or adjacent segment disease (ASDis) compared with fusion in lumbar spine. The authors compared the ASDeg and ASDis rate, reoperation rate, operation time, blood loss, length of hospital stay, visual analogue scale (VAS) and Oswestry disability index (ODI) improvement of the two procedures.

A total of 15 studies consisting of 1474 patients were included in this study. The meta-analysis indicated that the prevalence of ASDeg, ASDis and reoperation rate on the adjacent level were lower in motion-preservation procedures group than in the fusion group ($P = 0.001$). Moreover, shorter length of hospital stay was found in the motion-preservation procedure group ($P < 0.0001$). No difference was found in terms of operation time ($P = 0.57$), blood loss ($P = 0.27$), VAS ($P = 0.76$) and ODI improvement ($P = 0.71$) between the two groups. They concluded that the present evidence indicated that the motion-preservation procedures had an advantage on reducing the prevalence of ASDeg, ASDis and the reoperation rate due to the adjacent segment degeneration compared with the lumbar fusion and the clinical outcomes of the two procedures were similar.

Contributed by Mazda K. Turel


Degenerative cervical myelopathy (DCM) is an all-encompassing term that includes cervical spondylotic myelopathy (CSM), ossification of the posterior longitudinal ligament (OPLL), and other spinal abnormalities that cause cervical cord compression. It is unclear whether surgery is equally effective and safe for patients with OPLL as it is for those with other forms of DCM. The authors conducted this study to compare surgical outcomes of patients with OPLL and those with other forms of DCM. Four hundred and seventy-nine patients with symptomatic DCM were prospectively enrolled in the CSM-International study at sixteen sites. Of 479 patients, 135 (28.2%) had radiographic evidence of OPLL, and 344 (71.8%) had other forms of DCM. The two groups did not differ significantly in demographics, surgical approach, or baseline severity of myelopathy. Patients with OPLL achieved similar functional outcomes by two years following surgery compared with patients with other forms of DCM. With respect to quality of life, the Neck Disability Index and most of the subscales of the SF-36 were not different between the two diagnostic groups. There was a higher risk of perioperative complications in the OPLL group ($P = 0.054$), although this relationship did not reach statistical significance. Rates of neurological complications did not differ significantly between the diagnostic groups. The authors concluded that surgical decompression for the treatment of OPLL resulted in improvement in the functional status and quality of life comparable to those seen in patients with other forms of DCM. Patients with OPLL were at a higher risk of perioperative complications than patients with other forms of DCM. These similarities and comparable surgical outcomes support the inclusion of both OPLL and other forms of degenerative myelopathies under the single umbrella of DCM, rather than evaluating them differently, as was previously done.

Contributed by Mazda K. Turel


Although recombinant human BMP-2 is effective in promoting arthrodesis, many physicians avoid using it in anterior cervical spine fusions due to concern for increased incidence of dysphagia, significant pre-vertebral swelling, and airway compromise. The aim of this prospective, randomized, placebo-controlled, double blind trial study was to investigate whether the local administration of methylprednisolone (depomedrol) decreases the severity of dysphagia after anterior cervical discectomy and fusion (ACDF) surgery using bone morphogenetic protein (BMP). Fifty patients between 18 and 70 years of age, undergoing 1, 2, and 3-level ACDFs, were randomized to 1 of 2 groups: BMP-2 with depomedrol or BMP-2 with saline. A 1 × 3 cm collagen sponge was saturated by the nurse with either saline (1 cc) or depomedrol (40 mg/1 cc) based on the randomization protocol described above. Before closure, the sponge was placed ventral to the plate. Patients were followed for 4 weeks postoperatively by the study administrator. Dysphagia was measured at 5 time intervals (postoperative days 1, 4, 7, 14, and 28) using a 4-point Modified Dysphagia Scoring System. Additional data regarding overall length of hospital stay and the administration of dysphagia-directed treatments were also recorded. Twenty-seven patients were randomized to the treatment (depomedrol) group and 23 were randomized to the control (saline) group. The 2 groups were nearly identical in terms of their demographic and operative characteristics. Patients receiving depomedrol experienced decreased
The efficacy of fusion surgery in addition to decompression surgery in patients who have lumbar spinal stenosis, with or without degenerative spondylolisthesis, has not been substantiated in controlled trials. The authors randomly assigned 247 patients between 50 and 80 years of age who had lumbar spinal stenosis at one or two adjacent vertebral levels to undergo decompression surgery plus fusion surgery (fusion group) or decompression surgery alone (decompression-alone group). Randomization was stratified according to the presence of preoperative degenerative spondylolisthesis (in 135 patients) or its absence. Outcomes were assessed with the use of patient-reported outcome measures, a 6-minute walk test, and a health economic evaluation. The primary outcome was the score on the Oswestry Disability Index (ODI; which ranges from 0 to 100, with higher scores indicating a more severe disability) 2 years after surgery. There was no significant difference between the groups in the mean score on the ODI at 2 years (27 in the fusion group and 24 in the decompression-alone group, \( P = 0.24 \)) or in the results of the 6-minute walk test (397 m in the fusion group and 405 m in the decompression-alone group, \( P = 0.72 \)). Results were similar between patients with and those without spondylolisthesis. Among the patients who had 5 years of follow-up, there were no significant differences between the groups in clinical outcomes at 5 years. The mean length of hospitalization was 7.4 days in the fusion group and 4.1 days in the decompression-alone group (\( P < 0.001 \)). The operative time was longer, the amount of bleeding was greater, and the surgical costs were higher in the fusion group than in the decompression-alone group. During a mean follow-up of 6.5 years, additional lumbar spine surgery was performed in 22% of the patients in the fusion group and 21% of those in the decompression-alone group. The authors concluded that among patients with lumbar spinal stenosis, with or without degenerative spondylolisthesis, decompression surgery plus fusion surgery did not result in better clinical outcomes at 2 years and 5 years than did decompression surgery alone.

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In another randomized, controlled trial, a different group of authors assigned patients, 50 to 80 years of age, who had stable degenerative spondylolisthesis (degree of spondylolisthesis, 3 to 14 mm, excluding those with spinal instability, as confirmed on flexion–extension radiographs) and symptomatic lumbar spinal stenosis, to undergo either decompressive laminectomy alone (decompression-alone group) or laminectomy with posterolateral instrumented fusion (fusion group). The primary outcome measure was the change in the physical-component summary score of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36; range, 0 to 100, with higher scores indicating better quality of life) 2 years after surgery. The secondary outcome measure was the score on the Oswestry Disability Index (range, 0 to 100, with higher scores indicating more disability related to back pain). The patients were followed for 4 years. A total of 66 patients (mean age, 67 years; 80% women) underwent randomization. The rate of follow-up was 89% at 1 year, 86% at 2 years, and 68% at 4 years. The fusion group had a greater increase in SF-36 physical-component summary scores at 2 years after surgery than did the decompression-alone group (15.2 vs. 9.5; \( P = 0.046 \)). The increases in the SF-36 physical-component summary scores in the fusion group remained greater than those in the decompression-alone group at 3 years and at 4 years (\( P = 0.02 \) for both years). With respect to reduction in disability related to back pain, the changes in the Oswestry Disability Index scores at 2 years after surgery did not differ significantly between the study groups (-17.9 in the decompression-alone group and -26.3 in the fusion group, \( P = 0.06 \)). More blood loss and longer hospital stays occurred in the fusion group than in the decompression-alone group (\( P < 0.001 \) for both comparisons). The cumulative rate of reoperation was 14% in the fusion group and 34% in the decompression-alone group (\( P = 0.05 \)). The authors concluded that among patients with degenerative grade 1 spondylolisthesis, the addition of lumbar spinal fusion to laminectomy was associated with a slightly greater but clinically meaningful improvement in the overall physical health-related quality of life than laminectomy alone.
However, according to the authors, a moderate difference in the SF-36 score in favour of instrumented fusion does not justify the associated higher costs for implants and the longer duration of surgery than those with decompression alone. Given that the disease-specific ODI is a better outcome measure for the treatment of spinal stenosis than the general SF-36, the fact that both trials showed that the improvements in the scores on the ODI did not differ significantly between the two surgical approaches suggests that the costlier approach of instrumented fusion does not add value for patients. Both trials show clearly that for most patients, stenosis surgery should be limited to decompression when no overt instability is present. Evidence from the trials by Försth et al., and Ghogawala et al., suggests that fusion for the treatment of stenosis is no longer the best practice and that its use should be restricted to patients who have proven spinal instability.

**Contributed by Mazda K. Turel**


Resective surgery is a safe and effective treatment of drug-resistant epilepsy. If surgery has failed, reoperation after careful re-evaluation may be a reasonable option. This study was to summarise the risks and benefits of reoperation in patients with epilepsy. A total of 66 patients with a median follow-up of 10.3 years were included in the study. Fifty-one patients (77%) had surgery for temporal lobe epilepsy, and the remaining 15 cases for extra-temporal lobe epilepsies. The most frequent histological findings were a tumour (n = 33, 50%), followed by dysplasia, gliosis (n = 11, each) and hippocampus sclerosis (n = 9). The main reason for seizure recurrence was incomplete resection (59.1%) of the putative epileptogenic lesion. After reoperation, 46 patients (69.7%) were completely seizure-free and in International League Against Epilepsy grade 1 (ILAE 1) at the last available follow-up. The neuropsychological evaluation demonstrated that repeated losses in the same cognitive domain, that is, successive changes from better to worse performance categories, were rare and that those losses after the first surgery were followed by improvement rather than decline. However, reoperations lead to an increased rate of permanent neurological deficits (9%), overall surgical complications (9%) and visual field deficits (67%). The authors concluded that reoperation after failed resective epilepsy surgery led to approximately 70% long-time seizure freedom and reasonable neuropsychological outcome. However, there is an increased risk of permanent postoperative neurological deficits, which should be taken into consideration when counseling for reoperation.

**Contributed by Mazda K. Turel**


With the increasing life expectancy, neurosurgeons are now encountering an aging population with multiple chronic illnesses. Among these, a large proportion of the patients suffer from cardiac ailments, who are prescribed a regular dose of various anticoagulants such as vitamin K antagonists (VKA, e.g., warfarin) and low molecular weight heparin (LMWH) and new categories of drugs such as direct factor Xa and thrombin inhibitors. An intracerebral hematoma (ICH) accounts for 90% of all VKA related deaths. The increased morbidity and mortality in VKA-ICH is attributable to a large hematoma volume, ICH expansion and multiple comorbidities. Literature remains fractured over the management options for reversal of antithrombotics in ICH. The ‘Neurocritical Care Society’ and ‘Society of Critical Care Medicine’ have introduced evidence-based guidelines for reversal of antithrombotics induced ICH. Tabular summary of recommendations for reversal of antithrombotic agents is a quick first guide helpful for neurosurgery residents and caregivers. However, this guideline does not address antithrombotic reversal in the pediatric population and in patients suffering from intrinsic coagulopathies.

**Contributed by Dr. Manjul Tripathi.**


With the growing unrest in the world, war casualties are on the rise, especially injuries to the head and neck. During operation Iraqi Freedom and operation Enduring freedom, injured soldiers had been shifted from the war zone to the base hospital (4-6 hours) and finally to military hospitals in the United States of America (10 hours intercontinental flight) for definite treatment. Similarly, many patients were daily air lifted to the trauma centres throughout the world. Among these patients, majority suffer from head injuries. Transportation in air exposes the patients to additional risks of hypobaric pressure and hypoxemic conditions.
this interesting study, Skovira and team have evaluated the effects of hypobaric environment without the confounding effects of hypoxia in rat models of traumatic brain injury (TBI). Prolonged hypobaric pressures during air transportation may exacerbate cognitive deficits associated with increased neuro-inflammation and secondary brain injury, resulting in learning and memory deficits and hippocampal neuronal cell loss. Further studies are warranted to frame the guidelines for optimized oxygen supplementation levels, time delay between flights, optimal altitude levels, cabin pressurization and specialized enclosures for individual pressurization.

Contributed by Dr. Manjul Tripathi


As a nation, India is wide and diverse. This diversity is not only limited to language and customs but also to disease distribution, morbidity and mortality. In a nation-wide survey, Usha Ram and team have analysed the age and sex specific mortality risks in the adult (18-69 years) Indian population. It is interesting to note that in high mortality districts, the probability of a man or woman dying by the age of 70 years were respectively 62% and 54% whereas in low mortality districts, it remained 40% and 30%, respectively. It translates to roughly 10 years higher survival in low mortality districts than in high mortality districts. The contributing disorders for this gap are vascular disorders, tuberculosis, malaria and other infections. The adult mortality risk was the highest in north India and the lowest in west India. This report draws attention for better preventive and social programs to curtail infectious and communicable diseases. Apart from it, the vulnerability might be related to poor socio-economic status and geographical locations of particular states where susceptibility to non-communicable diseases and infections was due to childhood malnutrition.

Contributed by Dr. Manjul Tripathi


1012 patients with 1440 unruptured intracranial aneurysms (UIA) underwent 1080 craniotomies. The authors found that at a follow up of 12 months, 10% of all craniotomies (95% confidence interval (CI), 8.4-12.0) resulted in a complication which led to a modified Rankin scale (mRS) > 1. With the help of logistic regression analysis, the authors found that age (odds ratio, 1.04; 95% CI, 1.02-1.06), size (odds ratio, 1.12; 95% CI, 1.09-1.15), and posterior circulation location (odds ratio, 2.95; 95% CI, 1.82-4.78) were significant factors. Cumulative 10-year risk of retreatment or rupture was 3.0% (95% CI, 1.3-7.0). By dividing the complication risk by the 10-year cumulative freedom from retreatment or rupture proportion, the complication-effectiveness model was derived. Risk per effective treatment ranged from 1% for a 5-mm anterior circulation UIA in a 20-year-old patient to 70% for a giant posterior circulation UIA in a 70-year-old patient.

Contributed by Dr. Anant Mehrotra


The authors compared intensive (target systolic BP {SBP}, <140 mm Hg) versus guideline –recommended (SBP, <180 mmHg) lowering of blood pressure in 2839 patients within 6 hours of spontaneous intracerebral haemorrhage and who had elevated SBP (150-220 mm Hg). At 24 hours, 964 patients had a repeat cranial computed tomography. The authors found that a greater SBP reduction was associated with reduced hematoma growth (13.3, 5.0, and 3.0 mL for <10, 10–20, and ≥20 mmHg, respectively; \( P \) trend <0.001). In the intensive treatment group, the least haematoma growth was seen in those patients who had reduction of SBP in less than an hour (2.6 mL) as compared to those whose SBP was reduced in 1-6 hours (4.7 mL) or >6 hours (5.4 mL).

Contributed by Dr. Anant Mehrotra


The authors aimed to investigate the prognostic role of steroid administration in glioblastoma patients. The effects of corticosteroids, such as dexamethasone, on the cell growth in glioma models and on patient survival have remained controversial. A disease-relevant mouse model of glioblastoma was used to characterize the effects of dexamethasone on tumour cell proliferation and death, and to identify gene signatures associated with these effects. A murine anti-vascular endothelial growth factor A (VEGFA)
antibody was used in parallel as an alternative for oedema control. They applied the dexamethasone-induced gene signature to The Cancer Genome Atlas Glioblastoma Dataset to explore the association of dexamethasone exposure with outcome. Mouse experiments were used to validate the effects of dexamethasone on survival in vivo. Retrospective clinical analyses identified corticosteroid use during radiotherapy as an independent indicator of shorter survival in three independent patient cohorts. A dexamethasone-associated gene expression signature correlated with shorter survival in The Cancer Genome Atlas patient dataset. In glioma-bearing mice, dexamethasone pretreatment decreased tumor cell proliferation without affecting tumor cell viability, but reduced the survival when combined with radiotherapy. Conversely, anti-VEGFA antibody decreased proliferation and increased tumor cell death, but did not affect survival when combined with radiotherapy. Clinical and mouse experimental data suggested that corticosteroids may decrease the effectiveness of treatment like radiotherapy and shorten survival in a patient with glioblastoma. The authors concluded that dexamethasone-induced anti-proliferative effects might confer protection from radiotherapy- and chemotherapy-induced genotoxic stress. The authors thus advocated restricted use of steroids in the treatment of glioblastomas and rather highlighted the importance of identifying alternative agents such as vascular endothelial growth factor antagonists for managing oedema in glioblastoma patients.

Contributed by Dr. Kuntal Kanti Das


The authors investigated the temporal profile of microRNA (miRNA) expression during the development of secondary brain damage after experimental traumatic brain injury (TBI). Their hypothesis was that similar to other physiologic and pathologic conditions, miRNAs could represent a novel class of molecular targets for the management TBI. The authors utilized a controlled cortical impact model in C57Bl/6 mice (n = 6) to induce a cortical contusion. Subsequently, using microarray analysis, they studied miRNA expression in the traumatized cortex at 1, 6, and 12h after TBI. Of a total 780 mature miRNA sequences analyzed in this study, the authors could detect 410 sequences in all the experimental groups. Of these, 158 miRNAs were significantly upregulated or downregulated in TBI compared with the sham-operated animals. 52 miRNAs were increased more than two folds. Using quantitative polymerase chain reaction (qPCR), the authors validated the upregulation of five of the most differentially expressed miRNAs (miR-21**, miR-144, miR-184, miR-451, miR-2137) and the downregulation of four of the most differentially expressed miRNAs (miR-107, miR-137, miR-190, miR-541). They further investigated the most differentially expressed miRNA after TBI, miR-2137, using in situ hybridization. They found significant upregulation of miR-2137 in the neurons within the traumatic penumbra. Thus, the authors concluded that these miRNA sequences could act as crucial markers during TBI and may act as future novel targets for the management of brain trauma.

Contributed by Dr. Kuntal Kanti Das