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

K Sridhar, Mazda K Turel, Manjul Tripathi, Ravi Yadav, PR Srijithesh, Aastha Takkar, Sahil Mehta, Kuntal K Das, Anant Mehrotra


The authors conducted this study to compare the impact of robotic guidance in minimally invasive spine surgery (MIS) to fluoroscopy-guided open approach in lumbar fusions. Patients who had to undergo a 1- or 2-level spinal fusion were randomized between robotic-guided MIS (RO) and fluoroscopic-guided open surgery (FA). Thirty patients were recruited to each arm. Thirty-five levels were instrumented with 130 pedicle screws in RO versus 40 levels with 140 screws in FA, or 4.3 and 4.7 screws per surgery, respectively. The duration of use of fluoroscopy was 3.5 versus 13.3 seconds in the RO and FA, respectively (P < 0.001). By thermoluminescent dosimeters, the average per-screw radiation in RO was 3.5 versus 9.4 days in the RO compared with FA surgeries (P = 0.020). The authors concluded that MIS using robotic guidance significantly reduced radiation exposure and length of stay. However, patient outcomes were not affected by the surgical technique.


The authors from the International Spine Study Group (ISSG) conducted this study to describe the rate of neurologic complications in adult spinal deformity (ASD) surgery and also to describe the effect of these complications on clinical outcomes. A total of 564 patients with ASD, undergoing surgery between 2008 and 2014, were analyzed. Their average age was 57 years. A total of 116 neurologic complications occurred in 99 (17.6%) patients. There were 88 surgical procedure-related neurologic complications in 77 (13.7%) patients and 28 nonsurgical neurologic complications in 28 (5%) patients. The most common complications were radiculopathy (30%), motor deficits (22%), mental status changes (12%), and sensory deficits (12%). Revisions (odds ratio [OR] 1.7) and interbody fusions (OR 2.1) were associated with an increased risk of neurologic complications. Decompression and osteotomies (including three-column osteotomies) did not increase the risk of neurologic complications. Patients with neurologic complications were not more likely to sustain other complications; however, they were more likely to undergo another operation during the follow-up period (OR 1.9). The overall incidence of neurologic complications in ASD surgery was 17.6% with the incidence of surgical neurologic complications being 13.7%, especially in revision surgeries and when interbody fusion was required. These figures...
may be utilized to counsel patients prior to their undergoing surgery for adult spinal deformity.

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


The aim of the present study was to compare in patients undergoing anterior cervical discectomy, silicon nitride implants with polyetheretherketone (PEEK) cages filled with autografts harvested from osteophytes. The study was a prospective, randomized, blinded study of 100 patients with a 2 year follow-up. There was no significant difference in the neck disability index (NDI) scores between the groups at a follow-up of 24 months. At 3 and 12 months, the NDI scores were in favor of the PEEK cages although the differences were not clinically relevant. During the follow up assessments, there was no difference in the visual analog scale (VAS) neck and VAS arm scores between both the groups, and there was no statistically significant difference in the patients’ perceived recovery during follow-up. Fusion rate and subsidence were similar for the two study arms and about 90% of the implants were found to be fused at 24 months. Patients treated with silicon nitride and PEEK reported similar recovery rates during their follow-up assessment and no significant difference in the clinical outcome at 24 months was observed. The fusion rates improved over time and were comparable between both groups. Thus, either of these implants may be used in patients undergoing anterior cervical discectomy although better conclusions would be drawn with a longer follow-up assessment period.

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


The aim of the study was to examine the role of the MIS approaches on construct length and clinical outcomes in comparison to the traditional open approaches, when treating similar adult spinal deformity (ASD) profiles. Two multicenter databases for ASD, 1 involving MIS procedures and the other open procedures, were matched for clinical and radiographic parameters in 1215 patients where 84 patients were matched in each group. Statistical significance was found for mean levels fused, mean interbody fusion levels, blood loss, and hospital stay with the MIS techniques showing a better outcome. There was no significant difference in the preoperative radiographic parameters or the postoperative clinical outcomes (Oswestry Disability Index and visual analog scale) between the groups. There was a significant difference in the postoperative lumbar lordosis (43.3° in the MIS and 49.8° the open group) as well as in the pelvic incidence-lumbar lordosis correction (10.6° in the MIS and and 5.2° in the open group). There was no significant difference in the reoperation rate between the 2 groups. The authors concluded that MIS techniques for ASD may reduce the construct length, the reoperation rates, the amount of blood loss incurred, and the length of hospital stay without affecting the clinical and radiographic outcomes when compared to a similar group of patients treated with open techniques.

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


The authors examined the trends in reoperation after a single-level lumbar discectomy. The patients included in this study were followed for up to 4 years for assessing if they had undergone recurrent lumbar surgery, including spinal fusion, laminectomy, and additional discectomy. The analysis of data obtained from 13,654 patient records revealed a rate of additional lumbar surgeries after a single-level discectomy, of 4% (539/13654) within 3 months and 12% (766/6274) within 4 years of the index procedure. Lumbar spinal fusion was performed on 6% (370/6274) of patients within 4 years. Patients who received a re-exploration discectomy within 2 years of the index procedure went on to receive lumbar fusion at a rate of 38.4% (48/125) within the 4 years after the re-exploration discectomy. The average additional cost of lumbar reoperation, as measured by insurance reimbursement, was approximately $111,161 per patient per year. This study would be useful for seeking informed consent from the patients by providing them with valuable data regarding the frequency and nature of reoperations required after an initial discectomy has already been performed.

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

**Chugh AJ, et al.** Use of a surgical rehearsal platform and improvement in aneurysm clipping measures: Results of a prospective, randomized trial. *J Neurosurg* 2017;126:838-44

Surgical rehearsal platforms, that include surgical simulators that enable surgeons to rehearse a procedure prior to entering the operative suite, are helpful in planning surgery. This study was designed to determine if the use of a surgical rehearsal platform prior to performing an aneurysm surgery is helpful in decreasing the aneurysm dissection time and in clip manipulation of the aneurysm.

This was a blinded, prospective, randomized study comparing the key effort required and the time variables required in aneurysm clipping with and without the preoperative use of the SuRgical Planner (SRP) surgical rehearsal platform. 25 patients were randomly assigned to either of two groups: one in which surgery was performed after use of the SRP (SRP group) and one in which surgery was performed without use of the SRP (control group). All operations were videotaped. The videos were analyzed for the total microsurgical time taken, the number of clips used, and the number of clip placement attempts. The mean (± SD) amount of operative time per clip used was 920 ± 770 seconds in the SRP group.
The authors compared the effect of clipping and coiling on palsies induced by posterior communicating artery the treatment of patients with oculomotor nerve

Contributed by Dr. Mazda K. Turel


Symptomatic intracranial hemorrhage (SICH) following endovascular therapy (EVT) in acute ischemic stroke (AIS) with a large vessel occlusion may lead to serious consequences. The authors attempted to identify the predictors of SICH after EVT in patients with internal carotid artery (ICA) or proximal M1 segment of the middle cerebral artery (MCA) occlusion. Among 1442 AIS patients with a large vessel occlusion, admitted within 24 hours after the onset of AIS, 226 patients with an ICA or a proximal M1 occlusion were treated with EVT. SICH was defined as any type of intracranial hemorrhage with a decline in the National Institutes of Health Stroke Scale (NIHSS) score ≥4. Of the 226 patients, 204 patients with sufficient data were analyzed. SICH was observed in 10 patients (4.9%). Baseline NIHSS score (22 versus 17), serum glucose level (206 mg/dL versus 140 mg/dL), and prior antiplatelet therapy (60.0% versus 21.7%) were significantly higher in patients with SICH than in those without SICH (P < 0.01). SICH had a greater propensity to occur when the NIHSS score was ≥19 and serum glucose ≥160 mg/dL. The authors concluded that hyperglycemia, prior anti-platelet therapy, and a high baseline NIHSS score were associated with SICH after EVT in AIS patients with an ICA or a proximal M1 occlusion.

Contributed by Dr. Mazda K. Turel


The authors compared the effect of clipping and coiling on the recovery of oculomotor nerve palsy (ONP) during the management of patients with posterior communicating artery aneurysms (PcomAAs). Nine published reports of eligible studies involving 297 participants met the inclusion criteria. Overall, compared with endovascular coiling, surgical clipping had no statistically significant difference on the complete recovery of ONP, although there was an obvious trend in favor of clipping [RR = 1.48, P = 0.08]. There was no significant difference in any degree of change of ONP, in the incidence of overall complications, the efficacy on the complete recovery of ONP in patients without SAH, as well as the effect on the complete recovery of ONP in patients with pre-operatively complete or incomplete ONP. In a comparison of a small cohort of patients that had suffered an SAH (17 vs. 22), there was a significant difference on the effect on complete recovery of ONP between clipping and coiling [RR = 1.70, P < 0.05]. The authors concluded that a superiority of clipping over coiling for the complete recovery of oculomotor nerve palsy in patients who had suffered an SAH from a ruptured aneurysm of the posterior communicating artery was found in the present meta-analysis. The sample sizes in the two groups were small; however, there were no significant differences observed in the clinical outcome between coiling and clipping in the treatment of unruptured PcomAA causing ONP.

Contributed by Dr. Mazda K. Turel


The presence of a complex vascular anatomy might increase the risk of procedure-related stroke during carotid artery stenting (CAS). This randomized controlled trial attempted to study the influence that the vascular anatomy of the patient had on determining the choice between CAS and carotid endarterectomy (CEA).

One-hundred and eighty-four patients with symptomatic internal carotid artery stenosis were randomly assigned to the CAS or CEA groups in the ICSS (International Carotid Stenting Study). These patients underwent a magnetic resonance (n = 126) or a computed tomographic angiography (n = 58) at baseline and a brain magnetic resonance imaging before and after treatment. The authors investigated the association between different aortic arch configurations, angles of supra-aortic arteries, degree and length of carotid artery stenosis, and plaque ulceration with the presence of ≥1 new ischemic brain lesions, detected on diffusion-weighted magnetic resonance imaging (DWI+) after treatment. Forty-nine of 97 (51%) patients in the CAS group, and 14 of 87 (16%) patients in the CEA group were DWI+ (odds ratio [OR], 6.0; 95% confidence interval [CI], 2.9-12.4; P < 0.001). In the CAS group, aortic arch configuration type 2/3 (OR, 2.8; 95% CI, 1.1-7.1; P = 0.027) and the degree of the largest internal carotid artery angle (≥60° versus <60°; OR, 4.1; 95% CI, 1.7-10.1; P = 0.002) were both associated with DWI+, after correction for the patient's age. No predictors for DWI+ were identified in the CEA group. An increase in the largest internal carotid artery angle to ≥60° further increased the risk of the patient developing DWI+ lesions.
in the CAS group when compared to the group undergoing CAS where the angle was <60° (OR 3.4; P = 0.035). Thus, a complex configuration of the aortic arch and the presence of internal carotid artery tortuosity increased the risk of cerebral ischemia during CAS, but not during CEA. Vascular anatomy of the involved blood vessels should be taken into account when selecting patients for carotid artery stenting.

Contributed by Dr. Mazda K. Turel


The authors investigated the association between timing of treatment (0-7 days and >7 days after the qualifying neurological event) and the 30-day risk of stroke or death after carotid artery stenting (CAS) or carotid endarterectomy (CEA). This was done in a pooled analysis of individual patient data from 4 randomized trials by the Carotid Stenosis Trialists’ Collaboration. Among a total of 4,138 patients, a minority received their allocated treatment within 7 days after the symptom onset (14% CAS versus 11% CEA). Among patients treated within 1 week of symptoms, those treated by CAS had a higher risk of stroke or death compared with those treated with CEA (8.3% versus 1.3% [RR-6.7]). For interventions after 1 week, CAS was also more hazardous than CEA: 7.1% versus 3.6% (risk ratio [RR] 2.0). The authors concluded that, in randomized trials comparing CAS with CEA for symptomatic carotid artery stenosis, CAS was associated with a substantially higher peri-procedural risk during the first 7 days after the onset of symptoms. Early surgery is safer than stenting for preventing the development of future stroke.

Contributed by Dr. Mazda K. Turel


The authors aimed to evaluate the diagnostic accuracy of computed tomographic angiography (CTA) in the detection of intracranial aneurysms in the setting of subarachnoid haemorrhage (SAH). A single-center, retrospective cohort of 643 patients was reviewed. A total of 401 patients were identified whose diagnostic workup included both CTA and confirmatory digital subtraction angiography (DSA). 330 aneurysms were detected by CTA while DSA detected a total of 431 aneurysms. False positive CTA results were seen for 24 aneurysms. DSA identified 125 aneurysms that were missed by CTA and 83.2% of those were <5 mm in diameter. The sensitivity of CTA was 57.6% for aneurysms smaller than 5 mm in size, and 45% for aneurysms originating from the internal carotid artery. The overall sensitivity of CTA in the setting of SAH was 70.7%. They concluded that the accuracy of CTA in the diagnosis of ruptured intracranial aneurysm may be lower than previously reported. CTA has a lower sensitivity for detecting aneurysms less than 5 mm in size, in locations adjacent to bony structures, and for those aneurysms arising from small caliber parent vessels. They recommend that CTA should be used with caution when used alone in the diagnosis of ruptured intracranial aneurysms.

Contributed by Dr. Mazda K. Turel


Patients with acute ischaemic stroke within 8 h of symptom onset were randomly assigned to medical therapy (including intravenous alteplase) and neurovascular thrombectomy with Solitaire FR or medical therapy alone. From Nov 2012 to Dec 2014, 206 patients were randomly assigned to medical therapy plus endovascular 12 months post-randomisation, based on 205 of 206 outcomes available at 12 months, thrombectomy reduced disability over the range of the modified Rankin score [mRS] (with an odds ratio [OR] of 1.80), and improved functional independence (mRS = 0-2; 45 [44%] of 103 patients vs 31 [30%] of 103 patients). Health-related quality of life was superior in the thrombectomy group. The one-year mortality was 23% (24 of 103 patients) in the thrombectomy group versus 24% (25 of 103 patients) in the control group. These findings have important clinical and public health implications for evaluating the cost-effectiveness of the intervention in the long term.

Contributed by Dr. Mazda K. Turel


The prognosis of diffuse low-grade gliomas (DLGG) is variable and depends several factors, including the isocitrate dehydrogenase (IDH) mutation and the 1p19q codeletion. The authors aimed to analyse the correlations between the IDH and 1p19q status and the intracerebral distribution of the tumor (at the lobar and voxel levels), its volume, and its borders, on a consecutive series of 198 DLGG patients. Frontal tumors were more frequently IDH-mutant (87.1 vs. 57.4%) and 1p19q codeleted (45.2 vs. 17.0%) than tempo-ro-insular lesions. Tumors with sharp borders were more frequently IDH-mutant (P = 0.001) while tumors with indistinct borders were more frequently IDH wild-type and 1p19q non-codeleted (P < 0.001). Larger tumors at diagnosis (possibly linked to a slower growth rate) were more frequently IDH-mutant (P < 0.001). The authors concluded that IDH wild-type, 1p19q non-codeleted tempo-ro-insular tumors are distinct from IDH-mutant, 1p19q codeleted frontal tumors. Further studies are needed to determine whether the therapeutic strategy should be adapted to each pattern.

Contributed by Dr. Mazda K. Turel

Bevacizumab, as an antibody, was applied to inhibit tumor angiogenesis by preventing activation of vascular endothelial growth factor receptors. The authors analyzed four clinical trials, including 607 patients, to investigate the efficacy and safety of bevacizumab when combined with chemotherapy for the treatment of glioblastomas. Results demonstrated that bevacizumab when combined with chemotherapy improved progression-free survival (HR = 0.66; 95% CI 0.56-0.78; P < 0.00001) compared with bevacizumab or chemotherapy alone. Furthermore, the overall survival showed insignificant difference between the two arms (HR 0.99; 95% CI 0.8-1.21; P = 0.92). However, they found that patients treated with bevacizumab-containing therapy reported increased objective response rate (odds ratio [OR] 1.85, 95% confidence interval [CI] 1.17-2.93; P = 0.009), but had more treatment-related adverse events (OR 1.75; 95% CI 1.09-2.83; P = 0.02).

Contributed by Dr. Mazda K. Turel


The authors wanted to analyze the predictors for and the clinical impact of gross total resection (GTR) in patients with a glioblastoma (GBM). Patients were grouped based on the extent of resection into biopsy alone, subtotal resection (STR), and GTR. Univariable and multivariable (MVA) analyses were performed to investigate the factors associated with the likelihood of GTR and the overall survival (OS) following diagnosis. 27,865 patients met the inclusion criteria. Factors associated with increased odds of GTR on MVA included a younger patient age, the female gender, the patients’ race, a lower comorbidity score, a higher performance score, a smaller tumor size, unifocality, MGMT hypermethylation, radiotherapy, chemotherapy, and facility volume (each P < 0.005). After adjusting for each of these factors, compared to biopsy alone, GTR was associated with improved OS (hazard ratio 0.768, P < 0.001), while STR was not. While a prospective randomized trial on this topic is unlikely to be completed, this large retrospective analysis provides evidence to support the recommendation of GTR in patients with GBM.

Contributed by Dr. Mazda K. Turel


The authors conducted a trial involving patients 65 years of age or older with a newly diagnosed glioblastoma. Patients were randomly assigned to receive either radiotherapy alone (40 Gy in 15 fractions) or radiotherapy with concomitant and adjuvant temozolomide.

A total of 562 patients underwent randomization, 281 to each group. The median age was 73 years (range, 65 to 90 years). The median overall survival was longer with radiotherapy plus temozolomide than with radiotherapy alone (9.3 months vs. 7.6 months; P < 0.001), as was the median progression-free survival time (5.3 months vs. 3.9 months; P < 0.001). Among 165 patients with MGMT status, the median overall survival was 13.5 months with radiotherapy plus temozolomide and 7.7 months with radiotherapy alone (P < 0.001). Among 189 patients with unmethylated MGMT status, the median overall survival was 10 months with radiotherapy plus temozolomide and 7.9 months with radiotherapy alone (P = 0.08). The quality of life was similar between the two trial groups. The authors concluded that in elderly patients with glioblastoma, the addition of temozolomide to short-course radiotherapy resulted in longer survival than a short-course of radiotherapy alone.

Contributed by Dr. Mazda K. Turel


The authors attempted to assess the efficacy and safety of clonidine in reducing blood loss in pituitary adenoma surgery using a prospective randomized controlled trial. A total of 50 patients of pituitary adenomas were randomized into two groups. Group A (25 patients) was given 200μg clonidine orally, while Group B (25 patients) was given a placebo. The surgery, anaesthesiologist and patient were blinded to the group assigned. Sublabial trans-septal trans-sphenoidal approach to the sella and excision of the mass was performed in each of the patients. The blood loss during the surgery, operative time and bleeding grading by the surgeon were found to be significantly less in the clonidine group, while the quality of surgical field, condition of the specific part and extent of resection were found to be significantly better in the clonidine group (P value <0.05). There was no untoward adverse effect of the drug in the test group. They concluded that clonidine is a safe and effective drug to achieve reduction in the bleeding during the trans-sphenoidal microscopic surgery for resection of pituitary adenomas.

Contributed by Dr. Mazda K. Turel


The authors aimed to assess the effect of intensive insulin therapy (IIT) for preventing postoperative infection in patients with traumatic brain injury (TBI). 88 patients with TBI were randomly divided into 2 groups, 44 in each group. One
group (group ITT) received IIT and the other group (group CIT) received conventional insulin therapy (CIT). Outcomes included infection rate, mortality, and neurological outcome (measured by the Glasgow Outcome Scale [GOS]). A total of 81 patients completed the study. IIT showed a greater efficacy than CIT, with a decreased infection rate in the IIT group compared to the CIT group (31.9% vs 52.3%, P = 0.03), and also a reduced duration of stay in the intensive care unit (ICU) [IIT group, 4.5 ± 2.1 days vs CIT group, 5.7 ± 2.8 days, P = 0.02]. In addition, a significant difference in the scores on the Glasgow Outcome Scale was observed between the 2 groups (P = 0.04). The mortality rates in hospital and at the 26-week follow-up were similar between the two groups.

The authors concluded that IIT leads to a reduced infection rate, shorter stays in ICU, and improved neurological outcome when compared to CIT.

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


This study aimed to compare the clinical outcomes in patients with chronic subdural hematoma (CSDH) following a twist drill craniostomy (TDC) or burr hole craniostomy (BHC).

Thirty-eight and 45 patients received TDC and BHC treatment, respectively. There was no significant difference in age, gender, head trauma, diabetes mellitus, hypertension, antiplatelet usage, clinical manifestation, the Glasgow Coma Scale score and preoperative radiographic characteristics between the two groups. The patients in the TDC group had a significantly shorter operating time, but a longer draining time than those in the BHC group (16.9 ± 6.3 min vs. 44.4 ± 7.1 min, P = 0.001; 3.1 ± 1.0 d vs. 2.5 ± 0.9 d, P = 0.003; respectively). A smaller degree of midline shift reversal was observed in patients after TDC than those after BHC (2.6 ± 2.5 mm vs. 3.9 ± 2.8, P = 0.030). Seven patients (18.4%) in the TDC group, and 5 patients (11.1%) in BHC group experienced the recurrence of CSDH. There was no significant difference in the recurrence rate, in-hospital complications, and neurological outcomes between the two groups. The follow up was 3 months. This study indicates that TDC and BHC have similar clinical outcomes in the treatment of patients with CSDH. A shorter operating time, but a smaller midline shift reversal and a longer draining time may be expected in patients after a TDC than after a BHC.

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

**Price M. Study finds some significant differences in brains of men and women. Science 2017. DOI: 10.1126/science.aal1025**

While describing behavioural changes between men and women, various prolific works have been published, including the book “Men are from Mars, Women are from Venus.” Scientists have been trying to find some concrete evidence to prove gender based differences in the anatomy and physiology of the brain. With the earlier discovery of larger brain volume in males, patriarchal societies have utilized this data as an evidence to boost their ego and superiority over the other sex. But, apart from volumetric differences, do these translate to intelligence and/or functional significance? The answer still remains unanswered and is controversial too. In this regard, the largest anatomic study done so far by Stuart Ritchie details a few interesting facts such as women tend to have thicker cortices while men have a higher brain volume. Theoretically, cortical thickness contributes to higher cognitive ability and analytical power. Analysis of 68 different regions of the brain have revealed that men have higher brain volume in every subcortical area in comparison to women who have a thicker cortical volume. These indices are more variable in males than females. Interestingly, these mathematical parameters still fail to prove any correlation with intelligence and behaviour but will definitely fuel the ongoing war on popular conflicts over these heady issues.

**Contributed by Dr. Manjul Tripathi**


A significant proportion of patients with various benign and malignant disorders receive adjuvant, neo-adjuvant or concurrent radiotherapy, either in the form of radiotherapy or radiosurgery. One of the major complications after radiotherapy is attenuated higher order cognitive functions such as memory, attention or behavioural changes, etc., rather than somatosensory deficits, cortical blindness or paralysis. Conceptually, all intracranial structures are not uniformly sensitive to radiation but show a variable response. At present, the brainstem, optic pathway, cochlea, and cranial nerves are considered structures at risk while the brain parenchyma is considered essentially homogenous, in terms of their susceptibility to radiation therapy exposure. The treatment plans target particular areas in order to avoid overt radiation necrosis while maintaining the efficacy of radiotherapy. Challenging the current concepts of radiobiology, this article is the first study in the humans to show selective vulnerability of specific cortical subregions to atrophy related to radiation dependent dose. The authors hypothesize that the higher order association cortex is more vulnerable to radiation injury in comparison to the primary cortex, which is supported by greater volume reduction in the entorhinal cortex and the inferior parietal lobule in comparison to the primary cortical areas after administration of fractionated radiation therapy. Such a finding may dramatically change the treatment methodologies and radiation parameters, paving the way for more sophisticated radiation tools and targets.

**Contributed by Dr. Manjul Tripathi**

This interesting meta-analysis of more than 12820 records on this topic has highlighted the value of physical exercise for cognitive improvement in adult age population. With the shifting population base, dementia is a major health concern and the available interventions for silent epidemics such as Alzheimer’s disease are very insufficient. A combination pattern of exercise (including resistance training and aerobic exercise) helps in improvement of cognitive function in the general population above 50 years of age, regardless of their baseline cognitive status. The exercise should be of moderate intensity and should be done as many days every week as feasible. The minimum duration of exercise should be of 45 minutes per day. The study highlights that irrespective of the mode of the exercise viz. yoga, Tai Chi, resistance training, or multicomponent training, physical activity is helpful for a healthy brain. Inculcation of such habits early in the life will ensure a sound brain in a healthy body.

**Contributed by Dr. Manjul Tripathi**


The notable scientist and theoretical physicist, Albert Einstein maintains dominance in news even after 70 years of his death. His exceptional intelligence and analytical power garnered jealously among contemporary scientists and curiosity in subsequent generations. Dr. Dean Falk and his team have examined the external gross neuroanatomy of Einstein’s entire cerebral cortex from 14 recently discovered photographs taken at the time of block preparation after his death in 1955. Contrary to the popular belief, Einstein’s brain was unexceptional in weight and appearance. There were, however, some unusual findings, such as relatively expanded prefrontal cortices and larger inferior parietal lobules, which explains his extraordinary neuro-cognitive skills and visuospatial/mathematical skills respectively. The primary somatosensory and motor areas, which typically represent face and tongue area, were also exceptionally enlarged in the left hemisphere. Interestingly, these and the changed sulcal pattern in his brain are some changes which reflect a gradual evolution of the brain in human race with the evolution of higher cognitive abilities. A histopathologic review from these areas may illustrate some of these unanswered queries in hominid evolution.

**Contributed by Dr. Manjul Tripathi**


Radiation induced tumorigenesis (RIT) or malignant transformation are considered a collateral damage in the field of radiotherapy. To minimize its chances and to reduce the administration of sinister radiation to the surrounding brain parenchyma, sophisticated radiation tools such as gamma knife and proton radiosurgery have become popular. RIT is a significant risk factor which needs to be discussed with the patient while explaining different treatment options. Pollock et al., have evaluated the risk of RIT or malignant transformation in one of largest series of patients (n = 1837) receiving single fraction gamma knife stereotactic radiosurgery. They report a 0% risk of radiation induced tumor at 15 years of follow up, and a 2.2% risk of malignant transformation at 5 years. Literature review in the same article illustrates that the overall risk of RIT or malignant transformation remains 0.04%-2.6% at 15 years of follow up. The most common radiation induced tumors are glioma and meningioma. Among all, meningiomas are the most common primary brain tumors at risk for malignant transformation. There is no report of malignant transformation in pituitary adenoma or glomus tumor. Till date, there is no definite proof if this risk is because of heterogeneity in the histopathologic grade of the meningioma, which might show a variable response to radiation exposure. Based on this report, it can be concluded that single fraction radiosurgery is a very safe treatment option, which should be stressed upon as a justification for administering it while choosing alternate treatment options.

**Contributed by Dr. Manjul Tripathi**

**Fullston T, et al. The most common vices of men can damage fertility and the health of the next 3 generation. J Endocrinol 2017. DOI: 10.1530/JOE-16-0382.**

A man is considered a slave to his habits but the recent findings published by Tod Fullston suggest that such habits keep punishing the subsequent three generations, similar to the civil code practiced in North Korea. In this interesting study, the three most common vices of men (smoking, obesity and alcohol) were evaluated for their impact on fertility and the health of the next three generations. Smoking is a wishful sin which is the most dangerous vice of all the three. Not only is it a mutagenic substrate for numerous cancers but also contributes to increased incidence of childhood cancers in children born to male smokers. Reactive oxygen species from smoke have the tendency to cause permanent changes to the proteome of the seminal fluids, which further get transmitted to future generations. Similarly, the first and second generation of obese parents manifest an increased risk of developing metabolic syndrome and infertility. Till now, no specific correlation could be identified between alcohol consumption and sperm count, mobility or seminal fluid consistency but alcohol significantly reduces testosterone levels indirectly by its impact on liver metabolism. Paternal alcohol consumption has been linked to various neurological, behavioral, and growth anomalies in children. This article further strengthens the need for a simple lifestyle short of celibacy.

**Contributed by Dr. Manjul Tripathi**


Even after decades of the existence of the entity of “idiopathic intracranial hypertension” (IIH), the exact pathogenesis has...
not been deciphered. Female gender, obesity and recent weight gain have all been speculated to be the causative factors. This article captures attention in describing a 22-year old karyotypically 46XX patient undergoing a female-to-male gender reassignment, who presented with IIH. Interestingly, the patient had started testosterone injections (250 mg 3-monthly) just prior to the onset of symptoms. The role of hormones in IIH has always been suspected but has never been proven with certainty. The authors raise a possibility that IIH may be a distinct neuro-metabolic complication of circulating testosterone levels within a range. These observations present an interesting avenue for new research in IIH and warrant the need for further detailed characterization of the androgen metabolic phenotype in this condition.

Contributed by Dr. Aastha Takkar


Characterized by progressive onset of gait disturbances, dementia, and urinary incontinence, idiopathic normal pressure hydrocephalus (iNPH) is one of the important differential diagnoses in the causation of dementia or progressive gait disturbances. Early treatment with a ventriculo-peritoneal or a lumbo-peritoneal shunt can offer reversal of symptoms but non-invasive diagnostic markers are still insufficient to enable the diagnosis with certainty. Interestingly, this study used spectral domain-optical coherence tomography (SD-OCT)-based measures of retinal and choroidal thickness to assess for ophthalmological non-invasive markers in 12 patients with iNPH. The hypothesis considered was that vascular circulation abnormalities in iNPH may be reflected by changes in the subfoveal (SFChT) and peripapillary (PPChT) choroidal thickness. Non-shunted iNPH patients showed significantly lowered median PPChT and SFChT values compared to healthy controls, which reversed on shunting. Although limited by a small sample size, SD-OCT measures in this study reveal significant changes of choroidal thickness and support the hypothesis of choroidal susceptibility to hemodynamic alterations in iNPH, providing an interesting ophthalmologic approach to NPH, thus opening further domains for research.

Contributed by Dr. Aastha Takkar


The calcitonin gene-related peptide (CGRP) pathway is important in migraine pathophysiology. This phase 2, randomised, double-blind, placebo-controlled, multicentric study assessed the safety and efficacy of erenumab, a fully human monoclonal antibody, against the CGRP receptor, for adults with chronic migraine. The primary endpoint was the change in monthly migraine days from baseline to the last 4 weeks of double-blind treatment (weeks 9 – 12). Safety endpoints were adverse events, clinical laboratory values, vital signs, and anti-erenumab antibodies. In patients with chronic migraine, erenumab 70 mg and 140 mg, reduced the number of monthly migraine days with a safety profile similar to a placebo, providing evidence that administration of erenumab could be a potential therapy for migraine prevention. The applicability of this study to the real-world settings requires further evidence; however, this needs to be seen as a new hope for patients and physicians dealing with refractory, chronic migraine.

Contributed by Dr. Aastha Takkar, Dr. Ravi Yadav and Dr. Sahil Mehta


The eyes are a window to the brain. The retinal nerve fibre layer (RNFL) has long been thought as an extension of the central nervous system (CNS) and has been seen to be correlating with a plethora of degenerative/white matter diseases of the CNS. Since the retina belongs to the end-stream region of the internal carotid artery, the hypothesis was that a carotid artery stenosis, and importantly, even a clinically asymptomatic one, could cause a small ischemic infarct in the RNFL. It may result in an RNFL defect detectable by ophthalmoscopy or by another imaging technique. This community-based study of 3376 participants evaluated asymptomatic poly-vascular abnormalities in adults without a history of cerebrovascular/coronary incidents. The presence and degree of an intracranial arterial stenosis (ICAS) and extracranial carotid arterial stenosis (ECAS) was studied using the transcranial and colour Doppler ultrasound. Retinal nerve fibre layer thickness (RNFL thickness) was measured by the spectral-domain optical coherence tomography. A higher prevalence and degree of ECAS correlated with a thinner RNFL, and vice versa. Patients with an abnormally thin RNFL without any ocular disease may undergo a carotid artery examination to detect the presence of asymptomatic carotid artery stenosis. Interestingly, examination of the RNFL can provide a clue towards the diagnosis of cerebrovascular disease though the hypothesis requires confirmation utilizing larger studies with a longer follow up.

Contributed by Dr. Aastha Takkar


Intense measures to discover biomarkers in amyotrophic lateral sclerosis (ALS) are needed as reliable indicators for an early diagnosis, prognosis, and disease progression. Neurofilaments (NFL), as important scaffolding proteins of the cytoskeleton of the axon, may act as possible markers of neuronal injury. This single center, retrospective study was designed to assess the ability of NFLs to serve as diagnostic biomarker in ALS, and to study the prognostic value of
Cerebrospinal fluid NFLs in these patients. Cerebrospinal fluid samples were studied for the presence and levels of NFLs in 94 patients with ALS, 20 patients with frontotemporal dementia (FTD), 18 patients with motor neuropathies and in 44 controls. Log-transformed NFL (log[NFL]) concentrations were higher in the ALS and FTD groups compared with the motor neuropathies and control groups. Patients with typical ALS, progressive bulbar palsy and upper motor neuron dominant ALS had higher levels of NFLs than did those with flail arm or leg syndrome and progressive muscular atrophy. Interestingly, there was an inverse correlation between the log[NFL] concentration and overall survival. This study confirms the role of NFLs as biomarkers in ALS. Neurofilament light chain levels may help to discriminate amyotrophic lateral sclerosis from other diseases and also to differentiate between different phenotypes of amyotrophic lateral sclerosis; lower neurofilament light chain levels in patients with lower motor neuron signs could serve as a prognostic marker of a milder phenotypes of the disease.

Contributed by Aastha Takkar


The duration and definite benefits from individual treatment options in multiple sclerosis (MS) are controversial. Biomarkers may aid in predicting the long-term outcomes and in assigning patients to individual treatment regimens. This was an observational cohort study of 312 patients with relapsing remitting MS (RRMS) in 2 independent cohorts (with a shorter disease and a longer disease duration) to assess if the retinal layer volumes correlated with immune cell subsets and immunoglobulin indices in the cerebrospinal fluid, and if these are associated with worsening of the disease course. The common ganglion cell and inner plexiform layer (GCIPL) as well as the inner nuclear layer (INL) volumes were tested for the detection of their association with the immunoglobulin indices and the frequencies of immune cells in the cerebrospinal fluid. In both cohorts, with short and long disease durations, low GCIPL volumes were associated with an increased risk of worsening disability during the follow-up period compared with patients with higher GCIPL values. In both the cohorts, INL volumes correlated with the prospective increase in T2 lesion load and the number of gadolinium-enhancing lesions. Probably, retinal layers reflect different aspects of the disease activity during MS. Loss of GCIPL is associated with intrathecal B-cell immunity and constitutes an independent risk factor for worsening disability, whereas high INL volumes are associated with activity on magnetic resonance imaging in the brain parenchyma. Thus, retinal optical coherence tomography might be a means to support stratification of patients with MS for different therapeutic regimens. Conceptually, eye is the “mirror” of the brain.

Contributed by Aastha Takkar


In this paper, the two-year outcome data of ‘Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN)’ is reported. MR CLEAN was the first trial that reported unequivocal clinical efficacy of endovascular intervention in acute ischemic stroke due to large vessel occlusion. The two-year data was available for 391 patients (78.2%) and the data on death was available for 91.8% of the patients. The outcome was more favorable for endovascular treatment than the conventional treatment. The cumulative 2-year mortality rate was 26.0% in the intervention group and 31.0% in the control group.

This report shows that the favorable outcome of endovascular intervention in acute ischemic stroke due to large vessel occlusion is maintained in the long term. We await the two-year outcome data of other trials published on this topic for corroboration of this report.

Contributed by Dr. Srijithesh P


In this study, a retrospective analysis of the clinical syndrome associated with novel antibody against dipeptidylpeptidase–like protein 6 (DPPX) is described. DPPX is a regulatory protein of the Kv4.2 potassium channels that are involved in somatodendritic signal integration. A total of 35 patients were identified. All developed weight loss or diarrhea, followed by cognitive dysfunction, memory deficits, central nervous system (CNS) hyperexcitability, or brainstem or cerebellar dysfunction. All patients were positive for immunoglobulin (Ig) G4 and IgG1 DPPX antibodies. In neuronal cultures, the antibodies caused a decrease of the DPPX clusters and the Kv4.2 protein. The changes were reversible on removal of the antibodies. A triad of weight loss, cognitive-mental dysfunction, and CNS hyperexcitability is described. The features of CNS hyperexcitability included hyperekplexia, myoclonus, tremors, or seizures. Of the 35 patients, eight patients were not treated with immunotherapy. 60% had substantial or moderate improvement to immunotherapy, 23% had no improvement, and 17% died. Relapse occurred in 23% of the patients who responded to immunotherapy.

This report describes the phenotype of yet another novel autoimmune neurological disorder in the ever-increasing list of neurological autoimmune disorders. The gastrointestinal affection described in the disease is attributed to the presence of DPPX in myenteric plexus. The consideration of diverse clinical phenomena like myoclonus, seizures, tremors and hyperekplexia as an indication of the generalized CNS hyperexcitability would simplify clinical reasoning when dealing with multineuraxial neurological disorders that defy the established clinical phenotypes.

Contributed by Dr. Srijithesh P

Homocystenemia has been linked to atherosclerosis and vascular events in many observational studies. However, most of the interventional trials with folic acid were equivocal. Recently, a large randomized control trial (Chinese Stroke Primary Prevention Trial, the CSPPT) studying the effects of folate supplementation in patients with hypertension, stratified by the methylenetetrahydrofolate reductase (MTHFR) gene polymorphism was published. The study, unlike the previous studies, had first stroke as the primary outcome. This study has shown positive results in favor of folate supplementation. This systematic review and meta-analysis examined the efficacy of folic acid supplementation in the prevention of stroke. The study included randomized control trials (RCTs) and specifically looked at stroke, unlike the previous studies that studied the combined cardiovascular outcomes. It also examined the effect of folate fortification in the results of the trials. The study included 22 RCTs involving 82,723 participants, with 41,426 individuals assigned to the intervention group and 41,297 to the control group. The study found that folate acid supplementation significantly reduced the stroke risk by 11% (relative risk 0.89, 95% confidence interval [CI] 0.84–0.96). The effect was greater in low folate regions compared with high folate regions, and among patients without folic acid fortification compared with those with folic acid fortification. The study’s results were dominated by results obtained by CSPPT. However, the authors had conducted a sensitivity analysis that excluded CSPPT, which did not show results at variance from the main results of the study. The study analyses the differential effects of folate supplementation in stroke as compared to other cardiovascular diseases, especially in populations where food fortification with folate is not done. This study highlights the importance of biological heterogeneity in the study population that may result in equivocal or neutral conclusions, for interventions that have shown consistent results in observational studies. The differential effects of folate supplementation in stroke compared to other vascular disease calls for further investigation in this research area.

**Contributed by Dr. Srijithesh P**


The placebo response is known in many diseases whose clinical features are dominated by subjective symptoms. While the placebo response elicits a clinical response to the biologically inactive component, the nocebo response involves development of adverse events to biologically inactive components. Restless legs syndrome (RLS) is sensorimotor disorder characterized by paresthesia and dysesthesia in limbs, an urge to move the affected limbs, diurnal worsening of the symptoms, and improvement of symptoms on limb movement. The disease affects 10% of the population and causes significant impairment in sleep and life style. In this systematic review, the placebo and nocebo response demonstrated in the clinical trials on RLS was studied. The study included 85 randomized controlled trials involving 5,046 patients. The mean reduction in International Restless Legs Syndrome Study Group rating scale for the severity of restless legs syndrome (IRLS) was 6.58 points (95% confidence interval [CI] 4.86–8.29). The overall nocebo response was 43.36% (95% CI 40.47%–50.29%). The placebo and nocebo responses had similar direction of change.

The factors that determined the placebo and nocebo responses were longer duration studies, studies involving pharmacologic interventions, idiopathic RLS, industry-funded trials, and unpublished trials. All subjective outcomes like quality of life, quality of sleep, and daytime somnolence improved with the placebo administration, while the placebo response was small-to-absent for objective outcomes like periodic limb movement index (PLMI).

This systematic review highlights the magnitude of the placebo and nocebo responses in RLS. The magnitude of the response exceeded the threshold of the minimal clinically important score (MCIS) for IRLS maintained by more than 70% of the clinical trials that had defined MCIS in their protocol. This review underlines the care needed in designing and interpreting clinical studies in RLS.

**Contributed by Dr. Srijithesh P**


Elevation of cardiac troponin is frequently seen in patients with acute ischemic stroke. Most of these patients do not have myocardial infarction or acute coronary syndrome. Coronary angiographic studies in acute ischemic stroke patients with elevation of cardiac troponin have shown that stroke patients have less incidence of coronary occlusion as compared to patients with acute coronary syndrome with comparable troponin level. In this study, voxel-based lesion symptom mapping (VSLM) was used to relate the location of stroke within the anterior circulation against the temporal profile of cardiac troponin (hs-cTnT). Of the 1,239 patients screened, 299 patients had raised troponin without an identifiable cardiac cause. VSLM showed that the relative changes of elevated hs-cTnT were significantly associated with lesions in the right insular cortex, mainly in its dorsal anterior sub-region.

Understanding of the role of right insular cortex in the cardiac autonomic function would allow clinicians to better understand the neurogenic causes of cardiac injury in the context of the acute ischemic stroke.

**Contributed by Dr. Srijithesh P**

**Ciryam P, et al. Spinal motor neuron protein supersaturation patterns are associated with inclusion body formation in ALS. Proc Natl Acad Sci USA 2017; 114:3935-43**

This paper highlights the molecular findings in amyotrophic lateral sclerosis (ALS), which is a devastating neurodegenerative disorder. There are many different inclusion bodies due to the abnormal folding of primary ALS-related proteins like superoxide dismutase1 (SOD1), proteins encoded by the fused-in sarcoma (FUS) gene and TAR (trans-activator regulatory) DNA-binding protein (TDP)-43. The investigators showed that a common feature of these proteins is their aggregating ability in motor neurons of the spinal cord. This study shows that as protein metabolism becomes slowly
abnormal in ALS, supersaturated proteins in ALS patients fail to be sustained in their solvable states, leading to their presence in ALS-associated inclusions. This study gives a lot of insights about the supersaturation of these abnormally folded proteins in physiological conditions. This may help to develop therapeutic strategies against this grave illness.

Contributed by Dr. Ravi Yadav


The human being is capable of performing many tasks at the same time like walking, talking, driving and thinking. These are complex tasks which become impaired in patients with Parkinson’s disease (PD). In this paper, Nieuwhof and colleagues present their findings regarding impaired dual tasking in PD. The subjects performed a sensorimotor task, an executive flexibility task, as well as both tasks simultaneously (dual-task). The authors showed that there is motor and cognitive impairment in the cortical basal ganglia in patients with PD, which impairs the ability to carry out motor automatic tasks.

Contributed by Dr. Ravi Yadav


Ajiboye et al., have published this proof of concept study that has the potential to change the management of patients with chronic tetraplegia due to cervical cord injury in the future. The authors have utilized an implantable brain computer interface system to use the patient’s own cortical signals to move his paralyzed arm, utilizing the functional electrical stimulation. These finding were compared with a three-dimensional virtual system. This patient was a part of the Brain Gate-2 trial, which is testing the intracortical interface device. The subject started using his paralyzed arm 463 days after the implant and started feeding himself after about 700 days. It will be very exciting to see what this research has to offer in the near future.

Contributed by Dr. Ravi Yadav


This report is of promising value for the atypical Parkinsonian syndromes. Multiple system atrophy (MSA) is characterized by the pathological hallmark of alpha synuclein deposition in oligodendrocytes forming the glial cytoplasmic inclusions. In other degenerative disorders, impaired insulin/insulin-like growth factor-1 signaling (IGF-1) and insulin resistance (i.e., decreased insulin/IGF-1) has been seen. The authors of this study evaluated these changes in patients with MSA and mouse models showed that the glucagon-like peptide-1 analogue exendin-4, an antidiabetic drug, has positive effects on the insulin resistance and the α-synuclein burden in the putamen and caudate nucleus, as well as on the survival of substantia nigra cells. These findings may be important enough to carry out the testing of this drug in a clinical trial.

Contributed by Dr. Ravi Yadav


This paper provides evidence in favor of instituting adaptive deep brain stimulation (DBS) systems in patients with Parkinson’s disease. The adaptive DBS system helps in the detection of beta bursts and suppresses them with stimulation. These beta bursts in the subthalamic nucleus are associated with increased symptoms. The authors utilized this mechanism to test the hypothesis that effective adaptive deep brain stimulation reduces long beta bursts, shifting the distribution of burst duration away from a long duration stimulation. This paper shows that longer beta bursts are associated with clinical impairment in Parkinson’s disease.

Contributed by Dr. Ravi Yadav


Hepatocyte growth factor has been associated with risk factors related to haemorrhagic and ischaemic stroke. The author conducted a study to determine the existence of any association between the circulating hepatocyte growth factor (HGF) levels and incident stroke using data from the MESA (Multi-Ethnic Study of Atherosclerosis). Out of 6711 participants (aged 45-84 years), whose HGF was measured, 233 had an incident stroke during their follow up duration. Cox proportional hazards regression was used to calculate the hazard ratios and 95% confidence intervals for incident stroke. A secondary analysis stratified results by adjudicated stroke type (n = 183 ischemic; n = 39 hemorrhagic; n = 11 other). After adjustment for potential confounding variables, the risk of stroke was 17% higher with each standard deviation increase in HGF (hazard ratio, 1.17; 95% confidence interval, 1.03–1.34). The few haemorrhagic and other types of stroke were not associated with HGF. The authors concluded that the HGF may have utility as a prognostic marker for the assessment of risk of developing a stroke.

Contributed by Dr. Anant Mehrotra


To identify the risk factors for instituting a cerebrospinal fluid diversion procedure after aneurysmal SAH (aSAH), the authors used 1533 patients with aSAH s from the population-based collaborative stroke study (C3). The authors found that age of 60 years or older, Hunt-Hess grade of 4 or 5, Fisher grade of 3, and increased blood pressure on arrival were significant risk factors for the need for shunting. The authors also found that patients with aSAH who were 60 years of age or older and had Hunt-Hess grade of 4 or 5, Fisher grade of 3, and increased blood pressure on arrival were at higher risk of requiring shunting. The authors concluded that these factors should be considered in the decision-making process for patients with aSAH.
Eastern Finland Saccular Intracranial Aneurysm Database in a recursive partitioning analysis. The risk model was built and internally validated in random split cohorts. External validation was conducted on 946 aSAH patients from the Southwestern Tertiary Aneurysm Registry (Dallas, TX) and tested using receiver-operating characteristic curves. A total of 17.7% of patients who were alive for 14 days or more, required a shunt. 6 groups were defined with successively increasing risk for instituting a shunt based on the recursive partitioning analysis. These groups also successively risk stratified the functional outcome at 12 months, the shunt-related complications, and the time-to-shunt rates. The area under the curve–receiver-operating characteristic curve for the exploratory sample as well as the internal validation sample were 0.82 and 0.78, respectively, with an external validation of 0.68. The authors concluded that prediction modelling of shunt dependency is feasible with clinically useful yields.

Contributed by Dr. Anant Mehrotra


In this study, the authors studied the various magnetic resonance imaging parameters and their correlation with survival and molecular profile of lower-grade gliomas (LGGs). The authors analysed the preoperative MRI findings of 165 patients with diffuse low- and intermediate-grade gliomas (histological grades II and III). The imaging parameters were scored according to the Visually Accessible Rembrandt Images (VASARI) annotations. Radiomic models were built using automated texture analysis and VASARI features to predict the isocitrate dehydrogenase 1 (IDH1) mutation, 1p/19q co-deletion status, histological grade, and tumor progression. The imaging parameters analysed showed a good interobserver agreement (k = 0.703–1.000). On multivariate Cox regression analysis, no enhancement, and a smooth non-enhancing margin, were associated with longer overall survival (OS) after considering all potential confounding factors. The texture models were found to possess a higher prediction potential for IDH1 mutation, 1p/19q co-deletion status, histological grade, and progression of LGGs than the VASARI features, with areas under the receiver-operating characteristic curves of 0.86 ± 0.01, 0.96 ± 0.01, 0.86 ± 0.01, and 0.80 ± 0.01, respectively.

Contributed by Dr. Kuntal Kanti Das


In this interesting study, the authors compared the Response Assessment in Neuro-Oncology (RANO) criteria with various volumetric methods in the response assessment of recurrent glioblastomas treated with bevacizumab, factoring in the phenomenon of pseudo-response on the conventional post-treatment contrast enhanced T1 weighted MRI. The authors studied 148 patients from the BELOB trial (single-agent bevacizumab or lomustine versus a combination of bevacizumab plus lomustine in patients with recurrent glioblastoma) database. These patients were treated with bevacizumab, lomustine, or both. The disease progression at follow up (6 and 12 week) was determined using both the 2D RANO criteria and various volumetric methods. The differences in overall survival (OS) between patients with or without disease progression was assessed using appropriate statistical tests. The authors noted that the largest risk increase of death in patients with progressive disease at follow-up could be identified using the RANO criteria: Hazard ratio (HR) = 2.81 (95% confidence intervals [CI], 1.92–4.10) and HR = 2.80 (95% CI, 1.75–4.49), respectively. In the bevacizumab-treated patients, all methods assessed showed significant differences in the overall survival (OS) between the different groups of patients. There were no significant differences between the methods. Thus, the authors noted that volumetric methods did not provide significant improvement over the RANO criteria as a post-treatment prognostic marker in the initial 12 weeks of therapy.

Contributed by Dr. Kuntal Kanti Das

Barreto AD, et al. Randomized, multicenter trial of ARTSS-2 (argatroban with recombinant tissue plasminogen activator for acute stroke). Stroke 2017;48:1608-16

This was a randomized study to assess the safety and the probability of a favorable outcome with adjunctive therapy of argatroban, a direct thrombin-inhibitor, in patients of ischemic stroke, being treated with recombinant tissue-type plasminogen activator (r-tPA). 90 patients were randomised into 3 groups (29 treated with r-tPA alone, 30 with r-tPA + low-dose argatroban and 31 with r-tPA + high-dose argatroban). Safety was defined as a lack of symptomatic intracerebral haemorrhage. Probability of clinical benefit (modified Rankin Scale score 0–1 at 90 days) was estimated using a conservative Bayesian Poisson model. The authors noted similar rates of symptomatic intracerebral hemorrhage among the control, low-dose, and high-dose arms: 3/29 (10%), 4/30 (13%), and 2/31 (7%), respectively. At 90 days, 6 (21%) r-tPA alone, 9 (30%) low-dose, and 10 (32%) high-dose patients were having the modified Rankin Scale score 0 to 1. The relative risks (95% credible interval) for modified Rankin Scale score 0 to 1 with low, high, and either low or high dose argatroban were 1.17 (0.57–2.37), 1.27 (0.63–2.53), and 1.34 (0.68–2.76), respectively. The probability that adjunctive argatroban was superior to r-tPA alone was 67%, 74%, and 79% for low, high, and low or high dose, respectively. In patients treated with r-tPA, adjunctive argatroban was not associated with increased risk of symptomatic intracerebral haemorrhage.

Contributed by Dr. Kuntal Kanti Das


In this study, the authors assessed neurocognitive functions of adult moyamoya disease before and after direct external
carotid-internal carotid (EC-IC) artery bypass, a relatively lesser explored aspect of an uncommon disease. They carried out a structured battery of 13 neurocognitive tests on 84 adults with moyamoya disease before and 6 months after the EC-IC bypass. Twelve patients (14%) showed a significant decline postoperatively, 9 patients (11%) improved, and 63 patients (75%) were unchanged in their neurocognitive abilities. Similar results were obtained when the analysis was confined to those who underwent unilateral (33) or bilateral (51) revascularizations. Thus, the majority of patients showed neither significant decline nor improvement in their neurocognitive performance after the EC-IC bypass surgery. Therefore, the authors concluded that an uncomplicated EC-IC bypass seemed not to be a risk factor for cognitive decline in this patient population.

Contributed by Dr. Kuntal Kanti Das


The authors of this study intended to objectively investigate the effect of posterior fossa decompression (PFD) on the denervation status of the paraspinal muscles in patients with Chiari I malformation (CIM). They analysed 37 patients prospectively for this purpose. These patients had undergone two-stage surgeries at their institution, 6.5 months (average) apart. At the first stage, PFD was done; while, deformity correction for CIM-associated scoliosis was performed in the second stage. During both surgeries, the authors obtained biopsy from bilateral erector spinae muscles, the biopsy site being located within the spinal innervation region involved by the syrinx and near the level of upper instrumented vertebra. The muscle samples were examined for the expression levels of Bax and Bcl-2; as well as, for defining the histological features of the muscle fibres. The authors noted a significant rise in the mRNA level of, as well as the protein levels of antiapoptotic Bcl-2, with a coincident decrease for proapoptotic Bax at both concave and convex sides of the scoliotic curve (P < 0.001), the changes being more marked on the concave side. On an average, the Bax/Bcl-2 ratio decreased by 60% suggesting reduced apoptotic signalling and improved innervation of the paraspinal muscles. Histologically as well, the specimens demonstrated improvements in denervation-associated changes of the muscle fibres following PFD, with the number of atrophic and necrotic/degenerated fibres decreasing significantly, the decrease being more marked on the concave side (P < 0.001 Vs 0.012). The authors, thus, objectively proved the beneficial effect of PFD in Chiari I malformation, in amelioration of paraspinal muscle denervation.

Contributed by Dr. Kuntal Kanti Das


This study aimed to determine the interrater and intrarater reliability of the Knosp grading scale for predicting pituitary adenoma invasion into the cavernous sinus (CS). For this purpose, 50 MRI scans of biopsy proven pituitary adenomas were assessed independently by six raters (i.e., 3 neurosurgery residents, 2 pituitary surgeons, and 1 neuroradiologist). To avoid a potential confounding due to the level of training, the performance of residents was compared with that of faculty raters. There was no significant difference in reliability between residents and faculty and the intrarater reliability was moderate-to-strong and increased with the level of experience. The authors noted a strong interrater reliability (0.73, 95% CI 0.56–0.84). However, the percentage of complete agreement was rather low (10%), the agreement being marginally higher among resident raters than the faculty (30% vs 26%). In particular, the reliability of the middle scores (i.e., average rated Knosp Grades 1 and 2) was “very weak” (0.18, 95% CI 0.27 to 0.56), being only 5% among all raters. The reliability became strong (0.60, 95% CI 0.39–0.75) and the percentage of interrater agreement improved to 60% as soon as the scale was dichotomized into: tumors unlikely to have intraoperative CS involvement (Grades 0, 1, and 2) and those likely to have CS involvement (Grades 3 and 4). Therefore, the authors recommended, while recognising the overall acceptable interrater reliability of the Knosp grading scale, dichotomizing the scale into clinically useful groups. This would address the poor reliability and percent agreement of the intermediate grades for better utility in the surgical decision making.

Contributed by Dr. Kuntal Kanti Das


In this single center, open-label, randomized controlled trial (MRCT), the authors compared the clinical and radiological outcomes between isolated instrumented posterior fusion (PLF) and associated instrumented posterior fusion and interbody fusion by the transformaminal approach (posterior lumbar interbody fusion [PLF] + transformaminal lumbar interbody fusion [TLIF]) in patients with one-level lumbar degenerative spondylolisthesis (DS). Each group comprised 30 patients each. The clinical (pain and disability), surgical (blood loss and operating time), and radiological (alignment and fusion) parameters at baseline and at a 2-year follow-up were compared between the two groups. The authors noted significant improvement in both the groups with respect to pain and disability, although the two groups did not differ significantly. Radiographic bony fusion was better when TLIF was done additionally, although it did not affect the segmental lordosis. Thus, the authors concluded that TLIF was not mandatory in single level degenerative lumbar spondylolisthesis.

Contributed by Dr. Kuntal Kanti Das