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

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

Yan L, et al. A prospective, double-blind, randomized controlled trial of treatment of atlantoaxial instability with C1 posterior arches >4 mm by comparing C1 pedicle with lateral mass screws fixation. BMC Musculoskelet Disord 2016 Apr 14;17:164. https://dx.doi.org/10.1186%2Fs12891‑016‑1017‑8

This study attempted to compare the feasibility and clinical outcomes of C1 pedicle with lateral mass screw fixations for the treatment of atlantoaxial instability (AAI). A total of 140 patients with AAI were enrolled in this single-center, randomized, double blind trial. The patients were randomly assigned into two treatments, namely, C1 pedicle (group A; \( n = 67 \)) or lateral mass (group B; \( n = 63 \)) screw fixation. All 140 patients showed an overall improvement in clinical symptoms after surgery. The mean follow-up was around 2 years. In both the groups, the mean Japanese Orthopedic Association (JOA) scores improved significantly at the time of final follow-up compared to the prior surgery (group A: 7.1 vs 13.7; group B: 7.3 vs 13.1). The visual analogue scale (VAS) scores also decreased significantly in both the groups at the time of final follow-up compared to prior surgery. Bone fusion was achieved within 12 months postoperatively in the patients from both the groups. The operation time was significantly shorter and the volume of blood loss was significantly lesser in patients from group A compared to group B (\( P < 0.01 \)). Furthermore, 13 patients had burst bleeding from the C1-2 venous plexus, and 9 patients had immediate pain, and numbness in the occipitocervical region due to the C2 nerve root irritation during lateral mass screw replacement, which were not observed in the patients with C1 pedicle screw insertion.

The authors concluded that C1 pedicle screw fixation is less invasive and simpler, and has fewer complications. It renders better clinical outcomes than lateral mass screw fixation for treatment of AAI.


The authors conducted a meta-analysis to evaluate the reported rate of adjacent segment disease (ASD) following cervical disc arthroplasty (CDA) compared with anterior cervical discectomy and fusion (ACDF). Fourteen relevant RCTs involving 3235 individuals with a follow-up period of 2–7 years were included in the meta-analysis (1696 in the CDA group and 1539 in the ACDF group). The outcomes indicated that CDA was superior to ACDF, considering the lower rate of ASD (risk ratio, 0.57; \( P = 0.009 \)). Compared with ACDF, there were significantly fewer adjacent segment reoperations in the CDA group (risk ratio, 0.47; \( P = 0.0002 \)). The authors concluded that CDA was superior to ACDF with regard to a lower incidence of ASD and relative reoperations on the basis of available evidence from a meta-analysis of 14 RCTs. Further well-designed studies should continue to pay attention to the group of excellent
patients with a longer-term follow-up to evaluate the incidence of ASD following these two procedures.

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


The aim of this study was to evaluate the 5- to 8-year outcome of anterior cervical decompression and fusion (ACDF) combined with a structured physiotherapy program (30 patients) compared with that following the same physiotherapy program alone in patients with cervical radiculopathy (29 patients). After 5-8 years, the neck disability index (NDI) was reduced by 21% in the surgical group and 11% in the nonsurgical group ($P = 0.03$). Neck pain was reduced by a mean score of 39 compared with 19 ($P = 0.01$) and arm pain was reduced by a mean score of 33 compared with 19 ($P = 0.1$), respectively. Ninety-three percent of patients in the surgical group rated their symptoms as “better” or “much better” compared with 62% in the nonsurgical group ($P = 0.005$). Both treatment groups experienced significant improvement over the baseline for all outcome measures. The authors concluded that ACDF combined with physiotherapy reduced neck disability and neck pain more effectively than physiotherapy alone.

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


Some surgeons believe that the relief of back pain should not be an expected outcome of decompression and that substantial back pain may be a contraindication to carrying out solely a decompression procedure. The purpose of this study was to determine if patients with lumbar stenosis and substantial back pain, in the absence of spondylolisthesis, scoliosis, or sagittal malalignment, can obtain significant improvement after decompression without fusion or stabilization. Analysis of the National Neurosurgery Quality and Outcomes Database (N2QOD) identified 726 patients with lumbar stenosis (without spondylolisthesis or scoliosis) and a baseline back pain score $\geq 5$ of 10, who underwent surgical decompression only. The mean age of the cohort was 65.6 years, and 407 (56%) patients were male. The mean body mass index was 30.2 kg/m², and 40% of patients had a 2-level decompression, 29% had a 3-level decompression, 24% had a 1-level decompression, and 6% had a 4-level decompression. At 3 and 12 months, postoperatively, there was a significant improvement from baseline for back pain (7.62 to 3.19 to 3.66), leg pain (7.23 to 2.85 to 3.07), EQ-5D (0.55 to 0.76 to 0.75), and ODI (49.11 to 27.20 to 26.38). The authors conclude that through the first postoperative year, patients with lumbar stenosis (without spondylolisthesis, scoliosis, or sagittal malalignment) and clinically significant back pain improved after decompression-only surgery.

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


The authors conducted this study to compare the clinical and radiological outcomes of patients undergoing percutaneous vertebroplasty (PVP) versus those undergoing facet block (FB) for severe pain due to osteoporotic vertebral compression fractures (OVCFs).

Two hundred and six patients, who had OVCFs on spine radiography and intractable back pain for $\leq 8$ weeks, were included (165 females and 41 males, age $\geq 55$ years). Patients were randomly assigned to the PVP group (100 patients) or the FB group (106 patients).

Significantly lower visual analogue scale (VAS), Oswestry disability index (ODI), and Roland Morris disability (RMD) scores for patients in the PVP group compared to those in the FB group were observed at follow-up of 1 day and 1 week ($P < 0.05$). However, differences in the VAS, ODI, RMD and short-form (SF)-36 scores between the two groups at a follow-up of more than 1 month were statistically insignificant ($P > 0.05$). Difference in the numbers of new fractures in the two groups at the follow-up of 12 months was also statistically insignificant. The authors concluded that PVP produced better pain relief than FB in the short term ($\leq 1$ week). However, the difference in pain-relief between these two techniques was insignificant in the long term (follow-up between 1 month and 12 months).

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


The authors compared two different, single-modality treatment strategies of standard radiotherapy versus primary temozolomide chemotherapy in patients with a low-grade glioma, assessed progression-free survival outcomes, and identified predictive molecular factors. For this randomized, open-label trial, undertaken in 78 clinical centers in 19 countries, they included patients aged 18 years or older, who had a low-grade (World Health Organisation grade II) glioma (astrocytoma, oligoastrocytoma, or oligodendroglioma) with at least one high-risk feature (age $> 40$ years, progressive disease, tumor size $> 5$ cm, tumor crossing the midline, or neurological symptoms). Eligible patients were randomly assigned (1:1) to receive either conformal radiotherapy ($n = 240$) up to 50.4 Gy; 28 doses of 1.8 Gy once daily, 5 days per week for up to 6.5 weeks), or dose-dense oral temozolomide ($n = 237$; dose: 75 mg/m² once daily for 21 days, repeated every
28 days (one cycle), for a maximum of 12 cycles. At a median follow-up of 48 months, progression-free survival was 39 months in the temozolomide group and 46 months in the radiotherapy group. The median overall survival had not been reached. Grade 3–4 hematological adverse events occurred in 32 (14%) of 236 patients treated with temozolomide, and in one (<1%) of 228 patients treated with radiotherapy; and, grade 3–4 infections occurred in eight (3%) of 236 patients treated with temozolomide, and in two (1%) of 228 patients treated with radiotherapy. The authors concluded that, overall, there was no significant difference in progression-free survival in patients with low-grade glioma when treated with either radiotherapy alone or temozolomide chemotherapy alone.

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From the above mentioned study by Baumert et al., that is, temozolomide chemotherapy versus radiotherapy in patients with high-risk low-grade gliomas, no significant effect on progression-free survival had been noted. Hence, the authors postulated that, if these treatments have a different effect on health-related quality of life (HRQOL), it might affect the choice of therapy. In the same trial, the authors report the results for two key secondary endpoints: HRQOL [assessed using the European Organization for Research and Treatment of Cancer’s (EORTC) quality of life questionnaire (QLQ-C30) [version 3] and the EORTC Brain Cancer Module (QLQ-BN20)] and global cognitive functioning [assessed using the Mini-Mental State Examination (MMSE)]. The difference in HRQOL between the two treatment groups was not significant during the 36 months’ follow-up [mean between group differences (averaged over all time points)]. The authors concluded that the effect of temozolomide chemotherapy or radiotherapy on HRQOL or global cognitive functioning did not differ in patients with a low-grade glioma. These results do not support the choice of temozolomide alone over radiotherapy alone in patients with high-risk low-grade gliomas.

Contributed by Dr. Mazda K. Turel


Schwannomas are common peripheral nerve sheath tumors. The authors performed an integrative analysis to determine the genomic aberrations that are common to sporadic schwannomas. Exome sequence analysis with validation by targeted DNA sequencing of 125 samples uncovered in addition to the expected neurofibromatosis (NF) 2 disruption, recurrent mutations in ARID1A, ARID1B, and DDR1. RNA sequencing identified a recurrent in-frame SH3PXD2A-HTRA1 fusion in 12/125 (10%) cases, and genomic analysis demonstrated the mechanism as resulting from a balanced 19-Mb chromosomal inversion on chromosome 10q. The fusion was associated with male gender predominance, occurring in one out of every 6 men with schwannoma. Methylation profiling identified distinct molecular subgroups of schwannomas that were associated with anatomical location. Expression of the SH3PXD2A-HTRA1 fusion resulted in elevated phosphorylated ERK, increased proliferation, increased invasion, and in-vivo tumorigenesis. Targeting of the MEK-ERK pathway was effective in fusion-positive Schwann cells, suggesting a possible therapeutic approach for this subset of tumors. Targeted therapy to this fusion protein could revolutionize the treatment of schwannomas.

Contributed by Dr. Mazda K. Turel


The authors performed a retrospective analysis to evaluate the results and tolerability of BBBD therapy in combination with high-dose therapy supported by autologous stem cell transplantation. The authors analyzed 25 patients (age range: 40–71 years) who were treated in first or second line with BBBD therapy. Altogether 19 (76%) of the patients achieved a complete response (CR). Two-year progression-free survival (PFS) and overall survival (OS) rates were 61 and 57%, respectively, and the five-year OS was 47%. Patients who were treated with a five-drug therapy had a very promising prognosis. The CR rate was 100% in first-line therapy and 60% in relapsed cases. These findings suggest that BBBD is a promising therapy for PCNSL, especially for patients in the first line, but also for patients with relapsed or refractory disease after conventional chemotherapy, who commonly have a very poor prognosis. Treatment-related toxicity was generally manageable. Thus, BBBD followed by ASCT could be a treatment of choice in transplant-eligible patients with PCNSL.

Contributed by Dr. Mazda K. Turel


The authors conducted this study to analyze recent postoperative radiotherapy national treatment patterns and implications for overall survival in patients with medulloblastoma that occurred in patients in the age group of 3–8 years. Among 816 patients, 123 (15%) had deferred their postoperative radiotherapy, and 693 (85%) had an upfront postoperative radiotherapy; 36.8% of the 3-year-olds and 4.1% of the 8-year-olds had their postoperative radiotherapy deferred (P < .001). On survival analysis, with a median follow-up of 4.8 years, overall survival (OS) was improved for those receiving postoperative radiotherapy upfront vs postoperative radiotherapy deferred (5-year OS: 82% vs 63.4%; P < 0.001). On multivariable analysis, variables associated with a poorer OS were postoperative radiotherapy deferral, stage
MI-3 disease, and low facility volume. Their analysis reveals a higher-than-expected and increasing rate of postoperative radiotherapy deferral in children with medulloblastoma, who were in the age groups of 3–8 years. The analysis suggests that postoperative radiotherapy deferral is associated with worse survival in this age group, even in the modern era of chemotherapy.

Contributed by Dr. Mazda K. Turel


The authors conducted a retrospective study in which 140 consecutive patients taking low-dose acetysalicylic treatment (ASA), and undergoing surgical evacuation of chronic subdural hematoma (cSDH) were included. No statistically significant association was observed between the early postoperative resumption of low-dose ASA and recurrence of cSDH (P = 0.06). Corresponding odds ratios and risk differences for restarting ASA treatment on postoperative days 1, 7, 14, 21, 28, 35, or 42 were estimated at 1.53 and 5.9%, 1.42 and 5.1%, 1.33 and 4.1%, 1.23 and 3.2%, 1.15 and 2.2%, 1.07 and 1.1%, and 1.01, and 0.2%, respectively (P > 0.05). Cardiovascular event rates as well as surgical morbidity and mortality did not significantly differ between patients with or without ASA therapy. The authors concluded that given the few published studies regarding the use of ASA in cranial neurosurgery, their findings elucidate one issue, showing comparable recurrence rates with early or late resumption of low-dose ASA after burr-hole evacuation of cSDH.

Contributed by Dr. Mazda K. Turel


MISTIE was an open-label, phase 2 trial that was done in 26 hospitals in the USA, Canada, the UK, and Germany, randomizing patients aged 18–80 years with a nontraumatic (spontaneous) intracerebral haemorrhage of 20 mL or higher to standard medical care or image-guided minimally invasive surgery (MIS) plus alteplase (0.3 mg or 1.0 mg every 8 h for up to 9 doses) to remove clots using surgical aspiration followed by alteplase clot irrigation. Primary outcomes were all safety outcomes: 30-day mortality, 7-day procedure-related mortality, 72 h symptomatic bleeding, and 30-day brain infections. Ninety-six patients were randomly allocated and completed follow-up: 54 (56%) in the MIS plus alteplase group and 42 (44%) in the standard medical care group. The primary outcomes did not differ between the standard medical care and MIS plus alteplase groups: the 30-day mortality (4 vs 8, P = 0.5), 7-day mortality (0 vs 1, P = 0.5), symptomatic bleeding (1 vs 5, P = 0.2), and brain bacterial infections (1 vs 0, P = 0.4). Asymptomatic haemorrhages were more common in the MIS plus alteplase group than in the standard medical care group (12 vs 3; P = 0.05). The authors concluded that MIS plus alteplase appears to be safe in patients with intracerebral hemorrhage, but increased asymptomatic bleeding is a major cautionary finding. These results, if replicable, could lead to the addition of surgical management as a therapeutic strategy for intracerebral haemorrhage.

Contributed by Dr. Mazda K. Turel


A prospective randomized controlled study was performed on 20 patients (14 surgical and 4 medical) with primary intracerebral hematoma (ICH) of >20 mL volume within 48 hours of ICH onset. The authors used a contemporaneous medical control cohort (n = 36) from the MISTIE trial (Minimally Invasive Surgery and r-tPA for ICH Evacuation). They evaluated surgical safety and neurological outcomes at 6 months and 1 year. The intraoperative computed tomographic (CT) image-guided endoscopic surgery procedure resulted in immediate reduction of the hemorhagic volume by 68 ± 21.6% (interquartile range 59–84.5) within 29 hours of hemorrhage onset. Surgery was successfully completed in all cases, with a mean operative time of 1.9 hours (interquartile range, 1.5–2.2 hours). One surgically related incidence of bleed occurred perioperatively. However, no patient met surgical safety stopping threshold endpoints for intraoperative hemorrhage, infection, or death. The surgical intervention group had a greater percentage of patients with a good neurological outcome (modified Rankin scale score 0–3) at 180 and 365 days compared with medical control patients (42.9% versus 23.7%; P = 0.19). The authors concluded that early CT image-guided endoscopic surgery is a safe and effective method to remove acute intracerebral hematomas, with a potential to enhance neurological recovery.

Contributed by Dr. Mazda K. Turel


The authors sought to (1) compare patients with new-onset late seizures (i.e., delayed seizures), with those who experienced a recurrent late seizure following an immediately posthemorrhagic seizure; and (2) investigate the effect of late seizures on long-term functional performance after intracerebral hemorrhage. A total of 872 survivors of intracerebral hemorrhage were enrolled and followed for a median duration of 3.9 years. Early seizure developed in 86 patients, 42 of whom went on to experience recurrent seizures. Admission Glasgow Coma Scale, increasing hematoma volume, and cortical involvement were associated with recurrent seizure risk (all P < 0.01). Recurrent seizures were not associated with a long-term functional outcome (P = 0.6). Delayed seizures occurred in 37 patients, corresponding to an estimated incidence of 0.8% per year. Factors associated with delayed seizures included cortical involvement on index hemorrhage, pre-hemorrhage dementia, history of multiple...
prior lobar haemorrhages, and exclusively lobar microbleeds, as well as the presence of ≥ 1 apoenzyme (APOE) ε4 copies (all \( P < 0.01 \)). Delayed seizures were associated with a worse long-term functional outcome (\( P = 0.005 \)); however, the association was removed by adjusting for neuroimaging and genetic markers of cerebral small vessel disease. The authors concluded that delayed seizures are associated with a worse functional outcome; however, this finding appears to be related to the presence of underlying small vessel disease.

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


The authors conducted this study to identify the safety and efficacy of SVAT in a large multicentre patient cohort to evaluate the prognostic markers responsible for clinical outcome following SVAT. A total of 50 patients undergoing SVAT were identified. Patients presented, on average, 6.48 ± 4.45 days after subarachnoid haemorrhage. Hunt and Hess and Fisher grades were 1 (\( n = 7 \)), 2 (\( n = 12 \)), 3 (\( n = 14 \)), 4 (\( n = 15 \)), 5 (\( n = 2 \)), and 3 and 4 (\( n = 33 \)), respectively. The aneurysm location was distributed as follows: anterior (\( n = 32 \)), posterior (\( n = 16 \)), and anterior and posterior (\( n = 2 \)). Patients with a good clinical condition (Hunt and Hess score 1–3) had significantly higher odds of surviving [odds ratio (OR) =17.5], a favourable Glasgow Outcome Scale [GOS] (OR = 4.2), and a favourable 90-day modified Rankin Scale [mRS] (OR = 4.2). The authors concluded that SVAT is safe, with the majority of patients achieving a good clinical outcome. Patients with lower Hunt and Hess grades have higher odds of surviving and have a favorable clinical prognosis.

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


The authors aimed to study the cognitive dysfunctions among patients with ruptured intracranial aneurysms using magnetoencephalography (MEG). Before the MEG scans, neuropsychological tests were performed. Thirteen patients who had undergone coiling for aneurysmal subarachnoid hemorrhage, and 13 matched controls were included in the study. MEG data were acquired in a 151-channel, whole-head MEG system for resting state, and 2 cognitive tasks (go-no-go and set-shifting). The mean time from treatment to test was 18.8 months. Increased activation in the right anterior cingulate and inferior frontal gyrus was seen in cognitive tasks of inhibition, and a similar increased activation was seen in bilateral anterior cingulate cortical areas and the right medial frontal gyrus in cognitive set-shifting tasks (mental flexibility), in patients having an aneurysmal subarachnoid hemorrhage, with significantly different timing of activation between the groups. Resting-state, beta-band connectivity of the anterior cingulate gyrus correlated negatively with Montreal Cognitive Assessment scores (left: \( r = −0.56; P < 0.01 \) and right: \( r = −0.55; P < 0.01 \)); higher connectivity of this region was linked to a poorer cognitive test performance. The authors conclude that the subtle differences seen could be related to the common neurocognitive and behavioral complaints seen in this patient population.

**Contributed by Dr. Anant Mehrotra**


The authors identified 82 patients who had undergone coil embolization of their basilar top aneurysm and had a minimal follow up of 1 year. The three-dimensional data derived from rotational angiography was used to investigate the presurgical hemodynamic status using computational fluid dynamics (The data of 25 patients was excluded because of difficult geometry of the aneurysm). During the post-processing period, the rate of the net flow entering the aneurysm through its neck was quantified and the proportion of the aneurysmal inflow rate to the basilar artery flow rate was calculated. The authors also investigated the correlation between the basilar bifurcation configuration and the hemodynamic status of the aneurysm. Out of the 57 patients examined, 19 had recanalization. The proportion of the aneurysmal inflow rate to the basilar artery flow rate, and a coil packing density <30% were independent and significant predictors for the recanalization of coiled aneurysms. A small branch angle formed by the basilar artery and the posterior cerebral artery increased the blood flow into the aneurysm. The authors concluded that recanalization after coil embolization in the basilar tip aneurysms was affected by the proportion of the aneurysmal inflow rate to the basilar artery flow rate and was also influenced by the basilar bifurcation configuration.

**Contributed by Dr. Anant Mehrotra**


Partial resection of the occipital condyle is needed for the far lateral transcandular approach. The authors performed a study on 7 fresh cadavers. Using a robotic spine-testing system, multidirectional flexibility tests using cardinal direction and coupled moments combined with a simulated head weight “follower load” were performed to determine the effect of sequential unilateral joint-sparing condylectomy (25%, 50%, 75%, 100%) in comparison with the intact state. 5.2%, 8.1%, 12.0%, and 27.5% in flexion-extension (FE); 8.4%, 14.7%, 39.1%, and 80.2% in lateral bending (LB); and 24.4%, 31.5%, 49.9%, and 141.1% in axial rotation (AR) were the percent changes in the range of motion following sequential condylectomy compared with the intact state. Statistically significant values were achieved only on performance of 100% condylectomy. With coupled motions, however, –3.9%, 6.6%, 35.8%, and 142.4% increases in AR + F and 27.3%, 32.7%, 77.5%, and 175.5%...
increases in AR + E were found. Values for 75% and 100% condylar resection were statistically significant in AR + E. The authors concluded that as a significant increase in motion occurred after a 75% condylectomy or more, a stabilization procedure would be needed in these cases.

**Contributed by Dr. Anant Mehrotra**


The authors have conducted a phase 3, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of everolimus in two different concentrations, i.e. 3–7 ng/mL (low exposure) and 9–15 ng/mL (high exposure) compared with a placebo as adjunctive therapy for treatment-resistant focal-onset seizures (≥16 in an 8-week baseline phase receiving one to three concomitant antiepileptic drugs) in the tuberous sclerosis complex. Three hundred and thirty-three patients, aged between 2 and 65 years were included in the study from 99 centres across 25 countries. Patients were randomly assigned either to the low exposure group (n = 117), the high exposure group (n = 130), or the placebo group (n = 119) and randomization was stratified by age subgroup (<6 years, 6 to <12 years, 12 to <18 years, and ≥18 years). The primary endpoint was change from baseline in the frequency of seizures during the maintenance period defined as the response rate (the proportion of patients achieving ≥50% reduction in seizure frequency) and median percentage reduction in seizure frequency, in all randomized patients. The authors concluded that adjunctive everolimus treatment significantly reduced seizure frequency with a tolerable safety profile compared with a placebo in patients with tuberous sclerosis complex and treatment-resistant seizures.

**Contributed by Dr. Anant Mehrotra**


The authors conducted a randomized, double blind study in 328 children and adolescents (aged between 8 and 17 years) with migraine. Patients were randomly assigned in a 2:2:1 ratio to receive either amitriptyline (1 mg/kg/day; n = 132), topiramate (2 mg/kg/day; n = 130), or a placebo (n = 66). A relative reduction of 50% or more in the number of headache days in comparison to the 28-day baseline period within the last 28 days of a 24-week trial was taken as the primary outcome; and, headache related disability, headache days, number of trial completers, and serious adverse events were considered for the secondary outcome. In the primary outcome, there was no significant difference between the groups. Primary outcome occurred in 52% of patients of the amitriptyline group, in 55% of patients of the topiramate group and in 61% patients of the placebo group (amitriptyline vs. placebo, P = 0.26; topiramate vs. placebo, P = 0.48; amitriptyline vs. topiramate, P = 0.49).

There was no significant difference between the groups when headache-related disability, headache days or the percentage of patients who completed the 24-week treatment period were compared. However, patients receiving amitriptyline or topiramate had a higher incidence of adverse events than in the placebo group. The authors have concluded that there were no significant differences between the three groups in reduction in frequency of headache or headache-related disability in pediatric migraine.

**Contributed by Dr. Anant Mehrotra**


The authors conducted a phase 3, noninferiority, randomized trial in 69 centres in UK and three Australian centres in patients of nonsmall cell lung cancer (NSCLC) with nonresectable brain metastasis, which were also unsuitable for stereotactic radiosurgery. Five hundred and thirty-eight patients were randomly assigned (1:1) to either receive optimal supportive care (OSC) including dexamethasone along with whole brain radiotherapy (WBRT; 20 Gy in five daily fractions; n = 269) or OSC alone (including dexamethasone; n = 269). The dose of dexamethasone was titrated on an individual basis. The primary outcome measure was quality-adjusted life-years (QALYs). QALYs were generated from overall survival and patients’ weekly completion of the Euro-quality of life (EQ)-5D questionnaire. Treatment with OSC alone was considered noninferior if it was no more than 7 QALY days worse than treatment with WBRT plus OSC. The median age of the patients was 66 years (range: 38–85) and the other baseline characteristics were matched between the groups. There was no evidence of a difference in overall survival (hazard ratio, 1.06; 95% CI, 0.90–1.26), overall quality of life, or dexamethasone use between the two groups. The difference between the mean QALYs was 4.7 days (4634 QALY days for the OSC plus WBRT group vs 41.7 QALY days for the OSC group), with two-sided 90% confidence interval of −12.7 to 3.3. The authors concluded that the study suggests that WBRT provides little additional clinically significant benefit in this group of patients.

**Contributed by Dr. Anant Mehrotra**

**Wong J, et al.** Microsurgery for ARUBA trial (a randomised trial of unruptured brain arteriovenous malformation)-eligible unruptured brain arterio-venous malformations. Stroke DOI: http://dx.doi.org/10.1161/STROKEAHA.116.014660

The authors studied 155 ARUBA-eligible patients of arteriovenous malformation (AVM) who had undergone microsurgical resection. The demographic data, AVM characteristics, and treatment outcomes were evaluated. Outcomes were rates of early disabling deficits and permanent disabling deficits with modified Rankin Scale score ≥ 3, or any...
permanent neurological deficits with modified Rankin scale score ≥1. A total of 71.6% of patients underwent only surgery and the remaining underwent preoperative embolization as well. In 94.2% of the patients, complete obliteration was achieved after the initial surgery, and in 98.1% of the patients, complete obliteration was seen on final angiography. The mean follow-up period was 36.1 months. Early disabling deficits occurred in 12.3% and permanent disabling deficits in 4.5% of the patients, whereas any permanent neurological deficit (modified Rankin Scale score ≥1) occurred in 16.1%. Among unruptured brain AVMs of Spetzler–Martin grades 1 and 2, complete obliteration occurred in 99.2%, with early disabling deficits and permanent disabling deficits occurring in 9.3% and 3.4% patients, respectively. On multivariate analysis, the only significant predictor of early disabling deficits was major bleeding. The authors concluded that microsurgery in this cohort produced less disabling deficits than was seen in the ARUBA trial, with similar morbidity and AVM obliteration, as in other cohort series.

Contributed by Dr. Anant Mehrotra


The authors have examined the effect of left and right insular involvement on stroke outcomes among the patients from the IST-3 trial (Third International Stroke Trial). Among the 3035 recruited patients, 2099 had ischemic changes restricted to one hemisphere on CT scans, and out of these patients, 714 and 566 had infarction of the left and the right insula, respectively. The authors used multiple logistic regression to compare the outcomes of the left versus right insular and noninsular strokes at 6 months, with adjustment for the effects of age, lesion size, and presence of atrial fibrillation. At a follow-up of 6 months, the adjusted odds ratio comparing mortality after insular versus noninsular strokes on the left side was not significant but the right insular involvement was associated with increased odds of death when compared with noninsular strokes on the left side. The difference between outcome in right insular infarct and left insular infarct was more significant in mild/moderate strokes; however, in cases of severe stroke, the difference in outcomes was less substantial. The authors conclude that there is an association between right insular stroke and worse functional outcome.

Contributed by Dr. Anant Mehrotra


The authors studied 156 patients with intracanalicular vestibular schwannoma with a follow-up period of nearly 10 years to assess the long-term occurrence of tumor growth and hearing loss. In 37% of the patients, tumor growth occurred, and in 23% of the patients, growth occurred onto the cerebellopontine angle. In 15% of the cases, conservative treatment failed. Speech discrimination score (SDS) had reduced from 60% to 34%, and the pure tone average had increased from 51 to 72 dB hearing loss. There was a reduction in the number of patients with a good hearing (SDS > 70%) from 52% to 22%. Rate of hearing loss was higher in patients with growing tumors. The authors concluded that tumor growth occurred in a small number of patients who were diagnosed as a case of intracanalicular vestibular schwannoma over a follow-up period of 10 years. In patients with normal speech discrimination at diagnosis, the risk to hearing was small.

Contributed by Dr. Anant Mehrotra


Throughout the world, intracranial metastases form the most common indication for stereotactic radiosurgery (SRS). SRS has been an attractive option for the management of metastasis due to the relatively impenetrable nature of brain, and paucity of available options. However, approximately 5–10% patients of intracranial metastases suffer from radiation necrosis (RN) following SRS, which significantly affects the quality of life, overall survival, treatment related morbidity, and cost. Till now, prescription dose and tumor volume are considered the confounding variables affecting the chances of RN. However, the histopathology of the primary tumor has not been given much importance in the prognosis following SRS. Miller et al., tried to identify the role of other variables of questionable significance such as disease histopathology, receptor status, and mutational status of the primary tumor on the incidence of post-SRS RN. Renal cancer histology, lung adenocarcinoma histology, HER2 amplification, and ALK/BRAF mutational status are found to be the risk factors for RN. This research paper is a reference for prospective studies or clinical trials to evaluate the biological risk stratification or dose escalation in the presence of a pertinent pathology.

Contributed by Dr. Manjul Tripathi


Among brain tumors, diagnosis of a glioblastoma is a death sentence and its management remains challenging. Surgical resection alone provides overall survival ranging from 3–6 months, whereas adjuvant radiotherapy (RT) improves the longevity to 14–16 months. In this article, the American Society for Radiation Oncology (ASTRO) provided evidence-based guidelines for the management of glioblastoma. It concentrated on the best evidence for four key guideline questions. A, When is radiation therapy indicated after biopsy/resection of a glioblastoma, and how does systemic therapy modify its effects? The time interval between resection/biopsy and RT is mainly dependent on the...
morning, subconsciously. This finding is to be believed, surgeons might also be safer in the evening. There is no better chessboard than a human brain. If lead to faster but riskier and less successful moves towards the day, whereas night owls played more games towards dusk. Interestingly, both kind of players were 2.5% faster in their movements as wisely in the morning. These behaviors might treatment vary on the basis of pretreatment characteristics such as age or performance status? For patients, ≤70 years of age and KPS >60, optimal dose fractionation schedule for external beam radiation therapy (EBRT) is 60 Gy in 2 Gy fractions delivered over a 6-week period. Among patients >70 years of age, hypofractionated RT has been associated with superior survival and less corticosteroid requirement in comparison to conventional fractionation. An important conclusion is that adjuvant RT provides survival advantage without impairing the quality of life (QOL). Temozolomide monotherapy is an efficacious alternative for elderly patients with methyl guanine methyl transferase (MGMT) promoter methylation. For elderly patients, no consensus guidelines could be derived; however, shorter regimens were found as efficacious as longer duration regimens. C, What are the ideal target volumes for curative-intent external beam radiotherapy (EBRT) of glioblastomas? Partial brain irradiation is found to be as effective as whole brain radiotherapy (WBRT). Primary target volume encompasses edema (hyperintense region on T2 or FLAIR on MRI) and gross residual tumor/resection cavity, and boost target volume encompasses gross residual tumor/resection cavity. D, What is the role of re-irradiation among patients with a glioblastoma whose disease recurs after completion of standard first-line therapy? Re-irradiation is not supported in any patient group. With the best evidence based answers to the key questions, this paper is highly recommended for the effective management of glioblastoma; one of the most common patient groups subjected to surgery in neurosurgical practice.

Contributed by Dr. Manjul Tripathi

Bansal DG. You make more risky choices as the day wears on, chess study suggests. Scienccemag 2016. DOI: 10.1126/science.aal0460

This interesting article interprets the impact of diurnal variation on the professional game of prolific chess players. Indirectly, it examines the pervasive nature, risk taking behavior, and concentration of the players at different times of the day. As expected, early risers played more games in the morning, whereas night owls played more games towards dusk. Interestingly, both kind of players were 2.5% faster in their moves towards the end of the day and were not able to judge their movements as wisely as in the morning. These behaviors lead to faster but riskier and less successful moves towards the evening. There is no better chessboard than a human brain. If this finding is to be believed, surgeons might also be safer in the morning than in the later part of the days. Probably, principle of primum non nocere (First do no harm) is better followed in morning, subconsciously.

Contributed by Dr. Manjul Tripathi


Traumatic brain injury (TBI) is no more a hidden epidemic. TBI is an important cause of morbidity and mortality even in the developed nations; however, the true burden of the disease remains unrealized. In this cross-sectional analysis of TBI in Europe, the authors have analyzed the injury pattern, hospital-based incidence, and population wide TBI-related mortality in an analysis from 25 countries. In Europe, TBI is responsible for 37% of all injury-related deaths. However, there remain significant variations among countries. Similar to other studies on TBI, males outnumber females in its incidence, TBI-related age-adjusted mortality rates, and hospital discharge rates. A significant proportion of the population was >65 years of age; 72% of deaths in this age group occurred in female patients. This study remains important in serving as a background against which further prospective population-based analysis can be planned and the true burden of disease can be estimated. However, it also suffers from lack of uniformity in disease coding, hospital discharge, and mortality rates. In developing countries such as India, road traffic accidents (RTI) remain the leading cause of TBI. Similar to the countries of the European Union, Indian states also differ substantially in the care provided to trauma patients. An epidemiological study of appropriate design is needed to provide an estimate of the disease burden that may provide a framework for policy development and list the likely measures required for its correction.

Contributed by Dr. Manjul Tripathi


In 2015, Zika virus caused an epidemic among pregnant female patients in the South American countries, with Brazil being the worst affected. A sudden increase in the number of microcephalic infants and the temporal association with Zika virus outbreak led to a hypothesis that Zika virus is responsible for microcephaly. However, no population-based study has analyzed the causative association till date, and this association was proven on the basis of case reports and modeling studies. Zika virus infection leads to intrauterine growth retardation, and no radiographic brain abnormality apart from microcephaly could be detected in the majority of the cases. This finding suggests that Zika virus infection should be suspected in patients with microcephaly even in the absence of radiologic abnormalities. The timing of onset of Zika virus infection and its relation with Zika virus syndrome is still undefined. Identification of Zika virus specific IgM in the cerebrospinal fluid (Centers for Disease Control guidelines) and serum are the diagnostic methods for the detection of congenital Zika infection. This first case control study tries to fill the missing links in the causation of microcephaly and Zika virus infection. The authors have highlighted the need to rename the TORCH organisms as TORCHZ to include...
Zika virus as an important cause of intrauterine infections and presses on the need to be prepared for a possible global epidemic of Zika virus.

Contributed by Dr. Manjul Tripathi


Amyotrophic lateral sclerosis (ALS) is notorious in leaving a human being virtually speechless, helpless, and hopeless. Finally, there is some hope for these patients of ALS. The highly innovative brain–computer interface described in this article rests on the neuroelectrical properties of the brain. The authors describe a method for communication in a patient with late-stage ALS involving a fully implanted brain–computer interface. This interface was used in a 58-year-old patient of ALS and consisted of subdural electrodes placed over the motor cortex. Its transmitter was placed subcutaneously on the left side of the thorax. Moving the hand on the side opposite to the implanted electrodes, the patient could independently control a computer typing program, 28 weeks after the electrode placement. The software automatically extracts electrocortical signal features, allowing the patient to control commercial communication, albeit at a slow rate. Though, many factors may limit the use of the system (cortical damage, cognitive impairment, and level of caregiving), this system brings new hope for the patients of ALS who are unable to use conventional communication tools such as eye-trackers.

Contributed by Dr. Aastha Takkar


In this interesting retrospective cohort study published in Neurology, the authors attempt to determine the outcome of patients with psychogenic pseudosyncope (PPS) after the diagnosis was communicated to them. The attack frequency, factors affecting attack frequency, health care use, and quality of life using a questionnaire were studied from the records. Forty-seven of 57 patients with PPS could be traced, of whom 35 participated. Immediate reduction of attack frequency from the month before diagnosis to the month after was noted once the diagnosis was communicated and explained to the patients. The number of admissions decreased from 19 of 35 to 0 of 35. The authors mention that PPS is a serious condition. Rightly mentioned by the authors in this interesting article, “Anecdotally, digressions from a moral code are often described as a series of small breaches that grow over time.” Authors further provide an empirical evidence suggesting slow escalation of dishonest traits and reveal a central mechanism supporting the phenomenon. The gray zone of a human’s behavior is nicely demonstrated by depicting the extent to which humans can engage themselves in self-serving dishonesty, which on repetition further increases. Objective evidences of centres of dishonesty in amygdala using functional magnetic resonance imaging are also highlighted. Further, the reduced sensitivity of amygdala with persistent dishonest decisions predicts further escalated dishonest decisions in the next choices. The findings, interestingly enough support the theory of “slippery slope” – that small acts of dishonesty beget larger transgressions.

Contributed by Dr. Aastha Takkar


The European Friedreich’s Ataxia Consortium for Translational Studies (EFACTS) is a prospective international registry. It investigates the natural history of Friedreich’s ataxia (FA). The authors in this article published in Lancet Neurology used data from EFACTS to assess various characteristics of FA including disease progression and the predictive value of various factors on disease progression. A total of 605 patients of genetically confirmed FA were enrolled from 11 European study sites and followed for 2 years. Scale for the Assessment and Rating of Ataxia (SARA) was used as the primary endpoint. The authors conclude that SARA is a suitable clinical rating scale to detect deterioration and progression of symptoms in patients of FA and that younger age at disease onset is a major predictor for faster disease progression. Higher (more than 353) GAA repeats on the shorter allele of the FXN locus had a higher SARA progression rate thereby specifying the effect of load of GAA repeats on disease outcome. EFACTS longitudinal analysis is indeed providing results which might give a suitable outcome measure and help in sample size calculations for the design of upcoming clinical trials of FA.

Contributed by Dr. Aastha Takkar


Not so surprisingly, embarrassment seems to be a major motivator for seeking treatment in patients with essential tremor (ET). Approximately 30–40% patients of ET exhibit moderate-to-severe depressive symptoms. Authors in this prospective clinicoepidemiological study on 91 cases of ET attempt to assess the associations between the motor and psychosocial factors (tremor, depression, embarrassment) in ET. Center for Epidemiological Studies Depression Scale (CESD-10) was used to assess depression; embarrassment was assessed using Essential Tremor Embarrassment Assessment score (ETEA) and a detailed in-person neurological
examination was used as a measure for action tremors. Severe depression was noted to be significantly associated with higher ETEA score but not with increasing tremor severity. Rather at each level of tremor severity, cases with more depressive symptoms had more embarrassment. Depressive symptoms may be a secondary response to ET; however, in addition to their own ill-effects, they also amplify the level of embarrassment in these patients. Management of depressive symptoms in ET patients may indeed lessen the additional burden of embarrassment.

**Contributed by Dr. Aastha Takkar**


In this study, the authors evaluated lacosamide against carbamazepine as a first-line monotherapy in the treatment of newly diagnosed epilepsy in adults. This phase 3, randomized, double-blind, non-inferiority trial included 888 adults from different centers in Europe, North America, and the Asia Pacific region. Post randomization, each group of patients was put on a basic dose that was escalated at 2 weeks, which was followed by a week of stabilization and a 6-month assessment period. If a seizure occurred, the dose was re-titrated to the next target level for another 2 weeks with a 1-week stabilization period, and the 6-month assessment period began again. Patients who completed 6 months of treatment and remained seizure-free entered a 6-month maintenance period on the same dose. The primary efficacy outcome was the percentage of patients remaining seizure free for 6 consecutive months after stabilization at the last assessed dose. The predefined noninferiority criteria were −12% absolute and −20% relative difference between the treatment groups. Seventy-four percent of the patients in the lacosamide group and 70% in the carbamazepine-controlled release (CR) group completed 6 months of treatment without seizures. Treatment-emergent adverse events were reported in 74% of patients receiving lacosamide and 75% receiving carbamazepine CR. Thirty-two (7%) patients taking lacosamide, and 43 (10%) taking carbamazepine-CR had serious treatment-emergent adverse events, whereas 11% and 16% patients, respectively, had treatment-emergent adverse events that led to its withdrawal. Thus, the authors concluded that lacosamide was as good as carbamazepine and might be useful as first-line monotherapy for adults with newly diagnosed epilepsy.

**Contributed by Dr. Kuntal Kanti Das**


In this double blind, randomized, placebo-control trial, the authors sought to determine if the different components of working memory (WM) could be improved following adaptive WM training; and, whether improvements in WM would generalize to other cognitive (attention) and academic skills (reading and mathematics) in children with TBI. Twenty-seven children with moderate-to-severe TBI were randomized to adaptive (n = 13) or nonadaptive training (active placebo; n = 14) and evaluated at baseline, posttraining, and 3-months follow-up. Complete case (CC) and intention-to-treat (ITT) analyses were conducted. Children in the adaptive group demonstrated significantly greater gains on select WM tasks from pre to posttraining (pre-post) and pre-training to follow-up (pre-follow-up; CC and ITT analyses). No gains were found on tests of attention. Adaptive training resulted in significantly greater gains on reading (academic skills), reading comprehension prepost-training (ITT analyses), and reading accuracy pre-follow-up (CC and ITT analyses). The authors thus concluded that near and far transfer of training to WM and academic skills, respectively, was possible in these children.

**Contributed by Dr. Kuntal Kanti Das**


In this prospective study, the authors present the results of a policy where selected cases with small unruptured intracranial aneurysms (SUIAs; size less than 7 mm for anterior circulation, and less than 4 mm for posterior circulation, with no history of prior hemorrhage) were observed and secured only if signs of instability (growth) were documented. They analyzed 292 patients with 368 SUIAs between 2006 and 2014 with a mean follow-up of 3.2 years and 1177.6 aneurysm years. They observed aneurysm growth probability in the tune of 2.6 ± 0.1% per year. The rate of unexpected aneurysm rupture before treatment was 0.24% per year (95% confidence interval (CI): 0.17% to 2.40%). The calculated rate of aneurysm rupture after documentation of growth was rather high (6.3% per
Sridhar, et al.: The fourth dimension

aneurysm-year, 95% CI: 1–22%). They found that aneurysms located in the posterior circulation, aneurysms with lobulations, female sex, and patients suffering from hypertension were associated with an increased risk of aneurysm growth. The probability of aneurysm growth also increased with the size of the dome and was proportional to the number of aneurysms diagnosed in a patient. Thus, while it was safe to observe patients diagnosed with SUIAs using periodic imaging, some of them would grow and need to be treated.

Contributed by Dr. Kuntal Kanti Das


In this article, the authors evaluated the number of epilepsy surgeries at their center via a vis the number of patients undergoing presurgical evaluations. Between 1990 and 2013, 66.8% of a total of 3060 patients studied presurgically underwent epilepsy surgery. They observed that presurgical evaluations continuously increased, whereas surgical interventions did not. They also made a key observation that the numbers of patients with medial temporal sclerosis and benign tumors as well as temporal lobe resections decreased since 2009. The number of nonlesional patients and the need for intracranial recordings, however, increased. They noted that more than 50% of the evaluated patients did not undergo surgery between 2010 and 2013 because patients were either not suitable (mainly due to missing hypothesis: 4.5% in 1990–1993 up to 21.1% in 2010–2013, a total of 13.4%) or declined from undergoing surgery (maximum 21.0% in 2010–2013, a total of 10.9%). One potential reason for decline in epilepsy surgeries was found to be increasingly detailed information on chances and risks given over time. The increasing volume of the presurgical programme largely compensates for decreasing numbers of surgically remediable syndromes and a growing rate of informed choice against epilepsy surgery. Although comprehensive diagnostic evaluation was offered to a larger group of epilepsy patients, surgical numbers remained stable.

Contributed by Dr. Kuntal Kanti Das


This study was a retrospective study done on a cohort of multiple sclerosis (MS) patients who were prescribed rituximab as an off-label indication. The patients were identified from the Swedish MS register. Out of the 822 patients treated with rituximab, 557 were of relapsing-remitting MS type (RRMS), 198 of secondary progressive MS type (SPMS), and 67 of primary progressive MS (PPMS) type. Patients were treated with an intravenous (IV) 500 or 1000 mg rituximab every 6–12 months, during a mean of 21.8 (standard deviation, 14.3) months. Mean expanded disability score did not change in the RRMS group, but increased in the SPMS and PPMS group. Of the 89 adverse events, grades ≥2 (of which 76 were infections) were seen in 72 patients. Progressive multifocal leukoencephalopathy was not reported in any of them. This study reports the highest cohort of patients with MS who have used rituximab till date. The study provides class IV evidence regarding the efficacy and safety of the use of rituximab in patients with MS.

Contributed by Dr. Ravi Yadav


This single-blind, proof of concept, randomized controlled trial compared a 6 month, thrice weekly, progressive aerobic exercise training program (AT) with the usual care plus education on cognitive and everyday function and an assessment 6 months later. The primary outcome measures were the Alzheimer’s Disease Assessment Scale–Cognitive subscale (ADAS-Cog), Executive Interview (EXIT-25), and activities of daily living [Alzheimer’s Disease Cooperative Study–Activities of Daily Living (ADCS-ADL)]. At the end of the study, the intervention group with the aerobic exercises had significant improvement in the ADAS-Cog score as compared to the nonintervention group. This study is the first to provide class II evidence in adults with mild subcortical ischemic vascular cognitive impairment that aerobic exercises improves the ADAS-Cog score.

Contributed by Dr. Ravi Yadav


The role of steroids in the treatment of Duchenne muscular dystrophy (DMD) is established. This study was done to study the safety and efficacy of deflazacort (DFZ) and prednisolone (PRED) vs placebo in DMD. This was phase II double-blind, randomized, placebo-controlled, multicentre study that evaluated the muscle strength of 196 patients with DMD. In the 1st phase, patients were assigned into DFZ 0.9 mg/kg/d, DFZ 1.2 mg/kg/d, PRED 0.75 mg/kg/d or placebo for 12 weeks. In phase 2, the placebo participants were randomly assigned to one of the above three groups. The study results showed that there was improved muscle strength with 12 weeks of treatment with DFZ and PRED as compared to the placebo and the weight gain observed with DFZ was lesser than that seen with the PRD group. Class I evidence is provided by this study for boys with DMD regarding the beneficial effect of daily use of DFZ and PRED in preserving muscle strength.

Contributed by Dr. Ravi Yadav


This study aimed to assess the role of reduced serum calcium in patients with intracranial hemorrhage (ICH) and whether there is any association between the serum calcium level
and the size of hematoma. A cohort of 2130 patients with primary intracranial hemorrhage was recruited between 1994 and 2015. A level of less than 8.4 mg/dl was defined as hypocalcemia. The hematoma expansion was defined by an increase of more than 30% or 6 ml from baseline ICH volume. The hypocalcemia patients were found to have a higher baseline hematoma volume compared to patients with normal serum calcium. Low serum calcium was independently associated with higher baseline volume of hematoma. Interestingly, the patients with higher serum calcium had a reduced risk of hematoma expansion. The authors conclude that the serum calcium level is an important factor and correlates with the risk of bleeding in patients with ICH. A lower serum calcium was associated with a subtle coagulopathy, and hence is a potential therapeutic target in future drug trials.

Contributed by Dr. Ravi Yadav


The authors describe a novel autoimmune meningoencephalitis that is immunotherapy responsive. This is characterized by a seropositivity to glial fibrillary acidic protein (GFAP).

This study evaluated 103 patients at the Mayo Clinic from the records and included 16 patients who had antibodies to glial fibrillary acidic protein. The mean age of the patients was 42 years. The clinical features were headache, subacute encephalopathy, optic papillitis, inflammatory myelitis, and ataxia. Malignancies involving different parts of the body were diagnosed within 3 years of onset in 38% of the patients. The patients responded to doses of corticosteroids and had a tendency to relapse. Thus, this study adds to the existing lists of autoimmune encephalitis syndromes that are responsive to treatment.

Contributed by Dr. Ravi Yadav


This was a systematic review and meta-analysis of 25 studies involving 1547 patients with Parkinson’s disease and 1107 unique controls by two independent investigators. The main outcome measure was blood cytokine concentrations in patients with PD compared with controls. The main findings of this study were the higher levels of interleukin (IL)-6, tumor necrosis factor, IL-1B, IL-2, IL-10, C-reactive protein and (Regulated on Activation, Normal T Cell Expressed and Secreted) RANTES in patients with PD as compared to controls. The findings suggest that PD is associated with the systemic inflammatory response.

Contributed by Dr. Ravi Yadav


One of the palliative interventions in patients with amyotrophic lateral sclerosis (ALS) is non-invasive ventilation. The authors performed a multicentre, randomised, controlled, triple-blind trial in patients with probable or definite ALS in 12 ALS centers in France. A total of 37 patients were randomized into a phrenic nerve stimulation group and an equal number of patients were placed in the sham group. The trial was prematurely terminated due to a higher morbidity and mortality in patients with phrenic nerve pacing. Thus, although promising to begin with, the trial results were disappointing for patients with ALS.

Contributed by Dr. Ravi Yadav


There has been a surge in studies showing the beneficial effects of intravenous thrombolyis with alteplase and mechanical thrombectomy in patients with ischemic stroke. The THRACE trial was done at 26 centers in France. The patients aged 18–80 years with acute ischemic stroke, and proximal cerebral artery occlusion were randomized to intravenous (IV) alteplase group alone or the IV alteplase with mechanical thrombectomy group. At the end of the study, 208 patients received IV alteplase alone and 204 were stratified into the 2nd group (IV alteplase plus mechanical thrombectomy-IVTMT). 42% of the 202 patients in the IVT group and, 106 (53%) of the 200 patients in the IVTMT group, achieved functional independence at three months. The THRACE trial results show that mechanical thrombectomy with standard intravenous thrombolyis improves functional outcome in patients with acute stroke.

Contributed by Dr. Ravi Yadav


Amiselimod is a new compound that is a modulator of sphingosine one phosphate (SIP) receptor. It is a new oral drug being tested in various autoimmune disorders. MOMENTUM trial was a double-blind, phase 2 trial that recruited patients with relapsing-remitting multiple sclerosis from 84 centers in Europe and Canada. These patients were randomized to 0.1 mg, 0.2 mg, and 0.4 mg of amiselimod or placebo for 24 weeks. The primary endpoint was the total number of gadolinium-enhanced T1 lesions on monthly MRI scans from weeks 8 to 24. A total of 415 patients were randomized into four groups. The main finding was that the drug amiselimod 0.2 mg and 0.4 mg significantly reduced the total number of gadolinium-enhanced T1 weighted lesions. No serious adverse
effects were reported. The short duration and low power of the study are the reason why the results should be read with caution.

Contributed by Dr. Ravi Yadav


This meta-analysis showed that the prevalence of depression and suicidal ideation is significantly higher than the general population in medical students. The meta-analysis extracted data from 167 cross-sectional studies, with the patient number being 116628, and 16 longitudinal studies from 43 countries. The summary estimate of the prevalence of depression or depressive symptoms among medical students was 27.2%, and that of suicidal ideation was 11.1%, which was significantly higher than the data from the general population. This study raises important concerns regarding the need to develop strategies for the mental health of medical students.

Contributed by Dr. Ravi Yadav