COMMENTARY

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

K Sridhar, Mazda K Turel1, Manjul Tripathi2, Ravi Yadav3, Srijithesh PR3, Aastha Takkar4, Sahil Mehta4, Kuntal K Das5, Anant Mehrotra6, Chirag K Ahuja6

Spontaneous intraparenchymal hemorrhage (IPH) is a common neurosurgical emergency, with hemorrhage size and expansion associated with poor clinical outcomes. The authors studied 202 nontraumatic IPH transfer patients over two years. A maximum Youden index was calculated to determine thresholds of the initial IPH volume and expansion, most predictive of deterioration and mortality. Both intraventricular hemorrhage and hydrocephalus were independently associated with the elevated risk for deterioration and mortality, while anticoagulant use was associated with neurologic deterioration. An initial volume of over 32ccs was associated with an increased mortality risk, while the risk of neurologic deterioration appears to peak at a smaller volume of 18ccs. They concluded that any measurable IPH expansion suggests an elevated risk of deterioration and mortality.


There is no consensus on the comparative efficacy and safety of carotid artery stenting (CAS) versus carotid endarterectomy (CEA) in patients with asymptomatic carotid artery stenosis. The authors identified 11 reports of 5 randomized controlled trials for inclusion (n = 3019) in asymptomatic patients. The pooled incidences of any periprocedural stroke, periprocedural nondisabling stroke, and any periprocedural stroke or death trended toward an increased risk after CAS. However, they could not rule out clinically significant differences between the treatments for the long-term risk of stroke.


The authors compared the effectiveness of revascularization procedures in both adult and pediatric patients with moyamoya disease (MMD). The authors constructed a decision analysis model for treatment using a direct and indirect revascularization technique including 33 studies involving 4197 cases. Cases were divided into adult and pediatric populations. These were further subdivided into 3 different treatment groups: indirect, direct, and combined revascularization procedures. In the pediatric population, at a 5- and 10-year follow-up, there was no significant difference between the indirect and combination procedures but both were superior to direct revascularization. In adults, at a 4-year follow-up, indirect revascularization was superior to the direct one. The authors concluded that in the absence of factors that dictate a specific approach, the present decision analysis suggests that direct revascularization procedures are inferior in terms of quality-adjusted life years in both adults at 4 years and children at 5 and 10 years postoperatively, respectively. These findings were statistically significant, suggesting that indirect and combination procedures may offer optimal results at a long-term follow-up.


This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com
and the composite outcome of periprocedural stroke, death or myocardial infarction, or long-term ipsilateral stroke. They suggested that CEA is the preferred option for the management of asymptomatic carotid stenosis.


The authors performed a retrospective review of all surgically treated, unruptured pediatric AVM patients. Patients under 18 years were included. The average age of the 66 patients was 13 years. Nine patients were asymptomatic (13.6%), and seizure presentation occurred in 57.6% (n = 38) of them. During an average follow-up of 4.2 years, 12 (18.2%) patients experienced post-operative seizures, with 5 (7.9%) out of 28 non-seizure patients having a de novo seizure. In patients with the presentation of seizures, 81.6% were completely seizure-free throughout the follow-up. In a multivariable analysis, a larger AVM size and temporal location were found to increase the risk of follow-up seizures. On the contrary, seizure presentation and post-operative infection were not mutually associated. The authors suggest that for selected unruptured AVMs with a small size and non-temporal location, consideration of surgery as primary treatment for persistent seizures is a reasonable option.


Patients undergoing carotid endarterectomy (CEA) for symptomatic stenosis of the internal carotid artery benefit from early intervention. Heterogeneous data are available regarding the influence of timing of carotid artery stenting (CAS) on the procedural risk. 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 CAS or CEA in a pooled analysis of individual patient data from 4 randomized trials. Among a total of 4138 patients, a minority received their allocated treatment within 7 days after 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). For interventions after 1 week, CAS was also more hazardous than CEA (7.1% versus 3.6%). They concluded that early surgery is safer than stenting for preventing future stroke.


Atypical meningioma is a WHO grade II tumor, with intermediate prognosis and risk-of-recurrence. Optimal management following gross total resection (GTR) is controversial, with observation versus adjuvant radiotherapy (RT) being contentiously debated. In this study, 61 patients underwent observation and 8 received RT after surgery. Overall, 15 patients under observation and 3 patients undergoing RT experienced tumor recurrence (5-year progression free survival (PFS) 79% vs. 88%; P = 0.67); 19 patients under observation and 2 undergoing RT died (5-year overall survival [OS] 89% vs. 83%; P = 0.68). Systematic review identified 9 preceding studies reporting extractable data comparing observation and RT outcomes after gross total resection. Recurrence was 18% and 19% after observation and RT (P = 0.9), respectively; total survival was 84% and 93% (P = 0.2) respectively. At 5 years, PFS was 81% after observation and 88% after RT (P = 0.2), while survival was 87% after observation and 96% after RT (P = 0.4). The authors concluded that observation alone after GTR of atypical meningioma was not associated with an increased risk of tumor recurrence or mortality.


Postoperative cerebellar mutism syndrome (pCMS) occurs in 7%-50% of patients after cerebellar tumor surgery. In this study, the authors included 71 children with a medulloblastoma, 28 of whom developed pCMS after primary resection. Multiple regression analysis revealed that tumor size, tumor infiltration into or compression of the brainstem, and a higher mean body temperature during the first 4 postoperative days were independent and highly significant predictors for pCMS. These data suggest that an important focus for the prevention of pCMS in children who have undergone medulloblastoma surgery might be rigorous maintenance of normothermia as standard care after surgery.

Contributed by Dr. Mazda K. Turel


The aim of this study was to report the radiologic and clinical outcomes of patients treated with stereotactic radiosurgery (SRS) for pilocytic astrocytoma in the primary and salvage setting. Twenty-eight consecutive patients with a median age of 17.4 years who underwent SRS were identified. Overall, 46% of patients were treated with SRS as part of the initial treatment course after a biopsy or subtotal resection, and the remainder were treated with SRS as a part of the salvage therapy. The most common location was the cerebellum (28%) followed by brainstem and basal ganglia (21 and 18%, respectively). The median tumor volume was 1.84 cc, and 39% had a cystic component at SRS. The prescription dose was a median 16 Gy. With a median follow-up of 5 years, all patients remained alive at the last follow-up. Two patients demonstrated evidence of local radiographic progression at the last follow-up (7%). No toxicity could be directly attributed to SRS. In this SRS series, a durable tumor control was achieved in 93% of the patients with pilocytic astrocytoma, although a continued follow up protocol will be important, given the prolonged course of natural history of this disease.

Contributed by Dr. Mazda K. Turel
Sridhar, et al.: The fourth dimension


Up to one-third of patients with a posterior fossa brain tumor (PFBT) will experience persistent hydrocephalus mandating permanent cerebrospinal fluid diversion. The authors sought to compare the durability between endoscopic third ventriculostomy (ETV) and ventriculoperitoneal shunt (VPS) therapy in the pediatric population. A total of 408 patients were included from 12 studies, 284 who underwent ETV, and 124 who underwent VPS placement. No significant differences between the cohorts were observed with regard to age, sex, tumor grade or histology, metastatic status, or extent of resection. The cumulative failure rate of ETV was 21%, whereas that of VPS surgery was 29%. The median time to failure was earlier for ETV than for VPS surgery, 1.1 vs 4.7 months (P = 0.03). Initially the ETV survival curve dropped sharply and then stabilized around 2 months. The VPS curve fell gradually but eventually crossed below the ETV curve at 5.7 months. Overall, a significant survival advantage was not demonstrated for one procedure over the other. However, postoperative complications were higher following VPS (31%) than ETV (17%) (P = 0.012).

Contributed by Dr. Mazda K. Turel


The aim in this paper was to determine risk factors for the development of a postoperative cerebrospinal fluid (CSF) leak after an endoscopic endonasal approach (EEA) for resection of skull base tumors. Of the 615 patients studied, 103 developed a postoperative CSF leak (16.7%). Sex and perioperative lumbar drainage did not affect CSF leakage rates. Posterior fossa tumors had the highest rate of CSF leakage (32.6%), followed by anterior skull base lesions (21.0%) and sellar/suprasellar lesions (9.9%). There was a higher leakage rate for overweight and obese patients (body mass index [BMI] >25 kg/m²) than for those with a healthy-weight BMI (18.7% vs 11.5%; P = 0.04). Patients in whom a pedicled vascularized flap was used for reconstruction had a lower leakage rate than those in whom a free graft was used (13.5% vs 27.8%; P = 0.0015). In patients with a BMI >25 kg/m², the use of a pedicled flap reduced the rate of CSF leakage from 29.5% to 15.0% (P = 0.001); in patients of normal weight, this reduction did not reach statistical significance (21.9% [pedicled flap] vs 9.2% [free graft]; P = 0.09).

Contributed by Dr. Mazda K. Turel


A multicenter, prospective, randomized equivalence trial comparing a thoraco-lumbo-sacral orthosis (TLSO) to no orthosis (NO) in the treatment of acute AO Type A3 thoracolumbar burst fractures was recently conducted and demonstrated that the two treatments following an otherwise similar management protocol are equivalent at a 3-month post-injury time interval. The purpose of the present study was to determine whether there was a difference in long-term clinical and radiographic outcomes between the patients treated with and those treated without a TLSO. Here, the authors presented the 5- to 10-year outcomes. Subjects were enrolled if they had an AO Type A3 burst fracture between T-10 and L-3 within the previous 72 hours, kyphotic deformity <35°, no neurological deficit, and an age of 16-60 years old. The present study represented a subset of those patients: 16 in the TLSO group and 20 in the NO group. The Roland Morris Disability Questionnaire (RMDQ) score at 5-10 years post-injury was 3.6 for the TLSO group and 4.8 for the NO group (P = 0.4). Average kyphosis was 18.3° for the TLSO group and 18.6° for the NO group. The authors concluded that compared with patients treated with a TLSO, patients treated using early mobilization without orthosis maintained similar pain relief and improvement in function for 5-10 years.

Contributed by Dr. Mazda K. Turel


The objective of the present study was to use magnetic resonance imaging (MRI)-based propensity-score-matched analysis to compare postoperative outcomes between the anterior and posterior surgical approaches for degenerative cervical myelopathy. A total of 435 cases were included in the propensity score calculation, and 1-to-1 matching resulted in 80 pairs of anterior and posterior surgical cases; 99% of these matched patients had a multilevel compression. The anterior and posterior groups did not differ significantly in terms of the postoperative mean Japanese Orthopedic Association Scale [mJOA] score (15.1 versus 15.3, P = 0.53), Neck Disability Index (20.5 versus 24.1, P = 0.44), or Short Form-36 (SF-36) Physical Component Summary (PCS) score (41.9 versus 40.9, P = 0.30). The overall rates of perioperative complications were similar between the 2 groups (16% versus 11%, P = 0.48); however, dysphagia/dysphonia was reported only in the anterior group whereas surgical site infection and C5 radiculopathy were reported only in the posterior group. The authors concluded that anterior and posterior decompression for degenerative cervical myelopathy resulted in similar postoperative outcomes and rates of complications.

Contributed by Dr. Mazda K. Turel


1114 Neurology India | Volume 65 | Issue 5 | September-October 2017
The study was conducted to delineate whether ossified posterior longitudinal ligament (OPLL) continues to progress after a laminoplasty compared with fusion, and to clarify the relationship between radiological progression of OPLL and neurological decline. The authors included 11 studies involving 530 patients, of whom 429 underwent a laminoplasty and 101 underwent fusion surgery. The prevalence of radiological OPLL progression was 62.5% for the laminoplasty group and 7.6% for the fusion group. In the laminoplasty group, the prevalence of OPLL progression increased with time and reached 60% at about 10-year follow-up. The prevalence of neurological decline was similar for about 2 years, 8.3% for the laminoplasty group and 3.8% for the fusion group. They concluded that laminoplasty frequently induces progression of OPLL compared with fusion surgery, but this does not result in significant clinical deterioration. However, they suggested that laminoplasty should not be recommended for patients with OPLL because the latter can get worse with time.

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

Lee CW, et al. Which approach is advantageous to preventing the development of ASD? A comparative analysis of 3 different lumbar interbody fusion techniques (ALIF, LLIF, and PLIF) in L4-5 spondylolisthesis. World Neurosurg 2017; doi: 10.1016/j.wneu.2017.06.005

The purpose of this study was to compare radiological and clinical outcomes in patients with L-4-S lumbar spondylolisthesis who have undergone either instrumented anterior lumbar interbody fusion (ALIF), lateral lumbar interbody fusion (LLIF), or posterior lumbar interbody fusion (PLIF), especially with regard to the development of adjacent segment disease (ASD). Eighty-two patients with preoperative L-4-5 spondylolisthesis and minimal ASD who underwent instrumented L-4-5 fusion were divided into three groups according to the surgical approach used for treatment (ALIF: 27 patients, LLIF: 24 patients, PLIF: 31 patients). ASD was found in 37.0% (10/27), 41.7% (10/24), and 64.5% (20/31) of the patients in the ALIF, LLIF, and PLIF groups, respectively (mean follow-up duration: 35.42 ± 9.35 months). The ALIF and LLIF groups had significantly increased disc and foraminal height compared to the PLIF group. The ALIF group had significantly improved lordosis compared to the PLIF and LLIF groups. However, there were no statistically significant intergroup differences in the clinical outcomes assessed by the visual analog scale (VAS) and Oswestry disability index (ODI).

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


In this study, the authors compared the effects of early tracheostomy (ET) versus late tracheostomy (LT) on traumatic brain injury (TBI) related outcomes and prognosis.

Data on 152 TBI patients with a Glasgow coma scale (GCS) of ≤6 were collected. Patients who had tracheostomy before or at the sixth day of their admission were considered as the ET group and those who had tracheostomy after the sixth day of admission were considered as the LT group.

Patients who had undergone an ET had a significantly lower hospital stay (46.4 vs. 38.6 days; \( P = 0.048 \)) and intensive care unit (ICU) stay (34.9 vs. 26.7 days; \( P = 0.003 \)). Mortality rates were not significantly different between the two groups. Although not statistically significant, favorable outcomes [Glasgow outcome scale (GOS) >4] were higher and ventilator associated pneumonia rates were lower among the ET group. Multivariate analysis showed that the ET group had a significantly improved six month prognosis (GOS >4) (odds ratio [OR] = 2.5). The Glasgow Coma Scale (GCS) and Rotterdam score did not show any effect on the six month prognosis. Despite previous concerns regarding the increased mortality rates among patients who undergo an ET, performing a tracheostomy for patients with severe TBI less than six days after their hospital admission, in addition to decreasing hospital and ICU stay, will improve patient prognosis, according to this study.

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


The aim of the study was to evaluate the efficacy and safety of dexamethasone in 27 patients with recurrent CSDH. The follow-up for each patient consisted of CT or MRI scans every 28 days from admission to the resolution of hematoma. Among the 27 patients, only 3 patients with recurrent CSDH were treated by burr hole surgery. Of the other 24 patients who primarily underwent dexamethasone treatment, 17 (70.8%) patients were treated successfully with medical treatment, whereas 7 patients required reoperation. Complications were noted in 3 (12.5%) patients (hyperglycemia, urinary infect and pneumonia in one patient each, respectively). The single mortality (4.2%) was due to a massive brain infarction. Twenty-one of the 24 patients (87.5%) recovered to their previous functional levels. There was no statistical significance in between surgery and dexamethasone therapy regarding success, incidence of complications, and functional recovery rate. Hence, the authors concluded that patients with recurrent CSDH can be treated successfully and safely with the nonsurgical medical treatment of dexamethasone.

By the use of this method, reoperation may be avoided.

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


Bilateral chronic subdural hematoma (bCSDH) is a common neurosurgical condition frequently associated with the need for retreatment. In a national database of CSDHs (Danish Chronic Subdural Hematoma Study), the authors retrospectively identified all bCSDHs treated over a 3-year period. Two hundred and ninety-one patients with bCSDH were identified, and 264 of them underwent unilateral (136 patients) or bilateral
(128 patients) surgery. The overall retreatment rate was 21.6% (57 of 264 patients). Cases treated with unilateral surgery had twice the risk of retreatment compared with cases undergoing bilateral surgery (28.7% vs 14.1%, respectively, P = 0.002). The data also showed that a separated hematoma density and the absence of postoperative drainage were independent predictors of retreatment. The authors concluded that in bCSDHs, bilateral surgical intervention significantly lowers the risk of retreatment compared with unilateral intervention and should be considered when choosing a surgical procedure.

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


In 2016, World Health Organization (WHO) had revised the classification of tumors of the central nervous system (CNS). In view of the new pathological classification and prognostic markers, the treatment protocol is due for a significant shift. The ‘European Association for Neuro Oncology (EANO)’ recently published guidelines for management of adult patients with astrocytic and oligodendroglial gliomas. This article describes the consensus opinion of the EANO task force for management of glial tumors with special emphasis on the postoperative management including radiotherapy, chemotherapy, and radiosurgery. This guideline is a benchmark to guide the management decisions only when detailed immunohistochemical markers of gliomas especially IDH, 1p-19q, ATRX gene status etc., are reported, apart from the histological diagnosis. Although the present WHO update on gliomas has not taken MGMT methylation status and TERT mutation into consideration, this EANO guideline provides therapeutic approaches for focal and diffuse glial tumors in adults (for WHO grade II, III, IV, H3-K27M mutant) as per the IDH, 1p-19q, MGMT methylation, and TERT mutational status. This guideline emphasizes on two important issues: management of glial tumors should be on consensus basis by members of tumor board; and, neurosurgeons in India need to ensure the implementation of a detailed reporting by their pathology colleagues. Only then will we be able to do justice to the patients suffering from a glioma.

**Contributed by Dr. Manjul Tripathi**


Despite advances in molecular and surgical care, glioma still remains a formidable disease. As a care provider, neurosurgeons need to provide palliative care to patients and care givers in this terminal illness. An efficient palliative care is neccary to improve the quality of life of the patients and to destress their families. There are plenty of guidelines for surgical and adjuvant treatment of these patients but only few discuss the issues of care after their treatment is completed. The European Association for Neuro-Oncology (EANO) has recently published evidence based guidelines for the palliative care of glioma patients for commonly encountered issues such as headache, seizure and venous thromboembolism prophylaxis; fatigue, mood and behavioural changes; cognitive decline; and, nursing care. The guideline also discusses the key issues of pharmacological and behavioural therapy in patients in end-of-life phase. The article stresses on the early referral for palliative care and psychosocial support to involve patient and care givers in the early part of disease cycle. This will ensure that the patient can participate in key issues of life and end-of-life decisions while their cognition and communication skills are intact. Another frequently overlooked issue is the intense and inescapable fear of the anticipatory grief among the close family members, which adversely affects the dynamics of care, the sense of identity, and the relationship with the patient. This critical issue needs psychoeducation and cognitive behavioural therapy. This guideline is designed to help clinicians in managing adult patients with a glioma with the best available but clearly limited evidence for palliative care.

**Contributed by Dr. Manjul Tripathi**


There is nothing more confusing than an arteriovenous malformation of the brain as far as its natural history and management options are concerned. On a practical note, we shall never be able to know the natural history of an AVM as now, hardly any patient is left on observation alone. Our current knowledge of its natural history is based on observational studies of the clinical course in untreated patients. Intervention of any kind alters the natural history of the AVM. There have been significant differences in the management policy after the publication of the ARUBA trial and the first edition of recommendations by the American Heart Association (AHA)/American Stroke Association (ASA) in 2001. Even this updated guideline of AHA/ASA fails to answer the key question of the optimal management for AVM including the role of observation but it presents the best evidenced literature with discussion of the various available options. It supports the existing evidence that only surgery and stereotactic radiosurgery are the definitive treatment options available for an AVM, and endovascular intervention may be helpful in down-sizing some large volume AVMs. With the upcoming support for volume and dose fractionated GKRS, we are better equipped to treat large volume AVMs and malformations in eloquent areas in a cost effective way. This will help in mitigating the risk of surgical complications as well as collateral damage, and in maintaining the quality of life.

**Contributed by Dr. Manjul Tripathi**

For all practical purposes, cricket is the most common sport in India and the neighbouring countries. Being a non-contact sport, cricket is generally considered a safe game. In view of insufficient injury reporting, head injuries in cricket are viewed as unfortunate but rare accidents, or simply “a part of the risks of the game”. Although the risk of sustaining an injury cannot be completely obliterated despite every safety precaution introduced, all attempts should be made to significantly reduce the chances of significant injuries. An effective injury surveillance is the cornerstone of injury management. Among all the existing sports, organisers of cricket were the first to publish recommended methods for injury surveillance in 2005. This was followed by the organisers of soccer and baseball. Before the International Cricket Club’s world cup 2011 series, there was no standard injury surveillance report. Only 5/14 countries participated in that surveillance and the injury rate was 3.7 per 100 player days; thigh muscle sprain was the commonest injury. Craniofacial injuries are not uncommon and the recent tragic deaths of Philip Hudges and Ankit Keshari have redirected attention towards deficiencies in the safety parameters. Mild head injuries largely go unreported in view of poor awareness and negligence on the part of the players as well. This consensus statement is a robust effort to draft a uniform language of injury incidence and prevalence, considering all existing formats of the sport such as T20, one day international, and test cricket. Every cricket league should abide by these guidelines and report all injuries sustained during the game of cricket to identify the burden of trauma and to develop various modes for their prevention.

Contributed by Dr. Manjul Tripathi

Regis J, et al. Safety and efficacy of gamma knife radiosurgery in hypothalamic hamartomas with severe epilepsies: A prospective trial in 48 patients and review of the literature. Epilepsia 2017;58:60-71

Hypothalamic hamartomas (HH) are benign congenital heterotopic lesions, essentially epileptogenic when closely connected to the mamillary bodies. Most commonly, the patients are young children with drug resistant epilepsy as well as cognitive, and neuropsychological impairment. Usually the seizures start early in life and are drug resistant from the onset. Various surgical options such as microsurgical resection, radiofrequency thermocoagulation, laser interstitial thermal therapy etc., are efficacious only in 60% of the patients while 40% of the patients still present with seizures. In this study, a prominent radiosurgical centre has shared its experience with radiosurgery in patients of HH. The authors report a seizure control rate comparable to other management techniques but without the sinister complications of endocrinological, behavioural or neurocognitive deterioration. Except in the case of a large volume HH (grade V-VI), gamma knife radiosurgery proves to be the least invasive and least risky treatment option. With this favorable risk benefit profile, and absence of memory decline, radiosurgery should be considered as the first intention treatment for epilepsy associated with small volume HH. Interestingly, behavioural improvement precedes seizure control and patients with even partial seizure control start enjoying an improved quality of life.

Contributed by Dr. Manjul Tripathi


These are the times of evidence-based clinical decision making and treatment. Therefore, we rely on strong scientific evidence provided by randomized trials, metaanalysis and systematic reviews. The problems with the conduct of these clinical trials, however, are that these are not only challenging to carry out but also quite expensive. Therefore, many key clinical questions often go unanswered. Other alternatives for deriving high quality evidence, including precision medicine trials as well as mechanism based trials, have their own sets of hindrances. Master protocols represent a unique methodologic innovation that evaluate more than one or two treatments in more than one patient type or disease within the same overall trial structure, thus saving valuable time and money, while providing answers to more questions than the traditional clinical trials. The authors visit these master protocol based studies in this review and discuss their key design components and operational aspects to achieve better coordination among the different stakeholders. This review also brings forth certain bottlenecks of this approach like the need for extensive discussion between the sponsors contributing to therapies for evaluation and the parties involved in the conduct and governance of these trials (like the publication and data rights, and the timing of various regulatory submissions).

Contributed by Dr. Kuntal Kanti Das


Anterior cervical decompression and fusion (ACDF) is one of the most common procedures performed in neurosurgery. It is often one of the earliest surgeries performed in one’s neurosurgical career and it is indeed one of the most fruitful surgeries that we perform. Nevertheless, complications are part and parcel of any surgery and ACDF is no exception. Postoperative dysphagia is one of the less explored complications of ACDF, which can impair the patient’s quality of life, at least in the initial few days after surgery. In this paper, the authors aimed to determine the prevalence, risk factors and the impact of this complication on the short and long-term clinical outcomes, in patients undergoing ACDF. This multicenter prospective study included patients with a single-stage anterior as well as a two-stage anteroposterior cervical spine surgery (a total of 470 patients). A combination of standard follow-up parameters like the modified Japanese Orthopaedic Association scale (mJOA), Nurick score, Neck Disability Index (NDI), and Short Form-36 Health Survey (SF-36) were utilized to assess the outcomes between patients with and without dysphagia. The authors found on multivariate analysis that the incidence of postoperative dysphagia was significantly increased if the patients had an endocrinal disorder, a greater number of decompressed segments, or a 2-stage surgery.
The overall incidence of this complication was 6.2%. It was, however, transitory as the short and long-term improvements in functional disability, and quality-of-life scores were comparable between the two groups of patients.

Contributed by Dr. Kuntal Kanti Das


Competitive instinct and a strong will to succeed in life are present inside all of us in differing magnitudes. These attributes bring us accolades, define our character and provide us social prominence. However, the neural pathway of this complex higher mental function remains unexplored till now. Working in mice, Zhou et al., identified a dorsomedial prefrontal cortex (dmPFC) neural population as the special area responsible for the winning attitude. During moment-to-moment competition in the dominance tube test, the activation or inhibition of the dmPFC induced instant winning or losing, respectively. In vivo optogenetic-based long-term potentiation and depression experiments revealed that the mediodorsal thalamic input to the dmPFC mediated long-lasting changes that are affected by a history of winning. Once primed, the same neural circuit also ensured transfer of the behavior between different social contests. Therefore, this novel study provides interesting insights into the understanding of the neuronal circuitry underlying adaptive and pathological social behaviors.

Contributed by Dr. Kuntal Kanti Das


Deep venous thrombosis (DVT) remains an important complication faced by neurologists and neurosurgeons caring for their patients in the critical care setting. One of the fatal sequel of DVT is the prospect of pulmonary embolism which needs to be detected and treated promptly to improve patient outcomes. The Well’s criteria has been the traditionally utilized clinical algorithm, supplemented by blood D-Dimer estimation, in predicting the risk of pulmonary embolism (PE) in these patients. Considering the implications of PE, the high-risk patients often undergo repeated pulmonary CT angiograms (PCTA). This practice often leads to harmful exposure to the ionizing radiation and has financial implications too. Moreover, the Well’s criteria are a bit cumbersome to apply and can be time consuming, especially in the emergency setting. The YEARS clinical decision rule incorporates differential D-dimer cutoff values at presentation, added to three of the clinical criteria of the Well’s algorithm (clinical signs of deep vein thrombosis, haemoptysis, and whether or not pulmonary embolism is the most likely diagnosis). It was meant to provide a fast assessment of the risk of PE so that CTPA could be performed judiciously. In this multicenter study, the authors aimed to prospectively evaluate this novel and simplified diagnostic algorithm for suspected acute pulmonary embolism. They divided patients into three categories: 1) Patients without YEARS items and D-dimer less than 1000 ng/mL, 2) Patients with one or more YEARS items and D-dimer less than 500 ng/mL, and 3) all other patients. In the first two categories, PE was considered excluded. The third category of patients was considered to be having PE, and hence underwent CTPA. The authors found that only 18 of the 2946 patients in whom PE was ruled out at baseline (first two categories) eventually developed symptomatic venous thromboembolism during the 3-month follow-up (0.61%). Interestingly, they observed that the YEARS algorithm ensured that CTPA was not indicated in 48% of the patients, a figure which would otherwise have been 34%, had the Wells’ rule and fixed D-dimer threshold of less than 500 ng/mL been applied. Thus, the authors concluded that the YEARS diagnostic algorithm could exclude PE safely with 14% absolute decrease in CTPA examinations in all ages and across several relevant subgroups.

Contributed by Dr. Kuntal Kanti Das


Stroke remains one of the leading causes of neurological morbidity and mortality. Acute ischemic strokes (AIS) account for the lion share of these cases. The diagnosis and management of ischemic stroke has evolved rapidly over the last few years. Prompt diagnosis may allow institution of timely treatment in the golden hour for attainment of optimal outcomes. Diffusion weighted imaging (DWI) has remained one of the back-bones for making an early diagnosis of AIS. However, AIS may not always show diffusion restriction. This study aimed to focus on this rare subset of patients with a view to decipher the prevalence of DWI negative AIS and to clinically characterize these patients. For this meta analysis, the authors screened all relevant studies between 1992 (when DWI was first clinically used) till 2016. Having analyzed 3236 patients from 12 articles meeting the inclusion criteria, the authors found the pooled prevalence of DWI-negative AIS to be 6.8%. They also observed that posterior circulation ischemia was strongly associated with negative diffusion restriction (p < 0.001). Thus, the authors concluded that DWI negative AIS did account for a significant proportion of AIS patients, the odds being 5 times higher with posterior circulation ischemia. They emphasized the need to make the diagnosis on clinical grounds so that urgent reperfusion therapy could be considered even when an initial DWI scan was negative.

Contributed by Dr. Kuntal Kanti Das


This was a prospective multicenter study carried out on a cohort of 611 preterm neonates enrolled in the ‘Neonatal Seizure Registry’ at seven pediatric centers that follow the American Clinical Neurophysiology Society’s neonatal electroencephalography monitoring guideline. Seizure characteristics were evaluated by gestational age at birth and compared with term neonates. Hypoxic-ischemic encephalopathy and intracranial hemorrhage accounted for
the etiology in more than half of the preterm neonates. The presence of subclinical seizures, monotherapy treatment failure, and distribution of seizure burden was similar in preterm and term neonates. Phenobarbital was the most common initial medication for all gestational age groups, and failure to respond to an initial loading dose was high in both preterm and term neonates. Mortality was similar among the three preterm gestational age groups; however, preterm mortality was more than twice that of term infants.

Importantly, subclinical seizures were more common and mortality was higher for preterm than term neonates. The data highlights the importance of electroencephalographic monitoring and the potential for improved management in preterm neonates.

Contributed by Dr. Aastha Takkar


Ironically, it took decades together for neurologists to realize that the so called “benign intracranial hypertension” is not benign but has a potential to cause significant visual morbidity.

This was a prospective trial of patients with medically-refractory, medically-intolerant or fulminant idiopathic intracranial hypertension (IIH), in whom the safety and efficacy of stenting of venous sinus stenosis was analyzed. The main outcome measures were pre- to post-stent change in symptoms related to intracranial hypertension, mean deviation of visual fields, grade of papilledema (1–5), retinal nerve fiber layer (RNFL) thickness, trans-stenotic gradient, and opening pressure on lumbar puncture. Improvement or resolution of headaches, pulse-synchronous tinnitus, diplopia, and transient visual obscuration were observed in a considerable population. Improvement was also noticed in visual fields, papilledema, and RNFL thickness. A second stenting procedure was needed in one patient. Complications of the stenting procedure included one small, self-limited retroperitoneal hemorrhage, transient head or pelvic pain, and one allergic reaction to contrast. No serious adverse events were noted. It was concluded that stenting of venous sinus is safe and results in reduction of intracranial pressure in patients with IIH.

Contributed by Dr. Aastha Takkar


Antidepressants are one of the commonly prescribed drugs in the field of neurosciences. While the efficacy of antidepressants for chronic pain has been reported in large randomized-controlled trials (RCT), there is inconsistent data on their adverse effects and tolerability. In this article, systematic literature research and meta-analyses were performed to explore the adverse effect profiles and tolerability of antidepressants administered for the treatment of chronic pain. A higher risk for adverse effects compared to a placebo was observed in all antidepressants included in this analyses, except nortriptyline. The most prevalent adverse effects were dry mouth, dizziness, nausea, headache, and constipation. Amitriptyline, mirtazapine, desipramine, venlafaxine, fluoxetine, and nortriptyline showed the highest placebo effect-adjusted risk of adverse effects. The risk of withdrawal due to the adverse effects was highest in desipramine followed by milnacipran, venlafaxine, and duloxetine. There were distinct risk profiles for individual drugs but the overall tolerability was high. The data analysis confirmed overall tolerability of low-dose antidepressants for the treatment of chronic pain and revealed drug specific risk profiles. The results might be useful in defining multimodal treatment regimens for patients of chronic pain.

Contributed by Dr. Aastha Takkar


Patients with Parkinson’s disease (PD) and essential tremor (ET) are thought to have a higher risk of cognitive impairment than their age-matched controls. Only a few small studies are available to this day. This population based analysis of 2438 dementia free participants was aimed to compare the cognitive profile of patients with these two conditions to each other and to healthy individuals. A head-to-head comparison of ET and PD, adjusting for age and education was carried out. As expected, patients with PD and ET had a poorer cognition than controls. Patients with PD scored lower than those with ET, and both of these scored lower than controls, in memory and verbal fluency tasks. While patients with PD had lower scores in verbal fluency, patients with ET had a poorer cognitive processing speed. This large population-based study emphasized that both the conditions influence cognitive performance, that a continuum exists from normal controls to ET to PD (the cognitive defects in PD being more severe). It was also concluded that although deficits are in many of similar cognitive domains, the affected cognitive domains do not overlap completely.

Contributed by Dr. Aastha Takkar


Delirium is a common post-operative complication and implies significant financial burden, non-operative morbidity, and mortality. Continuous EEG data were obtained in 12 patients following their orthopedic surgery from the day of surgery until delirium assessment on post-operative day 2 (POD2). Sleep/EEG predictors of delirium present prior to the onset of symptoms of delirium were assessed. Loss of sleep on the night after the surgery and a longer latency to sleep onset on the first night in the hospital were found to be early predictors of the development of subsequent delirium. Electro-physiologically, EEG delta power alterations in waking and sleep appeared to be later indicators of impending delirium. Greater waking
EEG delta power on the first postoperative day and less non-REM sleep EEG delta power on the second postoperative night also predicted delirium severity. This novel concept may facilitate the development and targeting of therapies to avoid post-operative delirium that can be applied to the high-risk patients. Further studies may help to evaluate the reproducibility/generlizability of this hypothesis.

Contributed by Dr. Aastha Takkar


The 'freezing of gait' symptom in Parkinson's disease is quite disabling, and the exact localization of this symptom is not clear yet. This study tries to solve this question by a unique design. The authors chose 14 case reports from literature where the patient had a focal lesion in the brain that produced the symptom of freezing of gait. These lesions were then mapped on a known brain atlas. The symptom could be produced from various sites interconnected in that network. The networks were also mapped. The authors found that more than 90% of the lesions were functionally connected to an area in the dorsomedial cerebellum. This area was overlapped by areas of cerebellum activated by locomotor activity. The interesting findings of the study may help in many useful applications in the future and may help to further improve our understanding of the symptom of freezing of gait.

Contributed by Dr. Aastha Takkar

Writing Group; Edaravone (MCI-186) ALS 19 Study Group. Safety and efficacy of edaravone in well-defined patients with amyotrophic lateral sclerosis: A randomised, double-blind, placebo-controlled trial. Lancet Neurol 2017;16:505-12

There have been many clinical drug trials in the past on patients with amyotrophic lateral sclerosis (ALS) in an attempt to find a cure for this uniformly fatal disease. This phase 3, randomized, double-blind, parallel-group study was done on patients aged 20 – 75 years with ALS of grade 1 using the definite or probable ALS classification based upon the revised El Escorial criteria; the patients recruited had a disease duration of 2 years or less. These patients were recruited from 31 hospitals in Japan. These patients were allocated randomly 1:1 to receive 60 mg intravenous edaravone or intravenous saline placebo for six cycles (4 weeks per cycle on two weeks on, two weeks off) for a total treatment duration of 24 weeks. The primary outcome measure was the change in ALSFRS-R (Revised ALS functional rating scale) score from the baseline to 24 weeks. The primary endpoint and sensitivity analyses suggest that edaravone might maintain motor function in patients with type 2 or type 3 SMA over a period of 24 months.

Contributed by Dr. Ravi Yadav


This trial was conducted in patients with spinal muscular atrophy (a progressive motor neuron disease). In SMA, there is reduced life expectancy and few treatment options. This trial assessed the safety and efficacy of olesoxime in patients with type 2 or nonambulatory type 3 SMA. It was a randomized, double-blind, placebo-controlled, phase 2 study and was conducted in 22 neuromuscular care centers in Europe. The patients were randomized into 2:1 ratio and received olesoxime (10 mg/kg per day) in an oral liquid suspension or placebo for 24 months. The primary outcome measure was a muscle function scale assessing the differences between the two groups. The patients in the olesoxime group had the common side effects of pyrexia, cough, and nasopharyngitis. Olesoxime was found to be safe in the doses studied. The trial results failed to reach the primary efficacy endpoint. The secondary endpoint and sensitivity analyses suggest that olesoxime might maintain motor function in patients with type 2 or type 3 SMA over a period of 24 months.

Contributed by Dr. Ravi Yadav and Dr. Sahil Mehta


This is an important meta-analysis that provides an insight into the chance of recurrence of seizure in a patient with antiepileptic drug withdrawal. There is still a lack of clarity regarding the predictors of seizure recurrence after stopping the antiepileptic in a patient with a seizure disorder. This study done by Lamberink and colleagues assessed the predictors of seizure recurrence and long-term seizure outcomes through this systematic review and produced nomograms for estimation of individualized outcomes. They included 45 studies with 7082 patients for the final meta-analysis. The median follow-up of the patients was 5.3 years with a maximum follow up of 23 years. Seizure recurrence occurred in 812 (46%) of 1769 patients. 136 (9%) of 1455 patients for whom data were available, had seizures in their last year of follow-up. This showed that lasting seizure control was not achieved by this time point. Important predictors of seizures in the last year of follow-up were the duration of epilepsy before its remission, the seizure-free interval before the antiepileptic drug withdrawal was done, the number of antiepileptic drugs that were being administered before their withdrawal, the female gender, the family history of epilepsy, the number of seizures before remission, the incidence of focal seizures, and the epileptiform abnormality visualized on EEG before the drug withdrawal. This study provides nomograms that can be applied to patients in whom antiepileptic drug withdrawal is being contemplated.
Contributed by Dr. Ravi Yadav


The neuroprotective role of deep brain stimulation (DBS) has been debated for a while now. This study, performed on a rat model of Parkinson’s disease, demonstrated that there was an increase of the dopaminergic neurons in the rats who had undergone subthalamic nucleus DBS with concurrent improvement in motor tasks. This study is important as it provides a histopathological evidence in favor of the neuroprotective role of DBS.

Contributed by Dr. Ravi Yadav


The alphasynucleonopathies form the second commonest cause of neurodegenerative disorders in humans. The data regarding the survival and death in the patients of these disorders is sparse. This large study provides very useful information on this aspect of the disease and compares it with age- and gender-matched healthy adult population. This study was performed using the Rochester Epidemiology Project medical records linkage system to identify all residents in Olmsted County, Minnesota, who received a diagnostic code of parkinsonism from 1991 through 2010. An equal number of healthy people were also identified and matched. The investigators identified the age and gender adjusted risk of death for each type of synucleinopathy. The results showed that patients with any synucleinopathy died at a median of 2 years earlier than controls. Patients with multiple system atrophy with parkinsonism (MSA-P) had the highest risk of death (hazard ratio: 10.51) compared with the control group, followed by those with dementia with Lewy bodies (DLB) [hazard ratio: 3.94], Parkinson’s disease with dementia (PDD) [hazard ratio: 3.86], and Parkinson’s disease (PD) [hazard ratio: 1.75]. The study demonstrated that the survival in patients with MSA-P, DLB and PDD was significantly less than that in controls, but the survival in patients with PD was only moderately less than that seen in the general population. The commonest death certificate diagnosis was ‘neurodegenerative disease’ in these patients while ‘cardiovascular disease’ constituted the death certificate diagnosis in the controls.

Contributed by Dr. Ravi Yadav


Head positioning after acute stroke may have bearing on the outcome of the patient. Head and elevation to at least thirty degrees can reduce the intracranial pressure in large hemispheric strokes and can decrease the risk of aspiration pneumonia. Lying flat has the advantage of increasing cerebral blood flow to the infarcted hemisphere. This international, multi-centre, cluster-randomized open label trial (HEADPOST) recruited around eleven thousand patients from hundred and fourteen hospitals in nine countries. The patients were divided into two groups and the head position was maintained for twenty-four hours initiated after a median of fourteen hours after the onset of stroke. The authors found no difference in the disability outcomes at ninety days as well as no difference in the rates of aspiration pneumonia between the two groups.

Contributed by Dr. Sahil Mehta and Dr. Srijithesh PR


Various observational studies have reiterated the importance of physical activity and the lower risk of dementia. However, interventional studies have failed to demonstrate the benefits of exercise in lowering the risk of cognitive decline. This prospective cohort study with a mean follow up of twenty-seven years tested the hypothesis that physical activity in mid-life is not associated with a reduced risk of dementia. The authors conducted a battery of cognitive tests up to four times from the years 1997 to 2003. Mixed effects model did not show any association between the physical activity and the subsequent fifteen-year cognitive decline suggesting that there was no neuroprotective effect of exercise on cognitive functions.

Contributed by Dr. Sahil Mehta


Menopause is characterized by ovarian failure and elevated circulating FSH levels. There is also increase in the bone loss and enhanced visceral adiposity during this period. The authors of this study confirmed in their laboratories that blocking FSH in mice using an epitope specific polyclonal antibody resulted not only in an increased bone mass but also in a marked reduction in adiposity. This was also associated with the production of mitochondria-rich, highly thermogenic adipose tissue. This study may pave the way to the production of newer anti-obesity drugs and may envisage a potential role of FSH blocking agent in the treatment of both postmenopausal osteoporosis and obesity. However, the results of the study need to be proven in human trials.

Contributed by Dr. Sahil Mehta


This observational cohort study recruited five-fifty patients in investigating the association between alcohol consumption and brain structure and function. The authors found that a higher alcohol consumption over thirty year follow-up, increased the
odds of hippocampal atrophy in a dose-dependent fashion. The maximum chances of developing hippocampal atrophy were related to alcohol consumption (highest with more than thirty units per week). There was no protective effect of light drinking over abstinence. This study emphasizes that individuals should limit their alcohol consumption for maintaining a long-term optimal brain health.

**Contributed by Dr. Sahil Mehta**


Diabetic neuropathy is one of the most common complications of diabetes. Intensive blood glucose control has been shown to decrease the incidence of diabetic sensorimotor polyneuropathy and slow the progression in Type one diabetes. This single arm open label pilot trial recruited forty Type one diabetics and investigated the changes in cononal nerve fiber length and nerve conduction measures with omega three supplementations for twelve months. The authors found that omega three supplementations increased the cononal nerve fiber length in Type one diabetics and had a beneficial effect on neuropathy. There were, however, no changes in the parameters on nerve conduction studies. Additional clinical trials are needed before we can recommend the use of this supplement in clinical practice.

**Contributed by Dr. Sahil Mehta**

**Doumlele K, et al. Sudden unexpected death in epilepsy among patients with benign childhood epilepsy with centrotemporal spikes. JAMA Neurol 2017;74:645-9**

Benign epilepsy with centrotemporal spikes (BEFTS) is considered as ‘benign’ because seizures are infrequent and the disease usually resolves by adolescence. Due to the widely perceived ‘benign’ nature of BEFTS, many neurologists do not prescribe antiepileptic drugs (AED) to the patients. This study reports the occurrence of sudden unexpected death in epilepsy (SUDEP) in three patients with BEFTS from the records of 189 patients who died of SUDEP in the North American SUDEP Registry (NASR). The diagnosis of BEFTS and SUDEP was independently confirmed by two epileptologist. None of the three patients had been prescribed antiepileptic agents or had been counseled about the risk of SUDEP. All the three patients had a history of multiple episodes of seizures.

This study brings out another facet in the natural history of BEFTS. While the present study cannot give an explicit recommendation on the role of AEDs in BEFTS, it highlights the importance of counseling parents about the possibility of SUDEP, especially in patients who have higher than usual frequency of seizures. In the absence of large prospective data on the topic, an estimate from the present data indicates that 1000 patients with BEFTS need to be treated for preventing one case with SUDEP.

**Contributed by Dr. Srijithesh PR**


Glucose transporter type 1 deficiency (GID) was described by De Vivo in 1991 as an infantile epilepsy syndrome associated with delayed development, acquired microcephaly and low cerebrospinal fluid (CSF) glucose because of a defect in glucose transport across the blood-brain barrier. It is associated with mutation in the gene encoding the GLUT1 transporter (SLC2A1) on chromosome 1p34. Since the original description of the disease, the phenotypic spectrum has continued to expand. It accounts for 1% of idiopathic generalized epilepsy and 10% of early-onset absence epilepsy.

Hao J, et al., report the clinical spectrum and treatment outcomes of GID from a web-based global registry, the GID Registry from 2013 to 2016. The GID registry uses convenience sampling where patients are recruited from websites like the Rare Brain Disorders Program, clinicaltrials.org, direct referral from the authors, and links provided in the Glut1 Deficiency Foundation newsletters. The details were entered by the study participants.

In a majority of the cases, the diagnosis of GID was based on genotyping. The diagnosis based on CSF glucose estimation, and on positron emission tomography, were done less frequently. GID did not have any gender predilection. Most of the patients had a delayed development (69.7%). The epilepsy types include myoclonic epilepsy, absence epilepsy and unspecified epilepsy types, occurring either alone or in combination. Patients also presented with ataxia (56.1%), intermittent weakness (29%), dystonia (25.2%), intermittent involuntary gaze (23.2%), alternating hemiplegia (9.7%) and paroxysmal kinesogenic dyskinesias (7.7%). Psychiatric manifestations like obsessive compulsive traits were also seen in a minority of patients. 25% of the patients had white matter abnormalities in their magnetic resonance imaging.

In addition to ketogenic diet, patients also received modified Atkins diet or a low glycemic index diet. The usage of benzodiazepine was reported to have caused a high incidence of adverse effects. The most important prognostic determinant was the age at diagnosis. No genotype-phenotype correlation was forthcoming from the data.

This study provides another snapshot of the increasing clinical spectrum of GID. Given the wide phenotypic diversity and the absence of genotype-phenotype correlation, a high index of suspicion alone would help in securing an early diagnosis of the condition.

**Contributed by Dr. Srijithesh PR**


This study reports the results of the ‘minocycline in multiple sclerosis’ study, a multicentric, randomized double-blind, placebo-controlled trial that assessed the efficacy of minocycline in preventing the conversion of multiple sclerosis to a clinically
manifest syndrome. Minocycline, a tetracycline antibiotic, was found to have immunomodulating property in the preliminary studies.

The study randomized 143 patients to 100mg minocycline and a placebo. The primary outcome was conversion to multiple sclerosis (MS) within 6 months. The secondary outcome was conversion to MS within 24 months and the MRI outcomes at 6 months and 24 months. The study found that the unadjusted conversion to MS was less by 27.6% in the minocycline group. The absolute difference was 18.5% after adjustment for the number of enhancing lesions at the baseline. However, the study was not powered to show the difference at 24 months as the study could not enroll the planned sample size of 154 patients.

The study is an important breakthrough as the outcome (numbers needed to treat (NNT) 5.4) compares with the results of expensive disease modifying agents like interferon beta-1b (absolute risk reduction 24%; NNT 4.1), teriflunomide (absolute risk reduction 18%; NNT 5.5) and interferon beta-1a (absolute risk reduction 26%; NNT 3.8). A larger trial meeting the sample size requirements for all the outcome parameters is warranted.

Contributed by Dr. Srijithesh PR


The practice of telemedicine can be extended to many neurological diseases that can be reasonably diagnosed by clinical history. The majority of non-acute headaches are due to primary headache disorders like tension-type headache and migraine. These conditions can be diagnosed and managed by telemedicine consultations.

The present study reports the outcome of a randomized trial done in Northern Norway to evaluate the efficacy and safety of telemedicine consultation for non-acute headaches. The study aimed to test the non-inferiority of telemedicine consultation compared to traditional consultation in the treatment and safety at 12 months. The outcome factors were Headache Impact Test-6 (HIT-6) and visual analogue scale (VAS). The study found no difference between the telemedicine and the traditional consultation for HIT-6 and VAS, assessed at 3 and 12 months. The frequency of headache-related hospitalizations and specialist headache visits within 12 months after the study consultation were assessed as safety measurement. The study found that telemedicine consultation is non-inferior to traditional consultation in the outcome parameters assessed.

Contributed by Dr. Srijithesh PR


All the recently published endovascular intervention trials that reported positive results in favor of endovascular intervention had ensured a rigorous selection criteria based on angiography or perfusion studies. Identification of a select population that would benefit from intervention was the key to success of these trials. The same principle would apply to selection of patients for intravenous thrombosis as well.

Tenecteplase is biologically demonstrated to have a better fibrin specificity, a prolonged plasma half-life and a lesser activation of the systemic plasminogen activation system as compared to alteplase, the standard-of-care drug that is now being utilized for intravenous thrombolysis in acute ischemic stroke. The clinical trials comparing tenecteplase with alteplase were equivocal. The ATTEST trial, a phase 2, randomized trial that enrolled 355 ischemic stroke patients to compare tenecteplase over alteplase had equivocal results. However, an earlier trial, the Australian-TNK trial that selected patients based on computed tomographic (CT) angiography (CTA) and CT perfusion mismatch (CTP), had reported a benefit utilizing 0.25 mg/kg dose of tenecteplase in terms of the reperfusion rate and clinical outcomes. While the ATTEST trial did not select patients based on multimodal imaging, it had obtained CTP and CTA following randomization. In the present study, the data of all those patients who had a favourable CTP and CTA finding in the ATTEST trial were pooled with the arms of patients receiving 0.25 mg/kg tenecteplase and 0.9 mg/kg alteplase from the Australian-TNK trial. The data from the 0.1 mg/kg tenecteplase group of the latter trial was excluded. The 0.1 mg/kg tenecteplase arm was demonstrated to not be efficacious in the Australian-TNK trial.

The data of 146 patients were selected (96 patients from the ATTEST trial and 50 from the Australian-TNK study). Of these, 69 patients had a total vessel occlusion. The tenecteplase group had a better recanalization rate (absolute risk difference: 28%). The outcomes for an early clinical improvement and a better 90-day modified Rankin scale were statistically significant in favour of tenecteplase. The recanalization rates in patients treated with tenecteplase was as good (71% vs 43%) as seen with endovascular intervention in the recently concluded trials. The benefit of tenecteplase over alteplase was more pronounced in patients with complete vessel occlusion than those with partial vessel occlusion.

This posthoc analysis is a pointer to the importance of imaging based selection in the outcome of clinical trials. The ongoing phase 3 trial, tenecteplase versus alteplase for stroke thrombosis evaluation trial and alteplase-tenecteplase trial evaluation for stroke thrombosis 2, would be settling the questions raised by the study.

Contributed by Dr. Srijithesh PR


It is widely known that the incidence of stroke is higher in men than in women. However, the influence of sex-specific risk factors which have a bearing on the incidence of stroke and mortality are largely unknown. The authors have successfully attempted to conduct a systematic review and meta-analysis of female- and male-specific risk factors that contribute towards the incidence of ischemic and hemorrhagic stroke as well as
the associated mortality. Appropriate medical literature was searched including PubMed, EMBASE, and the bibliographies of articles for studies published over 30 years (1985 to 2015) which reported on the association between female- and male-specific characteristics and stroke. Of these, observational studies reporting associations between sex-specific risk factors and stroke were selected strictly following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. The main outcomes selected were ischemic stroke, hemorrhagic stroke, any stroke, and stroke-related mortality. In all, 78 studies comprising 10,187,540 persons were included. Women specific risk factors identified in acute ischemic stroke were hypertensive disorders in pregnancy (HDP) namely gestational hypertension [GH], pre-eclampsia, or eclampsia. Similarly, the risk factors for hemorrhagic stroke were late menopause (>55 years) and GH. The factors which were responsible for strokes of any of these types were oophorectomy, hysterectomy, HDP including eclampsia and GH, following a preterm delivery and after stillbirth. The stroke mortality risk was higher in the GH sub-group. In men, the risk of ischemic stroke was higher with androgen deprivation therapy (ADT) and orchiectomy. Ischemic stroke was also more common with ADT while erectile dysfunction contributed to both ischemic and hemorrhagic strokes. Strict blood pressure control during pregnancy is thus recommended for ischemic stroke prevention. Special attention should be taken in patients who have undergone oophorectomy, or who have suffered from HDP, preterm delivery, or stillbirth. Notably, hysterectomy proved to be possibly protective against any stroke. Males with medical androgen deprivation therapy and erectile dysfunction should be closely watched for and possibly medically managed for preventing the occurrence of stroke.

Contributed by Dr. Chirag K. Ahuja


At least five back-to-back landmark mechanical thrombectomy (MT) trials have revolutionised the treatment of acute ischemic stroke (AIS) claiming remarkable superiority of endovascular MT with intravenous thrombolysis (IVT) over IVT alone. A direct comparison of MT alone versus MT with IVT, however, has not been evaluated till date. The authors examined whether or not treatment with IVT before MT is beneficial in patients undergoing MT. They pooled data from two large, multicenter, prospective clinical trials that evaluated MT for AIS – Solitaire with the intention for thrombectomy (SWIFT) and Solitaire flow restoration thrombectomy for acute recanalization (STAR). A total of 291 patients from these trials were included and post hoc analysis was done after categorizing them into 2 groups: IVT and MT combined group and MT only group. Both the groups were appropriately matched demographically and with respect to time from symptom onset to groin puncture. Median Alberta Stroke Program Early CT Score (ASPECTS) at baseline was lower in the IVT and MT group (8 vs 9, P=0.04). The authors observed that the number of passes taken, rate of successful reperfusion, functional independence at 90 days, mortality at 90 days, and emboli to a new territory were similar among the two groups. No significant difference was noted in symptomatic intracranial hemorrhages and parenchymal hemorrhages in both the groups. However, vasospasm occurred more often in patients who received IVT and MT vs MT alone (P = 0.006). A multivariate analysis was done which showed no statistically significant association between IVT and MT vs MT alone for any of the outcomes. The authors concluded that there was no documented clinical benefit of IVT prior to MT over MT alone in management of patients of AIS. In our opinion, this may create a significant impact in terms of offsetting the shortcomings of administering IVT (drug adverse effects and economics) with direct MT being a feasible approach in such patients. Also, the time taken for administration of IVT can be overcome by taking the patients directly to DSA catheter laboratory following their imaging. A randomized clinical trial is warranted to derive further conclusions regarding management of these patients.

Contributed by Dr. Chirag K. Ahuja


Carotid revascularization currently forms the mainstay for symptomatic carotid stenosis as well as severe asymptomatic disease. Both carotid artery stenting (CAS) and carotid endarterectomy (CEA) can be employed based on the criteria elucidated by certain trials. No definite evidence based guidelines currently exist regarding the management of asymptomatic and symptomatic restenosis following these procedures. The authors aimed to study whether significant (>70%) restenosis following CAS or CEA increases the risk of late ipsilateral stroke. They conducted a systematic review according to the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement and identified 11 randomised controlled trials (RCTs) reporting rates of restenosis >70% (and/or occlusion) in patients who had undergone CEA/CAS for the treatment of primary atherosclerotic disease, and nine RCTs which reported late ipsilateral stroke rates. Proportional meta-analyses and odds ratios (OR) at the end of follow-up were performed. The observed weighted incidence of restenosis >70% was 5.8% after “any” CEA (at a median follow-up of 47 months) and 4.1% after a patched CEA (at a median follow-up of 32 months). This figure was 10% after CAS (median follow-up of 62 months). The incidence of late ipsilateral stroke with restenosis >70% following CAS was one in 125 (0.8%) as compared with 37 of 1839 (2.0%) patients of CAS with no significant restenosis (P = 0.8339). A similar incidence of stroke following CEA having restenosis >70% was seen in 13 out of 141 (9.2%) patients as against 33 out of 2669 (1.2%) patients, in patients with no significant restenoses (P < 0.0001). This clearly meant that the risk of stroke was greater with CEA than CAS in patients with untreated asymptomatic >70% restenosis. In conclusion, the authors recommended that routine duplex ultrasound surveillance offers little benefit to the CAS patient in view of the low incidence of ipsilateral stroke. Regular
follow-up duplex ultrasound should, perhaps, be offered to CEA patients for observing the degree of restenosis.

*Contributed by Dr. Chirag K. Ahuja*


Antiplatelet agents form an important medical constituent in the management and prevention of ischaemic strokes. Strangely, there is no data based on randomized trials or meta-analyses regarding antiplatelet therapy after carotid interventions. Barkat et al., devised this study with the objective of undertaking a systematic literature review and performing a meta-analysis to assess the effects of dual antiplatelet therapy in carotid endarterectomy (CEA) and stenting (CAS). A thorough search was initiated across electronic information sources (MEDLINE, EMBASE, CINAHL, CENTRAL) to identify randomised controlled trials (RCTs) and observational studies reporting comparative outcomes of dual versus single antiplatelet therapy in CEA and CAS. Primary outcomes were mortality and stroke within 30 days of intervention. Secondary outcomes were transient ischaemic attack (TIA), major bleeding, groin or neck haematoma, and myocardial infarction (MI). In total, three randomized clinical trials (RCTs) and seven observational studies were identified reporting a total of 36,881 CEA and 150 CAS procedures. In the CEA arm, there were no differences in stroke and death between single and dual antiplatelet therapy. The risks of major bleeding and neck haematoma with dual therapy was, however, statistically significant. Additionally, the rate of myocardial infarction was higher in the dual therapy group than the single therapy group. In the CAS arm, there was no difference in the major bleeding or haematoma formation rate, but a significant benefit of reduction in TIA with dual therapy was identified. In conclusion, the study reconfirmed the belief that dual antiplatelet therapy demonstrates advantages over single therapy in CAS; however, it was associated with an increased risk of bleeding complications in patients undergoing CEA.

*Contributed by Dr. Chirag K. Ahuja*


The authors conducted a meta-analysis of randomized controlled trials (RCTs) with the objective to compare outcomes among adult patients with Parkinson’s disease (PD) undergoing deep brain stimulation (DBS) of globus pallidus pars interna (GPi) and the subthalamic nucleus (STN) at various time points, including a 36 month follow-up. Among the 623 studies initially identified (615 through database search, 7 through manual review of bibliographies, and 1 through a repeat screen of literature prior to submission), 19 underwent full-text review; 13 of these were included in the quantitative meta-analysis. No differences in motor scores or activities of daily living were identified at 36 months. Medications were significantly reduced with STN stimulation (5 studies, weighted mean difference [WMD] −365.46, 95% CI −599.48 to −131.44, P = 0.002). Beck Depression Inventory scores were significantly better with GPi stimulation (3 studies; WMD 2.53, 95% CI 0.99–4.06 P = 0.001). The motor benefits of GPi and STN DBS for PD were similar. The authors concluded that the motor benefits achieved with GPi and STN DBS for PD are similar. DBS of STN allows for a greater reduction of medication, but is not of as significant an advantage as DBS of GPi with respect to mood.

*Contributed by Dr. Anant K. Mehrotra*


The authors report the result of the ANSWER trial (Adjunctive Neurovascular Support of Wide-neck aneurysm Embolization and Reconstruction), which was a prospective, non-randomized trial that tested the safety and benefit of the PulseRider (a novel neck reconstruction device that facilitates the treatment of wide-necked bifurcational aneurysms by preserving luminal patency and hemodynamic flow) for the treatment of broad-necked, bifurcation aneurysms. 34 patients with either basilar apex (n = 27) or carotid terminus (n = 7) aneurysms were enrolled in the study. The mean age was 60.9 years. The mean aneurysm height ranged from 2.4 to 15.9 mm with a mean neck size of 5.2 mm (range 2.3-11.6 mm). Delivery and deployment of the device was done in all the patients. Immediate Raymond I or II occlusion was achieved in 82.4% and progressed to 87.9% at a 6-month follow-up. A modified Rankin Score of 2 or less was seen in 94% of the patients at 6 months. The authors concluded that the PulseRider device is safe and offers probable benefits for the treatment of aneurysms arising from basilar top and carotid bifurcation.

*Contributed by Dr. Anant K. Mehrotra*


The authors conducted a systematic review to identify factors that influence reliability of the Glasgow Coma Scale (GCS). 41 studies which assessed the reliability of the GCS in adults or describing any factor that influences reliability were included. Methodological quality of studies was evaluated with the consensus-based standards for the selection of health measurement instruments checklist. Factors identified that may influence the reliability of GCS include education and training of the assessor, the level of consciousness, and the type of stimuli used. Conflicting results were found based upon the experience of the observer, the pathology causing the reduced consciousness, and the presence of an intubated/sedated patient. No clear influence was found for the professional background of observers.

*Contributed by Dr. Anant K. Mehrotra*

The authors conducted the study to determine the frequency of symptomatic in-stent restenosis (ISR) and its contribution to nonprocedural symptomatic infarction in the SAMMPRIS trial (stenting and aggressive medical management for the prevention of recurrent stroke in intracranial stenosis). Among the total of 183 patients included in the study, 27 (14.8%) had a symptomatic infarction (stroke or cerebral infarct with temporary signs) and 16 (8.7%) had transient ischemic attack alone in the territory during a median follow-up of 35.0 months. Among the 27 patients who developed infarction, 17 (9.3%) had an ischemic stroke and 10 (5.5%) had a cerebral infarct with temporary signs alone. Adequate vascular imaging to evaluate ISR was available in 24 patients with infarctions (showing ISR in 16 [66.7%]) and in 10 patients with transient ischemic attack alone (showing ISR in 8 [80%]). The 1-, 2-, and 3-year rates (with 95% confidence limits) for symptomatic ISR in the SAMMPRIS stent cohort were 9.6% (6.1%–14.9%), 11.3% (7.5%–17.0%), and 14.0% (9.6%–20.2%), respectively. The authors concluded that symptomatic ISR developed in approximately 14% (1/7) patients in the SAMMPRIS trial by a 3-year follow up.


The authors analysed a prospective database of 6488 patients of moderate to severe traumatic brain injury and found that 159 patients had a concurrent acute ischemic stroke (AIS). The median age of this group was 40 years. AIS was associated with intracranial mass effect, and carotid or vertebral artery dissection. High-velocity events more commonly caused TBI with dissection. AIS predicted a poorer outcome by all measures, accounting for a 13.3-point reduction in Functional Independence Measure total score (95% confidence interval, −16.8 to −9.7; \( P < 0.001 \)), a 1.9-point increase in the disability rating scale (95% confidence interval, 1.3–2.5; \( P < 0.001 \)), and an 18.3-day increase in the post-traumatic amnesia duration (95% confidence interval, 13.1–23.4; \( P < 0.001 \)). The authors concluded that ischemic stroke is observed in an acute setting in nearly 2.5% of cases of moderate to severe TBI survivors and predicts a worse functional and cognitive outcome. Half of the TBI patients with AIS were aged ≤40 years, and AIS patients more often had cervical dissection.