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PREOPERATIVE OPIOID USE AND READMISSION AFTER JOINT REPLACEMENT

In previous studies, preoperative opioid use has been associated with a worse clinical outcome. This study was designed to better understand the association between preoperative opioid use and the 30-day readmission rates among patients undergoing joint replacement surgeries.

This retrospective cohort study used data from the Truven Health MarketScan Commercial Claims and Encounters (commercial insurance) and the Medicare Supplemental and Coordination of Benefit (Medicare plus commercial supplemental insurance) databases. Patients were included who underwent total knee arthroplasty (TKA) or total hip arthroplasty (THA). Data were also obtained for opioid use in the six months before surgery. Opioid use was stratified as, no preoperative use (opioid naïve), 1-30 days of use, 30-60 days of use, and more than 60 days of use (chronic users). The primary outcome measure was the 30-day readmission rate after surgery.

Among the 324,154 patients, chronic opioid use was found in 15.6% of the TKA and 18.4% of the THA patients. For both TKA and THA patients, the 30-day readmission rates were greater in the chronic opioid users as compared to the opioid naïve patients ($p < 0.001$ for both comparisons). In a multivariate logistic regression analysis, compared to 0-60 day users, the one-year adjusted risk for a revision surgery among chronic users was 1.70 for the TKA and 2.26 for THA patients.

Conclusion: This study identifies preoperative opioid use as a risk factor for hospital readmission after total hip or total knee arthroplasty.

Weick, J., et al. Preoperative Opioid Use Is Associated with Higher Readmission and Revision Rates in Total Knee and Total Hip Arthroplasty. **J Bone Joint Surg.**

2018, July 18; 100-A (14): 1171-1176.

TRANSCRANIAL DIRECT CURRENT STIMULATION AND IMPULSIVITY IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER

In patients with attention deficit disorder with hyperactivity (ADHD), neuroimaging studies have linked cognitive deficits and impulsive decision making with reduced activity in several areas. These include the dorsolateral prefrontal cortex (DLPFC). As recent research has suggested that cognitive control circuits can be modulated using noninvasive direct current, this study tested whether direct current stimulation (DCS) can improve objective measures of cognitive control and impulsivity.

Subjects were adults between 18 and 65 years of age with a diagnosis of ADHD. The subjects were randomized to either an anodal DCS group or a sham DCS group. The anodal electrode was placed at F3 for stimulation over the left DLPFC, with the cathode placed over the right supraorbital area. Stimulation was increased over 30 s until 2.0 mA was reached, maintained for 19 min and ramped down over 30 s at the end of stimulation.

While receiving the DCS, participants performed a visual working memory training task with complex geometric figures. The primary outcome measure was false positive errors on the Continuous Performance Task (CPT).

Those in the DCS group had significantly better outcomes on the CPT ($p < 0.001$), which was driven by a reduction in false positive errors ($p < 0.001$). This did not persist after the stimulation had been discontinued. The stimulation did not seem to affect CPT true positive errors or CPT response time. The authors note that these findings suggest that the DCS reduced impulsivity.

Conclusion: This study demonstrates that transcranial direct current stimulation over the dorsolateral prefrontal cortex can decrease impulsivity in patients with ADHD.

Allenby, C., et al. Transcranial Direct Current Brain Stimulation Decreases Impulsivity in ADHD. **Brain Stim.** 2018, April 23. doi.org/10.1016/j.brs.2018.04.016.

TRANSCRANIAL DIRECT CURRENT STIMULATION AND MEMORY

Attention deficit hyperactivity disorder (ADHD) is characterized by abnormal levels of hyperactivity, impulsivity and inattention. Working memory deficits and long-term memory impairments are characteristic of this population. Studies have suggested that symptoms of ADHD are related to abnormal neuronal activity in the prefrontal cortex, striatum, hippocampus and cerebellum. Research has demonstrated that transcranial direct current stimulation (tDCS) can improve clinical symptoms, although the mechanism of action is unclear. This study used an animal model of ADHD to evaluate possible neurochemical substrates related to this treatment effect.

Adult rats were randomly assigned to active (tDCS) or sham treatment, conducted on eight consecutive days, with behavioral tests conducted at baseline and at 24 hours after the last stimulation session. Stimulation was applied at 0.5 mA, 20 minutes per day for eight days. The electrodes were placed to mimic tDCS protocols in ADHD, with the anode electrode placed over the right dorsal lateral prefrontal cortex (PFC), the left dorsolateral PFC, or the right inferior frontal gyrus.

In the discrimination phase, tDCS was associated with a reduction in the long-term memory deficits ($p = 0.01$). No change in working memory was noted. After autopsy,

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measures of oxidative parameters, including the production of reactive oxygen species increased in the hippocampus of the ADHD model rats and the levels of the antioxidant molecule, glutathione, increased in both strains. The inflammatory response was also noted to be modified by down regulating pro-inflammatory cytokines.

Conclusion: This animal study of attention deficit disorder found that transcranial direct current stimulation resulted in improvements in long-term memory, with associated mediations in the inflammatory responses in the brain.

Leffa, D., et al. Transcranial Direct Current Stimulation Improves Long-Term Memory Deficits in an Animal Model of Attention Deficit/Hyperactivity Disorder and Modulates Oxidative and Inflammatory Parameters. **Brain Stim.** 2018, July-August; 11(4): 743-751.

LIVING ALONE AND RISK OF DEMENTIA

Given the advance of worldwide aging, it is expected that the number of people living with age-related diseases, including Alzheimer's disease (AD) and other neurodegenerative conditions, will increase. This study was designed to understand the role of an individual's living situation on the development of dementia among people with mild cognitive impairment (MCI).

This longitudinal, clinically based study included consecutive patients referred to a cognitive dysfunction clinic with a diagnosis of MCI. The patients were assessed at baseline with a neuropsychological battery, with initial data collected including living situation, medical history, age, gender and years of education.

Data were assessed for 345 patients with an average age of 75.3 years at baseline and a mean follow up of 2.8 years. At follow-up, 50% had developed dementia. The fully adjusted multivariate analysis revealed that those with MCI who were living alone were more likely to develop dementia at follow-up (hazard ratio 1.5) than were those living with others.

Conclusion: This study of patients with MCI found that those living alone had a 50% greater risk of developing dementia at 2.8-year follow-up.

Grande, G., et al Living Alone and Dementia Incidence: A Clinical-Based

Study in People with Mild Cognitive Impairment. **J Geriatr Psychiat Neurol.** 2018, May 8; 31(3): 107-113.

HETEROTOPIC OSSIFICATION FOLLOWING ELBOW ARTHROPLASTY

Heterotopic ossification (HO) is a recognized sequela of both elbow trauma and total elbow arthroplasty (TEA). However, the true incidence of HO at the elbow is not well understood. This study was designed to better understand the incidence of HO following elective TEA and arthroplasty surgery for humeral fractures.

This retrospective study included all primary TEAs performed between 2007 and 2015, comparing those undergoing elective procedures and those with trauma related TEAs. All patients were assessed using elbow specific outcome scores and follow-up x-rays at a mean of 3.1 years.

At three years, among the 53 patients, the overall incidence of HO was 84%. The incidence was higher in the trauma group (96%) than the elective arthroplasty group (72%). There were no patients with Booker class IV (ankyloses), while 15/25 of the trauma group, and 3/21 of the elective group were Booker class II-III. At follow-up, the mean flexion/extension arcs were 97° in the elective group and 93° in the trauma group.

Conclusion: This study of patients undergoing total elbow arthroplasty revealed that the incidence of heterotopic ossification at three-year follow-up was 84%, with higher rates in the trauma than the elective surgery group.

Robinson, P., et al. Heterotopic Ossification following Total Elbow Arthroplasty. **Bone Joint J.** 2018, June; 100-B (761-771).

SPINE MANIPULATION FOR LOW BACK PAIN IN ADOLESCENTS

Low back pain (LBP) is now the leading cause of disability worldwide. While many studies have addressed LBP in adults, studies of children and adults are far less abundant. This study was designed to better understand the effectiveness of spinal manipulation plus exercise compared with exercise alone in an adolescent population.

This two-site, parallel group, randomized controlled trial included patients 12-17 years of age with

subacute and recurrent, or chronic nonspecific LBP. Chronic LBP was defined as 12 or more weeks of pain. Both groups received exercise training with no more than two sessions per week for 12 weeks. Those in the combined group attended 8-16 chiropractic visits, up to 20 minutes per session, no more than two times per week. The primary outcome measure was a self-reported typical level of LBP severity over the past week, as measured by a numerical rating scale. These were collected at baseline and at four, eight, 12, 26 and 52 weeks after enrollment. Secondary outcome measures included patient rated disability, quality of life, improvement in symptoms, frequency of medication use and patient satisfaction with care.

Compared with the exercise group, ratings of LBP were better in the combined group over the first year ($p<0.007$). For reduction in pain severity, the combined group had better adjusted mean scores than did the exercise group at 12 weeks ($p=0.083$), 26 weeks ($p<0.001$), and 52 weeks ($p=0.009$). In the secondary analyses, quality of life and medication use did not significantly differ between groups over the first year.

Conclusion: This study of adolescents with chronic LBP found that combining exercise with spinal manipulation was more effective than exercise alone for reducing pain.

Evans, R et al. Spinal Manipulation and Exercise for Low Back Pain in Adolescents: A Randomized Trial. *Pain*. 2018, July; 159 (7):1297-1307.

AGE THRESHOLD FOR ISCHEMIC RISK IN ATRIAL FIBRILLATION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the general population, with an associated fivefold increase in the risk of ischemic stroke. This study was designed to investigate the effect of the age of the patient, on the risk of ischemic stroke.

Data were obtained from the National Health Claims Database of the Republic of Korea. From the database were identified 426,650 adult patients with prevalent non-valvular AF. These patients received scores on the congestive heart failure, hypertension, age ≥ 75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), vascular disease, age 65–74 years, female score (CHA₂DS₂–

VASc), a widely used guideline to assess risk.

Of the 426,650 patients included in the analysis, 108,553 had no risk factors, 120,224 had one risk factor and 197,873 had two risk factors at baseline. The relative risk of ischemic stroke for AF patients without nongender risk (NGR) factors in different age groups was compared with patients with a one NGR risk score.

Patients 55 to 59 years of age with no NGR risk factors had a similar risk of ischemic stroke as did those with one NGR risk score. Patients 60 to 64 years with no risk factors had a higher risk of stroke than did patients with one NGR risk score.

Conclusion: This study of patients with atrial fibrillation found that age has a powerful influence on the risk of ischemic stroke, with this risk accelerating at 55 years of age.

Kim, T et al. Age Threshold for Ischemic Stroke Risk in Atrial Fibrillation. Cohort Data Covering the Entire Korean Population. *Stroke*. 2018, August 16; 49(8):1872-1879.

PULSED RADIOFREQUENCY VERSUS CORTICOSTEROID INJECTION FOR NECK PAIN

The prevalence of head and upper cervical pain in the general population ranges from 30-50%. Recent studies have suggested that the atlanto-occipital (AO) joint plays a major role in the occurrence of head pain and/or upper cervical pain. As pulsed radiofrequency (PRF) has been used for chronic musculoskeletal pain, this study compared the effectiveness of this technique with that of intra-articular steroid injections.

Subjects were 23 patients with spontaneous, chronic, suboccipital neck pain who were refractory to physical therapy and medication. Dysfunction of C2-3 in the lower cervical facet was excluded through a third occipital nerve block and a medial branch block with a negative response. Those randomized to an RF group received stimulation with a PRF needle in the AO joint, at 5 Hz and 5 ms pulse width for six minutes at 55 V. Those in the corticosteroid group received an intraarticular joint at the AO, of 0.75 mL of 2% lidocaine and 0.25 mL of triamcinolone 10 mg. Pain was assessed before treatment and at one, three and six months after the procedure using a 10-point Numeric Rating Scale (NRS).

Success was defined as greater than a 50% reduction in pain.

Compared with baseline, the mean NRS scores were significantly reduced in both groups ($p<0.001$). Greater than 50% improvement was achieved in 66.7% of the PRF group and in 63.6% of the corticosteroid group ($p=0.879$).

Conclusion: This study of patients with chronic suboccipital pain found that radiofrequency may be considered a reasonable treatment option to intra-articular steroids at the atlanto-occipital joint.

Shin, S., et al. Clinical Effectiveness of Intra-Articular, Pulsed Radiofrequency Compared to Intra-Articular Corticosteroid Injection for Management of Atlanto-Occipital Joint Pain. A Prospective, Randomized, Controlled Pilot Study. *Spine*. 2018, June 1; 43(11): 741-746.

COMPLICATIONS OF ANTICOAGULATION AFTER SPINE TRAUMA

Previous studies of spine surgery have examined the complications of prophylactic anticoagulation, but not therapeutic anticoagulation. This study was designed to better understand the incidence of complications among patients requiring an unplanned return to surgery with therapeutic anticoagulation.

This retrospective study included patients who underwent surgery for traumatic spinal column injury between 2001 and 2014 and who sustained a thromboembolic event (DVT, PE or MI). Patients who were then placed on anticoagulation were compared to matched patients who were not. The primary outcome variable was the rate of complications that required unplanned reoperation.

Of the 1,712 patients, 62 were diagnosed with a thromboembolic event after surgery. Of these, 18% receiving therapeutic anticoagulation required an unplanned return to the operating room, compared to 10% of those not receiving therapeutic anticoagulation ($p = 0.17$). A subgroup analysis showed a reoperation rate of 31% of patients receiving heparin infusion, compared to 6.5% in patients receiving low molecular weight heparin ($p = 0.02$).

Conclusion: In this study of patients with traumatic spinal injury with a post-surgical thromboembolic event, those placed on an anticoagulant had a higher rate of

return to surgery than did those not receiving an anticoagulant, especially among those receiving IV heparin.

Shiu, B., et al. Postoperative Deep Vein Thrombosis, Pulmonary Embolism and Myocardial Infarction: Complications after Therapeutic Anticoagulation in the Patient with Spine Trauma. **Spine**. 2018, July 1; 43(13): E766-E772.

ALTEPLASE VERSUS ASPIRIN FOR ACUTE ISCHEMIC STROKE

While intravenous alteplase has been shown to be effective for ischemic strokes, mild stroke is the most common reason for nonuse. This study was designed to test the efficacy and safety of alteplase, administered within three hours of onset of ischemic stroke, in patients presenting with minor deficits, defined as a National Institutes of Health Stroke Scale (NIHSS) score of zero to five.

This randomized, double-blind, clinical trial, the Potential of rTPA for Ischemic Strokes with Mild Symptoms (PRISMS) trial, included patients presenting within three hours of symptom onset. The primary outcome measure was the modified Rankin score (mRS) at 90 days. Secondary outcome measures, also reviewed at 90 days, were the consistent level of disability, global favorable outcome, defined as a mRS score of zero to one, an NIHSS score of zero or one, a Barthel Index of 95 to 100 and a Glasgow Outcome Scale score of one to five.

Of those enrolled, 281 completed the trial's primary outcome assessment. In the primary analysis, 78.2% of patients randomized to alteplase had favorable outcomes at 90 days, compared to 81.5% randomized to aspirin. No significant difference was seen between groups in the secondary outcomes. The primary adverse event, symptomatic intracranial hemorrhage within 36 hours, occurred in five patients, all treated with alteplase.

Conclusion: This study of patients presenting with mild, nondisabling, acute, ischemic stroke found that treatment with alteplase does not increase the likelihood of favorable functional outcome as compared to treatment with aspirin.

Khatri, P., et al. Effect of Alteplase versus Aspirin on Functional Outcome for Patients with Acute Ischemic Stroke and Minor, Nondisabling, Neurologic Deficits.

The PRISMS Randomized, Clinical Trial. **JAMA**. 2018, July 10; 320(2): 156-166.

RIVAROXABAN TO PREVENT RECURRENT CRYPTOGENIC STROKES

A large number of embolic strokes, sometimes termed cryptogenic strokes, have no clear source, despite an extensive work up. It is thought that these typically originate from the heart or blood vessels, and tend to recur. Rivaroxaban, a direct Xa inhibitor, has been shown to help prevent strokes in patients with atrial fibrillation. This study was designed to determine whether Rivaroxaban can reduce the recurrence of cryptogenic strokes.

This multicenter, randomized trial included patients with ischemic stroke, without a clear etiology. The patients were randomized to receive a daily dose of rivaroxaban at 15 mg plus placebo, or aspirin at 100 mg plus placebo. The patients returned for evaluation at one, six and 12 months, and then every six months thereafter. The primary outcome was stroke recurrence. The primary adverse event was major bleeding.

Recurrent stroke occurred in 5.1% per year in the rivaroxaban group, and 4.8% per year in the aspirin group (hazard ratio, 1.07; $p=0.52$). Major bleeding occurred in 1.8% per year in the rivaroxaban group, and 0.7% per year in the aspirin group ($p<0.001$), resulting in an early termination of the study.

Conclusion: This study of cryptogenic strokes found that rivaroxaban is not superior to aspirin in preventing recurrent strokes, and may result in an increased risk of bleeding.

Hart, R. et al. Rivaroxaban for Stroke Prevention after Embolic Stroke of Undetermined Source. **N Engl J Med**. 2018, June; 378(23): 2191-2201.

HEMOGLOBIN A1C AND ACUTE ANTERIOR STROKE

After an acute stroke, hemorrhagic transformation (HT) is a complication, often associated with clinical deterioration. As elevated admission blood sugar levels have been associated with adverse outcomes in patients with stroke, this study assessed whether chronic

hyperglycemia may be predictive of HT.

Subjects included 426 patients with acute anterior ischemic stroke. At admission, patients' assessments included hemoglobin A1c (HbA1c), measured the morning after hospital admission, and CT scans or gradient echo MRI, performed within one day after stroke onset. The HbA1c levels were compared with HT.

Of the 426 patients evaluated, 93 (21.8%) had HT. Of these, 54 received thrombolytic therapy. Multivariate analysis revealed that the odds ratio of HT was 1.294 among those with an elevated HgA1c, as compared to those with a normal HgA1c.

Conclusion: This study found that an elevated hemoglobin A1c on admission was a predictor of hemorrhagic transformation, as well as a predictor of worse outcome.

Zhang, G., et al. Hemoglobin A1c Predicts Hemorrhagic Transformation and Poor Outcomes after Acute Anterior Stroke. **Euro J Neurol**. 2018 July 20; <https://doi.org/10.1111/ene.13747>

CLOSTRIDIUM DIFFICILE AFTER SPINE SURGERY

Clostridium difficile (C Diff) infection is a common complication of inpatient hospitalization, and a significant cause of morbidity and mortality. This study was designed to determine the incidence, timing and risk factors of developing C Diff in spine surgery patients.

This retrospective, cohort study, utilized the 2015 National Surgical Quality Improvement Program (NSQIP) database. Subjects were 23,981 patients who underwent spine surgery in 2015. Patients undergoing emergency surgeries or those with diagnosis codes indicating trauma, tumor or infection were excluded. The researchers determined the rate of C Diff colitis within a 30-day post-operative period.

The incidence of C Diff colitis in the 30-day post-operative period was 0.11%. Of these, 70% were diagnosed post-discharge and 80% had no previous diagnosis of C Diff. The development of C Diff was associated with combined anterior/posterior fusion procedures (OR 12.29, $p=0.01$), increased age (OR 10.31 $p<0.001$ for patients 76 and older), hypoalbuminemia (OR 6.40, $p=0.023$) and anemia (OR 2.39, $p<0.001$).

Conclusion: This study found that C Diff is diagnosed within 30 days in 0.11% of patients undergoing spine surgery. Most of these cases occurred after discharge.

Bovonratwet P., et al. Incidence, Risk Factors and Impact of Clostridium Difficile Colitis after Spine Surgery. **Spine**. 2018, June 15. 43: 861-868.

SEIZURES AFTER CRANIOPLASTY

Decompressive craniectomy is often used with patients with severe traumatic brain injury and stroke. While many consider seizures to be the most common complication after this surgery, the reported incidence of seizures varies greatly. This study was designed to clarify the incidence of post-cranioplasty seizures.

This literature review was completed using publications through September of 2017. Studies which were considered described participants undergoing decompressive craniectomy, who then received a cranioplasty, and then described the incidence of seizures.

Of the studies reviewed, 16 were included in the quantitative analysis, with cumulative data for 3,212 patients. The interval time from craniectomy to cranioplasty ranged from three to 14 months, with six months determined as the cutoff point to distinguish early from late cranioplasty. The pooled incidence of seizures was 0.092. The adjusted incidence was 0.043.

The subgroup analysis revealed that the early cranioplasty group had a higher incidence of seizures than did the late cranioplasty group. In studies assessing antiepileptic drugs, seizures were found to be significantly reduced with the use of antiepileptic drugs, as compared with controls, with data suggesting that 80% of seizures were avoided with these medications.

Conclusion: This study of patients receiving cranioplasty after craniectomy found that the incidence of seizures was 0.043, and that antiepileptic drugs were effective in reducing this risk.

Yao, Z., et al. The Incidence and Treatment of Seizures after Cranioplasty: A Systematic Review and Meta-Analysis. **Br J Neurosurg**. 2018, June 6. DOI: 10.1080/02688697.2018.1481197.

CIRCADIAN PATTERNS OF MIGRAINES

Headaches, especially migraines, have been noted to have diurnal occurrence patterns, yet this phenomenon has not been extensively studied. This study analyzed the circadian patterns of migraines, including chronic migraines, and sought to clarify those factors associated with migraines at particular times of day.

This observational, cross-sectional study examined all first-time patients (786) who presented to an outpatient headache center over a two-year period. Patients were provided with a three-month headache diary. Time of day was recorded at each migraine occurrence. Also recorded were self-reported anxiety and depression.

Most patients reported no particular time of onset of the headaches (57.1%). The most common time of occurrence among those with a pattern was nighttime (24.4%). Two peaks of occurrence frequency were found, at 10 A.M. and 10 P.M.

Conclusion: This study suggests that most migraine patients do not show a consistent circadian frequency pattern of onset of symptoms nor clinical features associated with symptoms.

Tommaso, M., et al. Circadian Rhythms of Migraine Attacks in Episodic and Chronic Patients: A Cross Sectional Study in a Headache Center Population. **BMC Neurol**. 2018, doi: 10.1186/s12883-018-1098

GLUCOCORTICOIDS AND RISK OF VERTEBRAL FRACTURE IN RHEUMATOID ARTHRITIS

Previous studies have shown that patients with rheumatoid arthritis (RA) experience fractures more frequently than do those in the general population. Among the risk factors for fractures is the use of glucocorticoids, widely used in the treatment of RA. This study was designed to identify specific effects of glucocorticoid treatment on fracture types.

This study used a nationwide claims database in Korea, the Health Insurance Review Assessment Service, which covers 98% of the Korean population. From this database, patients with RA were identified, as were the prescriptions of disease modifying antirheumatic drugs (DMARDs) glucocorticoids and

a diagnosis of osteoporosis. Risk of fractures was compared to that of the general population.

Of the 138,240 patients with RA, fractures were identified in 9,964. A crude analysis revealed that the duration of glucocorticoid steroid use was associated with total fracture risk, with odds ratios of 1.22 for those treated from three to six months, and 1.81 for those treated for more than six months. An adjusted analysis revealed an increased risk for those treated for more than six months, of any fracture ($p < 0.05$) and of vertebral fractures ($p < 0.05$). Those taking a mean dose of five to 10 mg were at increased risk for total fracture ($p < 0.05$) and vertebral fracture ($p < 0.05$), as compared to those taking less.

Conclusion: This Korean study of patients with rheumatoid arthritis found that, for those treated with oral glucocorticoids, a higher dose and longer treatment duration were significantly related to an increased risk of hip or spine fracture.

Kim, D., et al. Glucocorticoids Associated with an Increased Risk for Vertebral Fracture in Patients with Rheumatoid Arthritis. **J Rheum**. 2018, May; 45 (5): 612-620.

REMOTE KINEMATIC TRAINING FOR CHRONIC NECK PAIN

Patients with neck pain often have reduced movement efficacy, with impairments in driving and symptoms such as dizziness or kinesiophobia. This study evaluated the efficacy of two methods of home delivery for chronic neck pain, including virtual reality and laser pointer feedback.

Patients with chronic neck pain were randomized to either a control group or one of two treatment groups. The treatment groups included kinematic training, with the use of virtual reality (KTVR) or a laser pointer (attached to forehead). All subjects underwent four weeks of training. In both intervention groups, the training was provided to increase the range of motion, velocity of motion and the accuracy of head motion. The primary outcome measure was the change in the neck disability index, global perceived effect and cervical motion velocity.

Of the patients recruited, 76 completed a one month, and 56 completed a three-month follow-up. The control group demonstrated no change in any variable. Compared with the control group, the neck disability index was significantly

improved with virtual reality ($p < 0.01$), as well as with laser training ($p < 0.01$). At three-month follow-up, neck pain was rated as much improved in 45.2% of the virtual reality group, and in 42.1% of the laser group.

Conclusion: This study of patients with chronic neck pain found that a minimally supervised home treatment using a laser pointer or virtual reality could significantly decrease disability and pain.

Bahat, S., et al. Remote Kinematic Training for Patients with Chronic Neck Pain: A Randomized, Controlled Trial. *Eur Spine J.* 2018, June; 27: 1309-1323.

POLYNEUROPATHY AND MYOPATHY AND VENTILATED CHILDREN

Critical illness polyneuropathy (CIP) and critical illness myopathy (CIM) are the most usual cases of neuromuscular weakness for patients in the intensive care unit (ICU). This study was designed to better understand CIP and CIM among ventilated children in an ICU.

This case-controlled study included 105 critically ill children, who underwent mechanical ventilation for seven or more days in a pediatric ICU. Patients were eligible who had been mechanically ventilated for at least seven days. At one week after awakening, those with severe muscle weakness underwent nerve conduction studies and electromyography. The patients underwent detailed clinical evaluations and neurologic assessments, including electrodiagnostic studies throughout their hospitalization. The electrodiagnostic results were compared with medical recovery data.

Of 105 children, 34 had clinically significant weakness and had electrodiagnostic evidence of CIP/CIM. Those with CIP/CIM had significantly longer ICU stays than did those without. The EMG studies showed normal motor units in all patients. There was a decreased interference pattern in 34 of the patients, of whom 27.6% were diagnosed with axonal polyneuropathy and 1.9% diagnosed with demyelinating polyneuropathy. In three patients (2.9%) the electrodiagnostic studies demonstrated a myelopathic pattern. Of those diagnosed with CIP/CIM, 62.1% failed weaning trials and died. Compared to those without, those identified with CIP/CIM had laboratory studies revealing elevated AST, ALT,

prothrombin times, serum calcium, serum sodium, and blood pH.

Conclusion: This study of critically ill, ventilated children found that 32.4% had CIP/CIM, which was associated with a delay in weaning and an increased risk of death.

Mahmoud, A et al. Neurophysiological Study of Critical Illness Polyneuropathy and Myopathy and Mechanically Ventilated Children: Additional Aspects in Pediatric Critical Illness Comorbidities. *Eur J Neurol.* 2018, March; 25:991-998.

TRAJECTORY OF FUNCTION AFTER MODERATE/SEVERE TBI

Traumatic brain injury (TBI) is a leading cause of long-term disability, affecting all age groups. This study was designed to characterize the functional trajectories during the first five years after a moderate to severe TBI.

This prospective cohort study was conducted at the Oslo University Hospital. Consecutive admissions of patients with moderate to severe TBI were screened between 2005 and 2007. Subjects were eligible for study inclusion who were 16-55 years of age, with a Glasgow Coma Scale score of 3-12. At admission all patients were assessed with a CT scan followed by a second scan between six and 12 hours after injury. All patients received neurosurgical and/or ICU care in the acute setting with 60% undergoing post-discharge inpatient rehabilitation. The primary outcome measure was the Functional Independence Measure (FIM) at five years. Data were analyzed to identify patient subgroups who shared the same functional profiles over time, so as to characterize the recovery trajectory of the different groups.

The combined total FIM scores for all participants was 104.6 at three months, 113.6 at one year, and 118.3 at five years after injury. From the data were identified three groups with distinct trajectories of physical functional recovery, and four groups with different trajectories of cognitive functional recovery. The most common group was the stable good recovery group, with the greatest gains among those initially requiring moderate assistance, with GCS scores of 9-12.

Conclusion: This prospective study of patients with moderate and severe traumatic brain injury clustered patients into groups with several distinct patterns of recovery. The most favorable outcomes were found in those with initial GCS scores of 9-12, who required moderate

physical assistance at initial evaluation.

Lu, J et al. Trajectory of Functional Independence Measurements during First Five Years after Moderate and Severe Traumatic Brain Injury. *J Neurotrauma.* 2018, July 15; 35 (14):1596-1603.

CLOPIDOGREL AND ASPIRIN IN ACUTE ISCHEMIC STROKE

The CHANCE trial showed a 32% lower risk of stroke recurrence among Chinese patients treated within 24 hours of a transient ischemic attack or minor stroke, with a combination of Clopidogrel and aspirin as compared to aspirin alone. Given the restricted ethnic population in that trial, this multi-national study was completed to broaden the applicability of these results.

This randomized, double blind, placebo-controlled trial was completed at 269 sites in 10 countries in North America, Europe, Australia and New Zealand. Subjects were 18 years of age or older within 12 hours of an acute ischemic stroke, with a score of three or less on the National Institute of Health Stroke Scale, or of a high-risk transient ischemic attack (TIA) with a score of four or more on the ABCD₂ scale. The patients were randomized to receive Clopidogrel plus aspirin or placebo plus aspirin, with patients followed for 90 days after randomization. The primary efficacy outcome was the composite risk of ischemic stroke, myocardial infarction or death from ischemic vascular causes.

This study was halted after exceeding the prespecified number of major hemorrhagic events in the combined group. At that time, 4,557 patients had completed the 90-day trial period. The primary efficacy outcome occurred in 5% of those receiving the combination and in 6.5% of those receiving aspirin alone ($p = 0.02$). The risk of total ischemic or hemorrhagic stroke was lower in the combined group than in the aspirin group ($p = 0.01$). The primary safety outcome of major hemorrhage occurred in 0.9% of the combined group and 0.4% in the aspirin group ($p = 0.02$).

Conclusion: This multi-national study, expanding on the results of the CHANCE trial, found that among patients with mild stroke or transient ischemic attack, combining aspirin and Clopidogrel, was superior to aspirin alone for decreasing the risk of ischemic stroke, myocardial infarction or death from ischemic

vascular causes, though with an increased risk of major hemorrhage.

Johnston, S et al. Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA. **N Engl J Med.** 2018, July 19:379(3):215-225.

TEN-YEAR TREND IN ATRIAL FIBRILLATION

Atrial fibrillation (AF) is the most common, sustained cardiac arrhythmia in the general population. This study investigated the temporal trends of the prevalence and incidence of non-valvular AF in the Korean population.

Data were obtained from the National Health Insurance Service Database (NHIS), containing the health care claims of the entire Korean population. Data were reviewed from 2006 to 2015 for the annual incidence of AF, defined as the rate of acquisition of new diagnoses. The annual prevalence was calculated by dividing the number of patients with AF who were alive at the end of each year, by the number of total Korean residents alive at that time. The prevalence rates were calculated by sex and by age group.

The prevalence of AF progressively increased from 0.73% in 2006 to 1.53% in 2015. Projecting to the year 2060, the expected prevalence is 5.81%. The median age of patients with AF increased from 65 years of age in 2006 to 71 years in 2015. The annual event rates for adverse events, including heart failure admission, myocardial infarction, intracranial bleed, and ischemic stroke all declined over the 10 years of the study ($p < 0.001$ for all).

Conclusion: This nationwide study of the entire Korean population found that while the prevalence of atrial fibrillation has increased, the risk of adverse events among those with atrial fibrillation has decreased.

Kim, D et al. 10-year Nationwide Trends of the Incidence, Prevalence, And Adverse Outcomes of Non—Valvular Atrial Fibrillation Nationwide Health Insurance Data Covering the Entire Korean Population. **Am Heart J.** 2018, August; 202:20-26.

BONE SCAN AND KETAMINE THERAPY IN CRPS

Complex regional pain syndrome (CRPS), can be a disabling condition, with a pathophysiology that is not yet fully understood. Studies have shown

that successful treatments have included bisphosphonates, calcitonin, corticosteroids and ketamine. While the three-phase bone scintigraphy (TPBS) is often used for the diagnosis of CRPS, the utility of this test for predicting treatment outcomes is not yet known.

This prospective study was completed between November 2011 and November 2016 with patients diagnosed with unilateral CRPS type 1, and treated with ketamine infusions. Prior to infusion, all underwent TPBS. For the three scintigraphic phases (vascular phase (VPr) tissue phase (TPr), and bone phase (BPr)), the ratio was calculated using tracer uptake in the affected to unaffected side. Ketamine infusions were performed continuously for five days with up to 1 mg/kg per day. The patients were followed for three days for changes in pain intensity using a visual analog scale (VAS). The TPBS findings were compared to the changes in VAS scores.

Of the patients treated, 59 were responders (greater than 50% pain relief) and 46 were nonresponders. The pain reduction was significantly correlated with disease duration before treatment. In addition, ketamine-induced pain relief was correlated with the ratio of BPr divided by VPr ($p = 0.005$), as well as by the TPr divided by VPr ($p = 0.02$). Using the criterion of <5% of responders, the cut-off values for nonresponse were <1.03 for BPr/TPr, <0.94 for BPr/VPr, and <0.84 for TPr/VPr.

Conclusion: This study of patients diagnosed with complex regional pain syndrome found that the results of the three-phase bone scan may be useful in predicting the efficacy of ketamine treatment.

Sorel, M., et al. Three-Phase Bone Scan Scintigraphy Can Predict the Analgesic Efficacy of Ketamine Therapy in CRPS. **Clin J Pain.** 2018, September; 34(9):831–837.

ANTIBACTERIAL ACTIVITY OF ESSENTIAL OILS

Respiratory tract infections are a significant cause of morbidity and mortality among patients admitted to rehabilitation hospitals with cerebrovascular accidents. As antibiotic resistant bacteria are of increasing concern, alternative interventions may need consideration. This study reviewed the effectiveness of essential oils against several antibiotic resistant bacteria common among upper respiratory infections.

The study organisms were the most frequent respiratory tract pathogens; *Streptococcus pneumoniae*, *S. mutans*, *S. pyogenes*, as well as gram negative strains including *Haemophilus influenzae*, *H. parainfluenzae*, and *Moraxella catarrhalis*. Using a Vapor phase test (VPT) as well as a Broth Macrodilution Test (BDT), the minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) were determined for the essential oils of clove, cinnamon bark, Eucalyptus, thyme, Scots pine peppermint and citronella. These results were compared to the activity of standard antibiotics including imipenem, amoxicillin/clavulanic acid and amikacin.

In the BDT, cinnamon bark, clove, citronella, and thyme presented the most potent inhibition against both Gram-negative and Gram-positive pathogens. Cinnamon bark oil produced the lowest MIC and thus the strongest overall antibacterial activity against all the respiratory tract pathogens in the study with MIC values in the range of 15.62–90 $\mu\text{L/L}$. However, the effect of the essential oils was less robust than that of the reference antibiotics.

Conclusion: This study of pathogens responsible for upper respiratory infections found that the essential oils of cinnamon bark, clove, citronella, and thyme provide antibacterial activity in either liquid medium or in the vapor phase. The effect is weaker than the referenced antibiotics, and the appropriate dose of the essential oils is not yet well understood.

Acs, K., et al. Antibacterial Activity Evaluation of Selected Essential Oils and Liquid and Vapor Phase on Respiratory Tract Pathogens. **BMC Complement Altern Med.** 2018. 18:227

IMPACT OF ATRIAL FIBRILLATION ON COGNITION AND EMOTION

Longstanding hypertension (HTN) and atrial fibrillation (AF) may produce ischemic lesions which can lead to progressive cognitive impairment, but the impact of AF alone is not well understood. This study compared the cognitive function, quality of life, psychological distress, and impulsiveness in people with AF with a matched control group.

Subjects included 30 patients with a history of AF of five years or more without a history of dementia or uncontrolled hypertension. These patients were matched with 30 healthy controls. Demographic and

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clinical characteristics were recorded, and all were assessed with the Mini-Mental State Examination, Hospital Anxiety and Depression, Heart Quality of Life, and Barratt Impulsiveness Scale.

The Mini-Mental State Examination score was 27.6 in the AF group and 29.5 in the control group ($p < 0.0001$). Anxiety disorders were observed in 20 patients (66.7%) in the AF group and eight patients (26.7%) in the control group ($p = 0.009$). The Heart Quality of Life mean score was 1.4 in the AF group and 2.6 in the control group ($p < 0.0001$). The impulsiveness and depression scores were not significantly different between the groups.

Conclusion: This small study found that cognitive status is worse and anxiety disorders more common among patients with atrial fibrillation as compared to matched controls.

Serpytis, R et al. Impact of Atrial Fibrillation on Cognitive Function, Psychological Distress, Quality Of Life, and Impulsiveness. *Am J Med.* 2018; 131: 703.e1–703.e5.

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