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PAIN AND DELIRIUM IN HOSPITALIZED PATIENTS WITH DEMENTIA

Data have shown that people with dementia are six times more likely to be admitted to the hospital with delirium. Further, delirium is associated with an increased risk of death or further hospitalization within the next 12 months. This study assessed the relationship between pain and delirium in patients with dementia in an acute hospital setting.

All hospitalized patients with a pre-existing, documented dementia were eligible to participate. Patients were screened at hospital admission with the Confusion Assessment Method (CAM). Those without delirium completed a Mini-Mental State Exam (MMSE). Data were gathered every four days, including assessments of dementia, self-reported and observational estimates of pain.

Of the 230 participants, 10% experienced pain at rest and 42% experienced pain during activity. The odds of delirium were 3.26 times higher among those with pain at rest ($p = 0.044$), with no increased risk among those with pain during activity. Over half of those with delirium who were unable to report pain were judged to be in pain during activity. No significant difference was seen in the occurrence of delirium between those who were prescribed analgesics and those who were not.

Conclusion: This study of patients with dementia found that, during hospitalization, the odds of delirium were over three times higher among those experiencing pain at rest.

Feast, A., et al. Pain and Delirium in People with Dementia in the Acute General Hospital Setting. **Age Aging.** 2018, November; 47(6): 841-846.

LOW CARBOHYDRATE DIET AND ENERGY EXPENDITURE DURING WEIGHT LOSS

According to the carbohydrate-insulin model of obesity, an increased ratio of insulin to glucagon after a meal with a high glycemic load directs metabolic fuels away from oxidation and toward storage in adipose tissue. Studies exploring this model have not produced conclusive results. This study compared the effects of diets varying in carbohydrate to fat ratios on energy expenditure during weight loss maintenance.

This randomized, controlled trial included adults at Framingham State University, studied between August of 2014 and May of 2017. During a run-in phase, energy intake was restricted to promote 12% weight loss over nine to ten weeks. The subjects who successfully lost this weight were randomized to high, moderate or low carbohydrate test diets for a 20-week phase. During this phase, energy intake was adjusted to maintain weight loss. The diets all contained protein at 20% of total calories, varying the energy contributions of carbohydrates at 60%, 40% or 20%, with the remaining calories obtained through fat. Outcome variables were energy expenditure, physical activity and metabolic hormones.

Of the 234 participants in the weight loss phase, 164 achieved the target 12% reduction in weight loss and were included in this randomized trial. Compared with the high carbohydrate diet, change in total energy expenditures were 91 kcal per day greater on the moderate carbohydrate diet and 209 kcal per day greater on the low carbohydrate diet. The data revealed that energy expenditure increased by 52 kcal/d for every 10% decrease in the contribution of carbohydrate to total

energy intake ($p=0.002$). This effect was most pronounced among those with high insulin secretion, as measured at pre-weight loss.

Conclusion: This randomized, controlled trial found that, with similar calories and similar protein intake, patients who consume low carbohydrate diets have significantly greater total energy expenditure.

Ebbeling, C., et al. Effects of a Low Carbohydrate Diet on Energy Expenditure During Weight Loss Maintenance: Randomized Trial. **BMJ.** 2018;363: k4583.

DURABILITY OF ANTIDEPRESSANT RESPONSE OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION

In cases of recalcitrant depression, repetitive transcranial magnetic stimulation (rTMS) has been shown to be of value as an additional treatment option. The durability of the antidepressant effects of rTMS is not yet clear. This meta-analysis was designed to better understand the efficacy of rTMS over time.

A literature review was completed for studies of rTMS for the treatment of depression. From this search, 23 articles, published between 2002 and 2018, were chosen for inclusion in the review. From the studies were extracted response rates at three, six and 12 months.

After successful rTMS induction, among 732 patients from 18 studies, 66.5% demonstrated a sustained response at month three. Among the patients followed through six months, 52.9% were still responders, while, at 12 months, 46.3% were still responders. A positive predictor of a positive response at both three and six months was the inclusion of maintenance treatment. Compared to those who did not receive maintenance treatment, the

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response rates of those who received maintenance treatment were 35.8% higher at three months and 58.7% higher at six months.

Conclusion: This systematic review and meta-analysis of studies of patients with depression treated with repetitive transcranial magnetic stimulation found that 66.5% were still responders at three months and 46.3% were responders at 12 months, with these results enhanced by maintenance therapy.

Senova, S., et al. Durability of Antidepressant Response to Repetitive Transcranial Magnetic Stimulation: Systemic Review and Meta-Analysis. **Brain Stim.** 2019, Jan-Feb; 12(1): 119-128.

COMPRESSION SOCKS DURING EXERCISE

While compression garments have been used to improve circulation, similar garments are worn during sports to improve performance. This study assessed the effect of compression socks worn during a five km run.

This counterbalanced, crossover design study included 12, well-trained, male runners. All were asked to maintain constant dietary patterns prior to each of three sessions. At each session, the runners performed a standardized warmup, followed by a five km timed trial and a one-hour recovery before a second warmup and five km timed trial.

The runners completed one session wearing compression socks for the first warmup and timed trial and one session with no compression socks. Blood lactate concentration was measured, with samples collected at completion of each stage of the warmup protocol, as well as three minutes after completion of the runs.

The declines in run performance between the first and second runs were moderate in the control group and significantly greater than in the compression stockings group ($p < 0.01$). No significant difference was found between the conditions on measures of oxygen consumption, blood lactate or calf volume.

Conclusion: This study of well-trained runners found that wearing compression stockings while running can reduce deterioration in performance one hour later.

Williams, N., et al. Wearing Compression Stockings During Exercise Aids Subsequent Performance. **J Science Med Sport.** 2019; 22(1): 123-127.

DYNAMIC BALANCE AND CONCUSSION

The Centers for Disease Control and Prevention estimates that up to

3.8 million concussions occur annually in the United States. Studies have shown that a history of concussion increases an athlete's risk of sustaining a subsequent concussion. This study investigated the association between dynamic balance performance and concussion injury. Subjects were 109 elite Irish rugby players. All participants underwent a baseline Y Balance Test (YBT), with an inertial sensor. The outcome variable of interest was the diagnosis of concussion during the ensuing season, with that diagnosis made using the Head Injury Assessment Tool (HIA) in compliance with the world rugby guidelines. Recorded for each player was a self-reported concussion history, playing position, age group and dynamic balance variables.

At baseline, 40% of the players reported of history of concussion, while 19.3% of the players sustained a concussion during the study season. There was no significant difference in baseline testing results between those who had a history of

concussion and those who did not. Those who sustained a new concussion demonstrated significantly worse dynamic balance when reaching in the anterior direction, as compare to the non-concussed group. A regression model revealed that, when controlling for concussion history, those with poor balance performance were at a 3.63 greater risk of sustaining a concussion, as compared with those with optimal balance performance.

Conclusion: This study of elite rugby players found an association between reduced dynamic balance performance and the risk of sustaining another concussion.

Johnston, W., et al. Association of Dynamic Balance with Sports-Related Concussion. **Am J Sport Med.** 2019, January; 47(1): 197-205.

MEDICAID HOSPITAL READMISSION REDUCTION

In the year 2012, seven percent of the United States population was hospitalized, with one in 12 adults readmitted within 30 days. It has been estimated that one fourth of all 30-day hospital readmissions are preventable, with many traceable to inadequate post-discharge follow-up. This study reviewed the effect of a primary care physician follow-up within seven days of discharge on the readmission rates of patients with Medicaid.

This study was conducted in Camden, New Jersey, where Medicaid covers 57% of the residents. This program engaged patients while they were still hospitalized, in order to facilitate a primary care appointment within seven days of discharge. During that visit, the patients were alerted to the benefits of primary care follow-up. Visits were scheduled, transportation offered and a 20-dollar gift card presented after appointment completion. In addition, the primary care practices were offered an enhanced reimbursement of \$100 for visits within 14 days and \$150 for visits within seven days. For each patient involved in the treatment group, five, matched patients were identified for a control group. The groups were compared for rates of rehospitalization within 30 days of discharge.

Between 2014 and 2016, there were 2,580 hospitalizations of adult patients. Of these, 450 discharges were followed by primary care within seven days, and 607 within 14 days. Of the hospitalizations in the intervention group, 12.7% had a readmission within 30 days, as compared with 17.5% among the matched controls ($p=0.03$). At 90 days post-discharge, 28% in the treatment group were readmitted, as compared with 30.7% in the matched controls ($p=0.002$).

Conclusion: This study of Medicaid recipients found that, after hospitalization, those seen for follow up by a primary care physician within seven days had a significant reduction in 30- and 90-day hospital readmission.

Wiest, D., et al. Outcomes of a Citywide Campaign to Reduce Medicaid Hospital Readmissions with Connection to Primary Care within Seven Days of Hospital Discharge. **JAMA Open.** 2019; January 25;2(1): 1-10.

LOWER EXTREMITY INJURY ON SYNTHETIC VERSUS NATURAL TURF

Grass turf has been shown to allow the release of the cleat from the surface at higher forces. This is thought to be a protection against certain injuries. Synthetic turf does not have this capacity. This study compared the injury rates between athletes who compete on synthetic turf and those who compete on natural turf.

Injury data were collected prospectively by medical staff for all

32 teams in the National Football League. Data for injuries of the lower extremities were compared between those which occurred on fields with natural surfaces and those which occurred on fields with synthetic surfaces. These data were reviewed for five seasons. Data was collected for 1,280 games, 555 which occurred on synthetic surfaces and 725 which occurred on natural surfaces.

For total injuries, play on synthetic turf resulted in a 16% higher rate of injuries as compared to natural turf. When the analysis was restricted to noncontact/surface contact injuries, the hazard ratios of synthetic surface/natural surface were 1.46 for knee injuries and 1.68 for ankle/foot injuries.

Conclusion: This study of National Football League athletes found higher rates of injuries to the lower extremity

when competing on synthetic turf than when playing on natural turf.

Mack, C., et al. Higher Rates of Lower Extremity Injury on Synthetic Turf Compared with Natural Turf among National Football League Athletes. Epidemiologic Confirmation of a Biomechanical Hypothesis. **Am J Sports Med.** 2019, January; 47 (1):189-196.

INTERLEUKIN-1 RECEPTOR ANTAGONIST FOR TENDINOPATHY

The cytokine, interleukin-1 (IL1), has been found in elevated levels in patients with tendinopathy. This study was designed to determine whether Anakinra, an IL1 receptor antagonist (IL1 RA), can effectively treat tendinopathy.

This animal study included 48, female, Sprague Dawley rats, all exposed to carrageenan (CAR), a reproducible means of developing inflammation. The animals were randomized to one of three groups, a control group (CON), a CAR group or a CAR plus Anakinra group (CAR+A). The CON group received 0.1 mL saline for six weeks. The intervention groups were treated with carrageenan for four weeks. Beginning at week three, the CAR+A group received Anakinra at 2.5 mg/kg added to the carrageenan and 0.94 mg of the carrageenan alone for the final two weeks, while the CAR group received saline for the final two weeks.

The CAR+A group demonstrated fewer plaque-like lesions than did the CAR group. In addition, the CAR group demonstrated shorter tendon lengths than the other two groups ($p<0.05$ for both). The CAR group demonstrated significantly greater histologic changes than did the CAR+A group. For all histologic factors studied, more pathology was noted in the CAR than in the CAR+A group ($p<0.05$). The tensile loads did not differ between the three groups.

Conclusion: This animal study of tendinopathy found that an antagonist to the IL1 receptor may reduce pathological signs of tendinopathy.

Eskildsen, S., et al. The Use of an IL1 Receptor Antagonist to Reverse the Changes Associated with Established Tendinopathy in a Rat Model. **Scand J Med Sci Sports.** 2019, January; 29 (1): 82-88.

SODIUM HYALURONATE AND PLATELET RICH PLASMA FOR ROTATOR CUFF TEARS

The treatment of partial thickness rotator cuff tears can include conservative and surgical interventions. Among the nonsurgical outcomes, sodium hyaluronate (SH) and platelet rich plasma (PRP) are relatively new. This study investigated the effects of SH combined with PRP for the treatment of partial thickness rotator cuff tears.

Subjects were 184 patients, 18 to 55 years of age, diagnosed with partial thickness rotator cuff tears, confirmed by magnetic resonance imaging. The participants were randomized to receive normal saline (4 mL), SH (4 mL), PRP (4 mL) or SH plus PRP (2mL +2mL), injected once per week for four weeks. The primary outcome measure was the Constant score. Secondary measures included the American Shoulder and Elbow Surgeons (ASES) and the VAS pain scores.

At one and three months, compared with the control group, the Constant and ASES scores were significantly improved in the SH and the SH+PRP groups. At one month, VAS pain scores were significantly lower in the SH and SH+PRP groups than in the normal saline and PRP groups. At six and 12 months, VAS score improvements were best in the SH+PRP group. At one year, compared with the other groups, the SH+PRP group showed the most improvement in the Constant, VAS and ASES scores, and rotator cuff tear size.

Conclusion: This study found that PRP can enhance the recovery of small to medium partial thickness rotator cuff tears, with better improvement when combined with sodium hyaluronate.

Cai, Y., et al. Sodium Hyaluronate and Platelet Rich Plasma for Partial Thickness Rotator Cuff Tears. **Med Sci Sports Exerc.** 2019, February; 51 (2): 227-233.

MELATONIN FOR TRAUMATIC BRAIN INJURY

After a traumatic brain injury (TBI), a complex cascade of processes often results in further significant (secondary) brain injury. As previous studies have suggested that melatonin may have neuroprotective qualities, this literature review and meta-analysis

explored the efficacy of melatonin for the treatment of acute TBI.

A literature review was completed for randomized, placebo-controlled trials involving patients with TBI treated with melatonin. From the review, eight articles were identified which had information suitable for a meta-analysis. The range of the melatonin dose was 0.625 mg/kg to 200 mg/kg, although the most frequent dose was 5 mg/kg.

Data revealed that melatonin decreased acute contusion volume by a standardized mean difference (SMD) of 2.22, decreased cerebral edema by a SMD of 1.91 and had a favorable effect on neurological status by a SMD of 1.35. In addition, those taking melatonin had an improved performance in cognitive tasks, by a SMD 1.16, and demonstrated improved memory by a SMD of 1.16. The overall outcome when effects were combined was a SMD of 1.51.

Conclusion: This literature review and meta-analysis, including data from animal studies, concerning acute brain injury, suggests that melatonin may have a protective effect on behavioral and pathological outcomes.

Barlow, K., et al. Melatonin as a Treatment after Traumatic Brain Injury: A Systematic Review and Meta-Analysis of the Pre-Clinical and Clinical Literature. **J Neurotrauma**. 2019, February; 36 (4):523-537.

INJECTABLE CARTILAGE FOR FOCAL CHONDRAL LESION

Among tissue engineering approaches to chondral repair are injectable hydrogels which can form three-dimensional networks. These can be delivered as a liquid solution and then polymerized *in vivo*. This animal study assessed the efficacy of a novel cartilage mimetic hydrogel for the repair of chondral defects.

A hydrogel was constructed, designed to polymerize within minutes. Bone marrow derived mesenchymal stem cells (MSC) were isolated and culture expanded, with those cells then encapsulated in the photopolymerized hydrogel. Ten rabbits underwent bilateral, surgical chondral lesions, with the lesions randomly assigned for

treatment with hydrogel (H), hydrogel plus MSCs (H+) or a placebo (P). In the H and H+ groups, 30 to 40 milliliters of polymer solution were injected, and then photopolymerized, using a 405 nm blue light for 40 seconds. At six months, the animals were euthanized for analysis.

At six months, the macroscopic evaluation showed nearly normal tissue repair in the H and H+ groups. The addition of mesenchymal stem cells did not enhance cartilage repair, with some cases suggestive of poorer outcomes. In both hydrogel groups, repaired tissues were scored as a mix of hyaline and fibrocartilage tissue. The H group had the best bonding to adjacent articular cartilage, with better cellularity and defect filling scores.

Conclusion: This animal study demonstrated that a cartilage mimetic hydrogel can be injected and then polymerized during surgery, with immediate weight bearing, resulting in good defect repair. The addition of mesenchymal stem cells did not enhance the repair.

Pascual-Garrido, C., et al. Photopolymerizable Injectable Cartilage Mimetic Hydrogel for the Treatment of Focal Chondral Lesions. A Proof of Concept Study in a Rabbit Animal Model. **Am J Sport Med**. 2019, January; 47 (1): 212-221.

ENGINEERED GLOVE TO DETECT RADIOLOGICALLY ISOLATED SYNDROME

A glove engineered to measure motor performance of the fingers has been shown to discriminate individuals with early-stage multiple sclerosis (MS) from healthy controls. This study assessed whether this glove could be useful in diagnosing individuals with radiographically isolated syndrome (RIS), who are asymptomatic with MRI findings suggestive of MS.

Subjects were 17 adults with a diagnosis of RIS and the presence of white matter lesions, all with no previous remitting clinical symptoms. A control group included 17 age and gender matched, healthy controls. All participants were asked to perform a bilateral

repetitive finger to thumb opposition sequence at maximum velocity, and then at two Hz, while paced by a metronome. All underwent brain MRI examination on the day of the glove experiment. Outcome measures were maximum velocity and coordination of movement between the hands.

Compared to that of healthy controls, the rate of maximum velocity in patients with RIS was lower ($p=0.005$). In addition, the hand movements were less synchronized in the RIS group ($p=0.006$).

Conclusion: This study of patients with asymptomatic radiologically isolated syndrome found that finger motor performance and bimanual coordination impairment could be detected with an engineered glove.

Bonzano, L., et al. Subclinical Motor Impairment Assessed with an Engineered Glove Correlates with Magnetic Resonance Imaging Tissue Damage in Radiologically Isolated Syndrome. **Europ J Neurol**. 2019; 26(1): 162-167.

IMPACT LOCATION AND BRAIN STRAIN

While the prevalence of concussion is not clearly understood, estimates ranged between 1.6 and 3.8 million sports related concussions in United States each year.

This study compared the relationship between the impact magnitude and direction to the subsequent variation of strain levels in regions of the brain. Using a model of the human head and brain, linear acceleration was recorded using an accelerometer, while rotational velocity was measured using a three-axis gyroscope. Twelve tests were conducted with constant energy impacts ranging from 20g to 200 g. These impacts were provided from the frontal, lateral and rear direction. Strains and pressures were measured at various portions of the brain, and compared by direction of impact.

The effect of the impact on different regions of the brain varied by direction of the impact. Both angular and linear accelerations were higher in lateral and rear

impacts as compared to frontal impacts. With the acceleration profile held constant, frontal impact produced the highest strains in the midbrain as compared to other regions of the brain. In contrast, strains in the corpus callosum were greatest when the impact was from a lateral direction.

Conclusion: This study, modeling the human brain, found that angular accelerations are up to 30% higher in lateral and rear impacts as compared to frontal impacts. Frontal impacts seem more likely to damage the midbrain while lateral impacts are more likely to impact the corpus callosum.

Tiernan, S et al. The Effect of Impact Location on Brain Strain. *Brain Inj.* 2019;10.1080/02699052.

GRANULOCYTE COLONY STIMULATING FACTOR FOR SPINAL CORD INJURY

For patients who have a traumatic spinal cord injury (tSCI), secondary mechanisms unfold in different phases, which can result in further clinical damage. Among the targets for blocking this secondary cascade, granulocyte colony stimulating factor (G-CSF) has been studied for its potential neuroprotective effect. This prospective, placebo-controlled trial assessed the neurologic effects of G-CSF among patients with incomplete tSCI.

Subjects were between 18 and 60 years of age, all with an incomplete (tSCI) of between one- and six-months' duration. The participants were randomized to receive seven daily injections of either placebo (n=26) or 300 micrograms of G-CSF (n=28). A neurologic evaluation was made at baseline and at follow-up, using the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI), with other measures including the American Spinal Injury Association (ASIA) and the International Association of Neurorestoration Spinal Cord Injury Functional Rating Scale (IANR - SCIFRS) and the Spinal Cord Independence Measure III (SCIM-III) for assessment of impairment.

After six months, the AIS grade remained unchanged in the placebo group, with 11 patients improving by at least one grade in the treatment

group. The mean changes in the ISNCSCI motor scores were 14.9 points in the treatment group and 1.4 points in the placebo group (p<0.001). Compared with the treatment group, IANR-SCIFRS functional scores were significantly better in the treatment group (p<0.001). Increased neuropathic pain was experienced in 10.7% of the treatment group, with 7.1% demonstrating increased spasticity.

Conclusion: This study of patients with incomplete spinal cord injury found that seven daily injections of 300 micrograms of G-CSF can significantly improve motor and sensory function.

Derakhshanrad, N., et al. Subcutaneous Granulocyte Colony Stimulating Factor Administration for Subacute Traumatic Spinal Cord Injuries, Report of Neurological and Functional Outcomes: A Double-Blind, Randomized, Controlled, Clinical Trial. *J Neurosurg Spine.* 2019, January; 30(1): 19-30.

DYNAMIC BALANCE AND RISK OF CONCUSSION

After a concussion, athletes are at a higher risk of sustaining a repeat concussion. This study investigated the association between dynamic balance performance and the risk of future concussion.

Subjects were 109, elite, male, rugby union players from four senior Irish teams. All underwent baseline testing sessions and received a single, inertial sensor to wear at the level of the fourth lumbar vertebra to match the body's center of mass. While wearing the sensor, the subjects completed four practice trials and three recorded trials of the pre-defined directions of the Y-balance test (YBT).

Reach distances were normalized to each individual according to leg length. The subjects were followed during the ensuing rugby season, with the incidence of concussions documented. Independent variables included self-reported concussion history, playing position, age group, dynamic balance variables and the entropy of the gyroscope magnitude signal during each YBT excursion.

Of the 109 players, 44 had a history of concussion, with 21 sustaining a concussion in the follow

- up season. Those with suboptimal balance at baseline were 2.81 times more likely to sustain a concussion during the following season, even after controlling for concussion history.

Conclusion: This study of professional rugby players found that those with suboptimal balance at baseline had a significantly increased risk of concussion during the following season.

Johnston, W., et al. Association of Dynamic Balance with Sports-Related Concussion: A Prospective, Cohort Study. *Am J Sport Med* 2019, January; 47 (1): 197-205.

BLOOD FLOW RESTRICTED EXERCISE FOR POWER LIFTERS

For strengthening, the traditional formula involves training with weights greater than 70% of the one-repetition maximum (1RM). However, similar effects have been found with reduced weights using blood flow restriction (BFR). This study assessed the effect of BFR training during six weeks of strengthening by elite power lifters.

A group of power lifters were assessed for their 1RM. The subjects were randomized to a conventional training group or a BFR group. The conventional training group performed front squats at 60 to 85% of their 1RM. The BFR group performed similar training, with BFR sessions inserted at weeks one and three, including four sets at 30% of the 1RM, with a blood pressure cuff at their proximal thigh inflated to 120mmHg. After 6.5 weeks of training, strength was assessed, muscle biopsies taken and US measurements made to determine the myofiber areas (MFA) and cross-sectional area (CSA) of m. rectus femoris (RF), m. vastus lateralis (VL), m. vastus medialis (VM) and m. vastus intermedius (VI).

The BFR exercise (BFRRE) group increased strength in knee extension (p=0.04) with no significant change in the conventional group. The difference between groups did not reach statistical significance. Type I fibers increased more in the BFR group than in the control group (p=0.003), with no increase in type II fibers. Muscle thickness (measured as the shortest distance between the

upper and lower aponeuroses) was also significantly greater in the BFR group than in the control group for the RF, VL and VM ($p=0.01$, 0.02 , and 0.02 , respectively). The number of myonuclei in type I fibers increased significantly more in the BFR group than in the control group ($p=0.01$).

Conclusion: This study of elite power lifters is found that adding two blocks of front squats with low load, blood flow restriction exercise resulted in an increased quadriceps cross-sectional area, and a preferential hypertrophy of type I fibers.

Bjornsen, T., et al. Type 1 Muscle Fiber Hypertrophy after Blood Flow Restricted Training in Powerlifters. *Med Sci Sports Exerc.* 2019, February; 51(2): 288-298.

DURATION OF SURGERY AND POSTOPERATIVE DELIRIUM AFTER HIP FRACTURE REPAIR

Research has shown that elderly patients with fractures are vulnerable to post-operative delirium, with the incidence ranging from five percent to 61%. This prospective study addressed the association between the duration of hip fracture surgery and the risk for postoperative delirium in elderly adults. This population-based cohort study used administrative data from Ontario Canada. Subjects were patients who received acute surgical management for hip fracture between April 1, 2009, and March 31, 2017. Procedures shorter than 30 minutes or longer than 240 minutes were excluded. Diagnoses, comorbidities and sociodemographic data were recorded. The primary outcome variable was the occurrence of postoperative delirium during hospitalization.

Of the 68,131 patients identified, 7,150 were diagnosed with postoperative delirium. Compared with those who received a regional anesthetic, those receiving a general anesthetic had a slightly higher rate of postoperative delirium (11% versus 10.2%; $p=0.001$). After controlling for comorbidities, increased surgical duration was associated with an increased risk of delirium, with an adjusted odds ratio of 1.06 per 30 minutes of surgery ($p<0.001$). This association was

stronger among those receiving general anesthesia than among those receiving a regional anesthetic.

Conclusion: This cohort study of elderly patients undergoing hip fracture surgery found a significant association between length of surgery and risk of postoperative delirium.

Ravi, B., et al. Association of Duration of Surgery with Postoperative Delirium among Patients Receiving Hip Fracture Repair. *JAMA Open.* 2019, Feb; 22: 4-11.

RESISTANCE EXERCISE AND CARDIOVASCULAR DISEASE

While the cardiovascular benefits of aerobic exercise have been well documented, most studies of resistance exercise have focused on bone health, physical function and quality of life. This study investigated the effect of resistance exercise on the risk of cardiovascular disease (CVD).

The Aerobics Center Longitudinal Study included 12,591 participants, 18 to 89 years of age. All underwent baseline, comprehensive medical examinations, with sociodemographic and lifestyle data also gathered. The subjects answered questions about their aerobic and resistance exercise during the previous three months. Four categories of resistance exercise exposure were established by total time, including zero, one to 59 minutes, 60 to 119 minutes and more than 120 minutes per week. The primary endpoint was CVD mortality.

At 10.5-year follow-up, among the 12,591 participants, there were 276 all-cause deaths. Compared with no resistance exercise, up to 60 minutes was associated with a 40 to 70% decreased risk of total CVD events, independent of aerobic exercise. No further reductions were found with resistance exercise of greater than 60 minutes per week.

Conclusion: This prospective study of adults up to 90 years of age found that up to one hour per week of resistance exercise is associated with a significantly reduced risk of cardiovascular events.

Liu, Y., et al. Associations of Resistance Exercise with

Cardiovascular Disease Morbidity and Mortality. *Med Sci Sports Exerc.* 2019, March; 51(3): 499-508.

THERAPEUTIC ELECTRICAL STIMULATION OF INJURED PERIPHERAL NERVE TISSUE

Previous studies have found that thin-film wireless receivers are able to reliably deliver electrical impulses to recruit peripheral nerve tissue and activate distal musculature for the purpose of tracking postoperative functional recovery. This study examined the effect of electrostimulation by an implanted stimulator on the recovery of an injured sciatic nerve.

Subjects were 25 male rats, all undergoing surgical implantation of a wireless nerve stimulator adjacent to the sciatic nerve. Group one served as a control and underwent surgical exposure with no injury. Groups two and three received a crush injury, while groups four and five underwent a transection and repair. Groups three and five received one hour of therapeutic stimulation immediately after surgery. All animals underwent weekly assessment of functional recovery, measured at the gluteus maximus (GM), tibialis anterior (TA), gastrocnemius (GS) and plantaris (PL) muscles.

At four weeks, EMG recordings in TA, GS and PL muscles revealed recovery of, respectively, 35.4%, 38.3% and 43.8% of native function with electrical stimulation, in contrast to 25.1%, 25.8% and 20.4% in its absence. At week 13 post-surgery, the TA, GS, and PL muscles demonstrated recovery of, respectively, 79.0%, 79.2% and 90.0% of native function in the presence of therapeutic electrical stimulation, and 65.4%, 64.2% and 66.8% in its absence.

Conclusion: This study found that a wireless implant successfully delivering therapeutic electrostimulation to injured peripheral nerve tissue can accelerate functional recovery.

MacEwan, M., et al. Therapeutic Electrical Stimulation of Injured Peripheral Nerve Tissue Using Implantable Thin Film Wireless Nerve Stimulators. *J Neurosurg.* 2019, February; 2:130:486-495.

HYDRODISSECTION FOR CARPAL TUNNEL SYNDROME

Carpal tunnel syndrome (CTS) is a common nerve entrapment that can be treated by conservative or surgical intervention. Hydrodissection is a procedure involving the injection of fluid into anatomic space to facilitate dissection and adhesiolysis. This study was designed to determine the clinical efficacy of nerve hydrodissection for mild to moderate CTS.

This prospective study included 40 patients with mild to moderate CTS of at least three months' duration.

All underwent electrodiagnostic testing, with the evaluations performed at baseline and at one, two, three and six months after intervention. The treatment group received an injection of three mL of normal saline (NS) to detach the median nerve from the transverse carpal ligament. An additional two mL of NS was injected to separate the median nerve from the flexor tendons. In the control group, five mL of normal saline was delivered into the subcutaneous region beyond the carpal tunnel. The primary outcome measures were scores on the Boston Carpal Tunnel Syndrome questionnaire and its two subtests, the Symptom Severity Scale (SSS) and the Functional Status Scale (FSS). The secondary outcome was the cross-sectional area (CSA) of the median nerve.

The treatment group demonstrated better improvement than the control group on the SSS, beginning at one month ($p=0.029$) and continuing through six months ($p=0.006$). The treatment group also had superior results on the FSS, beginning at month three ($p=0.016$) and continuing through months six ($p=0.041$). The treatment group had better recovery at one- and three-months' follow-up in sensory nerve velocities ($p=0.049$ and $p=0.018$, respectively), with the results falling at month six to marginally significant ($p=0.079$).

Conclusion: This study of patients with mild to moderate carpal tunnel syndrome found that hydrodissection with normal saline may improve functional outcome

and results on electrodiagnostic measures.

Wu, Y., et al. Nerve Hydrodissection for Carpal Tunnel Syndrome: A Prospective, Randomized, Double-Blind, Controlled Trial. *Muscle Nerve*. 2019, February; 59(2): 174-180.

IMMOBILIZATION FOR STABLE ANKLE FRACTURES

Data have shown that 70% of ankle fractures are Weber type B fibula fractures. Traditional non-operative treatment of stable Weber B fractures involves below the knee casting for six weeks. However, after cast removal, common sequelae include ankle stiffness and deep vein thrombosis. This study compared the outcomes of patients immobilized by casting for three versus six weeks.

Subjects with stable Weber B fractures were randomized in a 1:1:1 ratio to receive six-week casting, three-week casting or three-week immobilization with an orthosis. The primary outcome measure was the Olerud-Molander Ankle Score (OMAS), as measured at 52 weeks. Secondary outcome measures included the Foot and Ankle Outcome Score, the RAND 36-Item Health Survey and range of motion of the ankle.

Subjects included 247 patients, with 86% available at 52-week follow-up. At 52 weeks, the mean OMAS scores were 87.6 for the six-week cast group, 91.7 for the three-week cast group and 89.8 for the three-week orthosis group. Asymptomatic deep vein thrombosis was diagnosed in eight patients, five in the six-week cast group, three in the three-week cast group and none in the orthosis group. Two cases of nonunion were found, both in the three-week cast group.

Conclusion: This study of patients with stable Weber B type fibular fractures found that three-week immobilization, either in a traditional cast or a simple orthosis, results in ankle function and healing that is noninferior to conventional cast immobilization of six weeks.

Kortekangas, T., et al. Three-Week versus Six-Week Immobilization for Stable Weber B Type Ankle Fractures: Randomized, Multicenter,

Noninferiority Clinical Trial. *BMJ*. 2019; 36: K5432.

DULOXETINE AND PAIN AFTER TOTAL KNEE ARTHROPLASTY

Central sensitization due to chronic knee pain can occur in the 20 to 40% of those with advanced osteoarthritis of the knee. This is a known risk factor for persistent pain after total knee arthroplasty (TKA). This study investigated the effect of duloxetine for pain reduction among patients with centralized pain undergoing TKA.

This prospective, randomized, clinical trial enrolled patients scheduled for TKA. All were screened preoperatively with the Central Sensitization Inventory (CSI). Those with scores of 40 or greater were invited to participate. Eighty patients were randomized to either a duloxetine group or a control group. The treatment group took 30 mg of oral duloxetine the night before surgery, and then 30 mg per day for six weeks. All received 200 mg of celecoxib and 150 mg of pregabalin two hours preoperatively for preemptive pain control. The primary outcome measure was a visual analogue scale (VAS) for pain severity, as assessed by the sensory dimension of the Brief Pain Inventory. Those in the treatment group had better average and worst VAS pain scores during postoperative weeks two through six, ($p<0.01$) and week 12 ($p=0.014$). Pain while walking, resting and at nighttime was superior in the duloxetine group beginning at two weeks and continuing through 12 weeks ($p=0.012$ for resting pain at 12 weeks and $p<0.01$ for all other comparisons). There was no significant difference in adverse medical reactions between the groups.

Conclusion: This study of patients with centralized pain, each undergoing total knee arthroplasty, found that treatment with duloxetine beginning the day before surgery and continuing for 12 weeks resulted in significantly less pain beginning at two weeks post-surgery.

Koh, J., et al. Duloxetine Reduces Pain and Improves Quality of

Recovery following Total Knee Arthroplasty in Centrally Sensitized Patients. **J Bone Joint Surg.** 2019, January 2; 101 (1): 64-73.

METAL CHAPERONES FOR BRAIN INJURY

Traumatic brain injury (TBI) literature suggests that zinc homeostasis may be an important factor in the pathobiology of brain injury. Fluctuations in zinc are hypothesized to be neurotoxic, potentially through excitotoxicity, and are thought to contribute to neurodegeneration. This animal study assessed the effect of a zinc chelator, PBT2, for the treatment of acute brain injury.

The subjects were male mice, all of whom underwent controlled cortical impact, designed to produce a TBI. The animals were then randomized to be gavaged with vehicle or PBT2 30mg/kg once per day for the duration of the study. All underwent behavioral assessment, followed by postmortem histological assessment.

At 24 hours, no significant difference in lesion volume was seen between the treatment and control groups. At seven days, however, the PBT2 group had a significantly smaller lesion area ($p=0.01$). Histological assessment demonstrated a greater decrease in lesion area and a greater increase in the numbers of neurons in the treatment group, as compared to the control group. In addition, cognitive assessment, using the Y-maze test, and motor assessment, using a rotarod test, were normalized in the treatment group and maintained throughout the 26 days of the study.

Conclusion: This animal study provides evidence that a metal chaperone may be effective in reducing the effects of a traumatic brain injury.

Portbury, S., et al. Metal Chaperones: A Novel Therapeutic Strategy for Brain Injury? **Brain Inj.** 2019; 33 (3):305-312.

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