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ACUTE EFFECTS OF VITAMIN D3 SUPPLEMENTATION ON MUSCLE STRENGTH

Vitamin D is a complex hormone involved in a wide range of functions, with research confirming the link between muscle function and 25(OH) D3. This study examined whether vitamin D supplementation significantly increases serum 25(OH) D as well as muscle function in indoor athletes.

This prospective study included male, white, national level, judoka athletes, involved in full-time training. The group was randomized to receive either vitamin D3 (150,000 IU) or a placebo. All participants were assessed twice, eight days apart, before the start of training and after two days of rest. The subjects underwent anthromorphic measurements, blood tests, and muscle function tests. Concentric quadriceps and hamstring muscle function were measured using an isokinetic dynamometer.

At baseline the Judo athletes demonstrated insufficient levels of 25 (OH) D. The treatment group demonstrated a 34% increase in serum 25 (OH) D levels between days one and eight, while the placebo group remained constant. Muscle strength increased by a mean of 13% between days one and eight in the treatment group and by three percent in the placebo group.

Conclusion: This study of high-level indoor (judo) athletes found that levels of vitamin D were generally low at baseline, and that vitamin D supplementation resulted in significant increases in muscle strength within eight days.

Wyon, A., et al. Acute Effects of Vitamin D3 Supplementation on Muscle Strength in Judoka Athletes: A Randomized, Placebo Controlled, Double-Blind Trial. **Clin J Sport Med**. 2016, July; 26(4): 279-284.

VITAMIN D DEFICIENCY AMONG PROFESSIONAL BASKETBALL PLAYERS

Previous studies have shown an effect of vitamin D on muscle function and recovery. As vitamin D has been linked to a deficiency in sunlight exposure, indoor athletes may be at particular risk. This study investigated the prevalence of vitamin D deficiency among players in the National Basketball Association (NBA).

This retrospective study included participants in the NBA Combines 2009 to 2013. Data obtained included age, height, weight, body mass index and vitamin D level. Vitamin D deficiency was defined as below 20 ng/mL, insufficiency between 20 and 32 ng/mL and sufficiency as above 32 ng/mL. Data were reviewed to assess the relationship between any player parameter and vitamin D status.

Among the 279 players evaluated, 32.3% were vitamin D deficient. In addition, 47% were vitamin D insufficient. Only 20.8% were vitamin D sufficient. Vitamin D level was positively but weakly correlated with both height (p=0.002) and weight (p=0.012).

Conclusion: This study found a high prevalence of vitamin D deficiency and insufficiency among players attending the NBA Combine.

Fishman, M., et al. Vitamin D Deficiency among Professional Basketball Players. **Orthop J Sports Med**, July; 4(7): 2325967116655742.

CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY AND FALLS

It has been reported that up to 30 to 70% of patients receiving neurotoxic chemotherapy develop neuropathy. This prospective study monitored the severity of chemotherapy-related symptoms and the severity of falls among those beginning chemotherapy.

This study was a secondary analysis of a prospective, observational study using an automated telephone system to query patients receiving chemotherapy. The system used a series of questions developed by experts to track multiple chemotherapy-related adverse events. For each affirmative response, the severity level of the distress it caused was tracked. The primary outcome of the study was falls, with falls and near falls grouped as a single outcome. The patients were asked to call on the first day of the first cycle of their chemotherapy, and then daily for one chemotherapy protocol, or six months of therapy. Those with numbness and tingling severity scores of three or greater (on a one to ten scale) for 10 or more days were considered to have significant chemotherapy-induced peripheral neuropathy (CIPN).

A total of 116 patients, with an average age of 55.5 years, completed the study. During the study, 24 participants had a total of 74 fall events, including 37 falls and 37 near falls. Of those with CIPN symptoms 34.3% had falls, as compared with 15.4% of those without CIPN symptoms (p=0.03). In an adjusted analysis, those with CIPN symptoms were 2.5 times more likely to have a fall event (p<0.001) than were those without. There was no significant difference in the rate of injuries between those with CIPN symptoms and those without.

Conclusion: This study of patients receiving neurotoxic chemotherapy found that those with persistent numbness and tingling had a substantially higher risk of falling than did those without such symptoms.

Kolb, N et al. The Association of Chemotherapy-Induced Peripheral Neuropathy Symptoms and the Risk

of Falling. **JAMA Neurol.** 2016. July; 73(7): 860-866.

CHOCOLATE CONSUMPTION AND INSULIN RESISTANCE

Obesity, diabetes and insulin resistance are well known risk factors for cardiovascular disease. Recent studies have suggested that cocoa beans and their derivatives contain physiologically active compounds, including polyphenols and their flavonoid subclasses that may have health benefits. This study evaluated the effect of chocolate consumption on insulin sensitivity and liver enzymes.

Data were obtained from the Observation of Cardiovascular Risk Factors in Luxembourg (ORISCAV-LUX) survey, a nationwide, population based, cross-sectional study of the adult population. A stratified, random sample of 1,154 participants, ages 18 to 69 years were recruited. Data collected included chocolate consumption, as estimated by a food frequency questionnaire, demographic and socioeconomic data, tobacco use, physical activity, body mass index and total daily energy intake. Labs were drawn to determine lipid biomarkers and insulin resistance. The data were reviewed to compare demographic, lifestyle and cardiometabolic characteristics across the groups according to chocolate consumption.

More than 80% of the subjects reported chocolate consumption. A multivariable regression analysis found an inverse relationship between all liver biomarkers and chocolate consumption. Daily chocolate consumption was significantly associated with lower insulin resistance HOMA-IR (p=0.004), serum insulin levels (p=0.003) and liver enzymes, including γ-GT (p=0.009) and ALT (p=0.004). Daily consumption of 100 g of chocolate was associated with a reduction of HOMA-IR (insulin resistance) by 0.16, of serum insulin levels by 0.16 µg/l and of liver enzymes (γ-GT, ALT) by >0.10 mg/l.

Conclusion: This cross-sectional, population-based study of healthy adults found an inverse association between daily chocolate consumption and insulin resistance, serum insulin and liver enzymes.

Alkerwi, A., et al. Daily Chocolate Consumption Is Inversely Associated with Insulin Resistance and Liver Enzymes in the Observation of Cardiovascular Risk Factors in Luxembourg Study. **Br J Nutr.** 2016, May 14; 115(9): 1661-1668.

UNLOADING SHOES FOR KNEE OSTEOARTHRITIS

Previous studies have suggested that 10 -25% of women and 5 -15% of men, 60 years of age or older, have knee osteoarthritis (OA). Recent research has focused on the development of unloading shoes which reduce medial knee loads through changes in foot and ankle biomechanics. This study was designed to determine whether such shoes can reduce pain and physical dysfunction associated with knee OA.

This randomized, controlled trial included adults, 50 years of age or older, with knee pain on most days of the previous months, and with radiographic evidence of medial tibiofemoral OA. The subjects were randomly assigned to wear either unloading walking shoes, which significantly reduced measures of load across the medial knee, or commercially available, neutral walking shoes. The participants were asked to wear the shoes as much as possible during the day for six months and to avoid changing shoes. The primary outcome measures were self-reported pain and physical function, as measured with the numerical rating scale (NRS) and the Western Ontario and McMaster University Osteoarthritis index (WOMAC), at six months.

At six months, 160 had completed the questionnaires. While both groups reported improvement in function, no significant difference was found between groups in scores on the NRS or the WOMAC.

Conclusion: This study of patients with osteoarthritis did not find that shoes designed to unload the medial compartment of the knee reduced pain or improved function as compared with conventional shoes.

Hinman, R., et al. Unloading Shoes for Self-Management of Knee Osteoarthritis: A Randomized Trial. **Ann Intern Med** 2016. doi: 10.7326/M16-0453.

RESISTANCE TRAINING, MUSCLE MASS AND STRENGTH IN THE ELDERLY

Resistance training (RT) is important from the fifth to sixth decades of life, to control sarcopenia, as well as to enhance mobility and quality of life. Despite the efficacy of RT performed with heavy loads, some have suggested that strength and muscle mass gains are also achievable with lighter loads. This literature review and meta-analysis compared the efficacy of heavy and light load RT in elderly cohorts.

Online databases were reviewed to retrieve studies comparing the effects of light to moderate RT to conventional, intense RT programs. Intense RT was defined as the use of loads of 80% of a one rep maximum or higher, while low to moderate RT was defined as using loads of 60% of a one rep maximum or lower.

Fifteen studies were included in the analysis, including data from 448 subjects. Training was performed three times per week in all studies. The total population effect favored high intensity RT, although this finding failed to reach statistical significance ($p=0.06$). Compared to no-training control groups, both training interventions were found to provoke strong significant gains in muscle strength ($p<0.001$ for both comparisons). When matching for the amount of work, average increases in strength were 43% in the high and 35% in the moderate load RT groups. All studies found training with higher intensities of load to be more effective in provoking muscle hypertrophy.

Conclusion: This meta-analysis found that both intensive and light to moderate load resistance training programs can increase skeletal muscle mass and strength in elderly cohorts.

Csapo, R., et al. Effects of Resistance Training with Moderate versus Heavy Loads on Muscle Mass and Strength in the Elderly: A Meta-Analysis. **Scand J Med Sci Sports.** 2016, Sept; 26(9): 995-1006.

ISOMETRIC AND ISOTONIC EXERCISE REDUCES SYMPTOMATIC PATELLAR TENDINOPATHY

Patellar tendinopathy, also known as jumper's knee, is common in sports that involve jumping motions. As isometric exercise been found to decrease tendon pain in the short term, this study compared the effects of isometric and isotonic exercises during an athletic season.

Participants were volleyball and basketball players, 16 to 32 years of age, presenting with patellar tendinopathy. After baseline measures were obtained, the subjects were randomized to participate in an exercise program involving either isometric exercises, performed at 80% of maximum voluntary contraction with a knee joint angle of 60°, or isotonic exercises, at 80% of an eight repetition max. The primary outcome variable was pain during a single leg decline squat (SLDS), scored on a numeric rating scale, as well as the VISA-P, a questionnaire assessing the pain and function of the knee. The participants were also asked to rate the global rate of change of their patella pain from much worse (-4) to much better (+4).

Thirteen patients were randomized to the isometric group and 16 to the isotonic group. The median pain scores improved significantly over the four weeks of intervention in the isometric ($p=0.012$) and the isotonic ($p=0.003$) group. There was no significant difference between groups. In addition, the median VISA-P scores improved in both groups over the four weeks of intervention, with no difference between groups.

Conclusion: This study of basketball and volleyball players with patella tendinopathy, found that treatment during the season with both isometric and isotonic exercise could reduce pain over a four-week trial.

van Ark, M., et al. Do Isometric and Isotonic Programs Reduce Pain in Athletes with Patellar Tendinopathy in -Season? A Randomized Clinical Trial. **J Sci Med Sport**. 2016, September; 19(9): 702-706.

ISOMETRIC VERSUS ISOTONIC CONTRACTIONS FOR PATELLAR TENDON PAIN

Patellar tendon pain is often treated with exercise, injections, shockwave therapy and/or medications. While a number exercise therapies have been suggested for patellar tendinopathy, few studies have compared the effects of different exercise regimens on immediate analgesia. This study compared the acute effects of isotonic contractions with isometric contractions as an intervention for patellar tendon pain.

This randomized, clinical trial included 29 male and female volleyball and basketball athletes over 16 years of age. All were assessed at baseline with the VISA-P, a questionnaire of patellar pain and athletic function. The subjects were then randomized to receive one of two resistance protocols, isometric leg extension with the knee at 60° knee flexion, or isotonic exercises at 80%of the eight repetition maximum. All exercises were completed four times per week for a period of four weeks. The primary outcome measure was pain (VAS pain scale) experience during a single leg decline squat (SLDS) before and after each intervention session. The secondary outcome variable was the change in the VISA-P between baseline and week four.

The immediate reduction in pain between pre-measures and post-measures of each intervention session was greater for the isometric group than for the isotonic group ($p<0.001$). Both groups realized improvement on the VISA-P over the four weeks, with no significant difference between groups.

Conclusion: This study of patients with patellar tendon pain found that immediate analgesia was superior with isometric leg extension than with isotonic exercise.

Rio, E., et al. Isometric Contractions Are More Analgesic than Isotonic Contractions for Patellar Tendon Pain: An In-Season Randomized Clinical Trial. **Clin J Sport Med.** 2016; DOI:10.0:1097/JSM . 000000000000000364

INJECTIONS VERSUS HYDRODILATION FOR FROZEN SHOULDER

Frozen shoulder, also known as adhesive capsulitis, is a common disease that results in restricted passive and active range of motion in the glenohumeral (GH) joint. If conservative measures fail, treatment for this disorder may include intra-articular (IA) injections, subacromial (SA) injections or IA hydrodilation

(HD). This study compared these three injection techniques for their ability to improve range of motion, function and pain.

Subjects were 164 consecutive patients with primary frozen shoulder, all of whom were unresponsive to conservative treatment. All patients were assessed using a VAS for pain, the Simple Shoulder Test, a Constant Score and passive range of motion at baseline and up to six months after treatment. The intraarticular group (IA) received 1 mL of triamcinolone (40 mg), 4 mL of 2% lidocaine and 5 mL of normal saline, injected into the GH joint. The HD group were injected with 4 mL of contrast medium for joint space confirmation, and then 1 mL of triamcinolone (40 mg), 4 mL of 2% lidocaine, and 40 mL of normal saline into the GH joint. The SA group received 1 mL of triamcinolone (40 mg), 4 mL of 2% lidocaine and 5 mL of normal saline at the subacromial space.

Improvements from baseline to six months were noted for all measures in all groups (all p<0.001). Every patient in each group was satisfied with his or her results at six months. At one month, VAS scores were significantly more improved in the HD group than in the intra-articular group (p=0.035), with no significant differences between groups noted at three and six months. The HD group demonstrated better ROM and functional scores in the early follow-up, with no difference between groups at six months.

Conclusion: This study of patients with adhesive capsulitis found that, among three injection methods tested, hydrodilation resulted in better pain scores and range of motion at one month, with better functional scores up to three months after injection, with no difference between the injection methods at six months.

Yoon, J., et al. Intra-Articular Injection, Subacromial Injection, and Hydrodilation for Primary Frozen Shoulder: A Randomized, Clinical Trial. **J Shoulder Elbow Surg**. 2016, March; 25(3): 376-383.

RESTORING CORTICAL CONTROL OF MOVEMENT IN QUADRIPLEGIA

Previous studies have shown that intracortically recorded signals can be decoded to provide information related to motion, allowing nonhuman primates and paralyzed humans to control computers and robotic arms. This study demonstrates a real-time application of the use of such devices in a human with quadraplegia.

This subject was a 24-year-old male with stable, non-spastic, C5-6 quadriplegia, sustained four years prior to the study. The patient underwent the implantation of a microelectrode array at his left primary motor cortex. He was then trained to use his neuronal activity to control a neuromuscular electrical stimulator, positioned to allow for six different wrist and hand motions. To test the system, five trials of the six movements were performed.

During the trials, the subject achieved overall accuracy of 70%, ranging up to 93% for wrist flexion and 97.3% for thumb flexion. Assessing the upper limb function, using the Gradient and Redefined Assessment of Strength, Sensibility and Prehension (GRASSP), it was determined that the C5-C6 participant gained wrist and hand function consistent with a C7–T1 level of injury.

Conclusion: This case demonstrated, for the first time, that a human with quadriplegia could regain volitional movement through the use of intracortically recorded signals linked to neuromuscular signals in real time.

Bouton, C., et al. Restoring Cortical Control of Functional Movement in a Human with Quadriplegia. **Nature**. 2016, May 12; 533(7602): 247-250.

CAPSULAR RELEASE FOR ADHESIVE CAPSULITIS

Adhesive capsulitis of the shoulder is marked by the spontaneous onset of worsening shoulder pain and limited active and passive range of motion. Surgical options for recalcitrant cases include open release, manipulation under anesthesia or arthroscopic release. This study evaluated short-term recovery following arthroscopic capsular release of idiopathic adhesive capsulitis.

This retrospective study included adults, clinically diagnosed with idiopathic adhesive capsulitis, all with shoulder symptoms of at least four weeks' duration. All patients underwent arthroscopic capsular release. Before surgery, the subjects completed a standardized questionnaire evaluating shoulder pain and function, based on the Shoulder Rating Questionnaire. An independent examiner assessed shoulder strength and range of motion at baseline and at weeks one, six, 12 and 24.

Participants included 88 women and 45 men, with a mean age of 56 years. After release, the patients experienced immediate improvement in all ranges of shoulder motion (p<0.0001). External range of motion had a mean preoperative range of 21°, increasing to 76° after surgery, and regressing to 49° at 12 weeks, where it remained steady for the duration of the study. This pattern was similar for all other ranges of motion measured. At six, 12 and 24 weeks all ranges of motion were significantly better than before surgery. Activity pain was reported as "always" in 64% before surgery and in 22% at 24 weeks. Frequency of pain during sleep was "always" in 65% before surgery and in 16% at 24 weeks. Extreme pain was reported by 38% preoperatively and by 2% at 24 weeks. Overall shoulder function was rated as good by 0% preoperatively and by 45% at 24 weeks.

Conclusion: This study demonstrates that arthroscopic capsular release for patients with idiopathic adhesive capsulitis resulted in significant improvements in shoulder pain, function and range of motion within one week, with significant improvement persisting at 24 weeks.

Barnes, C., et al. Short-Term Outcomes after Arthroscopic Capsular Release for Adhesive Capsulitis. **J Shoulder Elbow Surg**. 2016, September; 25(9): e256-e264.

BLOOD PRESSURE, GLUCOSE AND TEMPERATURE AFTER CHILDHOOD STROKE

Few evidence based guidelines exist for the management of blood pressure, glucose levels or body temperature after a pediatric ischemic stroke. This study examined the association between blood pressure, hyperglycemia and fever with neurologic outcome in children after ischemic stroke.

This retrospective review included children with acute ischemic stroke,

ages 29 days to 18 years. Data collected for all patients included blood pressure, blood glucose levels and temperature from admission to hospital day five. Hyperglycemia was defined as a blood glucose level of 200 mg/dL or more and hypoglycemia as a blood glucose level less than 60 mg/dL. Hyperpyrexia was defined as an axillary temperature of 37.8°C or higher. Hypertension was defined as a systolic blood pressure and/or diastolic blood pressure at the 95th percentile or higher, while hypotension was defined as below the fifth percentile. The main outcome measure was a neurologic evaluation at three-year follow-up, using the Pediatric Stroke Outcome Measure (PSOM).

In the 98 children studied, hypertension was present in 65.3%, hypotension in 68.4%, hyperglycemia in 18.1% and fever in 37.8%. Many children had documented hypertension as well as hypotension. No association was found between hypertension and outcome at three months. Hyperglycemia was independently associated with poor neurologic outcome (p=0.02), while fever was not. Infarcts of four percent or greater of brain volume were associated with poor outcome (p=0.001).

Conclusion: This study of children with acute ischemic stroke found that hyperglycemia and infarct size were independently associated with increased disability at four months. No significant association was found between poor outcome and blood pressure or fever during acute hospitalization.

Grelli, K., et al. Association of Blood Pressure, Blood Glucose and Temperature with Neurological Outcome after Childhood Stroke. **JAMA Neurol.** 2016, July; 73(7): 829 -835.

TICAGRELOR VERSUS ASPIRIN FOR ISCHEMIC STROKE

After an ischemic stroke or transient ischemic attack, the risk of subsequent ischemic events is particularly high during the first 90 days. The role of aspirin for the secondary prevention of ischemic stroke has been found to be limited. As more intensive antiplatelet therapy through a different mechanism of action may be more effective than aspirin, this study compared ticagrelor (an antiplatelet agent that reversibly binds and inhibits the platelet P2Y12 receptor) with aspirin for their effectiveness in preventing major vascular events.

This multiple center, randomized, double-blind study enrolled subjects at 674 sites in 33 countries. Eligible patients presented with an acute ischemic stroke, with a National Institutes of Health Stroke Scale (NIHSS) score of five or lower or a high-risk transient ischemic attack, with an ABCD^2 stroke risk score of ≥four. Subjects who underwent thrombolysis or mechanical thrombectomy within 24 hours before randomization were excluded. The participants were randomly assigned to receive either ticagrelor, 90 mg twice per day, or aspirin, 100 mg per day. The primary endpoint was the time from randomization to the first occurrence of any stroke, myocardial infarction or death.

The primary composite endpoint occurred in 6.7% of the patients receiving ticagrelor and 7.5% of those receiving aspirin (p=0.07). Ischemic stroke occurred in 5.8% of the ticagrelor group and 6.7% of the aspirin group (p=0.046).

Conclusion: This study of patients with acute ischemic stroke or transient ischemic attack found that the primary endpoint, a composite of stroke, myocardial infarction or death, was not significantly less common among patients who received ticagrelor than among patients who received aspirin during a 90-day follow-up period.

Johnston, S., et al. Ticagrelor versus Aspirin in Acute Stroke or Transient Ischemic Attack. **N Eng J Med.** 2016, July 7; 375 (1): 35-43.

SERUM CHOLESTEROL, STATINS AND THE RISK OF INTRACEREBRAL HEMORRHAGE

Several studies have suggested that serum cholesterol is inversely associated with the risk of intracerebral hemorrhage (ICH). Despite the proven benefits of statins for reducing the risk of cardiovascular and cerebrovascular disease, some have raised concerns about the risk of hemorrhagic stroke, mainly ICH, among people treated with these agents. This study was designed to further understand the effect of statins on the relationship between serum cholesterol and intracerebral hemorrhage.

The Multicenter Study on Cerebral Haemorrhage in Italy (MUCH-Italy) investigated the epidemiology, risk factors and consequences of ICH. Eligible subjects had neuroimaging confirmed hemorrhagic stroke. Control subjects were enrolled in this Italian population-based study, recruiting citizens in the Molise region, with these individuals matched with cases by gender and age. The history of vascular risk factors was determined, with pre-ICH medications recorded. Fasting lipid measurements were obtained, with participants classified as non-hypercholesterolemic, hypercholesterolemic under treatment or not under treatment with statins. Patients with ICH were compared to controls.

Data were reviewed for 3,492 patients with ICH and 3,492 control subjects. Compared to control subjects, patients were more likely to have a pre-ICH history of coronary artery disease, hypertension and/or diabetes, and to be prescribed antithrombotic medications. Conversely, these patients were less likely to have a history of hypercholesterolemia. Increasing levels of serum cholesterol were associated with a decreased risk of ICH. Statin use was associated with an increased risk of ICH. The protective effect of serum cholesterol against ICH was reduced by statins, especially in lobar regions of the brain.

Conclusion: This study found that total serum cholesterol concentrations are inversely associated with ICH, with the protective effect of cholesterol reduced by statins, especially in lobar regions of the brain.

Pezzini, A., et al. Serum Cholesterol Levels, HMG COA Reductase Inhibitors and the Risk of Intracerebral Haemorrhage. The Multi -Center Study on Cerebral Haemorrhage in Italy. **J Neurol Neurosurg Psychiatry.** 2016, Sept; 87(9): 924-929.

CAUSES OF UNPLANNED EARLY READMISSION AFTER NEUROSURGERY

Among Medicare patients, the overall rate of readmission within 30

days of hospital discharge is nearly 20%. No large-scale studies of the causes of readmissions in a general neurosurgical population have been previously conducted. This study reviewed the causes of readmission in a broad group of patients cared for by neurosurgery.

Subjects were patients 18 years of age or older, admitted for neurosurgical or neuroendovascular procedures between January of 2009 and November of 2012. Using ICD-9 codes, the patients were classified according to one of four subgroups: cranial procedures with craniotomy, cranial procedures without craniotomy, spinal procedures and neuroendovascular procedures.

Of the 163,743 adult admissions, 2,791 were readmitted within 30 days of discharge, for an overall rate of 9.03%. Excluding those with elective or planned readmissions, the overall rate of unplanned readmissions was 8.63%. Of the four subgroups, spine procedures had the lowest rate, at 6.46%, followed by cranial non-craniotomy procedures, at 8.64%, neuroendovascular procedures, at 9.26%, and cranial craniotomy, at 15.88%. The most common causes of unplanned readmission were infection in 29.52%, other medical complications in 19.22%, new neurologic signs or symptoms in 8.68%, stroke in 6.09% and venous thromboembolism in 5.71%. The readmissions due to stroke occurred in 12.82% of the craniotomies. The median time to unplanned readmission was 10 days.

Conclusion: This study of a large group of neurosurgery patients found that the overall rate of unplanned readmission was 8.63%, with the most common reasons for readmission including infection and other medical complications.

Taylor, B., et al. Causes and Timing of Unplanned Early Readmission after Neurosurgery. **Neurosurg.** 2016, September; 79: 356-369.

LIMAPROST VERSUS PREGABALIN FOR LUMBAR SPINAL STENOSIS

Lumbar spinal stenosis (LSS) can produce neurogenic claudication. Some have recently suggested that neuropathic pain mechanisms are important in the genesis of leg pain among patients with LSS. Limaprost is a prostaglandin E1 derivative with effects that include the inhibition of platelet aggregation, improvement of erythrocyte deformability and inhibition of reactive oxygen production, in addition to potent vasodilation. As this medication can improve peripheral arterial circulation and increase blood flow in compressed nerve issue, pain can be improved in patients with LSS. This study compared the effect of this medication with that of gabapentin.

This prospective, double-blind, randomized trial included patients with LSS who were 20 to 75 years of age. The patients were divided into treatment groups to receive limaprost, at five micrograms three times daily, pregabalin, at 75 mg three times daily, or the combination of the two three times daily. The primary outcome measure was the Oswestry Disability Index (ODI) score at 8 weeks after treatment.

At eight weeks, data were available for 126 participants. Changes of the baseline-adjusted ODI scores, VAS scores for leg pain, EQ-5D scores and initial claudication distance during the follow-up assessments did not differ among the three groups. Compared with the limaprost group, the other two groups showed a significantly higher incidence of drug-related, adverse events (p=0.002 and p=0.009).

Conclusion: This study of patients with lumbar spine stenosis and neurogenic claudication found that limaprost is not inferior to pregabalin for the treatment of lumbar spine stenosis. No advantage was found by combining the two medications.

Kim, H., et al. Comparative Study of the Efficacy of Limaprost and Pregabalin as Single Agents and in Combination for the Treatment of Lumbar Spinal Stenosis: A Prospective, Double-Blind, Randomized, Controlled, Non-Inferiority Trial. **Spine J.** 2016, June; 16(6): 756-763.

TRAUMATIC BRAIN INJURY AND EARLY-ONSET FRONTOTEMPORAL DEMENTIA

The association between a history of traumatic brain injury (TBI) and the development of dementia has not been clarified in the literature. This study further examined whether TBI, with loss of consciousness, is associated with an earlier age of symptom onset among patients diagnosed with behavioral variant of frontotemporal dementia (bvFTD).

Since September of 2005, the National Alzheimer's Coordinating Centers have maintained an integrated database, with information gathered from 34 past Alzheimer's disease centers across the United States. From this database, data concerning patients with bvFTD were obtained. Subjects were queried for a history of TBI with loss of consciousness (TBI +).

Data were obtained for 678 patients with bvFTD. Of these, 75 reported a history of TBI + and 603 did not. Adjusting for gender, the age of symptom onset was 2.8 years earlier and the age of diagnosis 3.2 years earlier among those in the TBI + group than among the non-TBI group.

Conclusion: This study of patients with diagnoses of bvFTD found that a history of traumatic brain injury with a loss of consciousness is associated with earlier symptom onset and earlier age of diagnosis than among those with no history of TBI.

LoBue, C., et al. Traumatic Brain History is Associated with Earlier Age of Onset of Frontotemporal Dementia. **J Neurol Neurosurg Psychiatry**. 2016, August; 87(8): 817-820.

CONTINUOUS VERSUS ON-DEMAND DICLOFENAC FOR ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) is defined by the presence of structural bone damage, visible on x-rays of the sacroiliac joints and/or spine. This study was designed to determine whether nonsteroidal anti-inflammatory drugs (NSAIDs), given continuously, can reduce the progression of radiographic evidence of AS, as compared with NSAID on-demand therapy.

The Effects of Nonsteroidal Anti-Inflammatory Drugs on Radiographic Damage in AS (ENRADAS) study was a prospective, randomized, controlled trial conducted in 19 German centers. Using a block randomization method, patients were assigned to treatment with diclofenac continuously, at a dose of at least 50% of the maximally recommended

daily dose (150mg), or on demand, for a period of two years. The primary outcome variable was spinal radiographic progression, assessed by the change in the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Data concerning NSAID intake were collected at baseline and every 12 weeks thereafter during the two years of follow-up.

After correcting for baseline, the mean Bath Ankylosing Spondylitis Disease Activity Index values decreased during the two years of treatment to 2.7 in the continuous group and 3.2 in the on-demand group. The mSASSS progression, while numerically higher in the continuous group, was not significantly different than that for the on-demand group. In addition, looking only those who were C-reactive protein positive or had syndesmophytes at baseline, higher radiographic progression was noted in the continuous, as compared to the on-demand, group.

Conclusion: This study of patients with ankylosing spondylitis did not find that the use of continuous nonsteroidal anti-inflammatory drug treatment would reduce the progression of the disease more than on-demand medication.

Sieper, J., et al. Effect of Continuous versus on-Demand Treatment of Ankylosing Spondylitis with Diclofenac of Two Years on Radiographic Progression of the Spine: Results from a Randomized, Multicenter Trial (ENRADAS). **Ann Rheum Dis.** 2016, August; 75(8): 1438-1443.

TREATMENT OF ANKYLOSING SPONDYLITIS

For patients with ankylosing spondylitis (AS), nonsteroidal anti-inflammatory drugs (NSAIDs), and tumor necrosis factor-Alpha targeted therapies have proven efficacy. This study assessed the efficacy of treating patients with both medications, as compared to NSAIDs alone.

In the Infliximab as First-Line Therapy in Patients with Early Active Axial Spondyloarthropathies Trial (INFAST), patients with early active disease who had been treated with suboptimal doses of NSAIDs were selected. The patients were treated with naproxen 1000mg (if tolerated) plus either infliximab or placebo for 28 weeks. A post-hoc analysis of these data evaluated outcomes to determine who did or did not meet modified New York radiographic criteria for AS. The main efficacy measure was the percentage of patients who met the Assessment of SpondyloArthritis International Society (ASAS) partial remission criteria at 28 weeks.

The subjects included 94 patients who met AS criteria and 56 with non-radiographic axial SpA (nr-axSpA). For both the AS and the nr-axSpA groups, partial remission rates at week 28 were greater in the combination than in the naproxen group. The treatment effect was greater in the AS group than in the nr-axSpA group (p=0.0009 vs p=0.55). In addition, for both subgroups, the combination therapy group scored better on the BASDAI, ASDAS, BASFI and EuroQoL five-dimension questionnaires (EQ-5D).

Conclusion: This study of patients with early, active axial SpA found that greater partial remission occurs when treatment involves a combination of nonsteroidal anti-inflammatory therapy and infliximab than with non-steroidal anti-inflammatory therapy alone.

Sieper, J., et al. Partial Remission in Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthropathies Treatment with Infliximab plus Naproxen or Naproxen Alone: Associations between Partial Remission and Baseline Disease Characteristics. **Rheum**. 2016; 263: doi:10.1093/rheumatology/kew230

COMMUNITY ACQUIRED MRSA IN HIGH SCHOOL AND COLLEGIATE ATHLETES

Community acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) accounts for approximately 45% of all MRSA related hospitalizations. As athletes are a high risk population for this infection, this study assessed the standard of care and yearly incidence of CA-MRSA infections in high school and intercollegiate athletics settings.

Data were collected from 156 athletic trainers for the season 2012-2013, and 87 athletic trainers for the 2013- 2014 season. Questionnaires were distributed to determine demographic information, cases of physician confirmed CA-MRSA infection, and the treatment provided to those infected.

During the first season, 29% of the respondents reported a minimum of one CA-MRSA infection during the athletic year. Overall, the rates were 15.5 and 16.3 per 10,000 athletes in the 2012-2013 and 2013- 2014 seasons, respectively. The majority of infections occurred among football players (36%), followed by wrestlers (26%). The rates for wrestling and football were 90.2 and 42.3 respectively, per 10,000 athletes in the 2012-2013 season and 89 and 61.4 respectively per 10,000, in the 2013-2014 season. Isolation and decontamination were common school responses to these infections, with 60% of the athletes referred to their PCP for treatment.

Conclusion: This study of community acquired MRSA infections in high school and college athletes found the highest risk among those participating in wrestling and football.

Braun, T., et al. CA-MRSA Infection Incidence and Care in High School and Intercollegiate Athletics. **Med Sci Sports Exer**. 2016. August; 48 (8):1530-1538.

OFFLOADING FOOTWEAR FOR NEUROPATHIC DIABETIC FOOT ULCERS

Ulceration is thought to be responsible for up to 85% of diabetic foot amputations. Despite the efficacy of treatment with offloading, using total contact casts (TCCs), data suggest that this treatment is markedly underused. Suggesting that the underuse of TCC may be related to technical limitations, costs and acceptance by patients, the authors of this study compared the clinical efficacy of TCC with both removable and non-removable, commercially available, walking boots.

Subjects were patients with diabetic foot ulcers of at least one cm^2, stage IA or IIA. The patients were randomized to receive a total contact fiberglass cast (group A) or the Optima Diab Walker, either rendered irremovable by the application of a locking strap (group B) or maintained as removable (group C). The removable group was instructed to wear the device on all occasions, avoiding the use of other

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shoes or walking barefoot. All participants were followed weekly for up to 90 days or until the lesions had healed.

At follow-up, 95% had achieved complete healing in group A, as had 90% in group B and 80% in group C. The mean healing times of the three groups did not differ significantly. No severe, adverse effects were observed in the three groups throughout the duration of the study. Patient satisfaction was significantly higher in group C than in the other groups ($p<0.05$). When normalized for days treated, treatment costs were significantly higher in group A than in the other two groups.

Conclusion: This study of patients with diabetic foot ulcers demonstrated that an off-the-shelf walking boot was as effective and safe as a total contact cast for the healing of the ulcers. Patients preferred the removable device.

Piaggesi, A., et al. Comparison of Removable and Irremovable Walking Total Contact Casting in Offloading the Neuropathic Diabetic Foot Ulceration. **Foot Ankle Intern**. 2016, August; 37(8): 855-861.

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