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TARGETING RULE AND NFL CONCUSSIONS

Prior to the 2018 season, the National Football League (NFL) instituted a playing rule (Rule Eight), which forbids lowering the head to make contact with an opponent, termed "targeting". This study assessed whether the initiation of this rule has affected the occurrence of head injuries in the NFL.

This retrospective study included all NFL players from the 2016 through 2020 regular seasons. Data were obtained from weekly injury reports, detailing the name of the injured player, and a brief description of each injury. The records were used to collect demographic information. Injury rates before and after the initiation of the new targeting rule were compared.

During the study period, 479 concussions were reported, of which 62.4% occurred during the two years prior and 37.6% during the two years after initiation of the rule. The relative risks of concussion per athletic encounter (AE) were 3.3/1000 AEs after and 5.5/1000 before (RR 0.60) the rule change. This finding represents a 40% decrease in sport related concussion.

Conclusion: This study of injuries in the National Football League points to a significant reduction in sports related concussions after a rule change which disallowed the lowering of a helmet to initiate contact during competition.

Baker, H., et al. Playing Rule Article Eight Decreases the Rate of Sports Related Concussions in NFL Players over Two Seasons. **Physician Sports Med.** 2020. DOI: 10.1080/00913847.2020.1836945.

RIVAROXABAN IN PATIENTS WITH ATRIAL FIBRILLATION AND A BIOPROSTHETIC MITRAL VALVE

For patients with non-valvular atrial fibrillation (AF) the ROCKET-AF trial demonstrated that rivaroxaban is noninferior to warfarin for the prevention of stroke or systemic embolism. This study, the Rivaroxaban for Valvular Heart Disease and Atrial Fibrillation (RIVER), compared the efficacy and safety of Rivaroxaban to that of warfarin for the treatment of patients with AF and a bioprosthetic mitral valve.

Subjects were adult patients with permanent, paroxysmal or persistent AF or flutter and a bioprosthetic mitral valve. The subjects were randomized to receive rivaroxaban 20 mg daily or warfarin adjusted to an international normalized ratio (INR) of 2-3. The primary outcome variables were composite death, major cardiovascular events or major bleeding at 12 months.

A total of 1,005 patients were randomized. The mean time to reach the primary outcome was 347.5 days in the rivaroxaban group and 340.1 days in the warfarin group ($p<0.0001$). At 12 months, a composite, secondary outcome of death from cardiovascular causes or thromboembolic events occurred in 3.4% of the rivaroxaban group and in 5.1% of the warfarin group (hazard ratio [HR] 0.65) The incidence of stroke was 0.6% in the rivaroxaban group and 2.4% in the warfarin group (HR 0.25). Major bleeding events occurred in 1.4% of the rivaroxaban group and 2.6% of the warfarin group (HR 0.54).

Conclusion: This study of patients with atrial fibrillation who had undergone bioprosthetic mitral valve surgery found that rivaroxaban was noninferior to warfarin with respect to the mean time until the primary outcome of death, major cardiovascular events, or major bleeding at 12 months.

Guimaraes, H., et al. Rivaroxaban in Patients with Atrial Fibrillation and a Bioprosthetic Mitral Valve. **N Engl J Med**. 2020, November 26; 383 (22):2117-2126.

LONGITUDINAL PATTERNS OF PAIN IN OLDER ADULTS

Cross-sectional studies have found that pain and pain related functional limitations among older adults are common, though less is known concerning the longitudinal pattern of this pain. This study was designed to better understand the trajectories of pain in older adults

This retrospective cohort study used longitudinal data from the population based National Health and Aging Trends Study (NHATS), prospective cohort of community based ambulatory Medicare beneficiaries age 65 years or older. Data were collected annually for six years, including demographics, health characteristics including smoking, body mass index, self-rated health, number of pain sites, comorbid health conditions, the Patient Health Questionnaire–2 for depression, and the Generalized Anxiety Disorder–2 for anxiety, self-reported falls, and usual gait speed physical capacity measured by the Short Physical Performance Battery.

Summarized data for 6,783 adults found that in the prior month, 25% had used pain medications five to seven times per week. Pain trajectories were characterized as persisting, high bothersome pain (PH) in 35%, decreasing bothersome pain (DP) in 17%, increasing bothersome pain (IP) in 17%, and low bothersome pain (LP) in 32%. The same categories were produced for activity limiting pain. An adjusted logistic regression found that, compared to the LP group, a greater probability of PH was found in females, those with lower education, lower income, obesity, Medicaid coverage, fair or poor self-rated health, a greater number of comorbid health conditions, depression, anxiety and dementia.

Conclusion: This longitudinal study of elderly Medicare recipients found that 25% used pain medicine nearly every day and over half of older adults had either persistently high or increasingly bothersome pain.

Rundell, S., et al. Longitudinal Patterns of Pain Reporting among Community Dwelling, Older Adults. **Clin J Pain**. 2020, December; 36 (12): 912-922.

BEDSIDE PORTABLE LOW FIELD MAGNETIC RESONANCE IMAGING

In patients admitted to an intensive care unit (ICU), transportation to imaging suites can be cumbersome and often dangerous, particularly in the era of COVID-19. This study assessed a novel bedside neuroimaging device using a low energy (0.064-T) MRI (LE -MRI) for patients with COVID in a neuroscience intensive care unit. The LE-MRI has a five-Gauss (0.0005-T) safety perimeter and a radius of 79 cm from the center of the magnet.

The subjects were fifty patients admitted to the ICU with a diagnosis of acute brain injury. Scans were performed for those who demonstrated any neurological alteration during clinical examination requiring imaging. LE-MRI examinations were performed at the bedside using an eight-channel head coil. Twenty-nine patients (97%) also underwent conventional imaging, and were used for comparison.

Diagnostic-grade T1W, T2W, T2 FLAIR and DWI sequences were obtained for 37, 48, 45 and 32 patients, respectively. The mean examination time was 35 minutes and 40 seconds. All but one of the LE-MRI findings were in agreement with available conventional radiology reports. The exception was a finding of a diffuse subarachnoid hemorrhage ($p<0.001$).

Conclusion: This study demonstrates the feasibility of a low yield, portable MRI for use in the intensive care unit.

Sheth, K., et al. Assessment of Brain Injury Using Portable, Low Field Magnetic Resonance Imaging at the Bedside of Critically Ill Patients. **JAMA Neurol.** Published online September 08, 2020. doi:10.1001/ jamaneurol.2020.3263.

CHRONIC INFLAMMATORY POLYNEUROPATHY AND FATIGUE

Chronic inflammatory de-myelinating polyneuropathy (CIDP) is characterized by progressive or relapsing weakness or numbness. As fatigue can persist for years in patients with Guillain-Barre Syndrome (GBS), this study assessed fatigue among those with active CIDP and those with CIDP in remission.

This cross-sectional, multicenter study involved consecutive patients with CIDP between 2015 and 2017. The subjects were stratified as displaying active or immunotherapy-free remission status, as defined by CIDP disease activity status (CDAS). The clinical status was refined as cure (CDAS-1), remission (CDAS-2), stable active disease (CDAS-3), improvement on immunotherapy (CDAS-4) or unstable active disease (CDAS-5). Those with CDAS classifications of three, four, and five were grouped as active (A), whereas those classified as CDAS 1 or 2 were grouped as in remission(R). All participants were assessed for physical impairment, disability, fatigue, depression, sleepiness and sleep quality.

Eighty-five patients were enrolled in the study. Fatigue severity as measured by the Fatigue Severity Scale (FSS) was greater among those in the A group as compared to those in group R ($p=0.02$). Excessive or greater sleepiness (Epstein Sleepiness Scale (ESS) scores of >10) was reported by 39.1% of those in group A and 20.5% of those in group R. Only fatigue (with no excess sleepiness) was reported by 39% of group A and 46% of group R. Compared with healthy controls, both the A and R groups had significantly more fatigue overall ($p= 0.0001$). Poor sleep quality was reported by 73.9% of those in group A and 64.1% of those in group R.

Conclusion: This cross-sectional study of patients with chronic inflammatory demyelinating polyneuropathy found that fatigue is a common complaint, even among those in remission.

Gable, K., et al. Fatigue in Chronic Inflammatory Demyelinating Polyneuropathy. **Musc Nerve**. 2020, December; 62(6): 673-680.

PULSED RADIOFREQUENCY FOR HERPETIC NEURALGIA

Herpes zoster (HZ), resulting from the reactivation of latent varicella zoster, has a lifetime incidence of 30%. Pain is the most common and debilitating sequela of HZ. Post-herpetic neuralgia (PHN) is defined as chronic pain persisting for longer than three months after HZ rash onset. This lasts for over one year in 30% of patients. This meta-analysis was designed to clarify the efficacy of

pulsed radiofrequency (PR) in reducing symptoms of PHN.

A literature review was conducted to identify randomized, controlled trials involving patients with PHN which compared outcomes of PR with those of a control group. From this literature review, six randomized, controlled trials were selected, published between 2013 and 2019, for a final total sample of 504 subjects. From each study, data were obtained for measures of pain, quality of sleep, quality of life and use of rescue analgesic medications.

This meta-analysis revealed that those treated with PF had significantly lower pain scores than did controls at two to three days (weighted mean difference (WMD) 2.82), one week (WMD 2.95) two weeks (WMD 3.17), four weeks (WMD 2.59), eight weeks (WMD 3.02) and six months (WMD 1.94). Quality of life was significantly higher in the PF group than in the control group.

Conclusion: This study of patients with post-herpetic neuralgia found that pulsed radiofrequency significantly reduced pain within two to three days and persisted at six months.

Wu, C., et al. Efficacy of Pulsed Radiofrequency in Herpetic Neuralgia: A Meta-analysis of Randomized, Controlled Trials. **Clin J Pain.** 2020, November; 36(11): 887-895.

ARTIFICIAL TURF AND CONCUSSION IN CONTACT SPORTS

Since the introduction of artificial turf (AF) in 1965, safety concerns have been raised regarding its use in competitive contact sports. This literature review and meta-analysis compared the incidence of head injuries when competitions were played on (AF) and those who played on natural grass (NG).

An electronic database review was completed for studies of head injuries occurring during competitive sports, separating injuries sustained while competing on AF from those on NG. From this review, 12 papers published between 2004 and 2018 were selected, including eight reporting on injuries sustained during soccer, two on injuries sustained during American football and two on injuries sustained during Rugby.

From the combined data, 260 head injuries and concussions occurred on AF during 91,337 hours of match play. In addition, 7,055 head injuries and concussions occurred on NG during 220,201 hours of match play. Compared with NG, a lower rate of head injury and concussion occurred during play on AF (relative risk (RR) 0.89). Reviewing by sport, the relative risk was lower with AF for Rugby (RR 0.56) and American football (RR 0.72), while no significant difference was found in studies of soccer (RR 1.06).

Conclusion: This systematic review and meta-analysis found that the rate of concussion or head injury during competitive contact sports is less frequent when competing on artificial turf than on natural grass.

O'Leary, F., et al. Association of Artificial Turf and Concussion in Competitive Contact Sports: A Systematic Review and Meta-Analysis. **BMJ Open Sport Exercise Med.** 2020; 6(1): e000695.

RAPID RECOVERY PROTOCOL AFTER TOTAL KNEE ARTHROPLASTY

Approximately 500,000 total knee arthroplasties (TKA) are performed each year in the United States. This retrospective, observational, cohort study compared a rapid and a standard protocol for recovery after TKA.

All patients underwent primary TKA between January of 2012 and July of 2017. Those treated between January of 2012 and December of 2013 underwent a three-day hospitalization and physical therapy initiated within the first week after surgery (standard rehab protocol [SRP]). Beginning in 2013, the patients were discharged to home on the day of surgery with pain management including cryoneurolysis of the infrapatellar branch of the saphenous nerve and anterior femoral cutaneous nerve seven days before surgery. Physical therapy was initiated on the day of surgery (rapid rehab protocol (RRP)). Range of motion measures were taken at baseline and at follow-up visits up to 52 weeks post-surgery.

A total of 323 patients underwent TKA, including 129 treated with SRP and 194 with RRP. All subjects experienced significant improvement in flexion during the first year after surgery, with the greatest improvement occurring within the first 12 weeks. Compared to those receiving SRP those receiving RRP had greater flexion at weeks two, six and 12, but not at weeks 26 and 52. Those in the RPR group had less severe flexion contraction at two, six and 12 weeks.

Conclusion: This single surgeon study found that, compared with a standard rehabilitation protocol, a rapid rehabilitation protocol was associated with a reduced length of stay and a faster recovery of knee range of motion.

Plessl, D., et al. Rapid versus Standard Recovery Protocol is Associated with Improved Recovery of Range of Motion 12 Weeks after Total Knee Arthroplasty. **J Am Academy Ortho Surg**. 2020, November 1; 28(21): e962-e968.

RETURN TO PLAY FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN THE NFL

The rates of return to football after anterior cruciate ligament (ACL) reconstruction have been estimated to be 63% for high school and 69% for college athletes. This study evaluated the return to play of national football league (NFL) players undergoing ACL repair.

In the author's surgical practice, 55 NFL roster players underwent ACL repair surgeries. Data were available for 47 players who met inclusion and exclusion criteria. In all but one case, surgery involved an arthroscopic transtibial single bundle ACL repair, performed with a bone-patellar tendon-bone autograft.

Of the 47 repair procedures, 43 met the inclusion criteria, with 41 primary ACL repairs and six revisions performed. Return to game play (RTGP) was defined as returning to play in a regular-season game. Successful return to previous participation (RTPP) was defined as return to a level of participation equal to the level that the player had reached before injury. For this cohort, RTGP after primary ACL repair was 73% and RTPP 87.8%. A multivariate analysis revealed that an independent predictor of RTPP was age 25 years or less.

Conclusion: This study of 47 NFL active players found that successful return to play after primary anterior cruciate ligament repair was higher than previously reported, with an age of 25 years or less found to be an independent predictor of successful return.

Khair, M., et al. Return to Play following Isolated and Combined Anterior Cruciate Ligament

Reconstruction: Twenty-Five Plus Years of Experience Treating National Football League Athletes. **Orthop J Sports Med.** 2020, October; 8(10): DOI 10.1177/2325967120959004

NON-PHARMACOLOGICAL INTERVENTIONS FOR ALZHEIMER'S DISEASE

Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive memory deficits, cognitive decline and spatial disorientation. Currently the main pharmacotherapeutic options for AD are cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) and memantine. None of these can slow down or stop the progression of AD. This meta-analysis was designed to summarize the effects of non-pharmacologic interventions for AD.

A literature review was completed for studies of patients with AD involving non-pharmacologic interventions with outcome measures including the Mini-Mental State Examination (MMSE), activities of daily living (ADL), and Alzheimer's Disease Assessment Scale-cognitive section (ADAS-cog). From 41 potentially eligible studies, 10 were chosen for inclusion in the meta-analysis. Interventions within the studies were acupuncture, exercise, cognitive stimulation therapy, cognitive music therapy, and repetitive transcranial magnetic stimulation.

All studies were judged to be of low quality or critically low quality. From the studies chosen, exercise showed the potential to improve ADL and MMSE. The cognitive intervention resulted in improved MMSE. The rTMS improved ADAS–cog. Acupuncture improved MMSE, ADAS-cog, and ADLs. Music therapy was not effective.

Conclusion: This meta-analysis of studies of non-pharmacologic interventions for patients with Alzheimer's disease found some benefit of acupuncture, exercise, and repetitive transcranial magnetic stimulation, and no benefit of music therapy**.**

Wang, L., et al., Overview of Meta-analysis of Five Nonpharmacological Interventions for Alzheimer's Disease. **Front Aging Neurosci.** 2020, November 25. doi.org/10.3389/ fnagi.2020.594432.

LIFESTYLE FACTORS AND COGNITION IN OLDER ADULTS

Aging is accompanied by cognitive decline, evident as early as age 45 years. Previous studies have found that lifestyle variables may affect the process of aging. This study explored the association between modifiable lifestyle factors and cognition.

Data were obtained from the World Health Organization's Study on Global Aging and Adult Health (SAGE), a longitudinal study of adults age 50 years or older. Data for this study were obtained from Shanghai, China. Lifestyle factors included fruit and vegetable intake, physical activity, body mass index and waist to hip ratio. Cognitive function was assessed for immediate verbal recall, delayed verbal recall, digit span forward and backward, and verbal fluency. Covariates included age, gender, education, tobacco abuse, alcohol consumption and self-reported, chronic health conditions.

Data were assessed for 5,711 adults ranging in age from 50 to 95 years with a mean age of 62.29 years at baseline. Increased vegetable and fruit intake was positively associated with improved scores on all cognitive domains ($p<0.01$). Physical activity was also positively associated with scores on all cognitive domains ($p<0.01$). Body mass index was negatively associated with scores on all cognitive domains ($p<0.01$), were only significant in people up to 65 years old ($p<0.01$), but not in people older than 65 ($p>0.05$). A significant improvement was noted in immediate verbal recall, delayed verbal recall, digit span and verbal fluency with increases in vegetable and fruit intake ($p<0.01$ for all comparisons).

Conclusion: This Taiwanese study found that, among modifiable lifestyle factors, improvement in cognition occurs with increased fruit and vegetable intake.

Huang, Z., et al. Associations of Lifestyle Factors with Cognition in Community Dwelling Adults Aged 50 and Older: A Longitudinal, Cohort Study. **Front Aging Neurosci.** 2020, November; doi.org/10.3389/ fnagi.2020.601487.

FACET ARTHROPATHY FOLLOWING DISC REPLACEMENT

For patients with chronic low back pain (LBP) and lumbar disc degeneration, total disc replacement (TDR) is a surgical alternative for the spinal region. However, after TDR, facet arthropathy (FA) can appear, although the incidence and consequences of FA are unclear. This prospective, multicenter study assessed the long-term development of FA after TDR.

This study included 110 patients, 25 to 55 years of age, each with LBP of at least one year's duration and a history of at least six months of physiotherapy or chiropractic treatment without sufficient recovery. The subjects were randomly assigned to undergo lumbar TDR or multidisciplinary rehabilitation (MDR) with a cognitive approach and supervised physical exercise over three to five weeks. The participants were followed for ten years. The primary outcome measure was FA, as assessed with MRI at spine levels L4/L5 or L5/S1.

At eight-year follow-up, FA had appeared or increased more often in patients treated by TDR than in those treated with MDR ($p<0.001$). Index level FA developed in 36% of the TDR group and in two percent of the MDR group. In the TDR group, no significant association was found between FA changes and scores on the Oswestry Disability Index. This analysis could not be performed for the MRD group, given that only one patient in that group developed FA.

Conclusion: This randomized, prospective study of patients with chronic low back pain found that facet arthropathy progresses more frequently among those treated by total disc replacement, as compared to those treated with rehabilitation.

Furunes, H., et al. Facet Arthropathy following Disc Replacement versus Rehabilitation: A Prospective Study with Eight-Year Follow-up. **Spine.** 2020, November 1; 45 (21): 1467-1475.

COGNITIVE TELEREHABILITATION FOR MILD COGNITIVE IMPAIRMENT

Given the limited efficacy of pharmacologic treatments, novel interventions are needed to prevent or delay the onset of Alzheimer's disease (AD). A recent systematic review identified the efficacy of tele-rehabilitation on cognitive abilities in individuals with mild cognitive impairment (MCI). This study compared the efficacy of traditional face-to-face cognitive treatment to that of a virtual reality rehabilitation system (VRRS) with or without

supplemental telerehabilitation for patients with MCI.

This multicenter study included 49 patients diagnosed with MCI. A comprehensive, clinical, functional and neuropsychological evaluation was performed at baseline, at the end of face-to-face treatment and after four and seven months from baseline. Subjects were randomized to one of three groups a) face-to-face cognitive VRRS (12 sessions of individualized cognitive rehabilitation over four weeks) followed by telerehabilitation (36 sessions of home-based cognitive VRRS training; b) face-to-face cognitive VRRS followed by at-home unstructured cognitive stimulation (36 sessions of home-based unstructured cognitive stimulation); and c) face-to-face cognitive treatment as usual (12 sessions of face-to-face cognitive treatment as usual).The primary outcome variables were changes in two tasks of verbal episodic memory, the RAVLT and the FCSRT.

At the end of the first 12 sessions, the clinic-VRRS group improved more quickly than did the clinic-treatment as usual for, measures of memory (FCSRT IFR), language (FPC), attention (TMT A) and visuo-constructional abilities (CDT), though scores were similar. These gains were better maintained in those with subsequent home-based cognitive VRRS telerehabilitation compared to home-based unstructured stimulation

Conclusion: This study of adults diagnosed with mild cognitive impairment demonstrated that treatment with the cognitive face-to-face virtual reality rehabilitation system improved memory, language and visuo-constructional abilities significantly more than “treatment as usual”.

Manenti, R., et al. Effectiveness of an Innovative Cognitive Treatment and Telerehabilitation on Subjects with Mild Cognitive Impairment: A Multicenter, Randomized, Active Controlled Study. **Front Aging Neurosci.** 2020, November;12:400.

DICHLOROACETATE AND PAIN-RELATED BEHAVIOR

Pain conditions are associated with changes in the nociceptive neurons and glial cells, mainly in the spinal cord dorsal horn (SCDH). Studies have shown a role for microglial cells in initiating enhanced pain responses, whereas astrocytes have been implicated in pain persistence and chronification. As reduced mitochondrial respiratory function has been associated with glial reactivity, this study explored the effect of dichloroacetate (DCA) (known to reestablish mitochondrial function and reduce neuronal loss and glial reactivity in ALS models) in a chronic pain model.

This animal study included rats undergoing both a chronic and an inflammatory pain model. Chronic constriction injury (CCI) was produced in a hind paw. Persistent inflammatory pain was created by injections of freunds adjuvant (CFA) into the plantar surface of the hind paw. The animals were randomized to receive placebo or dichloroacetate 500 mg/L twice a week, starting on the day of injury. Mechanical allodynia was assessed, expressed as paw withdrawal threshold (PWT), comparing the affected to the unaffected side. Glial reactivity was measured at three, seven and 13 to 19 days. After animal sacrifice, tissue was assessed with immunofluorescence. Mitochondrial function was measured in the lumbar spinal cord, with tissue respiration measured by high-resolution respirometry (HRR).

DCA treatment significantly reduced ipsilateral pain-related behavior within five days in both pain models ($p<0.001$ for all comparisons). After DCA treatment, pain behavior did not differ between the affected and unaffected paws, at day 12 in the CCI group and at day six in the CFA group. The DCA significantly increased mitochondrial respiratory function by inhibiting pyruvate dehydrogenase kinase and decreasing glial fibrillary acidic protein and Iba-1 immunoreactivity in the spinal cord.

Conclusion: This animal pain model found that, following a pain-inducing injury, the pain was significantly reduced by oral dichloroacetate.

Lagos-Rodriguez, V., et al. Mitochondrial Bioenergetics, Glial Reactivity and Pain-Related Behavior Can Be Restored by Dichloroacetate Treatment in Rodent Pain Models. **Pain**. 2020, December; 161(12): 2786-2797.

HIGHLY BIOAVAILABLE CURCUMIN FOR KNEE OSTEOARTHRITIS

Curcumin has been used as an anti-inflammatory treatment in traditional eastern medicine. Curcumin regulates biochemical and molecular pathways by modulating several molecular targets. This study assessed the clinical efficacy and safety of orally administered Theracurmin in patients with knee osteoarthritis (OA) over six months of treatment.

Subjects were 40 years of age or older with OA of the knee, Kelgren levels II, III or IV. Theracurmin was administered orally twice a day for six months, corresponding to daily doses of 180 mg of curcumin. Blood draws were performed to assess high-sensitivity C-reactive protein (hsCRP) at baseline and at six months. Symptoms were evaluated monthly, for six months, using the Japanese Knee Osteoarthritis Measure (JKOM), the knee pain visual analog scale (VAS), and the knee scoring system of the Japanese Orthopedic Association (JOA). Thirteen patients were treated with only Theracurmin without combined therapy.

Data were completed for 45 patients with a mean age of 67.2 years. Scores on the VAS, JKOM and JOA all improved significantly ($p<0.001$, $p=0.003$ and $p<0.001$, respectively). Of the 45 patients, 34 were rated as effective cases (75.6 %) and 11 as not effective. Of the 13 patients treated with Theracurmin without concurrent therapy, JOA scores were significantly improved ($p=0.02$).

Conclusion: This prospective, uncontrolled open label trial suggests that curcumin at 180 mg per day may reduce pain and disability caused by osteoarthritis of the knee.

Nakagawa, Y., et al. The Efficacy and Safety of High Bioavailable Curcumin for Treating Knee Osteoarthritis: A 6-Month, Open Labeled Prospective Study. **Clin Med Insights Arthritis Musculoskelet Disord**. 2020. Volume 13: 1-8.

RECOMMENDED PHYSICAL ACTIVITY AND MORTALITY

In 2018, Physical Activity Guidelines for Americans recommended that adults engage in at least 150 minutes of moderate, or 75 minutes of vigorous intensity activity per week. This study compared level of exercise to risk of mortality.

Data were obtained from the National Health Interview Survey, an annual, cross-sectional, household interview conducted since 1957 by the United States Centers for Disease Control and Prevention. From 1997 to

2014, subjects reported the frequency and duration of leisure time aerobic and resistance training activity, categorized by intensity. From these data were obtained a sample of 479,856 adults, followed for mortality. Covariates included personal variables, education, marital status, lifestyle variables and chronic health conditions.

During a median follow-up of 8.75 years, 59,819 members of the cohort died. In a fully adjusted model, compared to participants not meeting the physical activity guidelines, the risks of all-cause mortality were found to be 11% lower in those who engaged in the recommended strengthening activity and 29% lower in those engaged in the recommended aerobic activity. The risk was 40% lower among those who engaged in both. Similar patterns were reported for cause-specific mortality from cardiovascular disease, cancer and chronic lower respiratory tract infections.

Conclusion: This study demonstrates that adults engaged in leisure time aerobic and strengthening activities at levels recommended by the 2018 guidelines are at reduced risk of all-cause and cause specific mortality.

Zhao, M., et al. Recommended Physical Activity and All Cause and Cause Specific Mortality in U.S. Adults: Prospective Cohort Study. **BMJ.** 2020; 370: M2031.

PLATELET RICH PLASMA AND FRACTURE HEALING

The incidence of delayed healing, or pseudoarthrosis ranges from one to six percent in long bone fractures. As platelets play an important role in the promotion of angiogenesis, mesenchymal cells and growth factors, this study investigated the effects of platelet rich plasma (PRP) for the treatment of pseudoarthrosis.

Subjects were 24 patients undergoing surgery for pseudoarthrosis between 2011 and 2014. Non-union was defined as the lack of union formation of the fracture line for at least nine months and no signs of fracture healing for three consecutive months. The patients' surgeries were categorized as those that used, and those that did not use, PRP during surgery. All were followed until fracture union.

The mean periods of pseudoarthrosis were 34.3 months in the PRP group and 11.3 months in the control group. Fracture union times were 5.3 months in the PRP group and 11.3 months in the control group (p=0.000).

Conclusion: This unblinded, retrospective study of patients undergoing pseudoarthrosis surgery found that the time to fracture union is significantly shorter among those treated with platelet rich plasma during surgery.

Basdelioglu, K., et al. The Effect of Platelet-Rich Plasma on Fracture Healing in Long Bone Pseudoarthrosis. **Euro J Orthop Surg Traumatol.** 2020, December; 30(8): 1481-1486.

MENTAL CHRONOMETRY TRAINING IN SUBACUTE STROKE

Motor imagery training involves the mental execution of an action in the absence of movement. This technique has been found to activate neural structures and processes similar to those activated during actual movement. To do this, one must be able to correctly estimate the duration of an imagined movement. The portion of this action that involves the temporal structure of simulated actions is called mental chronometry (MC). The MC involves the comparison of movement times during imagined and executed motor tasks. This study explored whether one session of motor imagery (MI) training induces performance changes in mental chronometry (MC), motor execution and/or motor excitability.

Subjects were 33 patients with stroke. Using a modified version of the Box and Block Test (BBT) the patients first performed the BBT mentally and then executed it as a motor task with one hand. For mental performance of the BBT, the subject received an auditory go-signal from the examiner, and then indicated orally when the task was complete. In a separate hand identification task (HIT), the subject was asked to watch a hand, displayed in eight different orientations on a computer screen, and to determine whether it was a right or left hand. The sequence of trainings (first MI training, followed by HIT training, or vice versa) were randomized for each patient. Transcranial magnetic stimulation (TMS) techniques were used to assess changes in motor excitability with each condition. The MC ability was calculated as [motor execution time – motor imagery time]/motor execution time.

After one session of MI, motor performance on the BBT improved significantly (p=0.006). No improvement in the BBT was found after a single session of HIT training. In addition, the MC ratio improved after MI training, but worsened after HIT training. Further, motor execution of the BBT significantly improved after MC training, but not after HIT training. Patients with severe sensory deficits performed significantly worse in BBT execution.

Conclusion: This study of patients with stroke found that a single session of mental chronometry could improve the execution of a fine motor task.

Liepert, J., et al. Effects of a Single Mental Chronometry Training Session in Subacute Stroke Patients-A Randomized, Controlled Trial. **BMC Sports Sci Med Rehab**. 2020. 12: 66. doi.org/10.1186/s13102-020-00212-w.

EYE TRACKING IN PEDIATRIC CONCUSSION

For patients with concussions, the quantification of eye movements has been shown to be effective and efficient in assessing concussion and central nervous system integrity. This study investigated the utility of eye tracking to identify concussion in the pediatric population.

Subjects were under 22 years of age and included 56 concussed children and 83 uninjured controls. All were assessed with eye movements recorded with an eye-tracker used to monitor eye movement while subjects viewed a video. The device recorded the position of the eye, obtained at 500 Hz while the chin was stabilized on a chin rest. The eye tracking data yielded 89 tracking metrics, with these reviewed to distinguish between the two populations.

From the metrics, 12 were found to differ significantly between the concussed and non-concussed children. Using these data, a model was constructed to identify those with concussion, with a 71.9% sensitivity and an 84.4% specificity. A separate model that included the ability to identify near point of convergence achieved a 95.8% specificity and a 57.1% sensitivity.

Conclusion: This pediatric study of concussion found that eye tracking correlates with concussion symptoms, demonstrating that eye movement could be useful in assisting with the diagnoses of concussion.

Zahid, A., et al. Eye Tracking as a Biomarker for Concussion in Children. **Clin J Sport Med.** 2020 Sep; 30(5): 433-443. doi: 10.1097/

JSM.0000000000000639. PMID: 30095503.

ACCURACY OF ANATOMY GUIDED BOTULINUM TOXIN NECK INJECTIONS

Several studies have determined that anatomy guided injections to the lower limbs are often inaccurate. This study reviewed the accuracy of anatomy guided botulinum neurotoxin (BoNT) injections to the cervical muscles using ultrasound (US) monitoring.

Subjects were consecutive patients presenting for BoNT injections for cervical dystonia. The target muscles were selected during the clinical examination, with injections placed by physicians with a mean of ten years' experience. After needle insertion, an US was used to locate the tip of the needle and the BoNT pool. The injection was considered accurate when the pool was seen in the targeted muscle.

Fifty-six participants received a total of 264 injections. Combining all injections, the target muscle was accurately injected in 76.6% of the attempts. Accuracy for specific muscles included 67.9% for the splenius capitis, 82.4% for the semispinalis capitis, 100% for the semispinalis cervicis, 86.7% for the sternocleidomastoideus, 75% for the trapezius, 78.3% for the levator scapulae and 100% for the scalenus medius.

Conclusion: This study of patients undergoing botulinum neurotoxin injections of the neck found that 76.6% of those injections reached the intended muscle.

Kreisler, A., et al. Anatomy Guided Injections of Botulinum Neurotoxin in Neck Muscles: How Accurate is Needle Placement? **Euro J Neurol.** 2020, November; 27(11): 2142-2146.

UPADACITINIB OR ABATACEPT IN RHEUMATOID ARTHRITIS

Upadacitinib is an oral, selective, Janus kinase inhibitor that is approved to treat rheumatoid arthritis (RA). Abatacept, which inhibits T-cell proliferation and B cell stimulation, has similarly been approved for the treatment of RA. This study compared the efficacy and safety these two medications.

Subjects were 18 years of age or older, diagnosed with RA for at least three months' duration, all with moderate to severe, active disease. All had failed treatment with at least one biologic disease-modifying antirheumatic drug (DMARD). The participants were randomized to receive either extended release oral upadacitinib (15 mg once daily) or intravenous abatacept (at day one and weeks two, four, eight, 12, 16 and 20 [500 mg for those <60 kg, 750 mg for those 60 to 100 kg, 1,000 mg for those >100 kg]). The primary endpoint was change from baseline to week 12 in the Disease Activity Scores for 28 joints (DAS28-CRP).

The participants included 303 in the upadacitinib group and 309 in the abatacept group. At week 12, the mean changes in the DAS28-CRP from baseline were -2.52 in the upadacitinib group and -2.00 in the abatacept group ($p<0.001$). Clinical remission occurred in 30% of the upadacitinib group and 13.3% of the abatacept group ($p<0.001$).

Conclusion: This study of patients with rheumatoid arthritis found that upadacitinib, an oral selective Janus kinase inhibitor, was superior to abatacept for improvement of DAS28-CRP scores and increasing rates of remission.

Rubbert-Roth, A., et al. Trial of Upadacitinib or Abatacept in Rheumatoid Arthritis. **N Engl J Med.2020,** October 15; 383: 1511-1521.

FATIGUE RELATED FEEDBACK AND MUSCLE STRENGTH

During fatiguing exercise, perturbations within the muscle increase the firing of small diameter group III/IV muscle afferents, giving rise to sensations of muscle work and pain. As their firing remains elevated during periods of post exercise blood flow occlusion (BFO), this study assessed whether maintained group III/IV afferent feedback from the plantar flexor muscles reduces voluntary activation of the knee extensors.

Subjects were 12, healthy participants with average age of 27.1 years. Assessments were made of maximal voluntary contractions (MVCs) of the knee before and after a three-minute fatiguing task of the plantar flexors (PFs), while monitored by an EMG. During one session, blood flow of the calf was occluded for two minutes after exercise(cuff) and for one without (no-cuff). Supramaximal stimulation of the femoral nerve elicited superimposed twitches during MVC of the knee extensors and resting twitches two to three seconds after relaxation.

The MVC of the plantar flexors on the cuff day was significantly lower than on the non-cuff day ($p=0.015$). Voluntary activation on the cuff day was 5.3% lower than on the non-cuff day ($p<0.14$). During the first two minutes of recovery, the average pain ratings were 6.1 (strong to very strong), on the cuff day, but 1.5 (very weak to weak), on the no-cuff day. The amplitude of the resting twitch on the cuff day was higher than that on the no-cuff day ($p= 0.004$). The quadriceps EMG was lower on the cuff day than on the no-cuff day ($p=0.03$). This finding suggests that high levels of fatigue-related group III/IV muscle afferent feedback from the calf impair the function of the knee extensors.

Conclusion: This study found that, when fatigue-related feedback from group III/IV afferents of the calf muscles is maintained by blood flow restriction after exercise, there are reductions in knee extensor maximal force, voluntary activation and EMG activity, despite the knee extensors performing no exercise.

Finn, H., et al. Fatigue Related Feedback from Calf Muscles Impairs Knee Extensor Voluntary Activation. **Med Sci Sports Exerc.** 2020. doi: 10.1249/MSS.0000000000002362.

SPLIT DOSE INTRAVENOUS STEROID AFTER TOTAL HIP ARTHROPLASTY

Studies have shown that inflammation plays a significant role in the development of postoperative pain. Reducing this inflammation with intravenous (IV) glucocorticosteroids has been found to reduce postoperative opiate requirements. This study compared the efficacy of single dose IV regimens to that of a split dose regimen in patients undergoing total hip arthroplasty (THA).

Subjects were 165 patients scheduled to undergo primary, unilateral THA. All participants received an IV injection prior to anesthesia, with a second 24 hours later. Those randomized to a control group received normal saline at both injections. Those in a single dose group received 20 mg of dexamethasone prior to anesthesia and normal saline 24 hours later. The split dose group received 10 mg of IV dexamethasone at both injections. The primary outcome measure, pain intensity, was reported at rest and during activity using a 10-point numerical rating scale (NRS). Blood samples were drawn preoperatively and at one, two, three and 14 days after THA to assess interleukin-6 (IL-6) and CRP levels. Patient satisfaction was measured on

(Continued from page 2)

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a 100 mm visual analog scale preoperatively and at three- and 90-days post-surgery.

Pain with movement was significantly, lower on postoperative days one two and three for both corticosteroid groups, as compared to the placebo group. Compared to those in the single dose group, patients in the split dose group had lower dynamic pain scores, higher patient satisfaction scores, as well as greater range of motion and, lower interleukin-6 and C-reactive protein levels on postoperative days two and three.

Conclusion: This study found that a split dose corticosteroid regimen is superior to a single high dose for reducing pain and inflammation, as well as for increasing patient satisfaction.

Lei, Y., et al. Is a Split Dose Intravenous Dexamethasone Regimen Superior to a Single High Dose in Reducing Pain and Improving Function after Total Hip Arthroplasty? A Randomized, Blinded, Placebo Controlled Trial. **Bone Joint J.** 2020; 102-B (11): 1497-1504.

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