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BOTULINUM TOXIN A FOR NEUROPSYCHIATRIC SYMPTOMS IN PARKINSON'S DISEASE

Parkinson's disease (PD) is a neurodegenerative condition characterized by motor symptoms and psychological dysfunction. Multiple randomized controlled trials have shown that Botulinum Toxin A (BoNT/A), when injected into the corrugator and procerus muscles, is an antidepressant. This study evaluated the impact of Botulinum toxin A (BoNT/A) injections on neuropsychiatric symptoms in PD.

The subjects were 64 patients with PD with neuropsychiatric symptoms. A healthy control group (n=45) without neuropsychiatric symptoms was included for comparison. The PD subjects were randomized to receive injections at the bilateral glabella, orbicularis oculi muscle, forehead, bilateral lateral canthus, and temporal area, with BoNT/A, diluted to 40U/mL (18 sites and 3-4 units BoNT/A per site) or an equivalent volume of 0.9% normal saline (Placebo). All were tested with the Cornell Medical Index (CMI) self-assessment questionnaire administered before and up to 12 weeks after treatment. The primary outcome was the change in depression scores and the proportion of patients showing symptom improvement at eight weeks.

At four weeks, compared to the control group, the treatment group had significantly improved depression and tension scores ($p<0.05$ for both). At eight weeks, compared to the control there were significant improvements in scores of anxiety, sensitivity, depression, and tension scores ($p<0.05$ for all). At 12 weeks, somatization, depression, sensitivity, and tension scores remained significantly lower in the treatment group ($p<0.05$). At eight weeks complete or significant relief of CMI-reflected neuropsychiatric symptoms was documented in 10/30 (33%) in the treatment group and two of 30 in the control group ($p=0.67$).

Conclusion: This study of patients with PD found that facial injections with Botulinum toxin A were effective in reducing depression, and anxiety.

Zhu, X., et al. Treatment of Neuropsychiatric Symptoms in Parkinson's Disease with Botulinum Toxin A: A 12 week Randomized, Double-Blind, Placebo-Controlled Trial. **J Geriatric Psych Neurol.** 2024 Sep 3: doi: 10.1177/08919887241281066.Epub ahead of print.

FLAVENOID RICH FOODS AND DEMENTIA

Flavonoids, found in plant derived foods, have been associated with a lower risk of dementia and cognitive decline. This study investigated the association between a novel flavonoid diet intake score and the risk of dementia.

This cohort study used data from the United Kingdom Biobank, a population-based, prospective, cohort study of more than 500,000 participants. Data were obtained from participants, 40 to 70, years of age who had appropriate dietary data documentation. Diet was assessed using the Oxford WebQ, which estimates the frequency of consumption of 206 foods and 32 beverages. The genetic risk was assessed using a polygenic risk score, as well as apolipoprotein ε4 status. The subjects were labelled as having a high genetic risk for dementia if they were carriers of the apolipoprotein E (APOE) ε4 genotype or were within the highest quintile of the Alzheimer's disease-related PRS.

Data were collected for 121,986 participants with a median follow up of 9.4 years. During that time there were 882 cases of incident dementia. A multivariable analysis found that those with the highest flavonoid scores were at the lowest risk for dementia ($p=0.03$). Consuming six additional servings per day of flavonoid-rich foods was associated with a lower risk of dementia among all participants (Hazard Ratio; 0.72).

Conclusion: This large, prospective, cohort study found that six additional servings per day of flavonoid-rich foods, specifically tea, red wine, and berries, was associated with a lower risk of dementia.

Jennings, A., et al. Flavonoid-Rich Foods, Dementia Risk, and Interactions with Genetic Risk, Hypertension, and Depression. **JAMA Open.** 2024, Sept 18; 7(9): e2434136.

INTENSIVE BLOOD PRESSURE CONTROL BY NON-PHYSICIANS

Hypertension (HTN) is the leading modifiable risk factor for cardiovascular disease and all cause death. Recent trials have demonstrated that intensive lowering of blood pressure (BP) can reduce the risk of cardiovascular disease. This study assessed the healthcare outcomes of a system of HTN control using community-based healthcare workers using electronic monitors, guided by physicians.

This is a 48-month follow-up study of the Chinese Hypertension Control Project (CRHCP). Eligible participants were hypertensive adults ≥40 years of age who were randomly placed in an intervention group (IG; n=11,289) or a usual care (UC; n=11,097) group. The IG received a stepped-care protocol based on clinical guidelines with a BP treatment goal of (<130/80 mm Hg). The IG group measured BP two to three days per week using electronic home-based monitors. Support included health coaching and social support between patients and families. The main outcome variable was CVD, defined as a composite of myocardial infarction, stroke, heart failure requiring hospitalization, and CVD death.

During a median four-year follow-up, the rates of CVD were 2.2% per year in the IG group and 3.0% in the UC group ($p<0$ .001). Among those

over 60 years of age, CVD occurred in 2.7% of the intervention group and 3.5% of the usual-care group ($p < 0.001$).

Conclusion: This rural Chinese study found that using electronic home-based monitors and nonphysician community healthcare workers, with a physician lead, could effectively reduce blood pressure and cardiovascular disease.

Guo, X., et al. Multifaceted, Intensive Blood Pressure Control Model in Older and Younger Individuals with Hypertension: A Randomized, Clinical Trial. **JAMA Cardiol.** 2024, September; 9(9): 781-790.

LESION LOWERING EFFECTS OF LDL-C REDUCTION AFTER HEART ATTACK

Among patients with atherosclerotic cardiovascular disease, a substantial rate of adverse events still occur, largely driven by those occurring in the arterial segment left untreated at the time of the event. This study was a lesion-level analysis of the Pac-Man AMI trial, designed to better understand the effects of LDL C lowering.

The PACMAN-AMI trial (Effects of the PCSK9 Antibody Alirocumab on Coronary Atherosclerosis in Patients with Acute Myocardial Infarction) multicenter, placebo-controlled trial included patients with acute myocardial infarction (AMI), randomized to receive alirocumab, 150 mg every two weeks (treatment group), or placebo (control group). All participants underwent high intensity statin therapy, with arterial evaluations using intravascular ultrasound (IVUS) at baseline and at one year follow up. A coronary lesion was defined as a coronary segment which had a more than 40% plaque burden at three or more consecutive slices. The main outcome variable was the change in the percent of atheroma volume.

At one year the mean reduction of percent atheroma volume (PAV) was 4.86% in the treatment group and 2.78% in the placebo group ($p<0.001$). At the minimum lumen area (MLA), the mean reduction in PAV was 10.14% with alirocumab and 6.70% with placebo ($p < 0.001$).

Conclusion: This study found that, compared to statin therapy alone, the addition of alirocumab resulted in a greater reduction in plaque burden, and a greater transformation from presumed high-risk plaque phenotypes into more stable, less lipid-rich, plaque phenotypes.

Biccire, F., et al. Lesion-Level Effects of LDL-C-Lowering Therapy in Patients with Acute Myocardial Infarction. A Post Hoc Analysis of the Pacman AMI Trial. **JAMA Cardiol.** 2024, Sep 2: e243200. doi: 10.1001/jamacardio.2024.3200. Online ahead of print.

SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS VERSUS DIPEPTIDYL PEPTIDASE-4 INHIBITORS AND RISK OF DEMENTIA

The World Health Organization has estimated that the number of people with dementia will reach 78,000,000 by the year 2030. As type 2 diabetes is known to be associated with a greater risk of dementia, anti-glycemic drugs may have a neuroprotective effect. This study compared the risk of dementia among adults who initiated treatment with sodium-glucose cotransporter-2 inhibitors (SGLT-2-I) to those who initiated treatment with dipeptidyl peptidase-4 (DPP-4-I).

Data were obtained from the Korean National Health Insurance Service Database, which includes all citizens of Korea, from the years 2013 to 2021. Dementia free adults, 40 to 69 years of age, with type 2 diabetes, who had initiated an SGLT-2-I or DPP-4-I, were eligible for inclusion. The primary outcome variable was incident dementia at a mean follow-up of 613 to 679 days.

Data were obtained from the records of 112,663 new users of SGLT-2-1 and 847,999 new users of DPP-4-I. During follow-up 1,172 had newly diagnosed dementia, with rates per 100 person years of 0.22 for initiators of SGLT-2-Is and 0.35 for initiators of DPP-4-Is. The lowered risk in the SGLT-2-I group was also true for Alzheimer's disease and vascular dementia.

Conclusion: This large Korean study of patients with type 2 diabetes found that those treated with an SGLT-2 inhibitor had a 35% reduced risk of dementia, as compared to those treated with DPP-4 inhibitors.

Shin, A., et al. Risk of Dementia after Initiation of Sodium-Glucose Cotransporter-2 Inhibitors versus Dipeptidyl Peptidase-4 Inhibitors in Adults Aged 40 to 69 Years with Type 2 Diabetes: Population Based, Cohort Study**. BMJ.** 2024; 386: e079475.

TENECTEPLASE VERSUS ALTEPLASE FOR ACUTE STROKE

Tenecteplase is a bioengineered variant of the tissue plasminogen activator alteplase. This phase three study assessed the non-inferiority of tenecteplase to alteplase in patients after an acute ischemic stroke (AIS).

The ORIGINAL study was a multi-center, active, controlled, parallel group, randomized, open label, phase three, non-inferiority study, conducted at 55 neurology clinics and stroke centers in China. Adults with AIS symptoms < 4.5 hours were randomized to receive either IV tenecteplase (0.25 mg/kg; maximum dose, 25 mg) or alteplase (0.9 mg/kg; maximum dose, 90 mg). A modified Rankin Scale (mRS) score was obtained at one and three months. National Institutes of Health Stroke Scale (NIHSS) scores were assessed for up to three months. The primary outcome variable was the proportion of patients who achieved an mRS score of zero (no symptoms) or one (no significant disability despite symptoms) by day 90.

Data were analyzed for 732 in the tenecteplase group and 733 in the alteplase group. The endpoint was achieved by 72.7% in the tenecteplase subjects and 70.3% in the alteplase group (p=0.003), demonstrating noninferiority of tenecteplase. Ninety-day mortality was 4.6% in the tenecteplase group and 5.8% in the alteplase group.

Conclusion: This Chinese study of patients presenting with an acute ischemic stroke found that tenecteplase was noninferior to alteplase for achieving a good functional outcome.

Meng, X., et al. Tenecteplase versus Alteplase for Patients with Acute Ischemic Stroke. The ORIGINAL Randomized, Clinical Trial. **JAMA.** 2024, Sep 12: e2414721. doi: 10.1001/jama.2024.14721. Online ahead of print.

VISUAL DISCRIMINATION TRAINING FOR CHRONIC STROKE

Visual field defects (VFDs) have been detected in approximately 20% of patients after a stroke. Visual perceptual learning (VPL) has been used to accelerate recovery from VFDs, with positive preliminary results. This study was designed to better understand the efficacy of VPL as a treatment for post-stroke VFDs.

This prospective study included eighteen patients, >20 years of age, diagnosed with VFDs secondary to a chronic stroke (more than six months in duration). After an eight-week period of no-training, the training phase began with sessions three times per week for eight weeks. During training, an LCD monitor displayed a centrally located letter, while simultaneously displaying a grating pattern (horizontal or vertical display) at varying distance from an orientation within peripheral vision, as well as at varying luminance. The subjects were asked to identify the letter and the orientation of the grating pattern. The primary outcome was the mean deviation (MD) from the age adjusted normative data. Vision related quality of life was assessed with the National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25).

Fourteen patients with a mean age of 53.9 years completed the study. The MD scores improved for the defective field during the training phase (p=0.004), but not during the no-training phase. The Vision-Specific Social Functioning sub score of the NEI-VFQ-25 improved from baseline after the 16-week study period (p=0.040).

Conclusion: This study of patients with a chronic stroke and visual field deficits found that visual field training could reduce the size of the visual field defect.

Namgung, E., et al. Customized Visual Discrimination Digital Therapy According to Visual Field Defects in Chronic Stroke Patients. **J Clin Neurol.** 2024, Sept; 20(5): 509-518.

PROTEIN ENRICHED SOUP AND WEEKLY EXERCISE IN THE ELDERLY

The PROT-AGE study demonstrated that individuals over 65 years of age should have a daily protein intake of 1.0 to 1.2 g/Kg of body weight to maintain and restore lean body mass and function. Those with acute or chronic conditions may benefit from intake up to 1.5g/Kg. This trial investigated the impact of a fixed dose, protein enriched soup, plus exercise on the muscle health physical performance in middle aged-elderly adults with insufficient protein intake.

Participants were 50 to 75 years of age and community dwelling, with at least one fall event within the past year. Eligible adults had daily protein intake < 1g/kg per day. All participants underwent a functional assessment, laboratory tests, and a body composition analysis. Those randomly assigned to an intervention group received a daily serving of protein-enriched soup containing 24 to 30 grams of protein, and participated in a weekly, one-hour group exercise, which encompassed moderate aerobic exercise and resistant exercise.

Participants were 100 adults with a mean age of 64.66 years. Compared to the control group, greater improvement was noted in the treatment group on the six-minute walking distance (p=0.006), the 5-time sit-to-stand (p=0.017), and handgrip strength (p<0.001). Additionally, the intervention group exhibited greater improvement in levels of triglycerides(p=0.022) and DHEA-S (p=0.040).

Conclusion: This study of elderly, community dwelling adults with low serum protein levels found that a daily intake of protein enriched soup, combined with one hour per week of exercise, significantly improved physical function, nutrition status, lipid metabolism, and dehydro-epiandrosterone sulfate levels.

Peng, L., et al. Protein-Enriched Soup and Weekly Exercise Improve Muscle Health: A Randomized Trial in Mid-to-Old Age with Inadequate Protein Intake. **J Cachexia, Sarcopenia Muscle.** 2024, August; 15: 1348-1357.

LIFE COURSE FINANCIAL STABILITY AND MEMORY FUNCTION

Positive socioeconomic trajectories across the life course are associated with better late life cognitive outcomes. However, the literature supporting this finding is sparce. This study was designed to better understand the relationship between financial status over time to later life cognitive outcomes.

Data were obtained from the cohorts of the KHANDLE and the Study of Healthy Aging in African Americans (STAR). The KHANDLE cohort included subjects 65 years of age or older on Jan 1, 2017, who participated in a health check-up examination between 1964 and 1985. The STAR cohort included individuals 50 years of age or older on Jan 1, 2018, identified as Black or African American, who participated in a health checkup examination between 1964 and 1985.

Life-course financial mobility was defined into categories based on self-reported financial measures from childhood to late adulthood. These included *consistently high* (high in childhood and later adulthood),

upwardly mobile (low in childhood and high in later adulthood), *downwardly mobile* (high in childhood and low in later adulthood), and *consistently low* (low in childhood and later adulthood). Verbal episodic memory was assessed using the Neuropsychological Assessment Scales over four waves from 2017 to 2023.

Data were reviewed for 1,712 in the KHANDLE group and 764 in the STAR group, with a mean age of 73.6 years. Individuals in the consistently *low* and *downwardly mobile* groups had lower mean verbal episodic memory scores at baseline than did the *consistently high* group. The rate of cognitive change over time did not differ between groups.

Conclusion: This study found that people with consistent financial stability or a downward financial stability had worse memory function, but no rate of change over time.

Kobayashi, L., et al. Life Course Financial Mobility and Later Life Memory Function and Decline by Gender, And Race/Ethnicity: An Intersectional Analysis of the U.S. KHANDLE and STAR Cohort Studies. **Lancet Healthy Longev.** 2024, September; 5(9): https://doi.org/10.1016/S2666-7568(24)00129-6.

COST EFFICACY OF PARTIAL MENISCECTOMY

Arthroscopic partial meniscus (APM) is among the most common orthopedic surgeries in the United States. Recent meta-analyses of randomized, controlled trials showed no treatment benefit of APM over non-surgical treatment or placebo surgery. This study was designed to determine whether APM reduced treatment costs post-surgically, compared to a placebo surgery.

Data were obtained from the Finnish Degenerative Meniscal Lesion Study (FIDELITY), a randomized, placebo-controlled, efficacy trial, including patients 35 to 65 years of age with degenerative medial meniscal tears. All patients had been unresponsive to conventional conservative treatment, and were randomly assigned to APM or placebo surgery, with 24-month follow-up.

Of the 146 patients, 70 were assigned to APM and 76 to placebo surgery. For the APM group, the torn meniscus was trimmed, with as much preserved as possible. Both groups received standardized postoperative care including a graduated home-based exercise program. Costs related to healthcare visits, community support, and loss of productivity were calculated. Cost effectiveness was computed as the incremental net monetary benefit for improvements in quality adjusted life years.

The mean total costs were £7,441 for the APM group and £6,780 for the placebo group. The vast majority of these costs were due to a loss of productivity £6102/ £7441 of the APM group and £5605/ £6780 of the placebo group.

Conclusion: This randomized, controlled study of patients with degenerative tears of the meniscus found that, compared to sham surgery, arthroscopic partial meniscectomy did not have a greater reduction in post-operative costs or improved quality of life.

Kalske, R., et al. Arthroscopic Partial Meniscectomy for a Degenerative Meniscus Tear Is Not Cost Effective Compared with Placebo Surgery: An Economic Evaluation Based on the FIDELITY Trial Data. **Clin Orthop Rel Research**. 2024, September; 482 (9):1523-1533.

NON-OPERATIVE ANKLE SPRAINS

Ankle sprains involving syndesmosis are referred to as high ankle sprains (HAS). Conservative treatment is recommended for most HASs without fracture or diastasis. This study reviewed the long-term outcomes of nonoperative management of HASs.

This study used data from a database of collegiate and high school athletes who experienced an HAS without fracture or diastasis. Treatment included a four-day period of immobilization, utilizing a posterior splint, with the ankle in neutral position. On day five, the splint was removed, with weight bearing as tolerated allowed. Passive range of motion was performed at zero to 15 degrees of plantarflexion and -15 to zero degrees of dorsiflexion. The participants used crutches until they could demonstrate a normal gait pattern. Balancing and proprioceptive training, and manual resistance exercises were progressively increased to improve strength, range of motion, proprioception, and function. The subjects were advanced to sport when they were able to pass sport-specific functional tests.

Thirty-one patients were available for 18-year follow-up. All returned to sporting activity at a mean of 13 days and rated their outcomes as good to excellent at six months. After the index injury, 42% of the subjects reported additional ipsilateral ankle injuries. Follow-up ankle radiographs were obtained in 11 (35%), with ten demonstrating osteoarthritis, and four demonstrating heterotopic ossification.

Conclusion: This long-term follow-up of athletes with high ankle sprains who were treated non operatively had acceptable patient reported functional outcomes, but with a high rate of subsequent ankle injuries.

Nussbaum, E., et al. Non-Operative Management of High Ankle Sprains. A Case Series With ≥18-Year Follow-Up. **Am J Sport Med.** 2024, Sep; 52 (11): 2807-2814.

PATIENT DISSATISFACTION AFTER ROBOT-ASSISTED PRIMARY TOTAL KNEE ARTHROPLASTY

Recent studies of patients undergoing total knee arthroplasty (TKA) have reported dissatisfaction rates ranging from 11% to 19%. As robot assisted (RA) surgery has significantly increased in the U.S., this study assessed the patient reported outcome measures (PROM) among those with RA-TKA.

This retrospective review included 800 consecutive patients with a mean age of 65 years who underwent primary RA-TKAs. At a mean of 36.6 months, patient satisfaction and PROMs were collected during office follow-up visits (451 patients) or via structured phone interviews (223 patients). Using Likert satisfaction scores, the groups were divided into group A, with scores of one (very dissatisfied), two (dissatisfied) or three (neutral), or group B, with scores of four (satisfied) or five (very satisfied). Additional PROMs included the Knee Society (KS) Knee Score, the KS function score, and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which were collected at both preoperative and postoperative office visits, and the Forgotten Joint Score-12 (FJS-12) and the Knee injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS, JR), which were collected postoperatively.

Of the 674 patients, 6.7% were in group A and 93.3% in group B. Lower scores were observed in Group A on the KS function ($p<0.001$), KS Knee ($p<0.001$), WOMAC ($p<0.001$), and KOOS, JR ($p<0.001$). The

multivariate binary logistic regression analysis found that independent predictors of dissatisfaction were preoperative opioid use (p=0.012), prior ACL repair (p=0.038), and male gender (p=0.006).

Conclusion: This study found a 93.3% patient satisfaction score with robot assisted total joint replacement of the hip.

Gardner, J., et al. Aetlology of Patient Dissatisfaction following Primary Total Knee Arthroplasty in the Era of Robotic Assisted Technology. A Review of 674 Cases. **Bone Jt Open.** 2024, September 12; 5(9): 758-765.

NEUROTOXICITY AFTER CHEMOTHERAPY

The most common neurologic complication in cancer patients is chemotherapy induced peripheral neurotoxicity (CIPN). Light chain neurofilament (NfL), an axonal protein, has emerged as a marker of peripheral nerve disease activity. This study compared changes in plasma NfL (pNfL) over time in cancer patients receiving several types of chemotherapy.

The subjects were adult patients diagnosed with breast cancer, gastrointestinal cancer, or lymphoma, each scheduled to receive paclitaxel (TX; n = 34), brentuximab vedotin (BV; n = 29), or oxaliplatin (PT; n = 19). All were assessed for neurologic changes using the Seven-Item Composite Total Neuropathy Score-Clinical Version. Venous blood was obtained to measure pNfL levels. The results were compared by treatment group.

Of the 82 patients included in the study, none reported baseline symptoms of neuropathy. Of the patients who received TX (29.4%), BV (31%), or PT (36.8%) developed CR-CIPN, respectively, without differences between them (p = 0.854). An early increase in pNfL at midtreatment was only observed in patients receiving TX, compared to BV or PT ($p < 0.001$). At treatment completion, increased pNfL levels were greater in the TX group, compared to the other two groups (p<0.001 for both comparison).

Conclusion: This study of patients treated for cancer with chemotherapy found that one third developed CR-CIPN significantly greater and earlier changes in pNfL levels compared to those receiving the other agents ($p < 0.001$)

Velasco, R., et al. Plasma Neurofilament Light Chain Levels in Chemotherapy Induced Peripheral Neurotoxicity According to Type of Anti-Cancer Drug. **Euro J Neurol.** 2024, September; 31(9): e16369.

PRIMARY TOTAL HIP ARTHROPLASTY INFECTION AND MORTALITY

With the aging of the population, the number of total hip arthroplasties (THAs) in the United States is expected to be > 600,000 annually by the year 2030. Worldwide, the risk of periprosthetic joint infection is estimated at two percent. This study assessed the 10-year mortality risk related to these infections.

This study included patients who underwent their first primary elective THA for arthritis between April 1, 2002, and March 31, 2021. The main exposure was the occurrence of peri-joint infection which required surgery within one year after the THA. Comorbidities were recorded. The primary outcome variable was death within 10 years after the index surgery.

During the study, 175,432 patients with a mean age of 67 years underwent a primary THA. Of these, 868 underwent surgery for the treatment of periprosthetic joint infection (PJI) within one year after the index surgery. In a matched comparison, those with PJI had significantly higher ten-year mortality than their counterparts (11.4% versus 2.2%, p<0.0001). In a separate matched analysis, of patients < 60 years of age, the PJI group had a higher 10-year mortality, with a hazard ratio of 10.18 (p<0.0001).

Conclusion: This population-based, cohort study of patients who underwent primary elective total hip arthroplasty found that a joint infection within one year after surgery was associated with a dramatic increase in their 10-year mortality.

Mundi, R., et al. Association between Periprosthetic Joint Infection and Mortality following Primary Total Hip Arthroplasty. **J Bone Joint Surg**. 2024, Sept 4; 106-A(17): 1546-1552.

PHYTOSOMAL CURCUMIN FOR MULTI-TRAUMA

Curcumin, derived from turmeric, has been shown to have anti-inflammatory and neuroprotective properties, but has poor oral bioavailability. Phytosomal curcumin involves binding curcumin to phospholipids that enhance the absorption of curcumin. This study investigated the effectiveness of phytosomal supplementation in ICU-admitted patients with multiple trauma.

This double-blind placebo-controlled trial included 53 patients admitted to an academic hospital intensive care unit with multiple trauma. The participants were randomized to receive phytosomal curcumin (P-Cur), 500 milligrams daily, or a placebo. Blood samples were taken before and after the study. The subjects were assessed clinically using the Acute Physiology and Chronic Health Evaluation II (APACHEII), the Glasgow Coma Scale (GCS), the Sequential Organ Failure Assessment (SOFA) score, and the Nutrition Risk in the Critically Ill (NUTRIC) Score.

At one week, the mean improvement in GCS scores from baseline was significantly greater in the P-Cur group than the placebo group (p= 0.028). The 28-day mortality rates were 7.7% in the placebo and 3.7% in the P-Cur group (p<0.01). Quantitative C-reactive protein (CRP) levels decreased (p= 0.044), while potassium (p= 0.01) significantly increased in the P-Cur group, compared with the placebo group. The reduction APACHE-II scores in the P-Cur group were marginally greater than those in the placebo group (p= 0.055).

Conclusion: This study of patients with polytrauma admitted to the ICU found that 500mg per day of phytosomal curcumin improved inflammatory indices, concussion scores, and one-month mortality.

Mirjalili, M., et al. The Effectiveness of Phytosomal Curcumin on Clinical and Laboratory Parameters of Patients with Multiple Trauma Admitted to the Intensive Care Unit: A Double-Blind, Randomized, Placebo-Controlled Trial. **BMC Complement Med Ther.** 2024, Sep 17; 24(1): 335.

SERUM NEUROFILAMENT LIGHT AND HEAVY ASSOCIATIONS WITH SIX-MONTH COGNITIVE PERFORMANCE AFTER BRAIN INJURY

The neurofilament proteins, neurofilament light (NF-L) and phosphorylated neurofilament heavy (pNF-H), are components of axonal cytoskeletons. These have been implicated as markers of axonal and dendritic injury. This study investigated the association between plasma levels of these proteins and cognitive function over time after a traumatic brain injury (TBI).

The subjects were 94 patients, 16 to 72 years of age, with moderate to severe TBI (msTBI). All completed a battery of neurocognitive tests up to six months post-injury. Blood draws were used to measure NF-L and pNF -H at three separate times, up to 90 days post-injury (DPI).

The NF-L at 0-16 DPI was significantly related to cognitive performance at six months (p=0.005), while NF-L levels taken more than 16 DPI demonstrated no such relationship. Serum levels of pNF-H at 16-90 DPI were significantly associated with executive composite scores at six months post-injury when controlling for age and level of education (p=0.003).

Conclusion: This study of patients with mild to moderate traumatic brain injury found that post-acute elevations of serum pNF-H levels may be associated with protracted/poor cognitive recovery.

Trifilio, E., et al. Temporal Profile of Serum Neurofilament Light (NF-L) and Heavy (pNF-H) Level Associations with Six-Month Cognitive Performance in Patients with Moderate-Severe Traumatic Brain Injury. **J Head Trauma Rehabil.** 2024, July; 41(13-14): 1609-1627.

MANAGEMENT OF METACARPAL SHAFT FRACTURES

Metacarpal shaft fractures (MSFs) are among the most common hand injuries in young adults. Despite this, evidence guiding treatment of these injuries is limited, with no consensus on the best management. This study described the epidemiology of MSF in adults and reviewed the variations in treatment across the United Kingdom.

This retrospective, multi-center, cross-sectional study focused on patients over 16 years of age with MSF of the second to fifth metacarpal. Given the population served by these centers, the incidence was calculated to be 40 per 100,000/year. Health records, operative notes, radiographic findings, and follow-up information were reviewed.

Data were analyzed from the records of 793 patients, with a median age of 27 years. Twelve types of non-surgical and six types of surgical treatment were used. The majority were treated non-surgically. Of the surgical treatments, plate fixation was the most common (55%). Ninety percent were simple fractures, and 97% were closed fractures. Forty -four complications were documented, including persistent pain (n=9), restricted movement at six weeks (n=9), malunion (n=8), infection (n=4), anatomic deformity (n=3), altered sensation (n=3), and hand weakness at six weeks(n=3).

Conclusion: This study of adult patients with metacarpal shaft fractures found that the conservative and surgical treatments vary considerably, with 5-6% experiencing complications.

Taha, R., et al. Management of Metacarpal Shaft Fractures. A Multicenter, Cross-Sectional Study. **Bone Jt Open**. 2024, August 8; 5(8): 652-661.

MELATONIN AND PALMITOYLETHANOLAMIDE FOR CHRONIC PAIN

Fibromyalgia (FM) is included in the spectrum of central sensitivity syndromes. Among the various mechanisms that are thought to contribute to the onset of FM include the activation of mast cells and microglia, increased proinflammatory mediators, disruption of the hypothalamic-pituitary-adrenal axis, and imbalance of certain neuromodulators. This study evaluated the efficacy of palmitoylethanolamide (PEA), an endogenous fatty acid amide which has displayed analgesic, anti-inflammatory, and neuroprotective benefits, for the treatment of FM.

This study enrolled 50 consecutive patients, 18-80 years of age who were diagnosed with FM and expressed dissatisfaction with their pharmacological therapy. The patients received 1,200 milligrams per day of PEA, and to assist with sleep, 0.2 milligrams of melatonin at bedtime. The patients were assessed at baseline and up to three months follow-up with a visual analog scale (VAS) for pain, the Insomnia Severity Index (ISI), and the Health Assessment Questionnaire (HAQ). An examination by a rheumatologist included the testing of tender points.

The mean VAS pain scores improved by 1.16 points at one month and an additional 1.18 points at three months. The ISI improved by 6.24 points at one month, 1.54 points at three months ($p<0.01$), and 0.36 points at four months ($p<0.01$). The HAQ improved by 0.295 points at one month ($p<0.01$) and by 0.4 points at three months ($p<0.01$) and stabilized at four months ($p<0.01$).

Conclusion: This open label study of patients with chronic fibromyalgia found that daily treatment with palmitoylethanolamide, 1,200 mg, combined with melatonin, 0.2 mg, could improve pain, sleep, and health related quality of life.

Terribili, R., et al. A Fixed Combination of Palmitoylethanol-amide and Melatonin for the Management of Pain, Sleep, and Disability in Patients with Fibromyalgia: A Pilot Study. **Nutrients.** 2024, Aug 21; 16(16): 2785.

TRANSCRANIAL DIRECT CURRENT STIMULATION WITH COGNITIVE TRAINING IN OLDER ADULTS

The lifetime risk of dementia is estimated to be 37% for women and 24 % for men. As studies have shown cognitive benefits of transcranial direct current stimulation (tDCS) on cognition, this study evaluated the effects on working memory of three months of bilateral tDCS combined with multimodal cognitive training.

The subjects were 290 adults 65 to 89 years of age, each with cognition below the 80th percentile based on the BrainHQ Cognitive Assessment. All subjects underwent 40 minutes per day of cognitive training using BrainHQ, a computerized cognitive training program, completing 40 hours of training over 12 weeks. After the first two weeks, the patients were randomly assigned to receive either sham stimulation or tDCS for 20 minutes during each the 40-minute training session.

A regression analysis indicated greater improvement of the longest digit span backward from baseline to post-intervention ($p=0.021$), with a trend toward greater improvement up to one year in the active tDCS group ($p=0.056$).

Conclusion: This study of patients with age related cognitive decline found that adding transcranial direct current stimulation to a cognitive training program improved working memory by improving the longest digit span backward performance at the three -month timepoint.

Aksu, S., et al. Facilitation of Working Memory Capacity by Transcranial Direct Current Stimulation: A Secondary Analysis from the Augmenting Cognitive Training in Older Adults (ACT) Study. **Gerosci.** 2024, October; 45(5): 4075-4110.

MUSCULOSKELETAL INJURIES AFTER CONCUSSION IN THE NFL

Concussions are associated with transient alterations in neuromuscular control, cognitive processing speed, vestibular and dynamic proprioceptive function. Some have suggested that these deficits create an increased risk of subsequent injury. This study was designed to determine whether National Football League (NFL) players who were diagnosed with a concussion have an increased risk of subsequent time loss due to injury.

Data were obtained from the League Wide Electronic Health Record (EHR), of the NFL. Players with a concussion were matched with a group who experienced time loss due to a musculoskeletal injury. After return to play both groups were followed for subsequent injury.

Data were analyzed for 641 players with a concussion, 4,878 players without concussion, and 653 players with time lost due to upper extremity (UE) injuries. Compared to time-loss musculoskeletal injuries, a greater proportion of players with a concussion sustained a subsequent time-loss injury at 30 days (Hazard Ratio (HR) 1.39). However, when factoring the time away from participation, the difference in risk of subsequent injury was similar between groups.

Conclusion: This study of NFL players found that, after a concussion, the driving factor behind the increased risk of subsequent injury may be the time lost due to injury, and not necessarily lingering neurologic dysfunction.

Wasserman, E., et al. Subsequent Musculoskeletal Injury after Concussion in National Football League Players. **Br J Sport Med**. 2024, September 9; 58 (18):1068-1074.

BLOOD FLOW RESTRICTION EXERCISE AFTER ACL REPAIR

The anterior cruciate ligament (ACL) is the most commonly injured knee ligament. Reconstruction using hamstring tendon graft is a standard procedure for these injuries. As an ACL injury adversely affects quadriceps strength, resistance training is recommended to stimulate muscle hypertrophy and increase muscle strength. While traditional resistance training is recommended at 60-70% of the one repetition maximum, post-surgical patients often do not tolerate this load. Blood flow restriction (BFR) exercise has emerged as an alternative procedure that requires less than half the weight with similar improvements in strength. This literature review was designed to better understand the relative benefits of these two resistance techniques after an ACL repair.

A literature review was completed for studies of adults hospitalized for ACL repair that engaged in post-operative rehabilitation, including resistance training with either traditional or BFR resistance.

The literature review identified five prospective blinded studies (n=130) that compared BFR to traditional resistance training as part of their post-operative rehabilitation. Two studies found that BFR training resulted in better strength gains than traditional resistance training while two found the opposite. One study measured passive range of motion showing better improvement in the BFR group, compared to traditional strengthening with no difference in muscle strength or size.

Conclusion: This literature review of patients undergoing rehabilitation after an ACL repair found that blood flow restriction training had results that were similar to traditional strength training, though the data were not conclusive.

Colombo, V., et. al. Comparison of Blood Flow Restriction Interventions to Standard Rehabilitation After an Anterior Cruciate Ligament Injury: A Systematic Review. **Am J Sports Med.** 2024;0(0). doi:10.1177/03635465241232002.

HEALTH OF CAREGIVERS SINCE 2015

Caregivers provide support to persons who might otherwise require placement in long term care facilities. Promoting the well-being of this large segment of the population is a public health priority. This study reviewed the change in health indicators for caregivers since 2015.

The Behavioral Risk Factor Surveillance System, (BRFSS) is an annual state-based random-digit-dialed telephone survey of non-institutionalized US adults. Data were reviewed from the 35 states and Puerto Rico where the optional caregiver module is included. The responses to questions about the prevalence of 19 health indicators were compared between caregivers and non-caregivers from 2015 to 2022.

Data were included from 92,461 caregivers and 353, 242 non-caregivers. The percentage of adults who self-identified as a caregiver in 2015-2016 and 2021-2022 were 20.2% and 20.1% respectively. During 2021–2022, compared to non-caregivers, caregivers were more likely to smoke cigarettes (11.7% vs 16.6%), have fair or poor self-rated health (16.9% vs 19.6%), have frequent mental distress (13.6% vs 20.5%), have frequent physical distress (11.2% vs 14.3%), have depression (18.6% vs 25.6%) have a chronic physical condition (6.3% vs 7.3%), have asthma (9.1% vs 12.8%) be obese (33.2% vs 38%) have a chronic medical condition (54.9% vs 65.7%), have multiple chronic physical conditions (24.2% vs 32.5%), and be unable to see a doctor due to cost (9.1% vs 13.2%).

Conclusion: This study found that one in five US adults provide care for a family member or friend with a chronic health condition or disability, and that most health indicators in this survey were worse for caregivers than for non-caregivers.

Kilmer G., et al. Changes in Health Indicators Among Caregivers — United States, 2015-2016 to 2021-2022. **MMWR Morb Mortal Wkly Rep** 2024;73:740–746.

RESCUE THERAPY FOR EARLY NEUROLOGICAL DETERIORATION AFTER LACUNAR STROKE

Early neurological deterioration (END) often occurs in patients with acute ischemic stroke and is linked to a poor prognosis. For those who fail to respond to volume expanders, alternative treatments include pharmacologically induced hypertension (PIH) and anticoagulation. As argatroban is an approved treatment in Japan and Korea, this study compared argatroban to PIH as a rescue therapy for END after a lacunar stroke.

This retrospective study included adults hospitalized for a lacunar stroke who developed END, diagnosed as an increase of two or more on the total NIHSS score or an increase of one or more on the motor NIHSS score within 72 hours of admission. For those unresponsive to volume expanders, data were reviewed from the charts of those who received PIH or argatroban. Phenylephrine was administered continuously over 24 hours and tapered after END symptoms improved. Argatroban was administered using 60 mg in IV fluid infused continuously over 24 h,

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followed by 10mg infused over two hours, twice per day. The primary outcome was proportion of END recovery within seven days.

Data were reviewed from the charts of 48 patients matched from each group. Recovery of END was noted in 77.2% of the PIH group and 51.5% of the argatroban group ($p< 0.01$). At three months the PIH group had better modified Rankin Scale (mRS) functional outcome scores with 34.2% achieving a good outcome (mRS 0-1) compared to 16.2% in the argatroban group ($p=0.04$).

Conclusion: This study of patients with early neurological deterioration after a lacunar stroke found that those treated with phenylephrine had better functional recovery than those treated with argatroban.

Park, S., et al. Rescue Therapy of Early Neurological Deterioration in Lacunar Stroke**. BMC Neurol.**2024; 2:329. https://doi.org/10.1186/s12883-024-03825-7**.**

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