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BIOMARKER CHANGES TWENTY YEARS BEFORE ALZHEIMER'S DISEASE

Preclinical Alzheimer's disease (AD) has been characterized by the presence of normal cognitive function and abnormal levels of cerebral spinal fluid (CSF) markers. This study was designed to determine the trajectory of changes in several CSF biomarkers comparing those who later received a diagnosis of AD, and those who remained cognitively intact.

The China Cognition and Aging Study (COAST) is a nationwide, prospective, cohort study which was to establish a large database pertaining to dementia in China. From this database researchers randomly selected 648 adults, 45 to 65 years of age, who later developed AD, and a matched group of 648 participants who maintained normal cognition. Data were obtained from clinical records, including blood and CSF samples [APOE genotyping, and levels of β -Amyloid 1-40, β -Amyloid 1-42, hTAU Ag, and PHOSPHO-TAU 181P, and NF-Light (NF-L)], neuropsychological tests, and MRI examinations every two to three years for 20 years. Cognitive status was determined by the Mini-Mental State Examination (MMSE), the Logical Memory Test (LMT), and the CDR-Sum of Boxes (CDR-SB). Mild cognitive impairment was diagnosed according to the Petersen criteria. The groups were followed for a median of 19.9 years.

The APOE ϵ 4 was present in 37.2% of those who developed AD and 20.4% of those who did not. Compared to the cognitively normal controls, CSF-A β ₄₂ levels began to differ in the AD group, 18 years prior to the diagnosis of AD. This interval was 11 years for the ratio of CSF A β ₄₂ to A β ₄₀, ten years for CSF phosphorylated tau 181, 10 years for total tau, and six years for CDR-SB.

Conclusion: This prospective study of Chinese adults found that, compared with controls, differences in cerebrospinal fluid biomarkers

occurred at 18 years for CSF A β ₄₂ to six years for CDR-SB.

Jia, J., et al. Biomarker Changes during 20 Years Preceding Alzheimer's Disease. *N Engl J Med.* 2024, Feb 22; 390(8): 712-722.

BLOOD FLOW RESTRICTION EXERCISE DURING SIT TO STAND MOVEMENTS

Blood flow restriction exercise (BFRE) has been shown to improve muscle strength with low intensity resistance, by temporarily restricting blood flow. This study assessed the effect of BFRE on pain and strength in patients with low back pain (LBP).

The subjects were 40 patients with LBP, with a visual analog scale (VAS) for pain score of four or greater, able to walk independently, and perform activities without assistive devices. The patients were randomized to either a control group or a BFRE group. All were asked to perform a sit to stand (STS) exercise 20 times in the first set and 10 times in the second to fourth sets. During the exercise, the BFRE group inflated their cuffs to a premeasured systolic blood pressure (SBP). Quadriceps muscle mass (QMM) was measured by ultrasound, at baseline and follow-up. Pain was measured using the visual analog scale (VAS) and the Oswestry Disability Index (ODI).

The rate of change in QMM was better in the BFRE group than the control group for the rectus femoris ($p=0.000$), vastus intermedius ($p=0.004$), vastus medialis ($p=0.001$), and vastus lateralis ($p=0.014$). Compared to the control group the BFRE group demonstrated a greater rate of improvement in VAS pain scores ($p=0.009$) and the rate of change of the ODI scores ($p=0.001$).

Conclusion: This study of patients with low back pain found that, compared to standard exercise, blood flow restriction exercises resulted in better pain relief and greater improvement in quadriceps muscle mass (QMM).

Lee, K., et al. Enhanced Pain Relief and Muscle Growth in Individuals with Low Back Instability: The Impact of Blood Flow Restriction Exercise during Sit to Stand Movements. *Med Sci Monit.* 2024, Jan 25; 30: e942508.

TOPICAL CURCUMIN FOR MILD TO MODERATE CARPAL TUNNEL SYNDROME

Carpal tunnel syndrome (CTS) is one of the most common neuropathies, caused by entrapment of the median nerve at the wrist. The most common manifestations of CTS are pain and paresthesia in the territory innervated by the median nerve. Typical treatments for this syndrome include splinting, corticosteroid injections, and surgery. This study assessed the efficacy of a topical treatment with curcumin for patients with mild and moderate CTS.

This prospective, randomized, placebo-controlled trial included 120 hands of 70 participants diagnosed with CTS. The patients were randomized to receive a placebo cream ($n=35$) or a topical curcumin gel ($n=35$), applied over the carpal tunnel twice per day for eight weeks. Both groups wore a volar cock-up splint at night. The primary outcome measures were the Symptom Severity Scale (SSS) and Functional Status Scale (FSS) of the Boston Carpal Tunnel Questionnaire (BCTQ). Baseline scores were compared to those at eight-week follow-up.

Compared to baseline, scores on the SSS improved by a mean of 12.45 points in the curcumin group and 3.28 in the placebo group ($p=0.0001$). Scores on the FSS were also significantly more improved in the treatment group than in the placebo group ($p=0.002$). After eight weeks, 22 patients in the treatment group and four in the placebo group reported that they were satisfied with the treatment. No significant changes in electrodiagnostic test results were noted in either group.

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Conclusion: This study found that topical curcumin gel may be effective for treating mild to moderate carpal tunnel syndrome.

Razavi, A., et al. Efficacy of Topical Curcumin on Mild to Moderate Carpal Tunnel Syndrome: A Randomized, Double-Blind, Placebo Controlled, Clinical Trial. *Pain Med*, 2024, Jan 27: pnae001. doi: 10.1093/pm/pnae001. Online ahead of print.

20-YEAR OUTCOME OF CERVICAL DISC ARTHROPLASTY

Anterior cervical discectomy and fusion (ACDF) is considered the gold standard for the surgical treatment of cervical radiculopathy caused by degenerative disc disease (DJD). However, this surgery can result in abnormal compensatory motion resulting in adjacent level disease. Cervical disc arthroplasty (CDA) was designed to reduce this abnormal motion. This study compared the outcomes of these two surgeries.

This prospective, randomized controlled trial included patients presenting with single-level cervical radiculopathy, and DJD at C3-4 and C6-7 that failed at least six weeks of non-operative treatment. Of the patients enrolled, twenty-two were randomized to undergo CDA and twenty-five to undergo ACDF. The clinical outcome measures included the neck disability index (NDI) and a visual analog scale (VAS).

At 20 years, both surgical groups demonstrated improvement from baseline scores on the NDI, VAS arm pain, and VAS neck pain scores ($p < 0.001$ for all comparisons). There were no significant differences at follow-up between the two surgical groups in mean scores for NDI (11.1 vs. 19.9, $p = 0.087$), mean VAS arm pain (0.9 vs. 2.3, $p = 0.095$), or mean VAS neck pain (1.2 vs. 2.9, $p = 0.073$). Reoperations occurred in 41.7% of the ACDF group and 10.0% of the CDA group ($p = 0.039$).

Conclusion: This prospective study of patients who underwent surgical intervention for cervical degenerative disc disease found that, at 20 years, clinical improvements were similar between those who underwent anterior cervical discectomy and fusion, and those who underwent cervical disc arthroplasty.

Sasso, W., et al. 20-Year Clinical Outcomes of Cervical Disc Arthroplasty. *Spine*. 2024, Jan 1; 49 (1): 1-6.

CHRONIC SPINAL CORD INJURY RECOVERY

Over the last several decades, researchers have demonstrated a crucial role of the cell and axon growth inhibitory properties of chondroitin sulfate proteoglycans (CSPGs) during normal neural development. These also serve to inhibit the re-growth of cells or their processes after spinal cord injury (SCI). This study assessed the effectiveness of a targeted enzymatic removal of the inhibitory chondroitin sulfate proteoglycan (CSPG), using a combination of interventions designed to reduce and overcome the inhibitory effects of CSPGs.

This animal study involved rats with experimentally induced SCIs. All were evaluated for forelimb function before and after injury. Three months post-injury, the rats were randomly assigned to begin 60 days of daily injections of a placebo solution or intracellular sigma peptide (ISP), combined with oral gavage feeding, with or without the small molecule (0.2 g/mL) perineuronal net inhibitor, PNNi. Two separate cohorts received ISP or PNNi alone. Forelimb/paw function was assessed using the Forelimb Locomotor Scale (FLS) and the IBB Forelimb Recovery Scale.

At baseline, all rats had FLS scores of 17. This fell to three immediately after the SCI, then rose, with spontaneous recovery to a mean of eight at 12 weeks. At 24 weeks, the animals that had been treated with ISP alone or PNNi alone reached an average FLS score of 11. The combination-treated rats achieved an average final score of 12. Upper extremity function was assessed by cereal eating, using the IBB. Before injury, all animals had IBB scores of nine. After injury, the control animals' scores averaged IBB scores of 2-3. At 24 weeks post-injury, the combined treatment group recovered to a mean IBB score of 5-6.

Conclusion: This animal study illustrates the crucial role of chondroitin sulfate proteoglycan mediated inhibition via the rPTP σ receptor in constraining functional synaptic plasticity following a spinal cord injury, suggesting clinically relevant, translational benefits.

Milton, A., et al. Recovery of Forearm and Fine Digit Function after Chronic Spinal Cord Injury by Simultaneous Blockade of Inhibitory Matrix Chondroitin Sulfate Proteoglycan Production and the Receptor PTP σ . *J*

Neurotrauma. 2023, Dec; 40(23-24): 2500-2521.

SUBLINGUAL EDARAVONE DEXBORNEOL FOR ACUTE ISCHEMIC STROKE

The Efficacy and Safety of Nerinetide for the Treatment of Acute Ischemic Stroke (ESCAPE-NA1) trial reported that eicosapeptide nerinetide had a potentially cytoprotective effect via inhibition of neuronal excitotoxicity, and decreased production of nitric oxide among patients with acute ischemic stroke. Sublingual edaravone dexborneol, composed of edaravone and dexborneol, can rapidly diffuse and be absorbed through the oral mucosa after sublingual exposure. Therefore, the Treatment of Acute Ischemic Stroke (AIS) with Sublingual Edaravone Dexborneol (TASTE-SL) trial investigated the effects of sublingual edaravone dexborneol on 90-day functional outcomes in patients with AIS.

This phase three, double-blind, placebo-controlled, multicenter, parallel group, randomized, clinical trial was completed in 33 centers in China between June of 2021 and August of 2022. The subjects presented to the centers with AIS symptoms and NIHSS scores of between six and 20. Within 48 hours of symptom onset, the eligible patients were randomized to receive either a sublingual placebo or sublingual edaravone dexborneol, 36 mg (edaravone, 30 mg; dexborneol, six mg), twice a day for 14 consecutive days. The primary efficacy outcome was the proportion of patients with a Modified Rankin Scale (mRS) score of one or less at 90 days after randomization.

A favorable outcome of an mRS score of one or less on day 90 occurred in 290 of 450 patients (64.4%) in the edaravone dexborneol group and in 254 of 464 patients (54.7%) in the placebo group ($p=0.003$). Edaravone dexborneol did not have a positive effect on the proportion of scores with a mRS score of two or less or changes in NIHSS scores to day 14.

Conclusion: This prospective study of adult patients hospitalized with acute ischemic stroke within 48 hours of symptom onset found that sublingual edaravone dexborneol can improve the proportion of patients achieving a good functional outcome on day 90, without increasing the risk of adverse events.

Fu, Y., et al. Sublingual Edaravone Dexborneol for the Treatment of Acute Ischemic Stroke. The TASTE-SL Randomized, Clinical Trial. *JAMA Neurol.* 2024. doi:10.1001/jamaneurol.2023.5716.

CONSERVATIVE VERSUS SURGICAL TREATMENT FOR CEREBELLAR INFARCTIONS

Surgical intervention is currently recommended for cerebellar infarctions in cases of neurologic deterioration in the setting of a mass effect, though this recommendation lacks clarity about the lesion volume implied. This study compared the functional outcomes of patients with cerebellar infarction who were treated surgically, to those treated conservatively.

This multicenter, retrospective study consisted of patients hospitalized with a cerebellar infarction. Information gathered during hospitalization included age, gender, medical history, Glasgow Coma Scale score, radiologic parameters, treatment modality, and associated complications. Surgical treatment was defined as either craniotomy with necrosectomy or suboccipital craniectomy. The primary outcome measure was the proportion of patients demonstrating favorable functional outcomes, comparing the surgical to the conservative group. A favorable outcome was defined as a modified Rankin Scale (mRS) score of zero to three.

Data were analyzed for 531 patients with cerebellar infarcts. There was no significant difference in favorable outcome at discharge between those treated surgically and those managed conservatively. In a subgroup analysis, those with infarct volumes of ≥ 35 ml had a higher rate of favorable outcome in the surgical group ($p=0.03$).

Conclusion: This cohort study of patients hospitalized with an ischemic cerebellar infarction found that surgical treatment was not associated with improved outcome, although subgroup analysis found that infarction volumes of 35 milliliters or greater did respond better to surgical intervention.

Won, S., et al. Functional Outcomes in Conservatively versus Surgically Treated Cerebellar Infarcts. *JAMA Neurol.* 2024, Published February 26: doi: 10.1001/jamaneurol. 2023. 5773.

FIVE TIMES SIT-TO-STAND AFTER TOTAL JOINT ARTHROPLASTY

Each year, over 1,000,000 total knee arthroplasties (TKAs) and total hip arthroplasties (THAs) are performed. A study of patients undergoing total knee or total hip arthroplasty found a statistically significant association between preoperative timed up and go scores and hospital length of stay. This study examined the clinical significance of the Five Times Sit to Stand Test (FTSTS) on hospital length of stay for patients undergoing total knee arthroplasty.

Included in the study were patients who had undergone total joint arthroplasty between January of 2020 and August of 2022. The FTSTS was administered to each subject, with the participants instructed to perform the test using a standard chair with arms. The data were analyzed to establish a score on the FTSTS which would be useful to stratify those with same day discharge (SDD) and those without.

High sensitivity ($>80\%$) was established for the test at a score of 18.5 seconds. High specificity ($>80\%$) was established for the test at a score of 11.3 seconds. The highest combined sensitivity and specificity for the SDD outcome occurred at a score of 13.6 seconds.

Conclusion: This study of patients undergoing total joint replacement surgery found that the Five Times Sit-to-Stand Test was useful in determining the likelihood of same day hospital discharge.

Camillieri, S., et al. The Five Times Sit-To-Stand Test Predicts Same-Day Discharge for Outpatients Undergoing Total Joint Arthroplasty. *Int Orthop.* 2024 Feb;48(2):351-356.

FROZEN SHOULDER, DIABETES, AND FASTING GLYCEMIC TRAITS

Frozen shoulders are one of the more common shoulder conditions, affecting up to five percent of the population. Patients typically present with early shoulder pain, followed by a decreased range of motion in their shoulder joint. As studies have suggested a correlation between blood sugar and the development of frozen shoulders, this study was designed to further clarify this association.

This study used two-sample, Mendelian randomization using single nucleotide polymorphisms (SNPs) associated with type 2 diabetes and

glycemic traits (fasting glucose (FG), fasting insulin (FI), glycated hemoglobin (HbA1c), and two-hour postprandial glucose (2hGlu)) as instrumental variables. The SNPs were obtained from a large-scale, genome-wide association study (GWAS), a meta-analysis which included 48,286 patients and 250,671 controls, encompassing 190,486 SNPs. To evaluate the causal association between type 2 diabetes (T2D) and glycemic related properties with frozen shoulders, the authors conducted a two-sample MR analysis.

A total of 89 SNPs were identified as instrumental variables for the MR analysis of T2D and frozen shoulder. The analysis revealed a significant genetic causal relationship between frozen shoulder and T2D ($p=0.00697$), and fasting glucose ($p=0.00035$).

Conclusion: This study, using Mendelian analysis, found a positive relationship between frozen shoulders and fasting glucose.

Xu, T., et al. Type 2 Diabetes and Fasting Glycemic Traits Are Causal Factors of Frozen Shoulder: A Two-Sample, Mendelian, Randomization Analysis. *J Shoulder Elbow Surg.* 2024, February; 33(2): 399-408

LUMBAR FLEXION VERSUS EXTENSION EXERCISES FOR CHRONIC LOW BACK PAIN

Low back pain (LBP) is among the primary causes of global disability. Axial LBP describes pain confined to the lower back region that does not travel to the extremities. This pain may be caused by degenerative disc disorders, facet joint disorders, or local soft tissue pathology. This study compared the effects of treatment using lumbar flexion with that of extension-based exercises for axial LBP.

The subjects were 56 patients with axial LBP > six months. Twenty-seven were randomized to a flexion group and 29 to an extension group. Clinical outcomes were observed at one, three, six, and 12 months. Each participant received four face-to-face sessions of 30-minute, supervised treatment once per week, to obtain instructions and principles for the allocated exercise. The patients were instructed to engage in daily home exercises for at least 30 minutes per day.

The extension group engaged in strengthening, including prone lying flat, prone propped on elbows, prone propped on hands, and standing

lumbar extension. The flexion exercises included pelvic tilt, knee to chest trunk flexion, and forward bending with hip flexor stretch. Adherence was monitored at each assessment visit. The primary outcome measure was the average pain score of the lower back region at one year, on a ten-point scale.

The mean pain scores in the flexion group were 5.86 at baseline and 3.78 at one-year follow-up. The mean pain scores in the extension group were 5.54 at baseline and 2.25 at one year ($p<0.002$). The extension group showed greater improvement on pain subscales, including least pain, current pain, and pain interference.

Conclusion: This study of patients with chronic, axial, low back pain found that extension exercises were superior to flexion exercises for improving this pain.

Park, C., et al. Long-Term Effects of Lumbar Flexion versus Extension Exercises for Chronic, Axial Low Back Pain: A Randomized, Controlled Trial. *Nature Scientific Reports.* 2024; 14: 2714. |

QUADRICEPS VERSUS HAMSTRING TENDON AUTOGRAFT IN ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

Anterior cruciate ligament reconstruction (ACL-R) is the standard treatment for patients with an ACL injury. With recent interest in using the quadriceps tendon (QT) autograft for the repair, this study compared the outcomes of patients undergoing ACL-R using hamstring tendon (HT) to those receiving bone-patellar tendon-bone (BPTB) grafts.

Subjects, who were 16 to 50 years of age and presenting for ACL-R, were randomized to receive either HT or QT autografts. Clinical assessments including passive range of motion were completed from three to 24 months post-surgery. Evaluations included the International Knee Documentation Committee Subjective Knee Evaluation Form, the Knee Outcome Survey Activities of Daily Living Scale, the Lysholm scale, the Cincinnati Knee Rating System, and the Tegner Activity Scale. Pain was measured with a ten-point pain visual analog scale (VAS) for the knee, and the graft harvest site.

Data collection was complete for 49 in the HT group and 48 in the QT group. Return to sport, was better in the HT group at post-surgery months

three ($p=0.008$), six ($p=0.010$), and 12 ($p=0.014$). In addition, the HT group demonstrated greater quadriceps strength at six and 12 months, while the QT group demonstrated better hamstring strength at the same intervals.

Conclusion: This study of patients undergoing anterior cruciate ligament repair, using autografts from the quadriceps or the hamstring tendons, found similar improvements in outcome measures, although return to sport favored the hamstring tendon group.

Ebert, J., et al. A Prospective, Randomized, Controlled Trial Investigating Quadriceps versus Hamstring Tendon Autograft in Anterior Cruciate Ligament Reconstruction. *Am J Sports Med.* 2024, Mar; 52(3): 660-669.

QUALITY OF LIFE 20 AND 35 YEARS AFTER ACL RECONSTRUCTION

After an anterior cruciate ligament (ACL) injury, the standard of care is surgical repair of the deficit. This study investigated changes in health and quality of life from 20-35 years after an ACL injury, comparing the outcomes of patients who did, and those who did not, undergo surgical repair.

This prospective, cohort study followed 139 patients for 20 and 35 years after injury. All underwent diagnostic arthroscopy at a mean of five days post-injury. Those who underwent surgical repair ($n=33$) were compared to those who were treated conservatively ($n=26$). After surgery, the subjects underwent a structured rehabilitation program focused on strength and coordination.

At 20 and then 35 years after their injury, the patients were given questionnaires including the Knee injury and Osteoarthritis Outcome Score QoL (KOOS-QoL) subscale (range, 1-100), ACL-QoL questionnaire (range, 1-100), European QoL-5 Dimensions Questionnaire, and visual analog scale.

At the 35 year-follow-up, symptomatic osteoarthritis (OA) was found in 52% of the surgical repair group and 38% of the no-surgery group. At 35 years, the mean scores on the ACL-QoL were the same (67/100) in both groups.

Conclusion: This study of patients with ACL injury found that, at 35 years, knee related quality of life was impaired, with no difference

between those treated surgically, and those treated conservatively.

Kvist, J., et al. Knee-Related Quality of Life Compared between 20 and 35 Years after an Anterior Cruciate Ligament Injury Treated Surgically with Primary Repair or Reconstruction, or Nonsurgically. *Am J Sports Med.* 2024, January; 52(2): 311-319.

HETEROTOPIC OSSIFICATION AND PLATELET RICH PLASMA IN CORE MUSCLES

Previous studies have investigated the phenomenon of heterotopic ossification (HO) among patients with core muscle injuries (CMI). This study was designed to determine whether HO is associated with a previous treatment with platelet rich protein (PRP)

A total of 3,642 patients were treated for a CMI involving the rectus abdominis, pectineus, adductor longus, adductor brevis muscles, and/or pubic fibrocartilage. Those who reported having previously been treated with PRP were compared to those with no such treatment. The cohort was segmented by age, gender, and athletic status, and by whether they had received PRP injections before their visits. The diagnosis of HO was established by the presence of calcification of the fibrocartilage and/or skeletal muscle, as detected by gross and/or microscopic pathology. The primary outcome measure was a self-reported, five-point scale of global performance, with five being at or above preinjury level and no discomfort, and one being worse than preoperatively. Those reporting a four or five were listed as surgical successes.

Among the cohort of 3,642 patients with new CMI, 68 (1.9%) developed HO in the core or adjacent muscles. Of these, 44 (64.7%) had received PRP injections. Of 108 patients treated with PRP injections into the core muscles, 44 (40.7%) developed HO in the core muscles. After surgical repair, three-month success rates were 67.9% and 96.4%, respectively, in the PRP and non-PRP groups ($p=0.006$).

Conclusion: This study of patients with core muscle injuries found that injections with platelet rich plasma are associated with an increased risk of heterotopic ossification within the core muscles.

Poor, A., et al. Heterotopic Ossification and Platelet Rich Plasma in Core Muscle Injuries: A Single Institution Experience Over Six Years. *Am J Sport Med.* 2024, January; 52(1): 54-59.

CONTINUOUS SUPRASCAPULAR NERVE BLOCK FOR ADHESIVE SHOULDER CAPSULITIS

Capsulitis is characterized by severe shoulder pain, restricted movement, and diminished quality of life. This study assessed the effect of a continuous block of the suprascapular nerve for improving adherence to exercise and function.

This retrospective cohort study included patients hospitalized for refractory adhesive capsulitis of more than six months' duration. During the 10-day hospitalization, the subjects underwent a suprascapular nerve block, delivered through a continuous infusion of ropivacaine, 5 ml per hour for four to nine days. The patients received intensive, standardized rehabilitation, including physical and occupational therapy for two hours per day. A 10-point visual analog scale was used to evaluate pain. The Disability of Arm, Shoulder, Hand (DASH) questionnaire was given at baseline and follow-up. The primary outcome measure was the change in range of motion over time.

By day ten, passive/active anterior elevation increased by $+ 31.5^\circ/32^\circ$ ($p<0.001$), passive/active frontal abduction by $+ 32^\circ/+ 35^\circ$ ($p<0.001$), passive/active internal rotation by $+ 20^\circ$ ($p<0.001$), and passive/active external rotation by $+ 23.5^\circ/+ 28.5^\circ$ ($p<0.001$). By day 180 the mean VAS scores decreased by a mean of 2.6 points ($p<0.001$) and the DASH by 9.5 points ($p<0.001$).

Conclusion: This study of patients with chronic adhesive capsulitis found that a continuous suprascapular nerve block, combined with intensive therapy, could significantly improve function and reduce pain.

Martens, G., et al. Continuous Suprascapular Nerve Blockade to Potentiate Intensive Rehabilitation for Refractory Adhesive Capsulitis: A Cohort Study. *Internat Orthop.* 2024, Feb;48(2):495-503.

CAFFEINE AND 800-METER RUN PERFORMANCE

A number of studies have demonstrated that caffeine ingestion

may improve physical performance. The exact mechanism of this effect is not completely clear. This study hypothesized that caffeine ingestion could improve pace-controlled simulated, 800-meter run performance, by increasing ventilation and, therefore, exercise induced arterial hypoxemia (EIAH).

The subjects were 16 college middle distance runners who were randomized to receive a placebo or caffeine dosed at six mg/kg of body weight prior to an 800-meter run. Prior to the run, an incremental treadmill test was completed to determine VO_2 max. Thirty minutes after caffeine injection, the subjects performed a simulated 800-meter run. The test involved 30 seconds of running at a pace of 103% of their 800-m seasonal best, followed by a speed of 98% of their seasonal best until exhaustion. The primary outcome measure was the time to exhaustion, comparing the control to the caffeine trials.

Compared to the control condition, the time to exhaustion in the caffeine condition was 7.3% longer ($p<0.04$). Arterial oxygenation, perceived exertion, minute ventilation and oxygen uptake were all similar between the two groups. The caffeine trials had higher heart rates ($p<0.01$) and postexercise blood lactate levels ($p=0.002$) compared to the control trials.

Conclusion: This study of college age middle distance runners found that caffeine ingestion improved 800-meter run performance, without affecting arterial hypoxia or ventilation.

Dobashi, K., et al. Caffeine Improves Simulated 800-Meter Run Performance without Affecting Severe Exercise-Induced Arterial Hypoxemia. *Med Sci Sport Exerc.* 2024, Feb 1;56(2):350-361.

COGNITION AND MEMORY AFTER COVID-19

While a number of research studies have suggested that memory and concentration may be impaired after COVID-19, objective data regarding cognitive performance are largely lacking. This study was designed to better understand the long-term effects of a SARS-CoV-2 (COVID-19) infection.

The Real-Time Assessment of Community Transmission (REACT) study of COVID-19 included a community sample of more than three million persons in England. Invitations

were sent to participate in a survey and cognitive testing. For those who agreed, an online assessment tool, including eight domains, was sent to assess cognitive function. The scores of these were reviewed and compared between those who had been previously infected with COVID-19 with symptoms that persisted for ≥ 12 weeks, and those who were uninfected (a no-COVID group).

The data demonstrated that COVID-19 was associated with longer-term, objective cognitive deficits, averaging three points on an IQ test. Those with resolved symptoms had an IQ score deficit of 0.2 standard deviations compared to the no-COVID group. Those with unresolved symptoms had a reduction in cognition of 0.4 standard deviations as compared to the no-COVID group.

Conclusion: This study found objective, measurable, cognitive deficits that may persist for a year or more after a symptomatic infection with Covid-19.

Hampshire, A., et al. Cognition and Memory after Covid-19 in a Large Community Sample. *N Eng J Med*. 2024, Feb 29; 390: 806-818.

EXTRACORPOREAL SHOCK WAVE THERAPY AND HIGH-INTENSITY LASER THERAPY IN LATERAL EPICONDYLITIS

Lateral epicondylitis is a commonly encountered extraarticular condition, classified as an overuse syndrome. Routine treatment includes conservative techniques, including anti-inflammatory drugs, splints, exercise regimens, local injections, kinesiotape, and shockwave therapy. The ideal conservative treatment remains unclear. This study compared the effect of treatment with high intensity laser therapy to that of extracorporeal shockwave therapy.

The subjects were adults with a diagnosis of lateral epicondylitis. The patients were randomized to receive HILT or ESWT. The HILT group received treatment at an average output power of 15 W at a frequency of 15 Hz with an energy density of 39 J/cm² per point, one session per day five days per week for three weeks. The radial ESWT was applied once a week for three weeks, with the ESWT device set to 8 Hz and 1,500 pulses/session at 0.18 mj/mm². Outcome measures included tenderness, Visual Analog Scale (VAS) scores, Quick Disabilities of the Arm scores, Shoulder and Hand scale(Q-DASH)

scores, and grip strength, all assessed at baseline, then at weeks three and twelve.

Both the HILT and ESWT groups demonstrated significant improvement in lateral epicondyle tenderness ($p < 0.001$ and $p = 0.003$ respectively), though the improvement was greater in the HILT group at week three ($p = 0.001$) and week twelve ($p = 0.003$). Improvement in the VAS-rest values was also better in the HILT group at weeks three ($p = 0.005$) and 12 ($p = 0.032$). A similar pattern was found for VAS-movement, and Q-DASH disability scores.

Conclusion: This study of patients with lateral epicondylitis found greater improvement in symptoms and function in a group treated by high intensity laser therapy as compared to extracorporeal shockwave therapy.

Sen, S., et al. Comparative Analysis of the Therapeutic Effects of Extracorporeal Shockwave Therapy and High-Intensity Laser Therapy in Lateral Epicondylitis: A Randomized, Clinical Trial. *Rheumatol Int*. 2024 Apr;44(4):593-602.

VITAMIN D LEVELS AND ROTATOR CUFF TEAR

Rotator cuff injury is a leading cause of shoulder disability. As prior research has demonstrated an association between vitamin D deficiency and muscle strength, this study assessed the effect of vitamin D deficiency on rotator cuff injury injuries and repairs.

This retrospective analysis was performed using de-identified data from a medical database from January 1, 2011, to October 31, 2018. This database includes all Humana, Incorporated insurance claims of over 150 million insured patients. The database was queried for patients 30 to 89 years of age diagnosed with vitamin D deficiency. This group was followed for diagnosis of rotator cuff injuries with these compared to those without a vitamin D deficiency.

Among the 150 million patients, 15% were diagnosed with vitamin D deficiency. A random sample of Vitamin D deficient patients was compared to a randomly selected group with normal levels of vitamin D. The subjects were followed for rotator cuff injuries. Within two years of a vitamin D deficiency diagnosis, 1,977 experienced a full thickness tear of the rotator cuff, compared to 842 of the matched control, with an

odds ratio (OR) of 2.36. Women between the ages of 70 and 89 had the greatest risk of tears, (OR 2.93 compared to men)

Conclusion: This study, utilizing a large insurance database, found that those with a vitamin D deficiency have more than double the risk of a rotator cuff tear.

Albright, J., et al. Significant Association between a Diagnosis of Hypovitaminosis D and Rotator Cuff Tear, Independent of Age and Sex: A Retrospective Database Study. *Med Sci Sports Exerc*. 2024, March; 56 (3): 446-453.

HIGH-RESISTANCE INSPIRATORY MUSCLE STRENGTH TRAINING AND EXERCISE TOLERANCE

High-resistance inspiratory muscle strength training (IMST) is a low-volume, time-efficient form of intensive respiratory exercise that improves respiratory muscle strength. This study was designed to determine whether IMST can improve cardiorespiratory fitness, exercise tolerance, and physical function in midlife and older adults.

This double-blind, randomized, sham controlled, parallel group design trial included healthy men and postmenopausal women 50-79 years of age. The subjects were randomized to perform high resistance IMST or low resistance sham training. All subjects performed 30 inspiratory maneuvers, five sets of six breaths, with one-minute rests between sets, six days a week for six weeks. The high resistant IMST group (H-IMST) trained at 55 percent of the maximal inspiratory pressure (Pimax) during week one, 65% of the Pimax during week two, and 75% of the Pimax during weeks three through six. All subjects were tested at baseline and at follow-up for peak aerobic capacity (VO₂ peak). Subjects performed a graded treadmill exercise test to exhaustion, physical performance battery (e.g., handgrip strength, leg press), and body composition testing (dual x-ray absorptiometry). Blood was drawn to perform an analysis of plasma acylcarnitines using high-throughput mass spectrometry.

Data were analyzed from 35 subjects. Compared to baseline, systolic blood pressure ($p < 0.001$) and diastolic blood pressure ($p = 0.050$) decreased, and Pimax increased ($p = 0.001$) with H-IMST but were unchanged with sham training. Exercise tolerance increased by 12% in the H-IMST group ($p = 0.009$) and was unchanged in the sham group.

Also noted were consistent associations between the change in plasma acylcarnitine levels and the changes in exercise tolerance with HIMST.

Conclusion: This study found that high resistance inspiratory resistance training of 30 inhalation-resistance breaths per day improved cardiorespiratory fitness, exercise tolerance, and physical function in healthy midlife and older adults.

Craighead, D., et al. Time-Efficient, High-Resistance Inspiratory Muscle Strength Training Increases Exercise Tolerance in Midlife and Older Adults. *Med Sci Sports Exer.* 2024 Feb 1; 56(2): 266-276.

REHABILITATION FOLLOWING TRAUMATIC SHOULDER DISLOCATION

The shoulder is the most frequently dislocated joint. Despite the prevalence of this injury, evidence comparing different rehabilitation interventions remains scarce. This study compared the clinical effectiveness of two rehabilitation interventions for adults with a first-time traumatic shoulder dislocation.

This study was conducted at 41 United Kingdom hospital trusts in the National Health Service (NHS). The subjects were adults with a first-time traumatic anterior shoulder dislocation. All were seen for a physical examination and provided with advice to aid self-management. This included specific progressive exercises and exercise planning to enhance self-management. The subjects were randomized to a group for advice only (A), or to a group for physiotherapy(P). The P group received therapy, with 30-minute sessions involving further teaching and supervised progressive exercises focused on range of motion and progressive strengthening of the muscles of the shoulder. The primary outcome measure was the Oxford Shoulder Instability Score, measured at six months. Secondary outcomes included the QuickDASH (a shortened version of the disabilities of the arm, shoulder, and hand (DASH) questionnaire).

Data was collected from 482 participants. In the intention-to-treat adjusted analysis the mean Oxford scores were 36.2 for group A and 38.4 for group P (p=0.11). At all time points measured, the P group had better improvement on the QuickDASH, though this difference was never statistically significant. The same pattern was seen for scores on

health-related quality of life as measured by the EQ-5D-5L.

Conclusion: This study of patients with traumatic anterior shoulder dislocations found that those who received advice only did as well as those who received physiotherapy.

Kearney, R., et al. Acute Rehabilitation following Traumatic Anterior Shoulder Dislocation (ARTISAN): Pragmatic, Multi Center, Randomized, Controlled Trial. *BMJ.* 2024; 384: E076925 | Doi: 10.1136/Bmj-2023-076925.

NEIGHBORHOOD ENVIRONMENTAL BURDEN AND CARDIOVASCULAR HEALTH

Cardiovascular disease remains the leading cause of death in the United States. This study evaluated the association between neighborhood-level environmental burden and the prevalence of cardiovascular risk factors.

This cross-sectional study of 71,659 United States neighborhoods used United States Census tract level data on environmental burden from the Centers for Disease Control and Prevention (CDC). The prevalence of cardiovascular risk factors and diseases within each neighborhood was extracted from the 2020 CDC data set.

In 2022, the CDC and the agency for toxic substances and disease registry released the environmental burden index (EBI), the first comprehensive measure of exposure to environmental factors influencing human health, including air pollution, hazardous and toxic sites, the built environment (recreational parks and neighborhood walkability), transportation infrastructure, and water pollution. The neighborhood-level social vulnerability index (SVI) was obtained from the CDC. The SVI is separated into four separate domains, including 1) racial or ethnic minority status, 2) socioeconomic status, 3) household characteristics (e.g., disability status and limited English-speaking ability), and 4) housing type.

A review of the data revealed that the most environmentally burdened neighborhoods had significantly higher rates of cardiovascular risk factors than the least environmentally burdened neighborhoods. These included hypertension, diabetes, and obesity. Similar patterns were observed across cardiovascular diseases, including higher rates of coronary heart disease and stroke, as compared to the least

environmentally burdened neighborhoods. Associations between environmental burden and cardiovascular diseases were also stronger at higher levels of social vulnerability, including that for coronary heart disease.

Conclusion: This cross-sectional study found that a greater cumulative environmental burden was associated with a higher prevalence of cardiovascular risk factors and diseases across United States neighborhoods, even after controlling for age, gender, social vulnerability, geography, and healthcare access.

Liu, M., et al. Neighborhood Environmental Burden and Cardiovascular Health in the U.S. *JAMA Cardiol.* 2024; 9(2): 153-163. doi:10.1001/jamacardio.2023.4680.

DECENTRALIZED, HOME-BASED ANTIHYPERTENSIVE TREATMENT

The Antihypertensive Treatment Evaluation in Multimorbidity and Polypharmacy Trial (ATEMPT) was designed to test the efficacy of decentralized, home-based blood pressure management.

This two arm, parallel group, open label, randomized, controlled trial included 230 adults living in southeast England, all 65 years of age or older with multimorbidity (three or more conditions) or polypharmacy (five or more medications). During the baseline home visit, blood samples were taken to check participants' renal function and electrolytes. Using a home visit to provide an upper arm cuff-based blood pressure monitor, participants took daily blood pressures and pulse. Depending on the number of antihypertensive medications and the systolic blood pressure at baseline, the artificial intelligence system divided participants into three strata to guide the treatment implementation. For those participants for whom deprescribing was recommended, one drug was reduced in dose or removed at each four-week assessment, following the reverse order of the European Society of Hypertension guidelines. For those scheduled for additional medications, drugs could be added every four weeks. The effect of the changes to medications were monitored remotely by a clinician and adjusted accordingly in 4-weekly intervals. Every 3–6 months, a telephone call assessment was made to review health and quality of life issues. The primary outcome was the change in remotely measured BP.

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Of the 230 participants, 136 (59%) were allocated to stratum 1 (two drug classes added vs no change), 75 (33%) were allocated to stratum 2 (one drug class added vs one drug class stopped), and 19 (8%) were allocated to stratum 3 (no change vs two drug classes stopped). The mean systolic blood pressure decreased from 134.5 mmHg at baseline to 122.1 mmHg in the more group and from 134.8 to 132.9 in the less group. At the end of the study, the mean difference between the groups was 10.7 mmHg. No change was noted in either group in scores on the PRISMA-7 questionnaire, the T-MoCA, or the EQ-5D-5L quality of life score.

Conclusion: The ATEMPT trial demonstrated that a substantial lowering of systolic blood pressure can be achieved by use of an IT system combined with remote monitoring, in a cohort of older patients with multimorbidity and polypharmacy.

Majert, J., et al. Efficacy of Decentralized, Home-Based, Antihypertensive Treatment in Older Adults with Multimorbidity and Polypharmacy: An Open Label, Randomized, Controlled Pilot Trial. **Lancet Healthy Longev:** 2024, March. 5(3): E-172-181.

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