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TRANSCRANIAL MAGNETIC STIMULATION FOR POSTSURGICAL PARESIS IN GLIOMA PATIENTS

Microsurgical glioma resection may lead to surgery-related functional deficits, originating from subcortical ischemia rather than tissue resection. This study assessed the clinical efficacy of navigated transcranial magnetic stimulation (nrTMS) in glioma-resected patients with acute surgery-related paresis.

Subjects were patients 18 years of age or older who underwent microsurgical glioma resection. The participants were randomized to seven consecutive days of sham or nrTMS treatment. Within one hour of surgery, the nrTMS group received low-frequency nrTMS of one Hz for 15 minutes at an intensity of 110% of the resting motor threshold, for seven consecutive days. Those in the sham group received a stimulation intensity of five percent of the resting motor potential. Both groups were followed by 30 minutes of upper extremity task -oriented physical therapy. The primary outcome measure was the Fugl-Meyer Assessment (FMA).

At three-month follow-up, the average changes on the FMA were 4.2 in the sham group and 31.93 in the nrTMS group ($p=0.001$). Improvement on the National Institute of Health Stroke Scale (NIHSS) scores was greater in the treatment group than the sham group ($p<0.01$), with a favorable outcome on the NIHSS motor arm score achieved in 92.9% of the treatment group and 40% of the sham group.

Conclusion: This study of patients with glioma resection found that low-frequency transcranial magnetic stimulation can improve upper extremity functional outcome.

Ille, S., et al. Navigated Repetitive Transcranial Magnetic Stimulation Improves the Outcome of Postsurgical Paresis in Glioma Patients-A Randomized, Double-Blind Trial. **Brain Stim.** 2021, July-Aug: 780-787.

ONASEMNOGENE ABEPARVOVEC FOR SPINAL MUSCULAR ATROPHY

Spinal muscular atrophy (SMA) is an autosomal recessive disorder with a life expectancy of six to eight months. Onasemnogene abeparvovec is a gene therapy designed to deliver a full-length functional copy of the human SMN gene via a self-complementary adeno -associated virus serotype vector that crosses the blood-brain barrier. This study evaluated the long-term effects of this gene therapy.

The START LTFU is an ongoing, observational, long-term, follow-up study of patients with a genetically confirmed diagnosis of SMA type I. The participants received a low-dose (6.7 × 1013 vg/kg) or a therapeutic dose (2.0x1014 vg/kg). The primary outcome measures were the determination of safety based on serious adverse events. Efficacy outcomes included motor milestone achievement and assessment of ventilation.

At a median of 5.2 years follow-up, all 10 patients in the therapeutic-dose cohort were alive and did not require permanent ventilation. All three of the patients in the low-dose cohort remained alive, and two of these three remained free of permanent ventilation. Serious adverse events were reported for eight patients (62%), one patient in the low-dose cohort and seven in the therapeutic-dose cohort. No treatment-related adverse events were noted (gene therapy-related adverse events, liver function enzyme elevations, new incidences of malignancy or hematologic disorders, or new incidences or exacerbations of existing neurologic or autoimmune disorders).

Conclusion: In this phase I study, a single intravenous dose of onasemnogene abeparvovec gene replacement therapy extended patient survival, with no treatment-related adverse events reported.

Mendell, J., et al. Five-Year Extension Results of the Phase I START Trial of Onasemnogene Abeparvovec in Spinal Muscular Atrophy. **JAMA Neurol.** 2021, July; 78(7): 834-841.

MUSCLE RELAXANTS FOR NONSPECIFIC LOW BACK PAIN

Low back pain (LBP) has been the leading cause of disability worldwide for the past 30 years. As international clinical practice guidelines have not been consistent in the recommendation of muscle relaxants for LBP, this study was designed to better understand the efficacy of these medications.

This meta-analysis included records of randomized, controlled trials involving adults with nonspecific LBP. Eligible studies included spasmolytic muscle relaxants compared to a control. The primary outcomes were pain intensity and acceptability (satisfaction with the treatment regimen measured by the number of patients who discontinued treatment for any reason).

Studies selected for this meta-analysis included a combined total of 6,505 participants. For acute LBP of two weeks or less, non-benzodiazepine antispasmodics (carisoprodol, cyclobenzaprine, metaxalone, methocarbamol, thiocolchicoside, tizanidine, tolperisone, and orphenadrine) were associated with a small reduction in pain intensity. These medications were not associated with reduced pain intensity at three to 13 weeks or disability at two weeks or less. There were no benefits of antispastic (baclofen, dantrolene) and benzodiazepine (diazepam) drugs for pain and disability at two weeks or three to 13 weeks. The one exception was benzodiazepines at three to 13 weeks, which reduced disability. No clear benefits were noted for subacute or chronic back pain for any of the medications.

Conclusion: This literature review and meta-analysis found that non-benzodiazepine and antispasmodics may provide small

reductions in pain intensity at two weeks or less.

Cashin, A., et al. Efficacy, Acceptability, and Safety of Muscle Relaxants for Adults with Non-Specific Low Back Pain: Systematic Review and Metanalysis. **BMJ.** 2021; 374: n1446.

GREEN LIGHT EXPOSURE FOR FIBROMYALGIA

Fibromyalgia (FM) is a syndrome involving widespread pain. Given recent anti-nociceptive effects associated with exposure to green light, this study explored the efficacy of exposure to green light-emitting diodes (GLED) for the treatment of pain among patients with FM.

Subjects were 18 years of age or older with a diagnosis of FM. All had failed attempts at pain control using medical therapy. In a crossover design, patients with FM were first exposed to white light-emitting diodes (WLED), one to two hours a day for 10 weeks. The protocol was then repeated with GLED. The patients were instructed to use the LED light in a dark room, with no other source of light. The primary outcome measure was the average pain intensity on a 10-point numeric pain scale (NRS).

The average NRS pain score for the WLED group was 8.71 at baseline and 8.14 at follow-up ($p=0.14$). For the GLED condition, the NRS pain score at baseline was 8.38 and that at follow-up 4.86 ($p<0.0001$). In the secondary outcome measures, compared to the WLED group, significantly greater improvements were noted in the GLED condition in the ability to fall asleep, ability to work, ability to exercise and ability to perform chores (all $p<0.0001$) and in the ability to stay asleep ($p=0.0004$).

Conclusion: This single-blind, crossover study of patients with recalcitrant fibromyalgia found that green light exposure can significantly improve pain.

Martin, L. et al., Green Light Exposure Improves Pain and Quality of Life in Fibromyalgia Patients: A Preliminary, One-Way, Crossover, Clinical Trial. **Pain Med.** 2021; 22 (1): 118-130.

GREEN LIGHT EXPOSURE FOR MIGRAINES

Previous animal studies have suggested that exposure to light of different wavelengths can affect nociception. In animal studies, exposure to green light-emitting diodes (GLED) was found to have an anti-nociceptive effect. This human study was designed to determine whether GLED therapy can reduce the symptoms in patients with migraine headaches.

Subjects were 29 patients with episodic migraine and chronic migraine headaches. Those participants were scheduled to be exposed to one to two hours daily of white light-emitting diodes (WLED) for two weeks. The patients were instructed to keep the LED strips in their fields of vision, but to not stare directly at the light.

After a two-week washout period, that treatment was followed by exposure for one to two hours daily of GLED for 10 weeks. The primary outcome measure was the number of headache days per month. Secondary outcomes included patient-reported changes in intensity and frequency of headaches.

The WLED produced a small, but statistically significant, reduction in headache days. After GLED, subjects reported a significant decrease in headache days, including 7.9 per month among those with episodic migraine headaches and 22.3 per month among those with chronic migraines.

Conclusion: This crossover study of patients with episodic or chronic migraines found that two hours per day of green light exposure could reduce the number of headache days per month by 60%.

Martin, L., et al. Evaluation of Green Light Exposure on Headache Frequency and Quality of Life in Migraine Patients: A Preliminary, One-Way, Crossover, Clinical Trial. **Cephalalgia.** 2021, Feb; 41(2): 135-147.

TANEZUMAB VERSUS NSAIDS FOR OSTEOARTHRITIS

Tanezumab is a neurotrophin nerve growth factor (NGF) monoclonal antibody, under investigation as an alternative to nonsteroidal anti-inflammatory drugs (NSAIDs) for the treatment of osteoarthritis (OA). This study compared the long-term effects of tanezumab and NSAIDs.

This phase III, randomized, double-blind study was conducted at 446 sites in four continents. The subjects were adults clinically diagnosed with hip/knee OA. Each subject received an oral NSAID (naproxen 500 mg twice daily,

celecoxib 100 mg twice daily, or diclofenac extended-release 75 mg twice daily) for at least the prior two weeks.

The participants were then randomized to receive oral NSAIDs twice per day or tanezumab 2.5 mg SC or tanezumab 5 mg SC every eight weeks. The efficacy endpoints at week 16 were changes in WOMAC pain and physical function scores and changes in Patient Global Assessment (PtGA) scores. The primary safety outcomes included a worsening of K/L grade, a significant decline in joint space width, or abnormal bone loss or destruction.

Data were completed for 2,996 patients. At week 16, compared to those receiving NSAIDs those treated with tanezumab 5mg obtained significantly better WOMAC pain and function scores (p=0.015 and p=0.003, respectively), but not better PtGA scores. The proportions of patients who received at least a 50% reduction from baseline in the WOMAC pain scores at week 16 were 54.9%, 56.5%, and 51.5% in the tanezumab 2.5mg group, tanezumab 5mg group, and NSAID group, respectively. Composite joint safety events were significantly more prevalent in the tanezumab group than in the NSAID group (p = 0.001 for tanezumab 2.5 mg versus NSAIDs; p< 0.001 for tanezumab 5 mg versus NSAIDs).

Conclusion: This study of patients with osteoarthritis found that treatment with subcutaneous tanezumab resulted in better pain relief, but also more joint safety events.

Hochberg, M., et al. Long-Term Safety and Efficacy of Subcutaneous Tanezumab versus Nonsteroidal Anti-Inflammatory Drugs for Hip or Knee Osteoarthritis: A Randomized Trial. **Arthr Rheumat.** 2021, July; 73 (7): 1167-1177.

HETEROTOPIC OSSIFICATION FOLLOWING FEMORAL NECK ARTHROPLASTY

Heterotopic ossification (HO) is the most frequent complication following primary total hip arthroplasty (THA). Whether HO alters outcomes of fracture repair remains uncertain. This study was designed to better understand HO following surgical repair of hip fractures.

Data were obtained from the Hip Fracture Evaluation with Alternatives of Total Hip Arthroplasty versus Hemiarthroplasty (HEATH) trial. This multicenter trial randomized patients, 50 years of age or older, with displaced femoral neck fractures, to receive a THA or a hemiarthroplasty. Participants were assessed clinically at one week, 10 weeks, and six, nine, 12, 18, and 24 months postoperatively. At 24 months, all available radiographs were reviewed to identify and classify HO. The primary outcome measure was the cumulative incidence of HO at 24 months.

Of the 1,441 patients, 287 developed HO. Only 4.4% developed high-grade (Brooker III-IV) HO. HO was evident at 10 weeks postoperatively in 26% of the cases. Hip function, as assessed with the WOMAC, did not significantly differ between those without and those with low-grade HO (grade I or II). However, as compared with those with no HO, grade III or IV HO was associated with worse WOMAC scores (p=0.006).

Conclusion: This study of patients with surgically repaired femoral neck fractures found that 18.9% developed heterotopic ossification within 24 months, though only 4.4% of these had clinically relevant heterotopic ossification.

Comeau-Gauthier, M., et al. Heterotopic Ossification following Arthroplasty for Femoral Neck Fracture. **J Bone Joint Surg.** 2021, July 21; 103(14): 1328-1334.

ELECTRIC SCOOTER-RELATED FRACTURES

After the introduction of electric scooter ride sharing services, the number of individuals using this mode of transportation has increased dramatically. This retrospective study reviewed the medical charts regarding injuries resulting from electric scooter-related accidents presenting to a level I trauma emergency department.

Data were recorded concerning the medical assessment and intervention. During the 34 months of the study, 3,331 electric scooter-related injuries presented to the emergency department. Of these, 563 patients presented with a total of 716 fractures. The most common mechanism of injury was a rider fall (85.6%).

Of the 224 upper limb fractures, 52.7% were intra-articular, involving the radial head and the distal portion of the radius. Of the 210 lower limb fractures, 50 were tibial fractures. Of the entire cohort, 58 were diagnosed with a concussion (8.1%), 14 with lung contusion (two percent), and 39 with laceration (5.4%).

Conclusion: This chart review of patients presenting to a level I trauma center with electric scooter-related injuries found that most injuries were caused by falls, with fractures accounting for 17% of those injuries.

Shichman, I., et al. Epidemiology of Fractures Sustained during Electric Scooter Accidents. A Retrospective Review of 563 Cases. **J Bone Joint Surg**. 2021, June 16; 103(12): 1125-1131.

REPETITIVE BRIEF ISCHEMIA FOR TIBIAL FRACTURE

After a tibial fracture, the rate of nonunion is approximately five to ten percent. As ischemic preconditioning has been shown to promote fracture healing in an animal model, this study assessed the efficacy of repetitive bone ischemia (RBI) for bone healing.

This five-year, prospective study randomized 32 subjects 18 to 65 years of age presenting with a tibial fracture requiring open reduction internal fixation. The patients were randomized to a control group or to a group to receive RBI. Those in the RBI group had an inflatable cuff placed at the proximal thigh with inflation to 50 mmHg for 30 seconds then deflated. This sequence was repeated 30 times, twice per day for one month. The patients were assessed postoperatively at one, two, three, four, six, eight, and 12 months, with evaluations including x-rays physical exams and blood draws.

The bone healing times were three months in the RBI group and four months in the control group (p<0.01). No patient in the RBI group was found to have delayed union or nonunion. Two patients in the control group had delayed union, with none experiencing nonunion. The mean Lysholm knee score was significantly better in the RBI group than in the control group at both six and 12 months (p<0.001 and p=0.014, respectively).

Conclusion: This prospective, controlled trial of adults with tibial fractures requiring surgical correction suggests that repetitive brief ischemia can accelerate healing and reduce the rate of nonunion.

Wang, D., et al. Repetitive Brief Ischemia Accelerates Tibial Shaft Fracture Healing: A Five-Year, Prospective, Preliminary, Clinical Trial (PCT). **BMC Musculoskeletal Disord.** 2021; 22:631.

EMBOLI AFTER THROMBECTOMY

Clot fragmentation with distal embolization is a known complication of endovascular thrombectomy (EVT). The frequency of these events during EVT is not well known. This study used susceptibility weighted magnetic resonance imaging (MRI) to visualize distal emboli after EVT.

Subjects were consecutive patients treated with EVT for an acute ischemic stroke due to large intracranial vessel occlusion. New post-treatment emboli were identified at follow-up and categorized as appearing in a previously involved vascular tree or uninvolved vascular tree. Infarct volumes in patients with anterior circulation involvement were assessed. The primary clinical efficacy endpoint was the modified Rankin Scale of Global Disability at discharge.

The subjects had a mean age of 70 years, with a median National Institute of Health Stroke Scale (NIHSS) score of 15. New emboli were evident on the post-procedure scan in 22% of the patients. All new emboli were in initial vascular territory, with 91% presenting as single emboli. Multivariate analysis revealed that predictors of new emboli included lower initial diastolic blood pressure, alteplase pretreatment and atrial fibrillation.

Conclusion: Among acute ischemic stroke patients treated with thrombectomy, imaging evidence of distal emboli was found in 22%.

Wong, G., et al. Frequency, Determinants and Outcomes of Emboli to Distal and New Territories Related to Mechanical Thrombectomy for Acute Ischemic Stroke. **Stroke.** 2021, July; 52(7): 2241-2249.

ANTITHROMBOTIC MEDICATION AND CEREBRAL MICROBLEEDS

Cerebral microbleeds (CMBs) are represented by small areas of hemosiderin deposition seen on magnetic resonance imaging (MRI). These are found in 23% of the cognitively normal population over 60 years of age. This study was designed to determine whether antithrombotic medications are associated with CMBs.

Subjects were enrolled in the Mayo Clinic Study of Ageing, a longitudinal, population-based study of cognitive decline among residents of Olmsted County, Minnesota. Clinical data were recorded, including medications, history of diabetes, smoking, hypertension, history of stroke, and dyslipidemia. All subjects underwent brain magnetic resonance imaging (MRI) and amyloid positron emission tomography (PET) imaging. Antiplatelet use was characterized as the use of aspirin, clopidogrel, ticagrelor, or prasugrel ≥3 days per week. Anticogulants included warfarin, dabigatran, rivaroxaban, apixaban and edoxaban.

A total of 1,253 of the subjects underwent MRI imaging, with 93% undergoing concurrent PET scanning. Of the participants, 26.3% demonstrated CMBs. Those with CMBs were older ($p<0.001$), more likely to be male ($p<0.001$), and more likely to be hypertensive ($p<0.001$). After adjusting for potential confounders, anticoagulant use, but not antiplatelet use, was associated with an increased number of CMBs.

Conclusion: This study, using data from the Mayo Clinic Study of Aging, found that cerebral microbleeds are correlated with the use of anticoagulants, but not with the use of antiplatelets.

Graff-Radford, J., et al. Cerebral Microbleeds. Relationship to Antithrombotic Medications. **Stroke**. 2021, July; 52(7): 2347-2355.

PLASMA NEUROFILAMENT LIGHT CHAIN AND IMPROVEMENT AFTER STROKE

Neurofilament light chain (NFL) is a blood and cerebral spinal fluid biomarker of axonal damage in multiple sclerosis and neurodegenerative diseases. This study explored the utility of this biomarker for predicting recovery after ischemic stroke.

Data were obtained from a single-blinded, randomized trial on the efficacy of rehabilitation in late-phase recovery after stroke. Subjects were 123 participants who had sustained a stroke 10 months to five years before inclusion. Blood samples were drawn to measure NFL, with these levels comparing baseline function and improvement with therapy. Follow-up occurred at three and nine months.

Higher plasma NFL levels were associated with lower baseline Berg Balance Scale scores ($p=0.014$), 10-meter fast walk test scores ($p<0.001$), and Letter/Number Sequencing scores ($p=0.048$). However, higher levels of NFL were associated with improvements in the Berg Balance Scale at three months ($p = 0.001$) and with improvements in the 10-m fast walking speed at nine months ($p=0.018$).

Conclusion: This study involving patients who were 10 months to five years post-stroke found that patients with higher levels of neurofilament light chain levels demonstrated greater improvement with rehabilitation.

Stokowska, A., et al. Plasma Neurofilament Light Chain Levels Predict Improvement in Late Phase after Stroke. **Euro J Neurol**. 2021, July; 28(7): 2218-2228.

ROBOT-ASSISTED VERSUS CONSTRAINT-INDUCED MOVEMENT THERAPY AFTER STROKE

Up to 80% of stroke survivors experience residual upper limb motor dysfunction and reduced ability to perform activities of daily living. Among techniques focused on upper limb motor recovery, constraint-induced movement therapy (CIMT) and robotic-assisted therapy (RT) have gained prominence. This study compared these two interventions.

Subjects were adults recruited between six and 36 months after a hemorrhagic or ischemic stroke. Those participants were randomly allocated to 36 sessions of RT or CIMT. The RT group used two robotic devices, one for the shoulder and one for the wrist, in three weekly sessions of 60 minutes for 12 weeks. The CIMT group received 10 consecutive days (except weekends) of intensive therapies for six hours per day. The CIMT group used a restraint mitt on the unaffected upper limb for 90% of their active day.

Clinical measurements were documented before the beginning of therapy, and up to 12 months after treatment completion. The primary outcome measures were the Wolf Motor Function Test (WMFT) and the Upper Limb Fugl Meyer Assessment.

Compared with baseline, both groups demonstrated significant improvements on all measurements. For the primary outcome measures, there was a slight, but not statistically significant, difference between groups. The mean change, measured by the FMA-UL, was 4.5 points for CIMT and 2.7 points for RT ($p = 0.187$). For the WMFT, the improvements were −24.36 and −11.09 for CIMT and RT, respectively ($p = 0.293$).

Conclusion: This study of patients with ischemic or hemorrhagic stroke demonstrated that, at six to 36 months post-stroke, significant gains

could be made through constraint induced or robotic therapy, with no significant difference between those interventions.

Terranova, T., et al. Robot-Assisted Therapy and Constraint-Induced Movement Therapy for Motor Recovery in Stroke: Results from a Randomized Clinical Trial. **Front Neurorobot.** 2021, July. doi.org/10.3389/fnbot.2021.684019.

PHYSICAL ACTIVITY AND WALKING BIOMECHANICS AFTER HIP REPLACEMENT

Total hip arthroplasty (THA) is a common intervention for the management of end-stage osteoarthritis of the hip. However, early studies suggest that postsurgical activity and sleep quality improve meaningfully during the first year after the surgery. This study investigated 24-hour activity patterns and gait biomechanics two years following THA.

Patients scheduled for THA between October 2016, and February 2018, were recruited prospectively and followed for up to two years postoperatively. All were assessed preoperatively with the Charnley Classification, the Charlson Comorbidity Index, and the American Society of Anesthesiologists (ASA) score. Patient reported outcome measures included the Hip Disability and Osteoarthritis Outcome Score (HOOS). All were assessed with three-dimensional gait analyses. The subjects wore a wristwatch activity monitor for 24-hour physical activity assessment.

Data were completed for 51 patients. Compared with baseline measures, significant gains were recorded at one year in all HOOS domains ($p<0.001$), gait speed ($p<0.001$) and step length ($p<0.001$), without further gains between years one and two. The participants were sedentary or asleep for a mean of 19.5 hours per day preoperatively, 19.5 hours at one year and 19.6 hours at two years. A post hoc analysis showed that the mean sleep time at one year postoperatively decreased by 53 minutes per day when compared to preoperative levels ($p=0.007$).

Conclusion: This prospective study found that, following total hip arthroplasty, patients have significant self-reported improvements in pain function and quality of life. Despite these improvements, physical activity does not increase after surgery.

Bahl, J., et al. Changes in 24-Hour Physical Activity Patterns and Walking Gait Biomechanics after Primary Total Hip Arthroplasty. **J Bone Joint Surg.** 2021, July 7; 103 (13): 1166-1174.

TEN-YEAR COURSE OF HIP OSTEOARTHRITIS

Hip osteoarthritis (OA) affects up to 25% of people older than 55 years. Despite its prevalence, little is known about the natural course of early signs of hip OA. This study describes the natural course of OA among middle-aged adults.

Data were obtained from the prospective Cohort Hip and Cohort Knee (CHECK) study, a prospective, 10-year follow-up of first-time presenters with hip and/or knee pain. Medical and psychosocial data were collected at five different points (at baseline, after two years (T2), T5, T8, and T10). The Western Ontario and McMaster Osteoarthritis Index (WOMAC) was used to measure pain, stiffness, and physical function. Radiographic OA (ROA) was defined as a Kellgren and Lawrence (K/L) grade of two or greater.

Of the 1,002 participants, 588 reported hip pain at baseline, including twenty-nine percent with only hip pain and 71% reporting both hip and knee pain. At 10 years, 53% had ROA in at least one hip and 12% underwent a hip replacement. At 10 years, only 51% still reported hip pain. The use of pain medication was found in 43% at baseline and 50% after 10 years. The number of physically active individuals remained stable over time.

Conclusion: This study of patients 45 to 65 years of age presenting with hip pain found that, at 10 years, 12% underwent a hip replacement, with the remaining demonstrating stable symptoms over time.

van Berkel, A., et al. Ten-Year Natural Course of Early Hip Osteoarthritis in Middle-Aged Persons with Hip Pain: A CHECK Study. **Ann Rheum Dis.** 2021, 80:487-493.

PLATELET RICH PLASMA FOR CHRONIC ACHILLES TENDINOPATHY

Chronic, midportion Achilles tendinopathy is characterized by swelling and pain over the midportion of the tendon. Platelet rich plasma (PRP) injections are thought to promote tendon repair by introducing a high concentration of growth factors to the site. This study assessed the efficacy of a PRP injection for chronic Achilles tendinopathy.

This multicenter, randomized trial included adult patients with pain at the midportion of the Achilles tendon for longer than three months. The subjects were randomized to receive a sham injection or an injection of autologous PRP, delivered into the Achilles tendon. The primary outcome measures were the Victorian Institute of Sport Assessment (VISA-A) scores of pain, function, and activity.

Data were obtained for participants with an average age of 52.2 years. At both three- and six-months follow-ups, no significant difference in VISA-A scores was seen between the treatment and sham groups. Among adverse events, more patients in the PRP group experienced injection site discomfort.

Conclusion: This randomized, placebo-controlled trial of patients with chronic Achilles tendinopathy investigated the effect of platelet rich plasma injected into the tendon, finding that treatment did not reduce tendon dysfunction or pain at six months.

Kearney, R., et al. Effect of Platelet-Rich Plasma Injection versus Sham Injection on Tendon Dysfunction in Patients with Chronic Midportion Achilles Tendinopathy. A Randomized, Clinical Trial. **JAMA.** 2021, July 13; 326 (2): 137-144.

DOWNSTREAM OF HIGH-SENSITIVITY TROPONIN TEST IMPLEMENTATION

Fewer than five percent of emergency room visits for chest pain are ultimately attributed to myocardial infarction (MI). This study assessed whether the use of a high-sensitivity cardiac troponin (hs-cTn) can alter the course of the workup for acute chest pain.

Data were obtained from the Mass General Brigham Enterprise warehouse, containing electronic health records from patients seen for chest pain at one of five emergency rooms in the Boston area. Data were compared one year before and one year after the introduction of hs-cTn for routine use. The primary outcome variable was the presence of any cascade event, defined as laboratory tests, cardiac studies, cardiac procedures, medications, cardiology service involvement, hospital admissions, or new diagnoses that

could potentially have been associated with an initial hs-cTn test.

The study sample included 7,564 emergency room visits for chest pain. Following the implementation of the hs-cTn test, those with chest pain had a 2.8% increase in testing, including multiple troponin tests and electrocardiograms. However, they experienced fewer CT scans, stress tests, and percutaneous coronary interventions and were less likely to receive cardiac medications, undergo a cardiac evaluation, or be hospitalized. There were no significant differences in costs between the two groups.

Conclusion: This study found that, for patients presenting with chest pain to the emergency room, the adoption of the hs-cTn was associated with more up-front tests, with fewer high cost, invasive tests.

Ganguli, I., et al. Downstream Cascades of Care following High-Sensitivity Troponin Test Implementation. **J Am Coll Card.** 2021, June 29; 77(25): 3171-3179.

REHABILITATION FOR HOSPITALIZED ELDERLY WITH HEART FAILURE

Patients who are hospitalized for acute decompensated heart failure have high rates of physical frailty, poor quality of life, delayed recovery, and frequent rehospitalizations. This study, the Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF), assessed the effect of early, transitional, progressive rehabilitation on physical frailty among patients hospitalized for heart failure.

Subjects were 60 years of age or older, admitted for acute decompensated heart failure. The participants were randomized to a usual care group or an intervention group. The intervention focused on strength, balance, mobility, and endurance and progressed through pre-specified functional levels. The intervention was initiated during hospitalization, with outpatient sessions occurring three days per week, 60 minutes per session, for 12 weeks. Outpatient sessions were complemented by home exercise of low-intensity walking and resistance exercise. At three months, the patients were provided with individualized exercise prescriptions and followed up every four weeks. Physical and cognitive function were assessed at baseline and follow-up.

At three months, those in the treatment group demonstrated significantly greater improvement on the Short Physical Performance than the controls ($p<0.001$). The rates of rehospitalization at six months were 1.18 in the intervention group and 1.28 in the controls. Falls were reported in 28% of the treatment group and 36% of the control group. Neither finding reached statistical significance.

Conclusion: This study of patients hospitalized for acute decompensated heart failure found that a 12-week program of progressive rehabilitation significantly improved physical function.

Kitzman, D., et al. Physical Rehabilitation for Older Patients Hospitalized for Heart Failure. **N Eng J Med.** 2021, July 15; 385(3): 203-216.

COFFEE CONSUMPTION AND TACHYARRHYTHMIA

Coffee consumption has been associated with several health benefits, including improved overall mortality. As some professional society guidelines have suggested avoiding caffeinated products to diminish the risk of arrhythmia, this study analyzed the association between coffee intake and cardiac arrhythmia.

Data were obtained from the U.K. Biobank prospective study of adults 40 to 69 years of age, recruited between January 2006, and December 2010. All completed questionnaires, physical examinations, and provided biologic samples. Information regarding coffee consumption was obtained through questionnaires. Using these data, participants were placed into one of eight categories corresponding to coffee intake: zero, less than one, one, two, three, four, five, or six or more cups daily. The primary outcome variable was incident tachyarrhythmia (atrial fibrillation or atrial flutter, supraventricular tachycardia, ventricular tachycardia, premature atrial complexes, or premature ventricular complexes).

Among the 502,543 participants, a median of two cups of coffee was consumed per day. During a mean of 4.5-years follow-up, 16,369 incident arrhythmias occurred. An adjusted analysis revealed that each additional cup of coffee per day was associated with a three percent lower risk of incident arrhythmia ($p<0.001$).

Conclusion: This large, prospective study found that greater amounts of habitual coffee consumption are associated with a lower risk of cardiac arrhythmia.

Kim, E., et al., Coffee Consumption and Incident Tachyarrhythmias. Reported Behavior, Mendelian Randomization and their Interactions. **JAMA Intern Med.** 2021, July 19: doi: 10.1001/jamainternmed.2021.3616. Online ahead of print.

UBROGEPANT IN PATIENTS WITH MAJOR CARDIOVASCULAR RISK FACTORS

Migraine is a chronic neurologic disease with episodic attacks characterized by headaches, photophobia, and nausea. However, ergots and vasoconstrictors are contraindicated for those with cardiovascular disease. Ubrogepant, an oral calcitonin gene related peptide (CGRP) receptor antagonist, has recently been approved as an alternative to these medications. This study assessed the cardiovascular risk factors associated with this medication.

The ACHIEVE I and II clinical trials were multicenter, randomized, phase III trials. Participants were randomized to receive a placebo or ubrogepant at 25 mg, 50 mg, or 100 mg as a treatment for a migraine of moderate to severe pain intensity. At baseline, participants were classified as one of three cardiovascular risk categories (high, moderate-low). Adverse events were recorded, separating these into those that occurred within 48 hours and those that occurred within 30 days.

Of the participants, 11% were categorized as moderately high, 32% as low, and 58% as having no cardiovascular risk factors. The rate of treatment-emergent adverse events within 48 hours was similar between groups, and compared to placebo, with 11.6% in the moderate to high-risk group, 11.5% in the low-risk group, and 12% in the no-risk group.

Conclusion: This prospective study of patients with migraine headaches found that treatment with Ubrogepant did not increase the rate of cardiovascular events, even among those with moderate to high cardiovascular risk factors.

Hutchinson, S., et al. Safety and Efficacy of Ubrogepant in Participants with Major Cardiovascular Risk Factors in two single-attack Phase 3 Randomized Trials: ACHIEVE I and

II. **Cephalalgia**. 2021, August; 41(9): 979-990.

DETECTING FUNCTIONAL DEFICITS FOLLOWING SUBCONCUSSIVE HEAD IMPACTS

Of the 413,858 traumatic brain injury (TBI) diagnoses made in members of the U.S. military in the last 20 years, 82.8% were classified as mild. Due to the prevalence of mild TBI and the difficulty of identification and diagnoses, this study examined the relationship between head impact biomechanics and performance on behavioral assessments in a military training environment.

Participants were U.S. Army soldiers attending the Basic Airborne Training Course. The participants wore two sensors to measure head impacts while participating in Parachutist Landing Fall (PLF) training, followed by six complete jumps from an airplane. At baseline and again at weeks one, two and three, data were collected including self-reported surveys and performance tasks. The visual-vestibular balance/sensory integration assessment an immersive environment for multimodal neurologic assessment. The task required the subject to roll a ball into a target area by tilting his/her head. Of the output variables, six measures of performance, were chosen based upon previous studies of athletes with concussion.

Comparing the sensory data with task performance, for sensor A, greater peak rotational velocity values and an increased number of impacts corresponded to decreased performance ($p=0.018$ and $p=0.007$, respectively). In addition, greater peak linear acceleration corresponded to a decrease in performance ($p=0.04$). For sensor B, greater peak linear acceleration and peak rotational velocity correlated with decreased performance ($p =0 .03$, $p = 0.04$, respectively).

Conclusion: This study found that visual-vestibular balance tasks may be useful in detecting subconcussive impacts.

Kelley, A., et al. Detecting Functional Deficits following Subconcussive Head Impacts: The Relationship between Head Impact Kinematics and Visual-Vestibular Balance Performance. **Brain Inj.** 2021, June 7; 35 (7): 812-820.

FUNCTIONAL OUTCOMES AFTER MODERATE TO SEVERE TRAUMATIC BRAIN INJURY

Survivors of moderate to severe traumatic brain injury (msTBI) experience long-term challenges in their daily lives. Long-term follow-up studies have reported considerable variability in the degree of residual disability after TBI. This study reports on data from the Transforming Research and Clinical Knowledge in TBI (TRACK-TBI), a prospective, observational study of the natural history of recovery after msTBI.

Patients were enrolled between February 26, 2014, and August 8, 2018, at 18 level I trauma centers in the United States. The Glasgow Outcome Scale-Extended (GOSE) and Disability Rating Scale (DRS) were used to assess global functional status 2 weeks and 3, 6, and 12 months postinjury. Data were included for participants 17 years of age or older with Glasgow Coma Scale Scores of three to eight (severe injury) and nine to twelve (moderate injury).

The 12-month mortality rates were 30.6% in the severe group and 13% in the moderate group. Of the deaths occurring in the first year, 33% occurred within three days of injury, 52% within the first week, and 70% within the first two weeks. For those with severe injury, a good recovery (GOSE of seven to eight) occurred in 8.3% at three months, 18.4% at six months, and 22.9% at 12 months. For those with moderate injury, a good recovery at 52 weeks occurred in 35%. Of those who remained in a vegetative state at two weeks post-injury, 22% died within the first year. Of the survivors, 84% recovered consciousness by three months, 94% by six months, and 100% by 12 months.

Conclusion: This prospective study of patients hospitalized for traumatic brain injury found that, at one year, 22% with severe, and 35% with moderate, TBI achieved a good recovery.

McCrea, M., et al. Functional Outcomes over the First Year after Moderate to Severe Traumatic Brain Injury in the Prospective, Longitudinal Track-TBI Study. **JAMA Neurol**. 2021. Published online July 06, 2021. doi:10.1001/jamaneurol.2021.2043.

WEARABLE SENSORS TO EVALUATE FRAILTY

As studies have shown that wearable sensors may assist in the identification of patients with frailty, this literature review and meta-analysis examined the efficacy of this monitoring.

A literature review identified 29 studies which assessed the efficacy of sensors worn by participants in a community setting. All involved the evaluation of frailty among participants 63 to 90 years of age. Studies included 13 body-worn sensors used in eight different body locations. Mobility measures included temporal-spatial gait parameters of speed, total steps, double support, stride length, time and variability, and postural transitions, including acceleration counts of sit to stand (STS), stand to walk, stand to sit trunk angular velocity, upper limb kinematics, the intensity of PA and percentage of time in walking, standing, sitting, and lying.

All but one study demonstrated an association between physical activity and level of frailty. All reported that slower gait speed correlated with tests of frailty.

Conclusion: This literature review of community dwelling elders found that wearable sensors can be successfully used to evaluate frailty in older adults.

Vavasour, G., et al. How Wearable Sensors Have Been Utilised to Evaluate Frailty in Older Adults: A Systematic Review. **J Neuro Engineering Rehab**. 2021; 18: 112.

DECOMPRESSION WITH OR WITHOUT FUSION IN SPONDYLOLISTHESIS

For patients with lumbar degenerative spondylolisthesis, surgical treatment is often recommended for those whose pain has not decreased with conservative management. In the last few decades, instrumented fusion, combined with decompression accounts for more than 90% of decompression surgeries in some countries. In the Norwegian Degenerative Spondylolisthesis and Spinal Stenosis (NORDSTEN-DS) trial, the authors investigated whether decompression surgery was non-inferior to decompression surgery with instrumented fusion in patients who have spinal stenosis with degenerative spondylolisthesis.

This multicenter non-inferiority trial included patients 18-80 years of age with degenerative spondylolisthesis, randomized to undergo decompression surgery alone or with instrumented fusion. The primary outcome was an

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improvement in the Oswestry disability index of 30% or more at two -year follow-up.

In the intention to treat population, 71.4% in the decompression alone and 72.9% in the fusion group met the primary outcome measure. For secondary outcome measures the percentage of patients with a clinically important improvement from inclusion to two years after surgery, as assessed by the Zurich Claudication Questionnaire, Numeric Rating Scale for leg pain, and Numeric Rating Scale for back pain were generally in the same direction as those of the analysis of the primary outcome. During the follow-up period, reoperation was performed in 12.5% of the decompression group and 9.1% in the fusion group.

Conclusion: This study of patients with degenerative spondylolisthesis found that decompression alone was non-inferior to decompression with fusion.

Austevoll, I et al., Decompression with or without Fusion in Degenerative Lumbar Spondylolisthesis. **N Eng J Med**. 2021, Aug 5 385(6):526-538.

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