

# REHAB IN REVIEW

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## COGNITION ONE YEAR AFTER COVID HOSPITALIZATION

Neurologic sequelae have been reported among patients hospitalized for COVID-19. This study was designed to determine the prevalence of cognitive deficits among patients one year after hospitalization for COVID-19.

Subjects were adults 18-75 years of age who had been hospitalized for COVID-19 and who had not been diagnosed with cognitive impairment prior to hospitalization. Clinical data were retrospectively collected, including the type and duration of oxygen therapy, hospitalization duration, comorbidities, and viral clearance time. Neuropsychological assessments were completed at five and 12 months after hospital discharge. Cognitive functioning at follow up was assessed using the Brief Repeatable Battery of Neuropsychological Tests (BRB-NT). The dependent variables were the raw scores to the eight tests of the BRB-NT.

Of the 76 patients who were assessed at five months, 53 returned for the one-year follow up. At five months 63% of patients had deficits in at least one test, and 40.8% in at least two tests. At 12 months 49.1% still showed cognitive deficits in at least one domain and 32.1% showed deficits in at least two domains. The most affected domains after one year were processing speed (28.3%) long-term visuospatial 18.1% and verbal (15.1%) memory. Given the number of dropouts, if all of those lost to follow up were negative for cognitive deficits the prevalence of cognitive deficits at one year would be 34%.

**Conclusion:** This study of patients hospitalized with COVID-19 found that, at one year, almost half demonstrated persistent cognitive deficits.

Ferrucci, R., et al. One-Year Follow-Up of COVID-19 Hospitalized Patients. *Europ J Neurol*. 2022, July;29(7):2006-2014.

## AMNESIC SYNDROME OF POSTERIOR CEREBRAL ARTERY INFARCTION

Ischemic amnesia (IA) is an impairment of episodic, mostly anterograde memory brought on by ischemia. This study explored IA in patients with acute posterior cerebral artery stroke, to better understand the prevalence and characteristics of memory impairment in these patients.

Eligible participants had an acute, first-ever, symptomatic, unilateral ischemic infarction involving the posterior cerebral artery territory. A neuropsychological assessment was completed with episodic memory assessed using the VLMT (Verbaler Lern- und Merkfähigkeitstest). The Rey Complex Figure Test was used to assess visual-spatial functions and figural memory. Neuropsychological assessments were completed an average of 6.4 days after admission. An MRI was also completed, with results reviewed using lesion mapping software.

Data were completed for 81 consecutive admissions. Of these, 69 scored at or below the fifth percentile in one or two modalities (M-). Only 15 patients were classified as having intact or only mildly impaired memory (M+). Approximately 70% of the M- patients self-rated their memory performance as equal to pre-morbid levels. To identify lesion locations most often associated with memory impairment, the territories representing M+ were subtracted from those in the M- group. The center of maximum damage was the superior and posterior of the left hippocampal formation, although 30% of lesions were extrahippocampal.

**Conclusion:** This prospective study of patients with acute ischemic stroke in the posterior cerebral artery territory found that memory is a key clinical manifestation, with amnesia more frequent and severe after infarctions to the left hemisphere.

Benke, T., et al. The Amnesic Syndrome of Posterior Cerebral

Artery Infarction. *Eur J Neurol*. 2022 Jun 16. doi: 10.1111/ene.15449.

## SELF-ADMINISTERED TRANSCRANIAL DIRECT CURRENT STIMULATION FOR KNEE PAIN

Osteoarthritis (OA) is the leading cause of work disability in the United States, with the highest incidence occurring in the knee. This study assessed the efficacy of self-administered transcranial direct current stimulation (tDCS) for older adults with OA of the knee.

This double-blind, placebo-controlled trial included 120 individuals, 50 to 85 years of age, with symptomatic OA of the knee. The participants were randomized to receive either active or sham stimulation. The active tDCS was delivered with a constant current intensity of 2 mA and was applied for 20 min per session daily for three weeks. The primary outcome measure was pain, assessed through the Numerical Rating Scale (NRS) up to three months. Data were also collected using the Western Ontario and McMaster University's Osteoarthritis Index (WOMAC).

At three weeks, the average decreases in NRS from baseline were 24.07 for the active group, and 1.08 for the sham group ( $p < 0.0001$ ). At three months, the average decreases in NRS pain scores were 14 for the active group, and 0.43 for the sham group. Responders, defined as those achieving at least a 30% improvement in NRS scores from baseline, included 36 of 60 in the active group and 14 of 60 in the sham group.

**Conclusion:** This study of patients with osteoarthritis of the knee found that significant pain reduction could be achieved through self-administered transcranial direct current stimulation.

Martorella, G., et al. Self-Administered Transcranial Direct Current Stimulation for Pain in Older Adults

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with Knee Osteoarthritis: A Randomized, Controlled Study. **Brain Stimulation** 2022, July-August; 15 4: 902-909.

**AMITRIPTYLINE AND FIBROMYALGIA**

Fibromyalgia (FM) is characterized by widespread, chronic pain, fatigue, cognitive problems, and affective issues. This study compared the efficacy of amitriptyline, the most commonly used off-label treatment, with the three FDA-approved medications.

This systematic review was completed with databases from 2018 through 2020, with included studies involving adults with FM. The search identified 10 clinical trials that evaluated amitriptyline, 11 that evaluated milnacipran, eight that evaluated duloxetine, and seven that evaluated pregabalin 600 mg.

Compared with placebo, duloxetine 120 mg was associated with the highest pain reduction, followed by pregabalin 450 mg. Milnacipran 100 mg was associated with the lowest reduction in pain. Among the studies evaluating depression, the greatest probability of improvement was found in those treated with duloxetine 120 mg, duloxetine 60 mg, and pregabalin 600 mg. The greatest improvement in fatigue was found with amitriptyline, followed by pregabalin 150 mg and pregabalin 600mg.

**Conclusion:** This systematic review of treatments for fibromyalgia found that amitriptyline was associated with a large improvement in sleep and quality of life, a small improvement in pain, and a moderate improvement in fatigue. Duloxetine, 120 mg, was associated with improvement in all efficacy outcomes, with the greatest improvements in pain and depression.

Farag, H., et al. Comparison of Amitriptyline and U.S. Food and Drug Administration Treatments for Fibromyalgia. A Systematic Review and Network Meta-Analysis. **JAMA Netw Open**. 2022 May; 5(5): e2212939.

**NONINVASIVE VAGUS NERVE STIMULATION FOR MIGRAINES**

Migraines are the leading cause of disability in individuals younger than 50 years of age. As vagus nerve stimulation (VNS) has proved to be beneficial for many primary headache

disorders, this study assessed the efficacy and safety of noninvasive VNS for migraine prevention.

This multicenter, randomized, double-blind, sham-controlled study included patients under 50 years of age with chronic migraine headaches. The participants were randomized to receive active VNS (A-VNS) or sham VNS (S-VNS) three times per day. The primary efficacy outcome was the mean change in the number of migraine days per month, with secondary outcomes including the number of “responders” who experienced a 50% or greater reduction in monthly migraine days.

Data were completed for 231 subjects. At weeks nine through twelve, the decreases in monthly migraine headaches were 3.5 days for the A-VNS group and 2.29 days for the S-VNS group (p=0.23). The responder rates were 44.87% in the active group and 26.81% in the sham group (p=0.048). More in the A-VNS group reported that they were very or extremely satisfied with treatment (p=0.0006).

**Conclusion:** This randomized, controlled trial of patients with chronic migraine headaches found that noninvasive vagus stimulation could reduce the number and severity of headaches.

Najib, U., et al. Non-Invasive Vagus Nerve Stimulation for Prevention of Migraine: The Multicenter, Randomized, Double-Blind, Sham Controlled, Premium II Trial. **Cephalalgia**. 2022. June; 42(7): 560-569.

**PARTIAL MENISCECTOMY VERSUS PHYSICAL THERAPY FOR TRAUMATIC MENISCAL TEARS**

Arthroscopic partial meniscectomy is the most frequently performed orthopedic surgery in the world. In middle age and older patients with chronic degenerative tears, multiple studies have shown that partial meniscectomy has no benefit as compared with nonoperative treatment. This study investigated whether arthroscopic partial meniscectomy was superior to physical therapy in young patients with traumatic meniscal tears.

The Study of Traumatic Meniscal Tears: Arthroscopic Resection versus Rehabilitation (STARR) included patients 18 to 45 years of age with a recent onset of traumatic, isolated, meniscal tear without knee osteoarthritis (OA). The subjects were

randomized to receive surgical repair or physical therapy. Those assigned to the surgical group underwent suturing of the injured meniscus. Those in the physical therapy group focused on restoring range of motion, strength and coordination, finishing with return to sport. The primary outcome variable was the International Knee Documentation Committee (IKDC) score at 24-month follow-up. Secondary outcomes were the Knee Injury and Osteoarthritis Outcome Score (KOOS), knee pain in rest and during activity [the Numeric Rating Scale (NRS)], the Lysholm measure, and the Western Ontario Meniscal Evaluation Tool (WOMET).

Data were completed for 100 subjects. At 24 months, there was no significant difference between the two groups in IKDC, KOOS, NRS-pain, Lysholm, WOMET, or Tegner scores or in patient satisfaction with knee function.

**Conclusion:** This study of patients with traumatic meniscal tears found that arthroscopic partial meniscectomy was not superior to physical therapy for the treatment of pain and function.

van der Graaff, S., et al. Arthroscopic Partial Meniscectomy versus Physical Therapy for Traumatic Meniscal Tears in a Young Study Population: A Randomized, Controlled Trial. **Br J Sports Med.** Published Online First: 08 June 2022. doi: 10.1136/bjsports-2021-105059.

### COOLED RADIOFREQUENCY ABLATION FOR HIP OSTEOARTHRITIS

For patients with osteoarthritis (OA) of the hip, thermal ablation has gained attention as a means of reducing pain through neurolysis. Cooled radiofrequency ablation (C-RFA) is a minimally invasive method that uses radiofrequency probes with temperatures of less than 100° C. This prospective study tested the efficacy of C-RFA for patients with OA of the hip.

This prospective study included 10 patients with OA of the hip. Using fluoroscopy, the femoral and obturator nerve sensory branches were targeted, with a small volume of local anesthetic injected for diagnostic verification. After verification, the patients underwent C-RFA of the obturator and femoral nerves. The primary outcomes included changes in scores on the Hip Pain and Function (HOOS), and

the Visual Analog Scale (VAS) for pain.

At a mean of 6.2 months after treatment, the mean total HOOS score improved from 17 to 52.9 ( $p<0.0001$ ). Significant improvements were also noted in HOOS subsets, including quality of life, function in sports, function in daily living, pain, and stiffness ( $p<0.0001$  for all). The mean VAS score improved from 8.3 to 2.5 ( $p<0.001$ ). There were no complications during or after the diagnostic injections or the C-RFA procedures.

**Conclusion:** This prospective study of 11 patients with severe osteoarthritis of the hip found that cooled radiofrequency ablation of the femoral and obturator nerve sensory branches significantly improved pain and function.

Tran, A., et al. Alternative Treatment of Hip Pain from Advanced Hip Osteoarthritis Utilizing Cooled Radiofrequency Ablation: Single Institution Pilot Study. **Skeletal Radiol.** 2022 May;51(5):1047-1054.

### RECREATIONAL SPORTS AND CALCANEAL BONE DENSITY

Optimization of peak bone mass (PBM) during the periods of childhood and adolescent bone development is a major determinant of later fracture risk. This study assessed the relationship between recreational sporting activity (RSA) and bone health in a group of adolescents and young adults.

Subjects were 16 to 35 years of age, recruited through local advertisement. All participants completed a validated sporting activity questionnaire reporting current and past recreational sporting activity history. A calcaneal quantitative ultrasound (cQUS) was performed to assess bone mineral density (BMD), the stiffness index (SI), the speed of sound (SOS), and broadband ultrasound attenuation (BUA). These findings were adjusted for age. Other data relevant to BMD were gender, ethnicity, age, BMI, height, weight, pubertal timing, smoking, alcohol consumption, fracture (age of first broken bone, fracture history, and family fracture history), and daily calcium consumption.

Associations were found between cQUS and BMI, later onset of puberty, physical activity, high impact weight-bearing sporting activity, non-weight-bearing sporting activity, past recreational sporting activity score,

ethnicity and alcohol intake above the median of 3.5 units per week.

A linear regression indicated that bone SI was significantly higher in those who reported running ( $p=0.022$ ) and playing soccer ( $p=0.047$ ), and significantly lower in participants who reported walking ( $p=0.009$ ). Bone SOS was significantly higher in participants who reported running ( $p=0.01$ ). Bone BUA was significantly higher in participants who reported playing soccer ( $p=0.042$ ).

**Conclusion:** This study of adolescents and young adults found that levels of past recreational sporting activity, as well as current physical activity, were associated with measures of bone health.

Patel, H., et al. A Cross-Sectional Study of the Relationship between Recreational Sporting Activity and Calcaneal Bone Density in Adolescents and Young Adults. **Phys Sports Med.** 2022, June; 50(3): 218-226.

### HAND OSTEOARTHRITIS

Hand osteoarthritis (HOA) is a highly prevalent disorder that may lead to severe pain and disability. This study was designed to better understand the prevalence, incidence, progression, and specific joint patterns of HOA.

The Osteoarthritis Initiative (OAI) is a multicenter cohort study of 4,796 adults, 45 to 80 years of age, with or at risk for symptomatic osteoarthritis of the knee. All participants underwent baseline radiographs of one or both hands, with a follow-up at 48 months. Questionnaires concerning hand pain were provided at both visits.

Subjective complaints were compared to radiographic imaging results. Prevalent symptomatic HOA was defined as radiographic HOA at baseline plus same-sided hand pain. Incident symptomatic HOA was defined as radiographic HOA accompanied by a new report of same side hand pain at the 48-month follow-up visit.

The prevalence of HOA was 41.4 per 100 persons. The prevalence of symptomatic HOA was 12.4 per 100 persons. Compared to men, women had a greater risk of prevalent, symptomatic HOA. The incidence over four years was 5.6 per 100 persons for radiographic HOA and 16.9 per 100 persons for symptomatic HOA. The most common joints for prevalent HOA in men were the thumb carpometacarpal (CMC) joint,

followed by the distal interphalangeal (DIP) joints. For women, the most common joint for prevalent HOA was the DIP joint of the index finger, followed by the thumb CMC and DIP joints, as well as the thumb STT joint.

**Conclusion:** This prospective study of adults 45 to 80 years of age found that the prevalence of hand osteoarthritis was 41.4%, with women at greater risk than men.

Eaton, C., et al. Prevalence, Incidence, and Progression of Radiographic and Symptomatic Hand Osteoarthritis: The Osteoarthritis Initiative. *Arthr Rheumat* 2022, Jun; 74(6): 992-1000.

### NUSINERSEN FOR TYPE II AND TYPE III SPINAL MUSCULAR ATROPHY

Spinal muscular atrophy (SMA) is a genetic disease characterized by muscle weakness and atrophy, resulting from progressive degeneration of lower motor neurons in the spinal cord and the brainstem nuclei. The antisense oligonucleotide, nusinersen (Spinraza), regulates the splicing of the survival motor neuron 2 (SMN2) messenger RNA to increase SMN protein expression. This study was designed to identify biomarkers that predict the response to nusinersen in type II and III SMA.

Subjects were 45 patients with type II or type III SMA. Cerebrospinal fluid was obtained to identify microRNAs. The patients received nusinersen on days one, 15, 29, and 64, followed by an additional maintenance dose after four months. Motor function was assessed at each visit using the Hammersmith Functional Motor Scale-Expanded (HFMSE). An improvement from baseline HFMSE scores of  $\geq 3$  points was considered clinically significant. The microRNA profile at baseline was compared between responders to nusinersen therapy (an increase of  $\geq 3$  points in the HFMSE) and those who responded poorly (HFMSE score change of  $\leq 0$  points).

Compared to responders, two microRNAs differed relative to non-responders. Lower baseline levels of two muscle microRNAs (miR-206 and miR-133a-3p), alone or in combination, predicted the clinical response to nusinersen after six months of therapy.

**Conclusion:** This study of patients with type II or type III spinal muscle atrophy found that two muscle microRNAs could help predict the

response to nusinersen after six months of therapy.

Magen, I., et al. Muscle MicroRNAs in the Cerebrospinal Fluid Predict Clinical Response to Nusinersen Therapy in Type II and Type III Spinal Muscular Atrophy Patients. *Euro J Neurol*. 2022 May 5. doi: 10.1111/ene.15382.

### PLASMA CEREMIDES

Ceramides are bioactive molecular lipids which have a role in several cellular functions and are implicated in apoptosis, inflammation, obesity, and insulin resistance. This study examined the predictive utility of measuring ceramides in the oldest old.

This cohort study included Caucasian men born between 1919 and 1934. They have been followed since midlife, in the 1960s, with regular questionnaires and surveys starting in 2000. Among the laboratory tests obtained, circulating ceramides in plasma samples were quantified. All-cause mortality through January of 2021 was retrieved from the National Population Information System, with a follow-up of 3.5 years. The levels of the ceramides were compared to all-cause mortality.

The preliminary analysis showed that, of the various ceramides measured, Cer (d18:1/16:0) was the best predictor in this cohort. In the adjusted regression analysis, higher levels of Cer (d18:1/16:0) as a continuous variable were associated with increased mortality. Compared with the bottom tertile, those in the top tertile were at an elevated risk of all-cause mortality, with a hazard ratio of 5.44.

**Conclusion:** This study found that the plasma ceramide Cer (d18:1/16:0) was independently associated with all-cause mortality among community-dwelling men 85 years of age or older.

Strandberg, T., et al. Plasma Ceramides Independently Predict All-Cause Mortality in Men Aged 85+. *Age Ageing*. 2022, June; 51(6): 1-6.

### NERVE COMBING FOR TRIGEMINAL NEURALGIA

Trigeminal neuralgia (TN) is a chronic pain disorder characterized by severe facial pain. While this disorder is often amenable to pharmaceutical management, surgical intervention may be

necessary. Internal neurolysis (INL) is a surgical procedure proposed as a safer alternative to partial sensory rhizotomy. This procedure involves a separation of the trigeminal nerve fibers between the pons and porus trigeminus. This prospective study was designed to better understand the outcomes of patients treated with INL.

Subjects were consecutive patients undergoing retrosigmoid craniotomy and INL between 2015 and 2017 at University Hospital, Southampton, the U.K. Patients with type I or type II refractory TN, were offered INL as an alternative to partial sensory rhizotomy. Eight patients with a median age of 55 years underwent INL. Six had type I and two had type II TN. All were assessed with the Barrow Neurological Institute (BNI) Pain Intensity Scale and the Brief Pain Inventory (BFI) facial score.

The median follow-up after surgery was 38 months. At immediate post-operative assessment and at three months, all patients were pain-free. At the last follow-up, six (75%) had remained pain-free (BNI grade I). There were no unexpected complications of the surgery. The median BFI-facial score was 20 at the last follow-up, reflecting a sustained and dramatic improvement in quality of life and activity scores.

**Conclusion:** This study of patients with trigeminal neuralgia found that, among those who were treated with a nerve combing technique, 75% were pain-free at 38-month follow-up.

Durnford, A., et al. Internal Neurolysis (Nerve Combing) for Trigeminal Neuralgia without Neurovascular Conflict - Early U.K. Outcomes. *Br J Neurosurg*. 2022, April; 36(2): 175-178.

### MR-GUIDED, FOCUSED ULTRASOUND FOR ESSENTIAL TREMOR

MR guided focused ultrasound (MRgFUS) uses high-intensity focused ultrasound waves to produce thermal ablation of target brain tissue. While early studies have shown some success with the use of MRgFUS to treat essential tremor (ET), the optimal target for the treatment remains unclear. This study assessed the efficacy of using sequential lesions in (anterior-VIM/VOP nuclei) the thalamus followed by the posterior subthalamic area (PSA).

Participants were over 21 years of age with moderate or severe ET

causing significant disability, and with an inadequate response to two or more anti-tremor medications. The subjects underwent procedures targeting the anterior ventralis oralis posterior (VOP) /ventralis intermedius (VIM) region and the posterior subthalamic area (PSA). The primary outcome measure was the Bain and Findley Spiral (BFS) score, with baseline scores compared with those obtained 12 months post-treatment. The Clinical Rating Scale for Tremor (CRST) was used to document tremor severity.

Data were collected for 13 patients with a mean age of 69 years at a mean age at tremor onset of 32 years. The BFS scores in the treatment arm improved by 43.5% at 12 months and 41.1% at 24 months. In the untreated arm, the mean changes were 7.7% improvement at 12 months, but worsening by 8.8% by 24 months. The secondary measures of CRST and QUEST scores showed significant improvements ( $p < 0.005$ ) in the treatment arm.

**Conclusion:** This study of patients with essential tremors found that MR-guided, focused ultrasound was effective in reducing symptoms and improving quality of life.

Jameel, A., et al. Double Lesion Treatment of Essential Tremor Targeting the Thalamus and Posterior Subthalamic Area: Preliminary Study with Two Years' Follow-Up. *Br J Neurosurg.* 2022; 36(2): 241-250.

### AMANTADINE AND CONSCIOUSNESS IN NON-TRAUMATIC BRAIN INJURY

Amantadine, an N-methyl-D-aspartate receptor antagonist and indirect dopamine agonist, exerts effects on multiple neurotransmitters and has been used as neurostimulant in patients with prolonged disorders of consciousness. This literature review examined the effect of amantadine in patients with non-traumatic brain injury (nTBI).

Data were pooled from five observational studies of patients with a Glasgow Coma Scale (GCS) scores of six or lower, treated with amantadine for sequela of intracerebral hemorrhage, ischemic stroke, subarachnoid hemorrhage, status epilepticus, and community-acquired bacterial meningitis. All received at least 100 milligrams of amantadine with the intention to improve consciousness. The primary outcome was defined as an increase

in GCS score of at least three points within five days.

The study's final sample consisted of 184 patients, of whom 84 (45.7%) received amantadine treatment. The primary outcome was achieved by 86.9% in the amantadine group at day five compared to 54% in the control group ( $p < 0.001$ ). At 90 days, all-cause mortality was 40% in the amantadine group and 30.9% in the control group.

**Conclusion:** This study pooled data from five studies of patients with non-traumatic brain injury, finding that treatment with amantadine was associated with improved consciousness.

Kuramatsu, L., et al. Amantadine Treatment Is Associated with Improved Consciousness in Patients with Non-Traumatic Brain Injury. *J Neurol Neurosurg Psychiatry.* 2022, June;93(6):582-587.

### GLUCOSE-6-PHOSPHATE DEHYDROGENASE AND INTRACRANIAL ATHEROSCLEROSIS

Intracranial atherosclerotic stenosis (ICAS) is a leading cause of ischemic stroke worldwide. This disorder is more prevalent in Asian, Black, Hispanic, and some Middle Eastern individuals as compared to Caucasians. Glucose-6-phosphate dehydrogenase (G6PD) deficiency, a hereditary enzyme defect, has been associated with atherosclerotic cardiovascular disease and worse post-stroke outcomes. This study compared the risk of ICAS in stroke patients with and without G6PD deficiency in a Chinese cohort.

This prospective study included 1,593 consecutive patients hospitalized in one of four centers in China, with acute ischemic stroke between June 2015, and July 2021. Stroke risk factors were collected at admission, including the G6PD enzyme activity. Patients with 50-99% atherosclerotic stenosis or occlusion of at least one major intracranial artery were categorized as having ICAS. The G6PD activity was compared to ICAS.

Of the 1,593 participants, G6PD deficiency was found in 11.4%. The prevalence of any symptomatic or asymptomatic ICAS was higher in G6PD-deficient patients than in those with normal G6PD levels ( $p < 0.001$ ). An adjusted analysis revealed that the baseline predictors of ICAS were greater age ( $p = 0.004$ ), hypertension

( $p = 0.006$ ), diabetes ( $p = 0.019$ ), and G6PD deficiency ( $p = 0.004$ ).

**Conclusion:** This study of patients hospitalized with a stroke found that those with a G6PD deficiency had a higher frequency of intracranial atherosclerotic stenosis.

Chen, J., et al. Glucose-6-Phosphate Dehydrogenase Deficiency and Intracranial Atherosclerotic Stenosis in Stroke Patients. *Euro J Neurol.* 2022. doi: 10.1111/ene.15418. Epub ahead of print.

### MULTIPLE COMPONENT INTERVENTION TO PREVENT DISABILITY IN FRAIL OLDER ADULTS

With advanced age, impaired mobility is associated with a higher risk of disability, poor quality of life, hospitalization, and admission to a residential care facility. The Sarcopenia and Physical Frailty in Older People: Multi-Component Treatment Strategies (SPRINTT) project was designed to develop a new, objective definition of physical frailty and sarcopenia and to test new interventions for this population.

The SPRINTT trial included community-dwelling adults 70 years of age or older with physical frailty and sarcopenia (a Short Physical Performance Battery (SPPB) score of three to nine points). The subjects who were randomized to a multicomponent intervention group, underwent moderate-intensity physical activity twice weekly at a treatment center and up to four times per week at home. The control subjects received education on healthy aging on topics relevant to older adults. The primary outcome variable was mobility disability, operationalized as the inability to complete the 400-meter walk test in less than 15 minutes without sitting.

Data were analyzed for 1,519 participants with an average age of 78.9 years and an average follow-up of 26.4 months. Among those with baseline SPPB scores of three to seven, mobility disability at follow-up was found in 46.8%, as compared with 52.7% of the controls ( $p = 0.005$ ). The change in SPPB scores favored the intervention group at 24 ( $p < 0.001$ ) and 36 months ( $p < 0.001$ ).

**Conclusion:** This study of an elderly sample with physical frailty and sarcopenia found that a multi-component intervention, based on moderate-intensity physical activity with technological support and nutritional counseling, was associated

with a reduction in the risk of mobility disability over 36 months.

Bernabei, R., et al. Multicomponent Intervention to Prevent Mobility Disability in Frail Older Adults: Randomised, Controlled Trial (SPRINTT Project). *BMJ*. 2022, May 11; 377: e068788.

### **WEIGHT LOSS AFTER KNEE REPLACEMENT**

For patients with end-stage osteoarthritis (OA) of the knee, total knee arthroplasty (TKA) is a common procedure. Weight reduction is recommended as part of the treatment of OA of the knee, with some recommending weight loss prior to surgery. As a TKA has been shown to improve an individual's tolerance of activity, this study assessed whether patients who undergo TKA will lose weight in the year after surgery.

This prospective study included patients undergoing a primary TKA from January of 2018 until January of 2019. Patients were weighed and heights measured preoperatively and at 12 months after surgery.

Data were completed for 247 patients, including 68 men and 179 women. At 12 months, the mean change in BMI was an increase of 0.48 kg/m<sup>2</sup>. As a group, 6.9% lost weight, 68% had no loss, and 25.1% gained weight.

**Conclusion:** This study of patients undergoing total knee arthroplasty secondary to osteoarthritis of the knee found that, on average, patients had a slight increase in body mass index one year after surgery.

Coelho, A., et al. Patients Lose Weight after a Total Knee Arthroplasty: Myth or Reality? *Int Orthop*. 2022; 46: 1299-1304.

### **CARE TRANSITIONS FROM HOSPITAL TO HOME**

Health care systems focus on the quality and value of care by improving patient experiences and clinical outcomes while minimizing costs. One potential route for increasing value involves improving the transition of care process, which begins before the patient's discharge and continues beyond the return home.

The Integrated Michigan Patient-Centered Alliance in Care Transitions (I-MPACT) included seventeen

hospitals, 12 practitioner organizations and six skilled nursing facilities (SNFs) in Michigan. These facilities collaborated to identify shared adult patients with congestive heart failure or chronic obstructive pulmonary disease, who had recently returned home or to an assisted living facility.

A survey was developed to query patients eight to 12 days after discharge, and conducted by telephone interviews. Data included sociodemographic information as well as the proportion of patients who experienced social determinants of health (SDOH) issues, received follow-up calls, and attended follow-up visits.

Over 20% reported not receiving a follow-up telephone call. This finding was more prevalent in Black patients (17.5%) versus other races (11.4%). Among patients who required medical equipment at home (e.g., oxygen, inhalers, or blood pressure monitors), 7.7% (68 patients) reported a lack of confidence in using such equipment, and 1.9% (17 patients) reported never receiving the prescribed equipment. The four most common SDOH concerns were 1) affording prescriptions, equipment, therapy, and home health care, 2) access to transportation, 3) affording medical visits and copayments, and 4) having enough help at home for appropriate care.

**Conclusion:** This study found that, in transitions from hospital to home, a number of communication and logistic issues inhibit appropriate post-discharge care.

Jones B., et al. Patient Perspectives on Care Transitions from Hospital to Home. *JAMA Netw Open*. 2022, May 6; 5: e2210774.

### **BOTOX ALONG SUTURES FOR MIGRAINE**

For patients with chronic migraine (CM) headaches, botulinum toxin injections are an FDA-approved intervention. This study reviewed the efficacy of a new technique using a reduced volume of onabotulinumtoxinA (BoNT-A) at sites along the pericranial sutures and neck muscles for patients with chronic migraine (CM).

The patients were 18 to 64 years of age with CM. Botulinum toxin was injected in 18 sites over the area of the cranial sutures. Adverse events and potential beneficial effects were recorded in a headache diary at least four weeks prior, and 12 weeks after,

the injections. Pain was recorded on a ten-point visual analogue scale (VAS).

Data were completed for 20 patients with a mean age of 40 years. Compared to baseline, the number of days with moderate to severe headache were reduced at 5-8 weeks after injections ( $p \leq 0.05$ ). All parameters, including acute medicine and triptan doses, and days with work absence, were reduced in the first two periods after injection.

**Conclusion:** This study of patients with chronic migraine headaches found that a treatment method that used significantly less botulinum toxin was effective for reducing the number of moderate to severe headaches.

Stovner, L., et al. Follow the Sutures: Piloting a New Way to Administer Onabotulinum Toxin for Chronic Migraine. *Cephalalgia*. 2022; 42(7): 590-597.

### **GREATER OCCIPITAL NERVE BLOCK FOR EPISODIC MIGRAINE**

Greater occipital nerve (GON) block with local anesthetic and steroids has been used to treat several types of headaches. This study assessed the efficacy of GON blocks for reducing the severity and duration of migraine headaches.

Subjects were 18 to 65 years of age with a history of migraine headaches without aura and randomized to one of four groups to receive injections with a) triamcinolone 20 mg combined with two ml of saline (T), b) 2 ml of lidocaine 2% and 0.5 ml of saline (L), c) 20 mg of triamcinolone and two ml of lidocaine 2% (T&L), or d) normal saline alone (S). Landmarks were used to provide bilateral injections at the area of the greater occipital nerve. The patients were asked to record the episodes, the duration, and the severity of headaches with a visual analog scale (VAS) of pain.

Fifty-five patients completed the study, with a mean age of 40.4 years, of whom 72.7% were female. All four groups experienced a significant reduction in the headache severity and duration, with no differences among the groups. A significant decrease from baseline in the number of headaches was found in patients in the L and the L&S groups, but not in the S or T groups.

**Conclusion:** This study found that injections at the greater occipital nerve which included lidocaine could

reduce the severity and number of migraine headaches.

Malekian, N., et al. Preventative Effect of Greater Occipital Nerve Block on Patients with Migraine: A Randomized, Double-Blind, Placebo-Controlled, Clinical Trial. *Cephalalgia*. 2022; 42(6): 481-489.

### POST-OPERATIVE AMINO ACID SUPPLEMENTATION

Among patients who must undergo surgical intervention for musculoskeletal trauma, complications and prolonged loss of function continue to impact clinical outcomes. Dietary deficiencies have been identified as a modifiable risk factor. This study assessed the effect of conditionally essential amino acid (CEAA) on the on post-operative complications including muscle wasting.

This prospective single-blinded single center randomized controlled trial including an intention-to-treat analysis included 400 patients with a mean age of 52.6 years with a combination of poly-trauma, fragility, and isolated fractures. All received standard post-operative nutrition. Those randomized to the CEAA group received twice daily supplementation for two weeks with a commercially available supplement containing 7 g of arginine, 7 g of glutamine, and 1.5 g of the leucine metabolite beta-hydroxymethylbutyrate. The primary outcome was complication rate (reoperation, nonunion, surgical site infection, mortality, and medical complications). Secondary outcomes were body composition (fat-free mass [FFM]) measured with A-mode via ultrasound, and grip strength via dynamometer measured up to 12 weeks postoperatively.

The complication rate was 30.5% in the CEAA group and 43.8% in the controls ( $p=0.008$ ). The FFM at six weeks was lower in the controls than in the CEAA group, although this did not reach statistical significance ( $p=0.3606$ ). No difference in grip strength was found between groups at any point.

**Conclusion:** This study of patients seen for fracture repair found that supplementation with conditionally essential amino acids could reduce the risk of post operative complications.

Hendrickson, N., et al. Conditionally Essential Amino Acid Supplementation Reduces

Postoperative Complications and Muscle Wasting After Fracture Fixation: A Randomized Controlled Trial. *JBJS*. 2022, May 4;104(9):759-766.

### CEREBELLAR INTERMITTENT THETA-BURST STIMULATION FOR DYSPHAGIA AFTER STROKE

After a cerebral vascular accident (CVA) traditional swallow training is not supported by strong evidence of efficacy. Theta burst stimulation (TBS) is a new model of transcranial magnetic stimulation that simulates endogenous oscillation frequencies in the hippocampus. As several studies have found that intermittent TBS (iTBS) may improve swallow outcomes in the elderly, this study explored the efficacy of cerebellar intermittent TBS (iTBS) for post-stroke dysphagia post-stroke.

This randomized double-blind sham-controlled trial included patients with first-ever stroke, with onset one week to six months prior to recruitment. The subjects were randomized to receive either true stimulation (T-iTBS) or sham stimulation (S-iTBS). The T-iTBS was delivered during ten 100% resting motor threshold (RMT) iTBS sessions, each lasting 190 seconds, for two weeks. Both groups received the same traditional dysphagia therapy over two weeks. The main outcome measure was the Fiberoptic Endoscopic Dysphagia Severity Scale (FEDSS) score, at baseline, at the end of treatment, and four weeks after the end of treatment. Secondary measures included the Functional Oral Intake Scale (FOIS), The Penetration - Aspiration Scale (PAS), and the Standardized Swallowing Assessment (SSA).

A multivariate analysis revealed that, compared to S-iTBS, FEDSS scores for the T-iTBS group were significantly improved after two weeks ( $p=0.02$ ) and four weeks ( $p=0.03$ ). Similar improvement relative to the sham group was seen in PAS, SSA, and FOIS scores ( $p<0.001$  for all comparisons).

**Conclusion:** This study of patients with post stroke dysphagia found that theta-burst intermittent transcranial magnetic stimulation could improve swallowing when added to traditional therapy.

Rao, J., et al. Bilateral, Cerebellar, Intermittent Theta Burst Stimulation Combined with Swallowing Speech Therapy for Dysphagia after Stroke: A Randomized, Double-Blind, Sham

Controlled, Clinical Trial. *Neurorehabil Neural Repair*. 2022, Jul;36(7):437-448.

### RETURN TO ACTIVITY AFTER REVISION ANTERIOR CRUCIATE LIGAMENT SURGERY

A primary goal after primary anterior cruciate ligament (ACL) reconstruction or revision (rACL) is to return to the pre-injury activity level. This study reviewed the characteristics of those who returned to activity after an rACL.

The Multicenter ACL Revision Study (MARS) included 1,205 patients undergoing revision rACL. A binary indicator was used to identify patients with same/better PROs versus worse outcomes compared with baseline. Options for level of return to sport included none, recreational, amateur (team or club), high school, National Collegiate Athletic Association Division I/non-Division I, semiprofessional, and professional.

At two years of the 862 patients with rACL, 15% had not returned to activity. A multivariate analysis found that failure to return to activity was associated with having worse patient-reported surgical outcomes at two years. Also, those less likely to have returned to activity included current smokers (odds ratio 3.3), female patients (odds ratio 2.9), recreational participants (odds ratio 2.0), and those with a previous medial meniscal excision (odds ratio 1.9).

**Conclusion** This study of patients undergoing revision of an anterior cruciate ligament surgery found that 15% had not returned to baseline activity in two years, with an increased likelihood found among smokers, females, those with a history of meniscal excision and those involved in recreational rather than higher level sports participation.

MARS group. Returning to Activity after Anterior Cruciate Ligament Revision Surgery. An Analysis of The Multicenter Anterior Cruciate Ligament Revision Study (MARS) Cohort at Two Years Post-Operative. *Am J Sports Med*. 2022; 50(7): 1788-1797.

### DORZAGLIATIN FOR TYPE 2 DIABETES

Dorzagliatin is a dual-acting, orally bioavailable glucokinase activator that enhances glucokinase activity in a glucose-dependent manner. This

(Continued from page 2)

Rachel Sunico, M.D.  
Wes Soliman, MS4  
Matthew Tan, MS2  
UC Irvine, Irvine, CA

\*David Quan, M.D.  
J Christian Belisaria, D.O.  
Ryan McLoughlin, M.D.  
Palak Patel, M.D.  
Univ. of Penn, Philadelphia, PA

\*Kelsey Lau, D.O.  
John Donovan, M.D.  
Martin Laguerre, M.D.  
Ellen Sloan, M.D.  
Jake Stephen, D.O.  
Univ. of TX SW Med Ctr., Dallas, TX

\*Trevor Ellico, D.O.  
Daniel Nguyen, M.D.  
Jessica Sher, M.D.  
Univ. of Washington, Seattle, WA

\*Peter Park, M.D.  
\*Alan Stupnitsky, M.D.  
Brittany Dukes, M.D.  
Michael Wright, M.D.  
Washington Univ, St. Louis, MO

**Executive Editor Emeritus**  
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trial (SEED) is a phase 3 placebo-controlled study designed to assess the efficacy of dorzagliatin in drug-naïve patients with T2D.

Subjects were drug-naïve adults, 18-75 years of age with T2D, HbA1c levels between 7.5% and 11.0%, and a BMI of 18.5-35.0 kg/m<sup>2</sup> at screening. The subjects were randomly assigned to receive dorzagliatin 75mg BID, or a placebo for 24 weeks of double-blind treatment, followed by 28 weeks of open-label treatment with dorzagliatin for all patients. The primary efficacy endpoint was the change from baseline in the HbA1c level at week 24.

At week 24, the HbA1c was reduced by 1.07% in the treatment group and 0.5% in the placebo group (p<0.001). The reduction in HbA1c in the treatment group started at week four and reached the maximum reduction at week twelve. There were no significant differences in adverse events between the two groups.

**Conclusion:** This study of patients with type 2 diabetes found that dorzagliatin 75 mg twice per day was effective in reducing the patients' HbA1c.

Zhu, D. et al., Dorzagliatin in Drug-Naïve Patients with Type 2 Diabetes: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial. **Nat Med.** 2022, May; 28, 965-973.

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