

# REHAB IN REVIEW

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## ULTRA-PROCESSED FOOD AND CARDIOVASCULAR AND RESPIRATORY DISEASE

A number of studies have investigated the association between ultra-processed foods (UPF) and the risk of cardiovascular disease (CVD). This study examined data from a prospective, cohort study to determine the association between UPF consumption and mortality due to cardiovascular or respiratory disease.

Data were obtained from the UK biobank, a population based, prospective cohort study of more than 500,000 participants recruited between 2006 and 2010. Data were gathered concerning sociodemographic factors, lifestyle factors, body mass index, personal history of disease, and diet. The dietary analysis was based on a food frequency questionnaire over 24 hours. The amount of UPF consumed was divided by the total amount of foods consumed in grams per day and expressed as a proportion. Outcome measures included cardiovascular disease and respiratory disease data obtained from medical and death records.

Data were gathered from 111,646 participants, followed over 10 years. Of these, 7,006 developed cardiovascular disease, and 9,785 developed respiratory disease. An adjusted analysis demonstrated that, compared to the group with the lowest UPF consumption, the group with the highest UPF consumption had an elevated risk for CVD (Hazard Ratio (HR) 1.19), cerebrovascular disease (HR 1.10), coronary heart disease (HR 1.24), CVD mortality (HR 1.46), respiratory disease (HR 1.12), and respiratory disease mortality (HR 1.12).

**Conclusion:** This large, prospective study found that higher consumption of ultra-processed food is associated with greater risk of cardiovascular and pulmonary disease.

Li, H., et al. Association of Ultra-Processed Food Intake with Cardiovascular and Respiratory Disease Multimorbidity: A Prospective, Cohort Study. *Mol Nutr Food Res.* 2023. Mar 17. Early View.

## CAFFEINE AND THE 100-METER SPRINT

The International Association of Athletics Federations has proclaimed that caffeine is an ergogenic aid which enhances running performance. As this consensus was based on studies of anaerobic sports, this study investigated the acute effect of caffeine on the performance of a 100-meter sprint.

Subjects were 15 male collegiate sprinters. In a preliminary experiment the participants were asked to ingest caffeine at 6 mg/kg of body weight to determine changes in plasma concentration over time. Serum levels were checked at 30, 60, 90, and 120 minutes after caffeine ingestion. At the second and third visits, the participants performed sprint running time trials after receiving either a placebo or a caffeine tablet. The following week, the capsule contents were reversed and the running trial repeated. Times were compared between the control and caffeine conditions.

As compared to the placebo trial, the 100-meter sprint time was shortened by 0.14 seconds in the caffeine condition ( $p=0.007$ ). The corrected sprint time at 60 meters was also significantly shorter in the caffeine than in the placebo condition ( $p=0.002$ ). No significant difference was noted between conditions in the time to run the final 40 meters.

**Conclusion:** This study of collegiate sprinters found that caffeine supplementation enhanced 100-meter sprint time by improving performance in the first 60 meters.

Matsumura, T., et al. Acute Effect of Caffeine Supplementation on 100-Meters Sprint Running Performance:

A Field Test. *Med Sci Sports Exerc.* 2023, March 1; 55(3): 525-533.

## COGNITIVE TESTING FOR LICENSE RENEWAL AND MOTOR VEHICLE COLLISIONS

In January of 2009, Japan introduced the mandatory screening test of cognition for drivers 75 years of age or older. The older drivers were allowed to renew their licenses and continued driving even when they screened positive for cognitive impairment. This study reviewed the incidence of collisions after the initiation of this mandate.

Data were collected concerning the number of motor vehicle collisions and road injuries among drivers, pedestrians, and cyclists for individuals 70 years of age or older between July of 2012 and December of 2019. Collisions were included in the data only when the driver was found to be responsible for the collision.

From the time of the policy change in March of 2017 to December of 2019, the number of collisions decreased by 3,670. During that same time the number of road injuries among pedestrians and cyclists 75 years of age or older increased by 959. The ratio of collisions/population of adults 75 years of age or older fell from 347 (July of 2012 to February of 2017) to 299 (March of 2017 to December of 2019).

**Conclusion:** This Japanese study found that mandatory cognitive screening of motor vehicle drivers  $\geq 75$  years of age was associated with a reduction in the rate of motor vehicle collisions but an increase in the number of pedestrians injuries.

Inada, H., et al. Association between Mandatory Cognitive Testing for License Renewal and Motor Vehicle Collisions and Road Injuries. *J Am Geriatrics Soc.* 2023, April; 71(4): 1145-1155.

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**OBESITY AND SHOULDER ARTHROPLASTY**

The prevalence of obesity has been increasing throughout the world. Recent literature has demonstrated increased intraoperative and postoperative complication rates in patients with obesity compared to those without. This study of patients undergoing shoulder arthroplasty compared the complication rates with baseline body mass index (BMI).

This retrospective, cohort analysis used data from the Pearl Diver Patients' Records Database, with over 150 million enrollees, covering dates from 2010 to 2021. BMI data were obtained, with categories of obesity determined. Data were reviewed for patients with primary total shoulder arthroplasty (TSA) or reverse total shoulder arthroplasty (RTSA), each of whom had five years of follow-up data available. The primary outcome measure was the five-year cumulative incidence for revision surgery.

Data were analyzed for 17,372 patients who underwent RTSA and 31,473 who underwent TSA. For the RTSA group, at five years, the cumulative revision rates among those in the normal and overweight group were 3.58%. For those in the class I and class II obesity group, revision rates were 4.38%. Finally, rates for those in the obesity class III group were 3.55%. The corresponding percentages for the TSA group were 3.69%, 3.39%, and 2.48%, respectively. Multivariate analysis revealed no significant difference in the two- and five-year surgical outcomes of all-cause revision for the overall obese cohort as compared to the non-obese cohort.

**Conclusion:** This study of patients undergoing shoulder joint replacement secondary to osteoarthritis found no significant association between revision rates and body mass index.

Agarwal, A., et al. Obesity Does Not Associate with Five-Year Surgical Complications following Anatomic Total Shoulder Arthroplasty and Reverse Total Shoulder Arthroplasty. **J Should Elbow Surg.** 2023, May; 32(5): 947-957.

**BODY MASS INDEX AND REVISION RATES OF KNEE REPLACEMENTS**

Studies have shown that those with an elevated body mass index

(BMI) have an increased risk of thromboembolic events, infection, and revision surgery. This study compared the effect of BMI on the long-term outcome of unicompartmental knee replacement (UKR).

Data were obtained from the National Joint Registry for England, Wales, Northern Ireland, and the Isle of Man, (NJR) and Hospital Episode Statistics Admitted Patient Care (HES-APC). The patients' BMIs were obtained from the records. Using these data, the cohort was divided into four groups, underweight (< 18.5 kg/m<sup>2</sup>) normal weight (18.5 to <25 kg/m<sup>2</sup>), overweight (25 to 30 kg/m<sup>2</sup>), and obese (> 30 kg/m<sup>2</sup>). Revision surgeries and medical complications were tracked over ten years.

Complete data were available for 10,440 patients. For those who received cemented replacements, the 10-year revision rate increased as BMI increased. However, for those who received cementless replacements, the 10-year revision rate was lower in the overweight and obese groups (HR 0.61 and 0.74, respectively) than in the normal weight groups.

**Conclusion:** This study of patients undergoing unicompartmental knee replacement found that, with increasing body mass index, 10-year revision rates significantly increased in a cemented group but decreased in a cementless group.

Mohammad, H., et al. Effect of Body Mass Index on the Relative Revision Rates of Cemented and Cementless Unicompartmental Knee Replacements. An Analysis of Over 10,000 Knee Replacements from National Databases. **J Bone Joint Surg.** 2023, April; 105: 527-536.

**BARIATRIC SURGERY AND OSTEOARTHRITIS**

Obesity is a major risk factor for osteoarthritis of the hip and knee. Bariatric surgery has been shown to be effective for long-term weight reduction. This study assessed the effect of bariatric surgery on the long-term risk of osteoarthritis (OA) and joint replacements at the hip and knee.

The Swedish Obese Subjects (SOS) study is a prospective, controlled, intervention trial comparing one group treated with bariatric surgery with a matched control group receiving usual obesity care. The primary endpoint was

overall mortality. Data were recorded at baseline from patients' records, including documentation of OA and arthroplasty of the hip and knee, as well as risk factors for OA. The subjects were recruited between 1987 and 2001 and followed for a median of 21.2 years.

At one year, the mean BMIs were 31.8 for the surgery group and 39.9 for the control group. The bariatric group demonstrated a lower incidence of hip OA but a similar incidence of hip, and a greater incidence of knee arthroplasty than did the controls.

**Conclusion:** This study found that bariatric surgery was associated with an increased incidence of knee replacement as compared to a control group.

Lohmander, L., et al. Bariatric Surgery, Osteoarthritis, and Arthroplasty of the Hip and Knee in Swedish Obese Subjects - Up to 31 Years' Follow-Up of a Controlled Intervention Study. **Osteoarth Cartilage.** 2023; 31(5): 636-646.

### HOME-BASED EXERGAMING AFTER TOTAL KNEE REPLACEMENT

After undergoing total knee replacement (TKR), rehabilitation protocols have been shown to maximize the individual benefits of the surgery. This study assessed the effectiveness of home-based exercise with custom exergames for post TKA rehabilitation in older adults.

The subjects were patients 60 to 75 years of age with arthritis of the knee, each of whom was scheduled for TKR surgery. Those patients were randomized to a standard protocol control group (CG) or to an exergame based home intervention group (IG). Assessments included the Oxford Knee Score (OKS), the timed up and go (TUG), and a visual analog scale (VAS) for pain. The CG followed the usual post-TKR treatment. The IG participated in 11 games, progressing over time by changing the weekly number, duration, and intensity of activities. The subjects were instructed to complete the program assignment several times per day.

Improvement in mobility as measured with the TUG improved more in the IG than in the CG at two months ( $p=0.019$ ) and four months ( $p<0.04$ ). The OKS improved by 9.8 points in the control group and 12.1 in the IG ( $p<0.27$ ). At four months VAS

pain scores had improved 26.7 points in the CG and 36.3 in the IG ( $p<0.18$ ).

**Conclusion:** This study of patients 60 to 75 years of age who had undergone a total knee replacement found that training at home with customized exergames was more effective for improving mobility and satisfaction than a standard exercise protocol.

Janhunen, M., et al. Effects of a Home-Based Exergaming Intervention on Physical Function and Pain after Total Knee Replacement in Older Adults: A Randomized, Controlled Trial. **BMJ Open Sport Exerc Med.** 2023; 9(1): e001416.

### RISK FACTORS FOR FIVE-YEAR, RECURRENT DISC HERNIATION AFTER PRIMARY, SINGLE-LEVEL LUMBAR DISCECTOMY

Lumbar discectomy is a surgical intervention performed to remove a degenerative or herniated disc from the lumbar spine. This approach is typically employed to treat radicular symptoms refractory to conservative treatment. Because primary, single-level, lumbar discectomy is one of the most common spine-related surgeries, this study was designed to clarify the risk factors and five-year incidence of same-site recurrent disc herniation (sRDH) and post-procedure re-operation.

This retrospective study included 754 patients who underwent a primary, single-level, lumbar discectomy at Spire Norwich Hospital in Norwich, UK, from 2008 to 2019. Data gathered included medical history, comorbidities, and scores on patient-reported outcome measures, including the Oswestry Disability Index (ODI) and the Visual Analogue Scale (VAS). Clinical notes and MRI studies were reviewed to evaluate postoperative sRDH, while the Kaplan-Meier method calculated the five-year sRDH incidence.

Five years after the primary discectomy, 63 of 754 patients (8.36%) had undergone an sRDH. These surgeries occurred at a median of 0.8 years after the initial surgery. The five-year Kaplan-Meier estimate for sRDH was 12.1%, the sRDH reoperation rate was 7.5%, and any procedure reoperation was 14.1%. Risk factors associated with sRDH included current smoking (Hazard Ratio (HR) 2.12) and worse scores on the preoperative ODI (HR 1.02).

**Conclusion:** This study determined that current smoking and

higher preoperative disability are independent risk factors for sRDH.

Geere, J., et al. Incidence and Risk Factors for Five-Year, Recurrent Disc Herniation after Primary, Single-Level, Lumbar Discectomy. **Bone Joint J.** 2023, Mar 1; 105-B(3): 315-322.

### THE SIX MINUTE WALK TEST AND LUMBAR SPINE CANAL STENOSIS SURGERY

After lumbar decompressive surgery, the functional gains are often measured by the Oswestry Disability Index (ODI). However, this test is time consuming and therefore not part of routine clinical follow up. As the six-minute walk test (6MWT) can be easily administered in less time, this study looked at the relationship between changes in the 6MWT and the ODI after spinal surgery.

Subjects were adults with severe claudication, scheduled for surgical repair of lumbar spine canal stenosis (LSS). Clinical assessments before and after surgery included the 6MWD, and the ODI. A positive response to surgery was defined as a change in the ODI of more than the minimal detectable change (MDC) of 12.8. The scores of the responders on the ODI were compared to the scores of the 6MWT.

The change in the 6MWD was significantly related to the changes in the ODI at both six and 12 months ( $p<0.001$  for all comparisons). The MCD of the ODI was correlated with the corresponding values on the 6MWD, of 102.3 m and 57.5m at 6 and 12 months postoperatively.

**Conclusion:** This study of patients undergoing surgical intervention for spinal stenosis found that the Six-Minute Walk Test may be useful as a short and valid estimate of improvement after surgery.

Takenaka, H., et al. Minimal Clinically Important Difference of the Six Minute Walk Distance in Patients Undergoing Lumbar Spinal Canal Stenosis Surgery: 12-Month Follow-Up. **Spine.** 2023, April; 48(8): 559-566.

### PLASMA METABOLITES AND DIETARY STROKE RISK

Medical literature has produced a well-documented association between diet patterns and the risk of stroke. This study was designed to identify metabolites associated with dietary patterns and to test whether

these were associated with incident stroke.

The Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort is a longitudinal design evaluating the long-term effects of dietary patterns. The first study identified metabolites associated with incident ischemic stroke.

The participants provided clinical demographic and lifestyle information, with clinical variables including smoking status, systolic blood pressure (SBP), hypertension (HTN), diabetes mellitus (DM), cardiovascular disease (CVD), left ventricular hypertrophy (LVH), and atrial fibrillation (AF). Using a targeted metabolomics approach, 162 plasma metabolites were quantified. Dietary questionnaires were scored for adherence to the Mediterranean and DASH diets. Incident strokes during the study were documented. An adjusted analysis was completed to assess the effects of diet patterns and metabolites on incident stroke risk.

Dietary data were available for 822 stroke cases and 630 controls. An adjusted regression analysis revealed that the metabolites associated with adherence to a plant-based diet were the gut microbial metabolite, indole-3-propanoic acid (IPA), guanosine, gluconic acid, and C7 carnitine. Those associated with an increased risk of stroke were guanosine (Hazard Ratio (HR) 1.44), gluconic acid (HR 1.29), and C7 carnitine. Those associated with a decreased risk of stroke were IPA (HR 0.92) and glyceric acid (HR 0.91).

**Conclusion:** This study found that the metabolites associated with a reduced risk of stroke are indole-3-propionic acid and glyceric acid.

Bhave, V., et al. Plasma Metabolites Link Dietary Patterns to Stroke Risk. *Ann Neurol.* 2023, March; 93(3): 500-510.

### SERUM MMP-3 AND OSTEOARTHRITIS OF THE KNEE

The gold standard for investigating the diagnosis of knee osteoarthritis (KOA) is radiograph of the knee. However, this diagnostic tool lacks sensitivity in early diagnosis. Several biomarkers have been reviewed for potential diagnostic utility. As studies have shown that serum MMP-3 is elevated among those with KOA, this study assessed the ability of serum MMP-3 to

differentiate between normal knees and those with primary KOA.

Subjects were 80 patients with primary KOA and 80 without features of KOA. Assessments included demographic, clinical and radiologic profiles as well as biomarker profiles. All underwent radiographs with grading of these films subdivided into KL grade, one to four.

The mean MMP-3 level of those with KOA was 59.85, and of the controls was 14.52 ( $p=0.0001$ ). The levels of MMP-3 were increased with increasing K-L grades on radiographs. Serum MMP-3 level increases with increasing K-L grade ( $p = 0.000$ ). Serum MMP-3 level differs significantly between K-L grade I and grade II ( $p = 0.004$ ), between K-L grade II-III ( $p = 0.007$ ), and between K-L grade III-IV ( $p = 0.02$ ). Using a receiver operative curve (ROC) analysis, the cutoff value of 20.03 ng/ml provided a specificity of 71.25%, sensitivity of 77.5% and an accuracy of 73.04% in distinguishing between controls and subjects with KOA.

**Conclusion:** This study found that serum levels of MMP-3 may be useful in discriminating between those with and those without knee osteoarthritis.

Singh, S., et al. Can Serum MMP-3 Diagnose Early Knee Osteoarthritis? *J Orthop.* 2023, Mar 9(38): 42-46.

### PERIOPERATIVE AMINO ACID SUPPLEMENTATION AND TOTAL KNEE ARTHROPLASTY

Perioperative essential amino acid (EAA) supplementation has been shown to reduce rectus femoral muscle atrophy up to four weeks after a total knee arthroplasty (TKA). This study assessed the effect of this supplementation two years post-surgery.

Subjects were patients scheduled for TKA as a treatment for knee osteoarthritis. All were randomized to receive a placebo or nine grams per day of EAAs. These were threonine (405 mg, 4.5%), lysine (756 mg, 8.4%), isoleucine (603 mg, 6.7%), valine (603 mg, 6.7%), methionine (603 mg, 6.7%), tryptophan (207 mg, 2.3%), phenylalanine (405 mg, 4.5%), leucine (684 mg, 7.6%), histidine (315 mg, 3.5%), arginine (630 mg, 7%), and glycine (1,089 mg, 12.1%) and 30% starch. The primary outcome was the rectus femoris muscle area as assessed by ultrasonography.

Sixty patients were enrolled in the study with four patients in each group

lost to follow up. The relative changes in the rectus femoris muscle area were significantly greater in the supplement group than in the placebo group at one year and two years after surgery. In addition, at two years, the change in strength in the quadriceps muscle was greater in the supplement group than in the placebo group.

**Conclusion:** This prospective study of patients undergoing total knee arthroplasty found that amino acid supplementation one week prior to, until two weeks after surgery resulted in better quadriceps strength and volume at two years.

Ueyama, H., et al. Peri-Operative Essential Amino Acid Supplementation Facilitates Quadriceps Muscle Strength and Volume Recovery after TKA. A Double-Blinded, Randomized, Controlled Trial. *J Bone Joint Surg.* 2023, March 1; 105(5): 345-353.

### TOFACITINIB FOR POLYMYALGIA RHEUMATICA

Polymyalgia rheumatica (PMR) is an inflammatory disorder characterized by pain and stiffness involving the shoulders and proximal arms. Tofacitinib, a Janus kinase inhibitor, has been shown to suppress the interferon- $\gamma$ -related downstream pathway, with the potential to alleviate the activity of PMR. This study evaluated the effect of tofacitinib on PMR.

Subjects were 14 participants with highly active PMR, defined as a PMR Activity Scale (PMR-AS) score of  $>17$ . The subjects were given tofacitinib, 10 mg/day, along with prednisone, 50 mg/day at baseline, with prednisone reduced to 2.5 mg/day or less within 20 weeks. The primary endpoint was the remission response, defined as the achievement of a PMR-AS of below seven, and with glucocorticoid independence for four weeks.

At two weeks, a significant reduction in PMR-AS scores was observed and maintained throughout the study. Quality of life, as assessed by the Modified Health Assessment Questionnaire and the EQ-5D-3L, was significantly improved ( $p<0.001$ ). In addition, a significant decrease was found in interleukin 6, tumor necrosis factor alpha, BASF, and Interleukin-1RA, ( $p=0.05$ ). At week 48, the average prednisone dose was 1.2 mg, with six patients discontinuing the medication.

**Conclusion:** This phase two trial involving patients with polymyalgia rheumatica found that tofacitinib, a Janus kinase inhibitor, reduced both symptoms and glucocorticoid use.

Zhang, L., et al. Efficacy and Safety of Tofacitinib in Patients with Polymyalgia Rheumatica: A Phase Two Study. *Ann Rheum Dis.* 2023, May; 82(5): 722-724.

### ANTI-CALCITONIN GENE RELATED PEPTIDE MONOCLONAL ANTIBODIES FOR TREATMENT RESISTANT MIGRAINES

Monoclonal antibodies against calcitonin gene related peptide (anti-CGRP MABs) have been shown to be effective for preventing episodic and chronic migraines. This study assessed the real-life treatment response to this category of medications at three and six months.

This prospective, clinical, cohort, observational study included 357 patients with a diagnosis of treatment resistance migraines. All had failed at least three classes of preventative medications. Baseline data included the Migraine Disability Assessment (MIDAS), the Headache Impact Test-6 (HIT-6), the Beck Anxiety Inventory (BAI), and the Beck Depression Inventory-II (BDI-II). The patients were treated with erenumab 140 mg monthly, or galcanezumab 120 mg monthly. All subjects maintained a headache diary. The response was categorized according to the reported reduction in monthly headache days (MHD): Sustained-response (SustainedR,  $\geq 50\%$  at M3 and M6), Short-Response (ShortR, M3  $\geq 50\%$  and M6  $< 50\%$ ), Late-Response (LateR, M3  $< 50\%$  and M6  $\geq 50\%$ ), Limited-Response (LimitedR, 25%–50% at M3 and M6), and No-Response (NoR,  $< 25\%$  at M3 and M6).

The distribution according to response pattern was 37.0% (110/297) SustainedR, 16.8% (50/297) LateR, 10.4% (31/297) ShortR, 22.6% (67/297) LimitedR, and 13.1% NoR (39/297). Only the SustainedR and LateR groups showed statistically significant anxiety and depression score reduction at M3 and M6, and the ShortR group only for depression.

**Conclusion:** This study of patients with recalcitrant migraine headaches treated with a new anti-calcitonin gene related peptide monoclonal antibody found that the initial response is not consistent in all

patients, with anxiety or depression associated with a diminished response at six months.

Torres-Ferrus, M., et al. Patterns of Response to Anti-Calcitonin Gene Related Peptide Monoclonal Antibodies during First Six Months of Treatment in Resistant Migraine Patients: Impact on Outcome. *Euro J Neurol.* 2023. 2023 Apr 10. doi: 10.1111/ene.15816. Epub ahead of print.

### INTERRUPTING PROLONGED SITTING AND CARDIOMETABOLIC RISK

Previous studies have suggested that sedentary lifestyles are associated with an increased incidence of cardiovascular disease. This study examines the effects of interruptions of sedentary activity using short bouts of light exercise.

Subjects were  $\geq 45$  years without persistent chronic medical conditions. Subjects were selected who were routinely sedentary for more than eight hours per day and accumulated  $\geq 50\%$  of their sedentary time from prolonged bouts of sitting. The subjects completed five conditions in random order, with a minimum of four days washout between these conditions. The conditions were: a) light intensity walking every 30 minutes for one minute; b) light intensity walking every 30 minutes for 5 minutes; c) light intensity walking every 60 minutes for one minute; d) and light intensity walking every 60 minutes for 5 minutes e) control. All trials were eight hours in duration. Before testing a screening was completed which included blood sugar and blood pressure, measured every 15 and 60 minutes respectively. The intervention groups were compared to the control group.

Compared to the control condition, significant reductions in glucose were realized in group b ( $p < 0.05$ ). Glucose was lowered in other conditions though these did not reach statistical significance. All intervention groups realized significant net decreases in systolic BP from baseline compared with the control condition ( $p < 0.05$ ). The largest reductions in systolic BP were observed for group c ( $p < 0.001$ ), followed by group b ( $p = 0.003$ ).

**Conclusion:** This randomized crossover study involving middle and older age adults who routinely engaged in prolonged sedentary activity, found that walking for one or five minutes every 30 or 60 minutes

could significantly improve blood pressure and blood sugar.

Duran, A., et al. Breaking Up Prolonged Sitting to Improve Cardiometabolic Risk: Dose-Response Analysis of a Randomized Crossover Trial. *Med Sci Sports Exerc.* 2023, May 1;55(5):847-855.

### ARTERIALIZATION OF DEEP VEINS IN CHRONIC LIMB ISCHEMIA

Despite advances in surgical and endovascular treatment, up to 20% of patients with chronic limb-threatening ischemia are not candidates for revascularization. Transcatheter arterialization of the deep veins is an endovascular revascularization procedure designed as an option for the treatment of chronic limb-threatening ischemia.

The subjects were patients with chronic limb threatening ischemia with no option for arterial revascularization. The patients underwent the creation of an arterial venous fistula, proximal to the diseased tibial arteries with oxygenated blood delivered from tibial arteries to the tibial veins. After surgery the patients were followed at week two and months one, two, three, 6, 9, and 12, with annual visits thereafter, until year three. The primary endpoint was amputation-free survival, defined as a composite of freedom from above ankle amputation or death from any cause at six months. The objective performance target was set at 54%.

During the study, a total of 219 patients with a median age of 70 years underwent screening, with 105 enrolled in the study. The procedure was successful in 104 of the 105. Amputation free survival at six months was 66.1%, greater than the performance goal of 54%. Of those presenting with a lower limb ischemic wound, 25% were healed at follow-up.

**Conclusion:** This prospective study of patients with no option chronic limb threatening ischemia found that, a new procedure, transcatheter arterialization of deep veins, could be performed with a high degree of procedural success.

Shishehbor, M., et al. Transcatheter Arterialization of Deep Veins in Chronic Limb Threatening Ischemia. *N Eng J Med.* 2023, March 30;388 (13): 1171-1180.

## EFFECT OF POLYPILL, ASPIRIN, OR BOTH ON COGNITION AND FUNCTION

While the prevalence and impact of cognitive decline is a global public health burden, few interventions have been clearly shown to reduce this burden. The International Polycap Study 3 (TIPS-3) tested whether a polypill (including antihypertensive agents and a statin), aspirin, or a combination of both could reduce major adverse cardiovascular events.

The subjects were 65 years of age or older, with no known cardiovascular disease, but with intermediate cardiovascular risk as scored on the INTERHEART Risk Score. The study used a 2 × 2 × 2 factorial design. Those taking the polypill received atenolol, 100 mg daily; ramipril, 10 mg daily; hydrochlorothiazide, 25 mg daily; and simvastatin, 40 mg daily. Those taking aspirin received 75 mg per day, and those taking placebo received a matching placebo.

The participants were assessed for cognition with the Montreal Cognitive Assessment (MoCA), the Digit Symbol Substitution Test (DSST) to assess psychomotor speed, attention, and executive function, and the Trail Making Test Part B (TMT-B) to assess attention. The primary outcome measure was the difference between groups on a composite of cognitive and functional assessment scores.

Data were collected from 5,713 participants, followed for a mean of five years. Over the course of the study, there was no significant difference between the study groups in the primary outcome. However, functional decline was decreased for both the polypill vs placebo and the polypill plus aspirin vs placebo comparisons ( $p=0.01$  for both).

**Conclusion:** This study of patients 65 years of age or older found that five years of treatment with a polypill did not reduce the risk of substantive cognitive decline but did reduce the risk of functional decline.

Bosch, J., et al. Effects of a Polypill, Aspirin, and the Combination of Both on Cognitive and Functional Outcomes. A Randomized Clinical Trial. *JAMA Neurol.* 2023, March; 80(3): 251-259.

## ATRIAL FIBRILLATION TREATMENT

Atrial fibrillation (AF) is a chronic and progressive disease, associated

with a high risk of cerebrovascular events. This study compared treatment options for initial rhythm control in patients with AF.

This randomized trial included adults with symptomatic paroxysmal AF who received an implanted cardiac monitor with an AF detection algorithm. The subjects were randomized to receive cryoballoon ablation or anti-arrhythmic drug therapy and followed for three years. The primary endpoint was the first occurrence of persistent AF, defined as continuous atrial tachyarrhythmia lasting seven days or longer or lasting 48 hours to seven days but requiring cardioversion for termination.

Over 36 months, persistent AF occurred in three of the 154 in the ablation group and 11 of the 149 in the medication group (Hazard Ratio (HR) 0.25). At 36 months, the recurrence of any AF tachyarrhythmia lasting 30 seconds or longer occurred in 56.5% of the ablation group and 77.2% of the medication group (HR 0.51). At 36 months, adverse events occurred in 11% of the ablation group in 23.5% of the medication group.

**Conclusion:** This study of patients with atrial fibrillation found that catheter cryoballoon ablation is associated with a lower incidence of persistent atrial fibrillation and a lowered burden of arrhythmia as compared to drug therapy.

Andrade, J., et al. Progression of Atrial Fibrillation after Cryoablation or Drug Therapy. *N Engl J Med.* 2023, Jan 12; 388(2): 105-116.

## MEDITERRANEAN DIET AND PARKINSON'S DISEASE

Several non-motor symptoms are known to precede the clinical diagnosis of Parkinson's disease (PD), suggesting early prodromal neurodegenerative processes. As several lifestyle factors have been implicated in this process, this study reviews the association between the adherence to a Mediterranean diet and the longitudinal changes in the probability of developing PD.

The Hellenic Longitudinal Investigation of Aging and Diet (HELIAD) is a large-scale multidisciplinary study evaluating the prevalence, incidence, and risk factors of several neuropsychiatric conditions involving aging. Participants were community dwelling populations in two areas of Greece, 65 years of age or older. Information collected included demographics, tobacco use, caffeine, physical

activity, pesticide exposure, medical, neurologic conditions neuropsychiatric symptoms, medical history and habits. An extensive structured physical exam was included with neurologic signs and symptoms recorded. Signs of PD were evaluated with the Unified Parkinson's Disease Rating scale part three (UPDS-3). These diagnoses were made of PD or dementia with Lewy bodies (DLB). Dietary intake was assessed using a semi quantitative food frequency questionnaire. Adherence to the Mediterranean diet was scored using the MeDi. Responses were divided into quintiles.

At the onset of the study 1,047 participants were recruited who were free of PD. During an average of three years follow up, 2% were diagnosed with prodromal PD. Adherence to the MeDi was associated with lower risk of PD over time on both unadjusted and adjusted analysis ( $p < 0.05$ ). Those in the highest quintile of adherence had a 21% lower probability for developing PD than did the lowest quintile.

**Conclusion:** This study found that higher adherence to the Mediterranean diet was associated with a lower increase in Parkinson's disease probability overtime.

Maraki, M., et al. The Mediterranean Diet Is Associated with a Lower Probability of Prodromal Parkinson's Disease and Risk for Parkinson's Disease Dementia with Lewy Bodies: A Longitudinal Study. *European J Neurol.* 2023, April; 30(4):934-942.

## POST-ACUTE REHABILITATION BEFORE AND DURING COVID

Skilled nursing facilities (SNFs) provide post-acute care for nearly 20% of hospitalized older adults. This study reviewed the changes in rehabilitation services provided by SNFs during the pandemic.

Data were obtained from a large, multi-state data sharing collaboration, representing 185,522 individuals in 776 SNFs. Data from patients treated from October of 2019 to March of 2020 (before the pandemic) and from October of 2020 and March of 2021 were compared. The data collected with the Minimum Data Set were used to compare two time periods.

The pre-pandemic cohort and pandemic cohorts included 61,017 and 47,505 patients, respectively. Compared with the pre-pandemic cohort, the pandemic cohort had worse cognitive scores, fewer days of

PT and OT, and slightly longer lengths of stay.

**Conclusion:** This study of patients admitted to skilled nursing facilities found that those admitted during the pandemic obtained poorer scores in cognitive function and had higher mortality than did those admitted before the pandemic.

Shi, S., et al. Post-Acute Care Rehabilitation Services and Outcomes in Skilled Nursing Facilities before and during the COVID-19 Pandemic. **JAMA Health Forum.** 2023;4(3): e230019.

### CHARCOT MARIE TOOTH PROGRESSION AND MPZ MUTATIONS

Dominant mutations in the Myelin Protein Zero (MPZ) gene account for five percent of all Charcot-Marie-Tooth (CMT) and 10% of all confirmed demyelinating forms of CMT. This study evaluated the natural history of MPZ neuropathies.

Subjects were patients with mutations in the MPZ gene, recruited from the National Institutes of Health Rare Diseases Clinical Research Network. All were tested with the CMT Examination Score (CMTES), seven-item, 28-point composite score, based upon patients' symptoms (three items), and the Rasch modified CMTES (CMTES-R). The change in CMTRS over time was monitored. Performance of the CMTES-R and the CMTES was evaluated by comparing the mean change from baseline to two years.

Scores for CMTES and CMTES-R were available for 67, 44, 38, 34, and 31 participants at years one through five respectively. The mean change in CMTES at two years was 0.87 points for axonal and 0.06 for demyelinating ( $p=0.057$ ). Only participants with moderate forms of neuropathy (CMTES of eight to 14) showed progression in CMTES over two years. In a subgroup analysis a greater change in CMTES at two years was more often noted among those with axonal as compared to demyelinating neuropathy ( $p=0.016$ ).

**Conclusion:** This study of patients with Charcot-Marie-Tooth found that worsening of symptoms over time was associated with axonal rather than demyelinating neuropathy.

Fridman, V., et al. Disease Progression in Charcot Marie Tooth Disease Related to MPZ Mutations: A

Longitudinal Study. **Ann Neurol.** 2023, March; 93(3): 563-576.

### HEALTH RELATED QUALITY OF LIFE AFTER KNEE REPLACEMENT

Knee osteoarthritis (KOA) is a common condition with pain, loss of function, and a negative impact on health-related quality of life (HRQOL). This study assessed the changes in HRQOL in patients 10 years after a total knee arthroplasty (TKA).

This prospective study included two previous adult cohorts with KOA who underwent TKA and were recruited between 2002 and 2006. All were evaluated at baseline and at six months and ten years using the Western Ontario and McMaster (WOMAC) arthritis index. Ten-year follow-up included the 36-Item Short Form Health Survey (SF-36).

Questionnaires were sent to 731 patients, of whom 471 responded at a mean of 10.11 years and a mean age of 69.73 years. From baseline to both six-month and ten-year follow-ups, changes in WOMAC scores showed significant improvement ( $p<0.0001$  for both comparisons). The changes between six months and ten years were not found to be significant. Compared to the general population, those in the TKA group had lower health related quality of life at 10 years.

**Conclusion:** This study of patients undergoing total knee arthroplasty found that health-related quality of life was significantly improved at both six months and 10 years but did not reach the level found in the general population.

Gonzalez-Saenz-de-Tejada, M., et al. Long-Term, Health-Related Quality of Life in Total Knee Arthroplasty. **BMC Musculoskel Dis.** 2023; 24: 327. doi: 10.1186/s12891-023-06399-6.

### TIME TO RECOVERY AFTER SPORT-RELATED CONCUSSION

After a concussion, the rate at which athletes can return to pre-injury levels of function remains unclear. To clarify this issue, this study uses data collected by the Concussion Assessment, Research, and Education (CARE) Consortium conducted between 2014 and 2020.

The subjects were college-level varsity athletes who completed baseline evaluations of mental status using the Standardized Assessment of Concussion (SAC). In addition, computer based neurocognitive

function was tested using the Immediate Post Concussion Assessment and Cognitive Test (ImPACT). Clinical balance was assessed using the Balance Error Score System (BESS). Participant-reported symptoms were assessed using the Sport Concussion Assessment Tool (SCAT) symptom inventory. Psychological health was tested using the Brief Symptom Inventory 18 (BSI-18). Medical staff at each site diagnosed injuries using a common definition and administered follow-up evaluations within six hours of injury and at 24 to 48 hours, when the athlete was cleared to return to play and when the athlete was cleared for unrestricted return to play. Recovery at the group level for each assessment was defined as the return to mean baseline level of functioning of the group.

Screening data were completed for 33,499 varsity athletes of whom 2,842 were diagnosed with a concussion. Of these 92% had no more than two previous concussions. At the group level, return to baseline levels of functioning on most clinical assessments occurred between two and seven days after the concussion. Visual memory recovery and reaction time recovery extended to 14 days and 18 days respectively.

**Conclusion:** This study of college level varsity athletes found that, as a group, the symptoms of concussion resolved within 18 days.

Broglio, S. et al. Time to Recovery as Measured on Clinical Assessments After a Sport Related Concussion. **N Eng J Med.** 2023, May 4;388:1717-1719.

### ATRIAL FIBRILLATION IN CRYPTOGENIC STROKE AND TRANSIENT ISCHEMIC ATTACK

Cryptogenic stroke is defined as an ischemic stroke without an identified cause where the etiologies are undetermined after extensive investigation. Approximately 1/4 of ischemic strokes remain cryptogenic. Cardioembolism due to occult atrial fibrillation is thought to be one of the more common causes of cryptogenic stroke. This study used data from the Nordic Atrial Fibrillation and Stroke (NOR-FIB) trial to better understand the contribution of atrial fibrillation to ischemic stroke.

The NOR-FIB was a prospective multi centered observational real-life study, which collected data from patients diagnosed with CS or cryptogenic transient ischemic attack

(Continued from page 2)

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(TIA). The patients received an ICM within 14 days of the event and monitored remotely for 12 months. Periods of AF for two minutes or longer were considered for a change of secondary prevention. The primary endpoint was AF detection rate within 12 months of continuous rhythm monitoring.

Between January 2017 and September 2020, 277 patients from 18 centers were enrolled. Remote monitoring data was available from 258 patients at six months and 254 patients at 12 months. During the 12 months of follow-up, 74 of 259 (28.6%) were diagnosed with paroxysmal AF or atrial flutter. The median time from index event to insertion was nine days. The detected arrhythmia was recurrent in 91.9% of the patients.

**Conclusion:** This study of patients with cryptogenic stroke and cryptogenic transient ischemic attack found that an insertable cardiac monitor (ICM) can be an effective tool for diagnosing underlying atrial fibrillation.

Ratajczak, R., et al. Atrial Fibrillation in Cryptogenic Stroke and TIA Patients in The Nordic Atrial Fibrillation and Stroke (NOR-FIB) Study: Main Results. *Eur Stroke J.* 2023, Mar;8(1): 148-146.

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