

# REHAB IN REVIEW

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## PHYSICAL ACTIVITY DURING PREGNANCY AND BIRTH WEIGHT

While moderate intensity physical activity seems relatively safe in uncomplicated pregnancies, some have expressed concerns about vigorous exercise. This study was designed to better understand the association between intensity of exercise and the child's birth weight.

Subjects were recruited from 10 tertiary care centers in Quebec, Canada from May of 2010 to August of 2012. Participating women were seen at the clinics in the first, second and third trimesters of their pregnancies.

Data collected included socio-demographic, obstetrical and medical history. Following each visit, the women completed a web-based version of the Pregnancy Physical Activity Questionnaire to document physical activity for the preceding month. The primary outcome measure was the infant's birth weight, collected from medical charts.

Overall, maternal energy expenditure decreased from pre-pregnancy to late pregnancy ( $p<0.0001$ ). Vigorous exercise was reported by 35.5%, 31.4% and 18.6% of women during the first, second and third trimesters, respectively. An adjusted analysis revealed that energy expenditure spent at sports and exercise during the first trimester was negatively associated with birth weight. However, this activity was not significantly associated with detrimental effects including the occurrence of small for gestational age and large for gestational age babies.

**Conclusion:** This study found that pregnant women who engaged in vigorous energy expenditure exercise during the first trimester delivered infants with a reduced birth weight, though without an increased risk of pathologically low birth weights.

Bisson, M., et al. Physical Activity during Pregnancy and Infant's Birthweight: Results from the 3-D

Birth Cohort. **BMJ Open Sport Exerc Med.** 2017;3(1):1-9.

## CAPSULAR SHRINKAGE FOR CHRONIC ANKLE INSTABILITY

Among patients with lateral ankle sprain, 30% to 40% develop chronic ankle instability (CAI). When conservative treatment is insufficient, surgical intervention may be considered. This study reviews the long-term outcomes of patients treated with a capsular shrinkage technique.

This retrospective, long-term follow-up included 25 adult patients diagnosed with CAI. All underwent shrinkage, using an arthroscopic probe with radiofrequency energy applied at 20 to 50 W. The primary outcome measure was the Karlsson score, which assessed pain, swelling, stability, stiffness, stair climbing, running, work activities and required ankle support. Secondary scores included the SF-36, the Tegner, the American Orthopaedic Foot and Ankle Society (AOFAS) and the Good score. Patients were assessed at baseline and then at nine months, five to seven years and 12 to 14 years post-surgery.

Of the 25 patients, 92% reported good or excellent treatment satisfaction. The Karlsson scores demonstrated significant improvement over the entire study ( $p<0.0005$ ), with no score change from the mid- to long-term follow-up. The SF-36 physical scale score showed significant improvement only at the first follow-up, while the Tegner score showed significant improvement over the short- ( $p<0.0005$ ) and long-term follow-ups ( $p<0.05$ ). Significant improvements were noted for all functional scores. Fourteen of the 25 patients reported a re-sprained ankle at least once a year.

**Conclusion:** This retrospective study of patients with chronic ankle instability suggests that an arthroscopic capsular shrinkage

technique may be effective in treating these patients.

Vuurberg, G., et al. Arthroscopic Capsular Shrinkage for Treatment of Chronic Bilateral Ankle Instability. **Foot Ankle Int.** 2017; 38(10): 1078-1084.

## VITAMIN E AND SEVERE KNEE OSTEOARTHRITIS

As evidence has demonstrated that oxidative stress is one of the inducing factors of osteoarthritis (OA), this study evaluated the effect of vitamin E on patients with severe symptomatic OA of the knee.

Subjects were adult patients with severe knee OA who were scheduled for total knee arthroplasty. During the study, the subjects were allowed to use only acetaminophen every six hours as needed for pain. The patients were randomized to a treatment group to receive 400 international units of vitamin E daily for two months, or to a control group to receive identical appearing placebos. The outcome measures included biochemistry, histology and clinical results.

At follow-up, those in the intervention group had significantly greater improvement than the placebo group in pain ( $p<0.01$ ), stiffness ( $p<0.01$ ) and function ( $p<0.01$ ), as measured by the Western Ontario and McMaster University Osteoarthritis Index (WOMAC). The changes in blood level markers of oxidative stress and antioxidative capacity were greater in the treatment group than in the placebo group, including malondialdehyde ( $p=0.03$ ), alpha-tocopherol ( $p<0.01$ ), FRAP ( $p=0.01$ ) and TEAC ( $p=0.03$ ). Similar differences were found in synovial fluids.

**Conclusion:** This study of patients with severe osteoarthritis of the knee found that vitamin E, at 400 international units per day, improved oxidative stress and clinical function.

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Tantavisut, S., et al. Effect of Vitamin E on Oxidative Stress Level in Blood, Synovial Fluid and Synovial Tissue in Severe Osteoarthritis: A Randomized, Controlled Study. **BMC Musculoskel Dis.** 2017; 18; 281: 1-9.

## **DUAL ANTITHROMBOTIC THERAPY AFTER PERCUTANEOUS CORONARY INTERVENTION IN ATRIAL FIBRILLATION**

For patients with atrial fibrillation (a-fib), the choice of antithrombotic therapy for those undergoing percutaneous coronary intervention is complicated by the risk of bleeding. This study, the Randomized Evaluation Of Dual Antithrombotic Therapy With Dabigatran Versus Triple Therapy With Warfarin In Patients With Nonvalvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention (RE-DUAL PCI trial), compared dual versus triple antithrombotic therapy.

Subjects included adults with nonvalvular a-fib who had undergone successful PCI within the previous 120 hours. The subjects were randomized to receive triple therapy with warfarin plus a P2Y<sub>12</sub> inhibitor (clopidogrel or ticagrelor) and aspirin (for one to three months), or dual therapy with dabigatran (110 mg or 150 mg twice daily) plus a P2Y<sub>12</sub> inhibitor (clopidogrel or ticagrelor) and no aspirin. The primary endpoint was the first major or clinically relevant non-major bleeding event.

Data were complete for 2,725 patients treated at 414 sites in 41 countries. The rates of the primary endpoint were 15.4% in the dabigatran 110 mg dual therapy group and 26.9% in the triple therapy group (p<0.001). The incidence of the primary endpoint in the dabigatran 150 mg dual therapy group was 20.2%, compared with 25.7% in the triple therapy group (p<0.001). By combining the two dual therapy groups, the primary endpoint was found to occur in 13.7%, as compared to 13.4% in the triple therapy group (p=0.0005). The incidence of thromboembolic events, death or unplanned revascularization was 13.7% in the composite dual therapy groups and 13.4% in the triple therapy group (p=0.005).

**Conclusion:** This study of patients with atrial fibrillation who had undergone percutaneous coronary intervention (PCI) found that dual therapy with dagabitrn and a P2Y<sub>12</sub> inhibitor resulted in a significantly

higher risk of thrombotic events and a lower risk of bleeding events than triple therapy.

Cannon, C., et al. Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation. **N Eng J Med.** 2017, October 19; 377(16): 1513-1524.

## **ASSOCIATIONS OF FATS AND CARBOHYDRATES WITH CARDIOVASCULAR DISEASE AND MORTALITY**

Cardiovascular disease represents 80% of the burden of disease in low and middle income countries. Current dietary recommendations suggest a low-fat diet and limiting saturated fatty acids to less than 10% of energy intake. However, these recommendations have been based upon limited populations. This study, the Prospective Urban Referral Epidemiology Study (PURE) assessed the impact of diet on total mortality and cardiovascular disease in diverse settings.

Subjects, ages 35 to 75 years, were recruited from 18, low-income, middle income and high-income countries on five continents. Standardized questionnaires collected information including demographics, lifestyle, health history and medication use. Physical exams included weight, height, waist and hip circumference and blood pressure. The median duration of follow-up was 7.4 years. Primary outcome measures were total mortality and major cardiovascular events.

Data were available for 135,335 individuals. At a median follow up of 7.4 years, 5,796 deaths and 4,784 major cardiovascular disease events were reported. Increased carbohydrate intake was associated with a higher risk of total mortality (p=0.0001) and non-cardiovascular disease mortality (p<0.0001). Total fat intake was associated with lower risks of total mortality (p<0.0001), stroke (p=0.0562) and noncardiovascular disease mortality (p<0.01). Total protein intake was inversely associated with total mortality (p=0.003) and non-cardiovascular disease mortality (p=0.002).

Looking at fat intake, higher intake of saturated fatty acids was inversely associated with the risk of total mortality (p=0.0088), stroke (p=0.0498) and non-cardiovascular disease mortality (p<0.01). Higher monounsaturated fatty acid intake

was associated with lower mortality ( $p<0.0001$ ) and lower non-cardiovascular disease mortality ( $p=0.0003$ ). Higher intake of polyunsaturated fatty acids was associated with a lower risk of total mortality ( $p<0.0001$ ) and non-cardiovascular disease mortality ( $p=0.0002$ ).

**Conclusion:** This multi-national study found that carbohydrate intake is associated with a higher risk of total mortality, while fats, both saturated and polyunsaturated, were associated with lower mortality.

Dehghan, M., et al. Associations of Fats and Carbohydrate Intake with Cardiovascular Disease and Mortality in 18 Countries from Five Continents: A Prospective, Cohort Study. *Lancet*. 2017, November 4; 390(10107):2050-2062.

### POWER TRAINING AND GAIT IN OLDER ADULTS

Slower walking speed in elderly adults has been associated with numerous medical, cognitive and motor dysfunctions. As studies have shown that a decline in knee extension activation contributes to muscle weakness and is associated with a slower gait, this study evaluated the effect of power training on gait velocity.

Subjects were participants in the Potsdam Gait Study of community dwelling adults over the age of 65 years without mobility limitations. All subjects underwent 10 weeks of power training, followed by 10 weeks of detraining. Power training consisted of three sets of six to 10 repetitions at 40% to 60% of the three-repetition maximum. Exercises were performed with the leg press, ankle press, knee extension and knee flexion. All assessments were completed with EMG evaluation to assess for EMG amplitudes, activation onset and offset.

In follow-up, power training was found to have increased isometric muscle strength of the knee flexors, extensors and plantar flexors, as well as EMG amplitudes of the knee flexors, knee extensors and plantar flexors. After training, fast gait velocity was increased by 3.5%, while habitual gait velocity did not change significantly. Gains in fast velocity seemed to be significantly influenced by gains in plantar flexor activation during push off.

**Conclusion:** This study found that power training increased neuromuscular activation during

isometric contracture in older adults, with neuromuscular adaptations associated with increases in strength and fast gait velocity.

Beijersbergen, C., et al. Power Training-Induced Increases in Muscle Activation during Gait in Older Adults. *Med Sci Sports Exer*. 2017, November; 49(11): 2198-2025.

### FRUIT, VEGETABLE AND LEGUME INTAKE VERSUS CARDIOVASCULAR DISEASE

Guidelines recommending the consumption of five or more servings per day of fruits, vegetables and legumes are largely based upon observational data from Europe and the United States. This prospective study analyzed data from 18 countries in seven geographical regions to better understand this relationship.

This prospective, cohort study, the Prospective Urban Rural Epidemiology (PURE) study, included individuals 35 to 70 years of age without cardiovascular disease, sampling from low, middle and high income countries in seven geographical regions. At baseline, dietary intake was calculated using country specific food frequency questionnaires. In addition, questionnaires were used to obtain information concerning demographics, socioeconomic status, lifestyle, health history, including medications, and family medical history. The main outcome variables were major cardiovascular disease, fatal and nonfatal myocardial infarction/stroke, cardiovascular mortality and total mortality.

During the median 7.4 year follow-up of 135,335 individuals 35-70 years of age there were 4,784 major cardiovascular disease events. Higher total fruit, vegetable and legume intake was inversely associated with major cardiovascular disease, myocardial infarction, cardiovascular mortality, non-cardiovascular mortality and total mortality. The adjusted analysis revealed that only non-cardiovascular mortality ( $p=0.0038$ ) and total mortality ( $p=0.0001$ ) remained significant. Total mortality was lowest for three to four servings per day, with no further improvement noted with higher consumption.

**Conclusion:** This global, prospective study, including 18 countries, found that three to four servings per day of fruits, vegetables and legumes can reduce non-

cardiovascular and total mortality, with higher levels of consumption offering no further advantage.

Miller, V., et al. Fruit, Vegetable, and Legume Intake and Cardiovascular Disease and Deaths in 18 Countries (PURE): A Prospective, Cohort Study. *Lancet*. 2017, November 4; 390(10107):2050-2060.

### STATIN INTENSITY AFTER STROKE

The use of statins in acute ischemic stroke can be effective in reducing secondary cardiovascular events and death. This study investigated the effects of statin intensity and adherence on long-term prognosis after acute ischemic stroke.

This retrospective study used data retrieved from the National Health Insurance Service, a national sample cohort of South Korea. Data were mined for all patients 20 years of age or older with acute ischemic stroke between 2002 and 2012. Data were also collected from the prescription records of statins, with adherence estimated by the number of days covered by any statin prescription during that year. Poor adherence was defined as less than 40%, while good adherence was defined as greater than 80%. The primary outcome variable was a composite of recurrent stroke, myocardial infarction and all-cause death.

Of the 8,001 patients with acute stroke, 4,377 received no statin, 1,206 had poor adherence, 706 had intermediate adherence and 1,712 had good adherence. Among those with good adherence, 9.1% had low intensity, 83.1% had moderate intensity and 7.9% had high intensity dosing. A significant, positive relationship was seen between increased statin adherence and a lower risk of adverse events ( $p<0.001$ ). Among the patients with good adherence, the risk of adverse events was lower in those with high-intensity statin use than among those with low-intensity statin use. There was no significant increase in risk of hemorrhagic stroke with statin use.

**Conclusion:** This retrospective study demonstrated that, after stroke, adherence to high-intensity statins can provide a substantial, long-term benefit for the prevention of recurrent stroke, myocardial infarction and all-cause death.

Kim, J., et al. Effects of Statin Intensity and Adherence on the Long-Term Prognosis after Acute Ischemic

Stroke. **Stroke**. 2017, October; 48 (10): 2723–2730.

### HEALTHFUL VERSUS UNHEALTHFUL PLANT-BASED DIET AND CORONARY HEART DISEASE

While plant-based diets have been associated with a lower risk of various diseases, studies often treat all plant foods equally. This study compared different types of plant-based diets with their effect on coronary heart disease (CHD).

From the Nurses' Health Study, dietary data were mined from responses to the food frequency questionnaires. Using these data, scores were obtained for an overall plant-based diet index (PDI) which emphasizes the consumption of plant food and reducing animal food intake. In addition, a healthful plant-based diet index (hPDI) score was calculated, which emphasized intake of whole grains, fruits/vegetables, nuts/legumes, oils and tea/coffee, as well as an unhealthful plant-based diet index (uPDI) score which emphasized the consumption of juices/sweetened beverages, refined grains, potatoes and sweets. The primary outcome measure was CHD.

Data were obtained for 73,710 women, of whom 8,631 developed CHD. In the pooled analysis, the PDI was inversely related to the development of CHD ( $p=0.003$ ). When analyzed separately, the inverse association between CHD and hPDI was stronger than that for overall PDI. In contrast, there was a positive association between uPDI and CHD ( $p<0.001$ ).

**Conclusion:** This study, using data from the Nurses' Health Study demonstrates that, while adherence to a plant based diet is associated with a lower risk of CHD, this effect is enhanced when individuals exclude unhealthy plant-based items including juices, refined grains, potatoes and sweets.

Satija, A., et al. Healthful and Unhealthful Plant-Based Diets and the Risk of Coronary Heart Disease in U.S. Adults. **J Am Coll Cardio**. 2017, July; 70 (4): 411–422.

### ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: YOUNG VERSUS OLD

The population of individuals older than 65 years of age is expected to increase significantly in the next

decades. As the incidence of anterior cruciate ligament (ACL) repair surgery is likely to increase with the growing population of elderly, this study evaluated the effect of age on the outcome of ACL repair.

This retrospective study included patients between 20 and 30 years of age, as well as those between 50 and 70 years of age, at the time of their primary ACL reconstruction. At a minimum of two years after the index surgery, the patients were administered a questionnaire, including clinical outcome measures. Demographic characteristics were recorded, and patient satisfaction was measured on a 10 point scale.

Data were available for 85 patients, including 52 in the younger group and 33 in the older group. All patients improved on all outcome scores, with the exception of the International Knee Documentation Committee (IKDC) score ( $p<0.001$ ). Improvements were similar between age groups in the SF-12 PCS, SF-12 MCS, WOMAC total, Lysholm, Tegner Activity Scale and patient satisfaction scores.

**Conclusion:** This study of patients undergoing anterior cruciate ligament repair found similar function and satisfaction improvement in those 50 to 70 years of age when compared to those 20 to 30 years of age at the time of repair.

Cinque, M., et al. Outcomes and Complication Rates after Primary Anterior Cruciate Ligament Reconstruction Are Similar in Younger and Older Patients. **Ortho J Sports Med**. 2007. 5(10): 1-6.

### FEMOROACETABULAR IMPINGEMENT IN PROFESSIONAL FOOTBALL

Femoroacetabular impingement (FAI) can result in significant hip pain and disability. Studies have shown that early chondral and labral lesions continue to progress if impingement is not adequately addressed. These injuries have been found to result in significant game and practice time lost among players in the National Football League (NFL). This study describes the rate of return to play (RTP) for NFL players after arthroscopic treatment of FAI.

Subjects were 51 professional football players undergoing 60 arthroscopic procedures for FAI between 2000 and 2014. Data were obtained from historical and current player websites. Successful RTP was defined as playing in a single

preseason or regular season game post-surgery. All players underwent a physical examination, including radiographic assessment.

After the 60 arthroscopic procedures, 52 returned to play. Of the nine players undergoing bilateral surgery, 89% return to play. By position, linemen were less likely to return to play than were other players ( $p=0.04$ ). Microfracture that was performed during the surgery was not associated with RTP.

**Conclusion:** This study of professional football players found that, after acetabular repair, 87% returned to play for an average of 38 games.

Menge, T., et al. Femoroacetabular Impingement in Professional Football Players. **Am J Sport Med**. 2017, August; 45(8):1740-1744.

### AUTOLOGOUS CHONDROCYTE IMPLANTATION AFTER 20 YEARS

Autologous chondrocyte implantation (ACI) was first performed in 1987, with the first generation of this technique using an autologous periosteal flap to cover the defect. This study evaluated the long-term, clinical outcomes of patients undergoing this procedure.

Between 1995 and 1996, 23 patients were treated with ACI for symptomatic, full-thickness, chondral defects. The surgical procedure included arthroscopic cartilage biopsy at the initial surgery, with chondrocytes expanded for cell implantation. At the second surgery, a membrane was placed over the defect, with the chondrocytes injected underneath the membrane. At follow-up, patients were assessed with the Western Ontario and McMaster University's Osteoarthritis (WOMAC) index, a Visual Analog Scale for pain, the Short Form-36 (SF-36) and the Modified Cincinnati Knee Rating System.

The survival rate was 63% at 20 years. Survival rate did not differ by age, gender or cartilage defect size. Only the WOMAC stiffness subscale and the SF-36 mental component summary failed to significantly improve after surgery. The greatest improvements in clinical scores were observed during the first two years after surgery. Of the failures, five underwent revision ACI and four underwent arthroplasty at a mean of 1.7 and 5.9 years, respectively.

**Conclusion:** This 20- year follow-up of patients undergoing first-generation autologous chondrocyte

implantation found satisfactory survival rates and clinical improvement.

Ogura, T., et al. A 20-Year Follow-Up after First Generation Autologous Chondrocyte Implantation. **Am J Sports Med.** 2017, October; 45 (12): 2751-2761.

### **COCOA, BLOOD PRESSURE AND VASCULAR FUNCTION**

Cardiovascular disease is the most common cause of death in the Western world. Studies have shown that the consumption of polyphenol rich foods is related to a lower risk of cardiovascular events. Fruits, vegetables, tea, chocolate and wine contain high amounts of polyphenol. This literature review summarized the effects of cocoa and chocolate on blood pressure and vascular function.

A number of epidemiologic studies have shown that cocoa consumption is associated with a reduction in blood pressure, reduced cardiovascular mortality and decreased all-cause mortality. In addition, studies have shown a reduction in stroke. Intervention studies have demonstrated that the regular consumption of chocolate milk is associated with a reduction in blood pressure, LDL cholesterol, oxidative stress, insulin resistance and lipid peroxidation. In addition, cocoa-containing drinks have been to have a positive effect on cognitive performance and improved endothelial function.

**Conclusion:** This literature review outlines a number of epidemiologic studies demonstrating a positive relationship between routine cocoa intake and better cardiovascular outcome, with interventional studies demonstrating improvements in vascular function, including blood pressure.

Ludovici, V., et al. Cocoa, Blood Pressure, and Vascular Function. **Front Nutr.** 2017, August; 4(36).

### **PAIRED ASSOCIATIVE STIMULATION AFTER INCOMPLETE SPINAL CORD INJURY**

The combination of transcranial magnetic stimulation (TMS) with peripheral nerve stimulation (PNS) has been found to induce plasticity in motor and sensory tracts in healthy subjects. This combination, termed "paired associative stimulation (PAS)"

was used in this study of patients with incomplete SCI.

Subjects were five patients, 36-68 years of age with incomplete chronic tetraplegia. The patients received 16 sessions of stimulation over four weeks. Serving as their own controls, TMS was combined with PNS in one hand (involving the median, ulnar and radial nerves), and with sham PNS in the contralateral hand. The subjects were assessed using the Daniels and Worthinghams Muscle Test (DWMT).

Immediately after intervention, DWMT scores increased significantly in both hands, with the PAS improving by 0.74 and the PNS by 0.55, resulting in no significant difference between the two ( $p=0.5$ ). At one month after treatment cessation, the PAS hand was found to have improved further, with total improvement in the PAS hand of 1.02 points, as compared with 0.65 in the PNS hand ( $p<0.0001$ ). No difference in hands was noted in sensory or spasticity scores.

**Conclusion:** This study of patients with incomplete tetraplegia found that combining transcranial magnetic stimulation with peripheral nerve stimulation can enhance motor output more than peripheral nerve stimulation alone.

Tolmacheva, A., et al. Long-Term Paired Associative Stimulation Enhances Motor Output of the Tetraplegic Hand. **J Neurotrauma.** 2017, September 15; 34: 2668-2674.

### **TRIGEMINAL NERVE STIMULATION FOR MIGRAINE**

Migraine headaches are primarily treated pharmacologically. Recent studies have indicated that neurostimulation may be helpful for the treatment of headaches. However, data are limited regarding the efficacy of external trigeminal nerve stimulation (e-TNS) for the acute treatment of migraine. This study investigated whether e-TNS can effectively and safely treat an acute migraine attack.

Subjects were patients 18 to 65 years of age with a history of episodic or chronic migraines. All had presented to a clinic complaining of a migraine attack lasting for at least three hours, with no recent migraine medication use. The patients were treated with a 60-minute session of e-TNS, programmed with a pulse frequency of 100 Hz and a pulse width of 250  $\mu$ s. All patients were asked to rate their pain on a 10-point visual analog scale (VAS) before

treatment, and at one and two hours after beginning treatment. Rescue medicine intake was documented at two and 24 hours.

Thirty patients completed the one-hour treatment, with no dropouts. The mean VAS pain score was reduced from 5.63 to 2.42 after one hour ( $p<0.001$ ), and to 2.66 after two hours ( $p<0.001$ ). Of the 26 patients contacted within 24 hours, 17 had not used a rescue medication.

**Conclusion:** This study of patients with chronic migraine headaches found that stimulation of the trigeminal nerve may be effective for reducing pain.

Chou, D., et al. External Trigeminal Nerve Stimulation for the Acute Treatment of Migraine: Open-Label Trial on Safety and Efficacy. **Neuromodulation.** 2017; 20: 678-683.

### **PATENT FORAMEN OVALE CLOSURE VERSUS MEDICAL THERAPY AFTER STROKE**

Studies have shown a strong association between cryptogenic strokes and the presence of a patent foramen ovale (PFO). While previous studies have failed to demonstrate a benefit of PFO closure over medical treatment, those studies have been based upon moderate durations of follow-up. This study was designed to understand the long-term effects of these two intervention techniques.

Eligible patients were adults, 18 to 60 years of age, with a PFO confirmed following a cryptogenic ischemic stroke. The subjects were randomly assigned to medical therapy alone group or to a PFO closure group. The closure group received aspirin plus clopidogrel daily for one month, followed by aspirin for five months. In the medical therapy group, four therapies were allowed including aspirin, warfarin, clopidogrel and aspirin combined with extended-release dipyridamole. The participants were followed for a median of 5.9 years. The primary efficacy end point was a composite of recurrent nonfatal ischemic stroke, fatal ischemic stroke, or early death.

Data were analyzed for 980 patients with an average age of 45.9 years, including 499 in the PFO closure group and 481 in the medical-therapy group. Of these, 46 had a primary endpoint event, with 45 % fewer noted in the PFO closure group than in the medical therapy group ( $p=0.046$ ).

**Conclusion:** This study of adults with a cryptogenic ischemic stroke found that surgical closure of the patent foramen ovale was associated with a lower risk of recurrent ischemic stroke than with medical treatment alone.

Saver, J., et al. Long-Term Outcomes of Patent Foramen Ovale Closure or Medical Therapy after Stroke. *N Engl J Med.* 2017, September 14; 377 (11): 1022-1032.

### INPATIENT REHABILITATION AND SKILLED NURSING AFTER STROKE

Multiple guidelines recommend that stroke survivors receive appropriate post-acute care to enhance recovery and minimize disability. This study was designed to describe the use of inpatient rehabilitation facilities (IRFs) and skilled nursing facilities (SNFs) after ischemic stroke.

Data for this study were obtained from the American Heart Association Get with the Guidelines-Stroke Registry (GWTG-Stroke). This system records information including demographics, medical history, diagnostic history, brain imaging and in-hospital treatment outcomes. The sample included 31,775 adults who were hospitalized for acute ischemic stroke and were discharged to either an IRF or a SNF between January of 2006 and December of 2008.

Among the stroke survivors, 55.6% were discharged to an IRF and 44.4% to a SNF. Those discharged to a SNF were younger, more likely to be male, had less health-service use in the six months pre-stroke and had fewer comorbid conditions and in-hospital complications. Those patients with an NIHSS of <9 were more likely to receive IRF care ( $p<0.001$ ), while those with NIHSS scores of nine or more likely go to a SNF ( $p<0.001$ ). Those who lived farther away from an IRF than an SNF were less likely to receive care at an IRF.

**Conclusion:** This study of Medicare beneficiaries found that patients with lower NIHSS stroke scale scores are more likely to go to an inpatient rehabilitation facility, while the relative distance from the patient's home to a skilled nursing facility versus an inpatient rehabilitation center influenced the choice of the discharge destination.

Thomas, Y., et al. Unexplained Variation for Hospitals' Use of

Inpatient Rehabilitation and Skilled Nursing Facilities after an Acute Ischemic Stroke. *Stroke.* 2017, October; 48(10): 2836-2842.

### GRAY MATTER AND CHRONIC BACK PAIN

Chronic back pain (CBP) is a major contributor to functional impairment and disability throughout the world. Studies of patients with back pain have demonstrated structural and functional reorganization in brain areas involving nociceptive processes. This meta-analysis was designed to identify the most consistent gray matter (GM) changes in patients with CBP.

A comprehensive literature search was made of studies from January of 2000 through May of 2016. Studies chosen focused on CBP and voxel based morphology (VBM) of the GM of the brain. These studies included 293 patients with CBP and 624 healthy controls.

The meta-analysis found a decrease in GM in the bilateral, medial prefrontal cortex (mPFC) of patients with CBP, as compared with controls ( $p=0.00028$ ). This area has been identified as being involved in negative emotions, response conflict and detection of unfavorable outcomes, especially in relationship to the self. Patients with CBP also had greater GM reductions in the left anterior insula than did controls ( $p=0.00023$ ).

**Conclusion:** This meta-analysis of studies involving patients with chronic back pain demonstrates a reduction in gray matter in the medial prefrontal cortex, as well as the left anterior insula, as compared with controls.

Yuean C., et al. Gray Matter Abnormalities Associated with Chronic Back Pain: A Meta-Analysis of Voxel-Based Morphometric Studies. *Clin J Pain.* 2017, November; 33(11): 983-990.

### TRENDS IN SELF-REPORTED, HEALTHY OLDER ADULTS

Given the growing number of elderly in population, this study was designed to understand the distribution of healthy older adults in the United States.

This investigation used a nationally representative data sample from the Medical Expenditure Panel survey to identify adults, 65 years of

age or older, who reported their general health to be excellent or very good between 2000 and 2014. The data were reviewed by socioeconomic status and region.

The number of healthy, older adults increased from 14 million in 2000 (42.4% of all older adults) to 22.4 million in 2014 (48.2% of all older adults). The rate was higher for non-Hispanic whites, those with a higher education and those in the bracket of highest family annual income. Improvements over time in self-reported good health were noted in non-Hispanic whites and "others", those with some college education, those with middle income or greater and those who had ever been married. Self-reported good health rates declined among non-Hispanic blacks, Hispanics, those with a high school education or less, those in low income families and those who were never married. No regional differences were reported.

**Conclusion:** This study found that, while the percentage of elderly individuals who self-report good or excellent health has risen over the past decade, there has been a decline in some elements of the population.

Davis, M., et al. Trends and Disparity in the Number of Self-Reported, Healthy, Older Adults in the United States, 2000 To 2014. *JAMA Intern Med.* 2017. doi:10.1001/jamainternmed.2017.4357.

### TAI CHI AND THE KINESTHESIA IN ELDERLY WOMEN

Postural control has been found to decrease with age, resulting in an increased risk of falling among the elderly. Studies have shown that reduced lower limb proprioception is a contributing factor to falls. This study assessed the effect of tai chi (TC) on the kinesthesia of the lower extremities of elderly patients.

Women, 55 to 68 years of age, were recruited and randomly assigned to a TC group or to a control group. At baseline, all subjects were assessed to determine kinesthesia thresholds of the knee and ankle joints. The participants were assessed at the end of the 24-week TC intervention (at least four sessions per week), and at the end of 48 weeks of TC intervention.

At the end of the 24-week intervention, the kinesthesia levels of knee flexion ( $p<0.05$ ), knee extension ( $p<0.05$ ) and ankle dorsiflexion ( $p<0.05$ ) of the TC group were

significantly better than those of the control group, while the kinesthesia of ankle plantar flexion showed no significant change. At the end of the 48-week intervention, the kinesthesia level of each dependent variable of the TC group was significantly better ( $p < 0.01$ ) than that of the control group. Moreover, the kinesthesia of each variable of the control group remained unchanged.

**Conclusion:** This randomized study found that 24 weeks of tai chi intervention significantly improved the kinesthesia of the knee and ankle with further improvements noted after 48 weeks.

Cheng, L., et al. Effects of Different Periods of Tai Chi Exercises on the Kinesthesia of the Lower Limbs and Joints of Elderly Women. *Res Sports Med.* 2017; 24(4): 462-469.

### DOXYCYCLINE AND HEALING OF ACHILLES TENDONS

After Achilles tendon injury, the tendon undergoes three stages of repair, including inflammatory, proliferative and remodeling phases. In the remodeling stage, matrix metalloproteinases (MMP), are produced, which have been shown to degrade the extracellular matrix. As doxycycline has been found to inhibit local MMP activity and improve local collagen fiber organization, this animal study examined the effects of daily doxycycline administration on the healing of Achilles injuries.

Subjects were adult, male rats who underwent surgical transection of the Achilles tendon. The animals were then randomized to a treatment group receiving 10 mg/kg of oral doxycycline, or to a control group. At three, six and nine weeks post-injury, 18 animals were euthanized for tendon analysis.

Compared to the control group, those in the treatment group had a significant reduction in the expression of MMP-3. Those treated with surgical repair plus doxycycline exhibited better structural repair as well as better histological scores than those treated with surgery or doxycycline alone ( $p < 0.005$ ). The doxycycline groups also exhibited accelerated recovery of biomechanical properties, including greater equilibrium modulus ( $p < 0.001$ ), higher dynamic modulus ( $p < 0.001$ ) and lower creep strain ( $p = 0.04$ ).

**Conclusion:** This animal study found that after surgical resection, the recovery of the Achilles tendon was

accelerated by combining surgical repair with daily oral doxycycline.

Nguyen, Q., et al Therapeutic Effects of Doxycycline on the Quality of Repaired and Unrepaired Achilles Tendons. *Am J Sports Med.* 2017, October; 45(12): 2872-2881.

### BIOMARKERS AND MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment is the pre-dementia phase of Alzheimer's disease (AD). Over half of patients with MCI remain clinically stable or return to a normal state, while 50% progress to dementia over three years. This study was designed to construct prognostic models based on findings on MRI and cerebrospinal fluid (CSF) biomarkers.

Data were obtained from the Alzheimer's Biomarkers in Daily Practice (ABIDE) study, included 525 patients with MCI, seen in a memory clinic between 1997 and 2014. All underwent MRI and CSF analysis for A $\beta$ 1-42 and total tau. A model was constructed by using a Cox proportional hazards regression to assess for the risk of progression after three years.

Progression to AD after three years occurred in 30.9% of the patients. The rate of progression was 86% when MRI results were abnormal, 82% when CSF test results were abnormal and 89% when the results of both tests were abnormal. The rate of progression at three years was six percent when CSF results were normal, 18% when MRI was normal and four percent when both were normal.

**Conclusion:** This study of patients with mild cognitive impairment found that progression to dementia at three years was 86% when MRI results were abnormal, and only six percent when CSF levels of A $\beta$ 1-42 and total tau were normal.

Maurik, I., et al. Interpreting Biomarker Results in Individual Patients with Mild Cognitive Impairment in the Alzheimer's Biomarkers in Daily Practice (ABIDE) Project. *JAMA Neurol.* 2017, doi:10.1001/jamaneuol.2017.2712.

### FISH INTAKE AND COGNITION IN THE ELDERLY

As a number of studies have demonstrated that long chain omega-3 fatty acids may delay cognitive aging, this study pooled data from

one French and four US cohort studies to investigate the relationship between fish intake and cognitive decline.

Data were obtained from the French Three-City study, and four US cohort studies (The Nurses' Health Study, The Women's Health Study, The Chicago Health and Aging Project, and the Rush Memory and Aging Project). All studies included Caucasian participants 65 years of age or older, with at least one food frequency questionnaire, and repeated cognitive evaluations over 4-9 years. The data were assessed for the relationship between cognitive decline and fish intake, APOE4 alleles, and single nucleotide polymorphisms.

The primary analysis included data from 23,688 participants with a mean age of 71.9 years. In the combined analysis, a significant association was found between increasing intake of fish and slower cognitive decline ( $p = 0.031$ ). In addition, a significant relationship was found between an increase in fish intake and a reduced decline in episodic memory ( $p = 0.024$ ), with those consuming less than one serving per week declining more rapidly than those consuming four or more servings per week ( $p = 0.018$ ). There was no interaction between fish intake and APOE status or nucleotide polymorphisms.

**Conclusion:** This pooled analysis from five large cohorts of older Caucasian subjects in Europe in North America found that an increased intake of fish was modestly associated with slow rates of cognitive decline, particularly episodic memory decline.

Samieri, C., et al. Fish Intake, Genetic Predisposition to Alzheimer's Disease and Decline in Global Cognition and Memory in Five Cohorts of Older Persons. *Am J Epidemiol.* 2017. <https://doi.org.proxy.library.emory.edu/10.1093/aje/kwx330>.

### B-TYPE PEPTIDES AND TRAUMATIC BRAIN INJURY

While traumatic brain injury is a considerable worldwide health issue, diagnosing moderate traumatic brain injury (mTBI) is often complicated. A number of studies have reviewed the potential for biomarkers to assist with this diagnoses. This literature review and meta-analysis evaluated whether B-type natriuretic peptide could serve as a biomarker for TBI.



(Continued from page 2)

\*Justin L. Weppner, D.O.  
Sara Raiser, M.D.  
University of VA, Charlottesville, VA

\*Anna Coles, M.D.  
Alicia Fuhrman, M.D.  
Sean Matsuwaka, M.D.  
University of Washington, Seattle, WA

\*Hazel DeHut, D.O.  
Bonnie Weigert, M.D.  
Karen Laursen, M.D.  
University of Wis., Madison, WI

\*Joe Seacrist, M.D.  
VCU, Richmond, VA

\*Sean Smith, M.D.  
Gregory Decker, M.D.  
Washington U. in St. Louis, St. Louis, MO

**Executive Editor Emeritus**  
Donald F. Langenbeck, Jr., M.D.

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Michael P. Burke, M.S.

**\*Regional Managing Editors have  
attested that they have no financial  
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A literature review was conducted for studies including patients with a diagnosis of TBI, where plasma/serum concentrations of B-type natriuretic peptide (BNP), and N-terminal fragment BNP/NT-proBNP were measured. The strength of the relationship between BNP/NT-proBNP and a diagnosis of TBI was calculated. Of the 1369 potentially relevant studies, 21 were included in the meta-analysis. Of the 21 studies included the meta-analysis, 17 were considered to be high quality. The results of the meta-analysis showed that BNP/NT-proBNP was significantly higher in patients with TBI than in controls.

**Conclusion:** This meta-analysis suggests that serum levels of BNP/NT-proBNP may be an effective biomarker for assisting with a diagnosis of patients with traumatic brain injury.

Zang, Y et al. Could B-Type Natriuretic Peptide be a Biomarker for Traumatic Brain Injury? A Systematic Review and Meta-analysis. **Am J Emerg Med.** 2017, November; 35 (11):1695-1701.

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