

# REHAB IN REVIEW

TM

WWW.REHABINREVIEW.COM

Volume 26 Number 9

Published by Physicians  
In Physical Medicine and Rehabilitation

September 5, 2018

## WORKING HOURS AND VENOUS THROMBOEMBOLISM

Previous studies have demonstrated an association between longer working hours and the risk of coronary heart disease, myocardial infarction, cardiac arrhythmias and stroke. This study assessed the effect of long working hours on the risk of deep venous thrombosis (DVT) or pulmonary embolism (PE).

Data were obtained from the Individual Participant Data Meta-Analysis in Working Populations (IPD-Work) consortium, including data from 13, independent cohort studies in multiple nations. Long working hours were defined as 55 hours per week or longer, and standard working hours as 35 to 40 hours per week. The subjects were followed for incident venous thromboembolisms (VTE). The sample was followed for a mean of 9.7 years, with work hours compared to the incidence of VTE.

Among the 77,291, full-time employees included in the analysis, 539 first-time VTE events were recorded, with an incidence of 64.9 per 100,000 person/years. Compared to those working 35 to 40 hours per week, the risk of VTE was greater among those with longer working hours (HR 1.5). The risk with longer hours was greater for DVT (HR 1.7) than for PE (HR 1.4).

**Conclusion:** This study expands on our understanding of the cardiovascular risks of working 55 hours per week or longer, demonstrating an increased risk of venous thromboembolism.

Kivimäki, M., et al. Long Working Hours and Risk of Venous Thromboembolism. *Epidem.* 2018, September; 29(5): e 42-e44.

## CAFFEINE, CYP1A2 GENOTYPE AND ENDURANCE PERFORMANCE

Over 95% of caffeine is metabolized by the CYP1A2 enzyme which is encoded by the CYP1A2

gene. In addition, the 163A>C single nucleotide polymorphism, has been shown to alter the CYP1A2 enzyme inducibility and activity. This study explored the relationship between variations in CYP1A2 genotype and the ergogenic effects of caffeine.

This randomized, double-blinded, placebo-controlled study recruited 101 competitive athletes to complete a 10-km cycling time trial. At week one, saliva samples were collected to determine fast caffeine metabolizers (AA genotype) and slow caffeine metabolizers (AC or CC genotype). During weeks two through four, the athletes were randomly assigned to ingest caffeine at a low dose (2 mgkg<sup>-1</sup>) a moderate dose (4 mgkg<sup>-1</sup>) or a placebo.

The genotypes of the participants were, 49% AA, 43 % AC and 8% CC. For the AA genotype, cycling time improved by 4.8% at a caffeine dose of 2 mgkg<sup>-1</sup> (p=0.0005), and by 6.8% at 4 mgkg<sup>-1</sup> (p<.0001). In contrast, among those with the CC genotype, 4 mgkg<sup>-1</sup> of caffeine worsened cycling time by 13.7% (p=0.04), with no change seen with 2 mgkg<sup>-1</sup> or placebo. No significant effects were observed among those with the AC genotype at any caffeine load.

**Conclusion:** This study of competitive athletes found that the ergogenic effect of caffeine is greatly influenced by the 163A>C single nucleotide polymorphism, with the greatest positive ergogenic effect seen among those with the AA genotype.

Guest, N., et al. Caffeine, CYP1A2 Genotype and Endurance Performance in Athletes. *Med Sci Sports Exerc.* 2018, August; 50(8): 1570-1578.

## ASPIRIN AND CLOPIDOGREL AFTER ISCHEMIC STROKE OR TRANSIENT ISCHEMIC ATTACK

In 2013, the CHANCE trial found a 32% lower risk of stroke recurrence at 90 days by using a combination of clopidogrel and aspirin, as compared to aspirin alone, in a Chinese sample.

This study, the Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) trial was designed to generalize these results to the international population.

This randomized, double-blind, placebo-controlled trial enrolled 4,881 patients from 10 countries. Patients with NIHSS stroke scores of less than three were randomized within 12 hours after an acute ischemic stroke. The treatment group received a loading dose of clopidogrel 600mg, followed by 75mg daily, in addition to aspirin for 90 days for the duration of the study. The control group received aspirin plus placebo. The primary efficacy outcome measure was the risk of a composite of ischemic stroke, myocardial infarction and death from ischemic vascular causes. The primary safety outcome variable was the risk of major hemorrhage.

After 90 days, five percent of the patients who received combination therapy and 6.5% who received aspirin monotherapy achieved the primary efficacy outcome (p=0.02). Major hemorrhage occurred in 0.9% of the combination group and in 0.4% in aspirin group (p=0.02), with nonfatal, extracranial hemorrhage accounting for most of the hemorrhages. The risk of ischemic or hemorrhagic stroke was greater in the aspirin group than in the combination group (p=0.01).

**Conclusion:** This international study of patients who had sustained an acute ischemic stroke found that combining aspirin and clopidogrel reduces the risk of ischemic stroke, myocardial infarction or death from ischemic vascular causes while increasing the risk of major hemorrhage.

Johnston C., et al. Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA. *N Engl J Med.* 2018 Jul 19; 379(3): 215-225.

## SYMPTOMATOLOGY FOLLOWING TRAUMATIC BRAIN INJURY

Patients who experience a traumatic brain injury (TBI) report a

### **Editor-in-Chief**

David T. Burke, M.D., M.A.  
Emory University, Atlanta, GA

### **Executive Editor**

Randolph L. Roig, M.D.  
Emory University, Atlanta, GA

### **Copy Editor**

Roberta Alysoun Bell, Ph.D.  
Emory University, Atlanta, GA

### **Assistant Copy Editor**

Tracie McCargo  
Harvard Extension Sch., Cambridge, MA

### **Contributing Editors**

\* Michael Rozak, M.D.  
Iain Bailey, M.D.  
Natasha Bhatia, M.D.  
John Hermansen, M.D.  
Dana Norall, M.D.  
Benjamin Sirutis, M.D.  
Emory University, Atlanta, GA

\*Anthony Mazzola, M.D.  
Ariana Gluck, D.O.  
Icahn Sch. of Med at Mt. Sinai, N.Y., NY

\*Ethan Rault, M.D.  
\*Alex Richerand, M.D.  
Trevor Boudreaux, M.D.  
Wesley Miller, D.O.  
Ryan Wehle, M.D.  
LSU Health Sci. Ctr., New Orleans, LA

\*Alexander Sheng, M.D.  
Laura Malmut, M.D.  
Ishan Roy, M.D.  
N.W.U. /R.I.C., Chicago, IL

\*Yu Chiu, M.D.  
Yekaterina (Kathy) Plavnik, D.O.  
Rosa Pasculli, M.D.  
Kyle Seko, D.O.  
Perry Zillinger, M.D.  
NYU/Rusk Inst., New York, NY

\*Nicole Diaz-Segarra, M.D.  
Kathryne Bartolo, M.D.  
Nicole Diaz-Segarra, MD.  
Mohammad Zaidi, M.D.  
Hee-jin Jung, Touro, M.D.  
Rutgers-NJMS/Kessler, W. Orange, NJ

\*Richard Lau, M.D.  
Miles Bonner, M.D.  
Ryan Hafner, M.D.  
Richa Lamba, M.D.  
Anton Matveev, M.D.  
Luke Musser, M.D.  
Temple University, Philadelphia, PA

range of physical, cognitive and emotional sequelae. This study investigated the wide variety of persisting symptoms following TBI.

Data were collected from 311 patients (six were later excluded) who had attended a multidisciplinary neurotrauma TBI clinic from 2013 to 2016. Falls were the most common mechanism of injury (53.1%) with CT scans revealing mostly contusions (37.4%) and subdural hematomas (27.9%), located most commonly at the frontal (21.6%) and temporal (16.1%) lobes. Of the persisting symptoms, headache was the most common (47.9%), and dizziness and fatigability the second most common. Cognitive symptoms at three months included memory loss, reported by 43.4% of those with mild TBI, 41.1% of those with moderate TBI and 44.2% with severe TBI. A total of 7.1% experienced new-onset seizures, and 23% reported anxiety. Of the 184 employed prior to injury, 48.4 % returned to work. Of those driving before the injury, 28.5 % did not return.

**Conclusion:** This study of patients with traumatic brain injury found that headaches, dizziness, fatigability and memory loss were persistent issues three months after injury.

Bell, C., et al. Symptomatology Following Traumatic Brain Injury in a Multidisciplinary Clinic: Experiences from a Tertiary Centre. **Br J Neurosurg**, 2018. DOI: 10.1080/02688697.2018.1490945.

### **EXERCISE FOLLOWING RESOLUTION OF POST-CONCUSSIVE SYMPTOMS**

For children and adolescents, guidelines for return to play following concussion recommend a gradual increase in activity, with monitoring for post-concussive symptoms. The authors examined the effect of exercise on PCS and cognition in children and adolescents following the resolution of symptoms post-concussion.

This study included 41 males and 39 females, ranging in age from eight to 18 years, each of whom had been diagnosed with a concussion at an emergency room visit, (CON group). Healthy controls, (HC group), were also recruited, comprising non-injured adolescents, matched for age and cognitive function.

At day two following symptom resolution, the subjects completed an exercise protocol (the McMaster All-Out Progressive Continuous Cycling Test) and post-exercise tests of post-

concussive symptoms, using the Cog Sport Symptom Scale (CogSport SS) and a computer-based assessment of cognitive efficacy (the CogSport).

Results of the CogSport SS demonstrated that the HC group reported an average increase of three symptoms from pre-to post-exercise, while the CON group reported an average decrease by nearly 1.5 symptoms. For the CogSport SS composite, the CON group demonstrated faster reaction times than did the HC group, with this effect more pronounced on the more demanding tasks.

**Conclusion:** This study of children and adolescents, ranging in age from eight to 18 years, found that exercise did not result in a cognitive decline or greater symptom emergence, as compared with healthy controls.

Anderson, V., et al. Impact of Moderate Exercise on Post-Concussive Symptoms and Cognitive Function after Concussion in Children and Adolescents, Compared to Healthy Controls. **Int J Sports Med**. 2018; 39(9): 696-703.

### **SHORT-TERM MUSCULAR EFFECTS OF KINESIOTAPE**

A number of studies have suggested that Kinesiotape may be effective for the treatment of shoulder pathologies. This study explored the effects of Kinesiotape after rotator cuff surgery.

Subjects were adults with a rotator cuff tear, with surgical repair less than six weeks prior to enrollment. The patients were randomized to receive either Kinesiotape (KT), sham tape (ST) or no tape (NT). Those randomized to the KT condition underwent taping according to the method of Kenzo Kase. Those in the sham tape (ST) condition were taped horizontally at the distal insertion of the deltoid.

At six and 12 weeks, the subjects answered questions of the Quick Disabilities of the Arm Shoulder and Hand (DASH) to assess physical function symptoms. For each testing condition, the muscular activity of the trapezius, deltoid and infraspinatus were measured using EMG, conducted by an evaluator held blind to the condition (with taping hidden by a long sleeve shirt worn by the patient)

There was no significant difference between the groups in scores on the DASH and VAS pain scores at six and 12 weeks. At six weeks, during active forward flexion, muscular activity was greater in the

KT than the ST condition for the posterior deltoid ( $p=0.013$ ) and the infraspinatus ( $p=0.004$ ). At 12 weeks the muscular activity was greater in the KT than in the ST group in the middle as well as the posterior deltoid ( $p=0.001$  for both comparisons). A decrease in the upper trapezius recruitment was found in the KT group with increased flexion ROM at six weeks in both the KT and ST groups.

**Conclusion:** This study of patients with recent rotator cuff surgical repair found that Kinesiotape decreases activity of the upper trapezius, as compared to sham taping, with no difference between the groups in pain at six or 12 weeks.

Reynard, F., et al. Immediate and Short-Term Effects of Kinesiotaping on Muscular Activity, Mobility, Strength and Pain after Rotator Cuff Surgery: A Crossover, Clinical Trial. **BMC Musculoskel Dis.** 2018; 19:305.

### CONDOLIASE FOR LUMBAR DISC HERNIATIONS

Condoliase is a mucopolysaccharidase, with a high specificity for chondroitin sulfate and hyaluronic acid of the nucleus pulposus. This phase three, randomized, clinical trial was designed to verify the efficacy and safety of condoliase for the treatment of lumbar disc herniation (LDH).

Subjects were 163 patients, ranging in age from 20 to 70 years, each with symptomatic LDH. The subjects were randomized to receive either 1 mL of condoliase or a placebo, delivered under fluoroscopy into the nucleus pulposus, and then followed through week 52. The primary endpoint was the reduction in patient-assessed leg pain at week 13, using a 100 mm visual analogue scale (VAS).

Secondary endpoints included the "responder rate" (defined as at least 50% improvement in worst leg pain), and changes at week 52 on the VAS, the Oswestry Disability Index (ODI), the 36-Point Health Survey Form, neurologic exam results, volume of disc herniation, disc height and the need for lumbar surgery.

Significant reductions in VAS scores were noted in both groups, with mean improvements of 49.5mm after condoliase and 34.3mm after placebo ( $p=0.001$ ). The responder rate was higher in the condoliase group at weeks 13 and 52 ( $p=0.008$  and  $p=0.002$ , respectively). Also, at week 52, the condoliase group had superior results in the change in disc

height and volume, hypesthesia, straight leg test results and the physical component scores on the SF-36.

**Conclusion:** This study of patients with symptomatic lumbar disc herniation found that chemonucleolytic treatment with condoliase may improve pain and function.

Chiba, K., et al. Condoliase for the Treatment of Lumbar Disc Herniation: A Randomized, Controlled Trial. **Spine.** 2018 Aug 1; 43(15): 869-876.

### SURGERY VERSUS BRACE FOR PATELLAR DISLOCATION

Lateral patellar dislocation (LPD) is estimated to occur with an incidence of up to 1.2 per 1,000 children nine to 15 years of age. This study compared the outcomes of those patients with LPD treated with surgical repair with those of children treated with bracing.

This prospective study recruited patients between nine and 14 years of age with an acute, primary LPD. The subjects were randomized within two weeks of the injury, and after diagnostic arthroscopic surgery. Those randomized to a knee brace group received a lateral stabilizing soft knee brace, applied 24 hours per day for one month, combined with physical therapy. The operative group underwent arthroscopic-assisted repair of the medial patellofemoral ligament. The main outcome variable was a redislocation at two years.

At two-year follow-up, the redislocation rates were 22% in the surgical group and 43% in the bracing group. During that time, six patients from the bracing group were surgically stabilized. Within the two years, 14% suffered a dislocation of the contralateral knee. Knee Injury and Osteoarthritis Outcome Score for Children's-Sports Play and Quality of Life Subscale scores were better in the surgical group than in the bracing group. Of those without redislocation, objective and subjective knee function was comparable between groups.

**Conclusion:** This study of children with a primary patellar dislocation found that surgical repair resulted in a reduced redislocation rate as compared to conservative treatment with bracing and PT.

Askenberger, M., et al. Operative Repair of Medial Patellofemoral Ligament Injury versus Knee Brace in Children with an Acute, First-Time, Traumatic Patellar Dislocation: A Randomized, Controlled Trial. **Am J**

**Sports Med.** 2018, August; 46 (10): 2328-2340.

### RISK FACTORS FOR HAMSTRING INJURY IN PROFESSIONAL SOCCER

In elite soccer play, hamstring injuries are the most common noncontact injury. As the evidence supporting the use of stretching exercises for the prevention of these injuries is limited, this study examined the relationship between hamstring injuries and the flexibility of the hamstring and ankle.

Over two consecutive soccer seasons, players in all 18 teams in the Qatar Stars league were assessed for injuries. Data collected also included age, playing season, team, leg dominance, playing position, ethnicity, body mass index, as well as ankle and knee range of motion. Hamstring injury was defined as acute pain in the posterior thigh, occurring during training or match play, and resulting in an immediate cessation of participation.

Of the 438 players completing the study, 78 sustained an index hamstring injury. Goalkeepers were significantly less likely to sustain a hamstring injury than were other players. In addition, injured players were, on average, 18 months older than the uninjured. A multivariate regression analysis revealed that age ( $p=0.002$ ), player position ( $p=0.02$ ), passive knee extension test results ( $p=0.008$ ) and dorsiflexion lunge test results ( $p=0.02$ ) were significantly related to hamstring injury.

**Conclusion:** This prospective study of professional soccer players found that modifiable factors related to an increased risk of hamstring injury are decreased knee extension and ankle dorsiflexion passive range of motion.

Van Dyk, N., et al. Hamstring and Ankle Flexibility Deficits are Weak Risk Factors for Hamstring Injury in Professional Soccer Players: A Prospective, Cohort Study of 438 Players, Including 78 Injuries. **Am J Sport Med.** 2018, July; 46 (9): 2203-2210.

### MESENCHYMAL STEM CELL REPAIR OF KNEE CHONDRAL LESIONS

As mesenchymal stem cells have the capacity to differentiate into a variety of cells, many have explored the use of those cells for the treatment of chondral defects. This study used such cells to develop a

three-dimensional, tissue-engineered construct (TEC), containing undifferentiated, synovial-derived mesenchymal cells, surrounded by extracellular matrices synthesized by the cells.

Subjects were five patients, 20 to 60 years of age with isolated, full-thickness cartilage defects of the knee. After an arthroscopic biopsy, a volume of TEC was created, and later implanted onto the defect site. Partial weight bearing was allowed at six weeks, and full weight bearing at eight weeks. Assessments occurred on the date of surgery, on postoperative day one, and then at weeks one, two, four, six, 12, 24 and 48. The participants were followed with MRI for up to two years postoperatively. The primary outcome was the safety of the procedure.

No serious adverse events were noted within the first two years. At two years, the defect filling rate reached 100% coverage, with good integration to adjacent cartilage in all cases. All outcomes scores, including pain and function scores, were significantly improved and remained high at 24 weeks.

**Conclusion:** This study of adults with knee chondral defects found that, by using a new, scaffold-free, tissue-engineered mesenchymal stem cell repair, patients could have complete defect repair combined with significant improvement in function and symptoms.

Shimomura, K., et al. First In-Human Pilot Study of Implantation of a Scaffold-Free Tissue-Engineered Construct Generated from Autologous Synovial Mesenchymal Stem Cells for Repair of Knee Chondral Lesions. **Am J Sports Med.** 2018, August; 46 (10): 2384-2393.

#### USE OF A COMPUTERIZED CRYOTHERAPY DEVICE FOLLOWING TOTAL KNEE ARTHROPLASTY

The benefits of cryotherapy after orthopedic surgeries such as total knee arthroplasty (TKA) are well-documented, and include reduced surgically-induced intra-articular inflammation, lower post-operative analgesia requirements and shortened post-operative lengths of stay. This study investigated whether a new computerized cryotherapy device with continuous cold flow (cTreatment) could improve post-operative rehabilitation outcomes, as compared to standard cold pack therapy, in patients undergoing TKA.

This randomized, prospective, single-blind, controlled trial, assigned 97 patients undergoing unilateral TKA to either conventional cold pack therapy (applied for 20 minutes TID) or the cTreatment, which was applied for two hours twice per day, until post-operative day six. Outcome measures included range of motion and pain reduction.

As compared to the cold pack group, the cTreatment group showed better improvement in post-operative range of motion ( $p=0.021$ ), and pain scores on post-operative day two ( $p=0.034$ ). There was no significant difference between groups in pain medication requirements. No adverse events were reported for either intervention.

**Conclusion:** This study found that a computerized cryotherapy device which regulates temperature can improve post-operative range of motion and pain reduction more than the traditional cold pack.

Sadoghi S., et al. Impact of a New Cryotherapy Device on Early Rehabilitation after Primary Total Knee Arthroplasty (TKA): A Prospective, Randomized, Controlled Trial. **Int Orthop.** 2018, June; 42(6): 1265-1273.

#### DAYS BETWEEN MATCHES AND MUSCLE INJURY RATES IN SOCCER

Studies have found that muscle fatigue may last more than 72 hours after a professional soccer match. However, nearly one third of matches for top level professional soccer teams are played within a 72-hour interval. This study compared the injury rates to the days of rest between match play.

This study used a *post hoc* analysis of data gathered during 14 consecutive seasons in a prospective cohort study of 57 professional European soccer teams from across 16 countries. All first team players were invited to participate, with a total of 2,672 players included. Individual exposure during matches was recorded, with injuries and participation records reviewed. The intervals between matches and the total number of hours of match exposure were compared to the rate of injury.

During 166,433 match hours, 4,083 injuries were reported, resulting in an injury rate of 24.5/1,000 match hours, and a muscle injury rate of 9.4/1,000 match hours. Compared with three or less days between matches, the muscle injury rate was 20% lower with six to ten day

intervals. There was no difference in injury rates between three or less days and four days between matches, suggesting that a recent rule change by the World Football Academy would have no effect on the rate of injury.

**Conclusion:** This analysis of elite professional soccer players found that muscle injury rates were lower when players were given at least six days between match play, as compared to three or less days.

Bengtsson, H., et al. Muscle Injury Rate in Professional Football is higher in Matches Played within Five Days since the Previous Match: A 14-Year, Prospective Study with More Than 130,000 Match Observations. **Br J Sports Med.** 2018; 52(17): 1116-1122.

#### ACHILLES TENDON ELONGATION AFTER REPAIR

The Achilles tendon, while the strongest tendon in the human body, is susceptible to complete rupture, occurring most frequently in men 30 to 50 years of age. While the treatment for these ruptures can involve surgical or nonsurgical repair, a consensus has not been reached regarding the optimal intervention. For both interventions the length of the tendon may elongate, with this occurring within 6-12 weeks after surgery. This study was designed to better understand this phenomenon.

Subjects were 75 patients with acute tendon rupture, all presenting for surgical repair. During that procedure, metal beads were implanted on either side of the rupture. After surgery, an orthosis was used for the first six weeks, with three heel wedges placed within the orthosis, with one wedge removed each week to allow for increased dorsiflexion. The participants were randomized to one of three separate rehabilitation regimens, including late weightbearing with immobilization (LWB + IMMOB), late weightbearing with mobilization (LWB + MOB) or early weightbearing with mobilization (EWB + MOB), which involved partial weightbearing from day one and full weightbearing from week five. The primary outcome variable was tissue elongation at rest.

Elongation increased from six to 12 weeks ( $p<0.01$ ) and from 12 to 26 weeks ( $p<0.001$ ), but not from 26 to 52 weeks. There was no group difference in the amount of elongation that occurred. For tendon cross-sectional area, no interaction or group effect was found, but a significant effect of time was noted ( $p<0.0001$ ).

**Conclusion:** This study of patients undergoing surgical repair of a ruptured Achilles tendon found that elongation occurs over the first six months, without being influenced by a patient's weightbearing or mobilization protocol.

Eliasson, P., et al The Ruptured Achilles Tendon Elongates for Six Months after Surgical Repair, Regardless of Early or Late Weightbearing in Combination with Ankle Mobilization. **Am J Sport Med.** 2018, August; 46(10): 2492-2502.

### UPPER EXTREMITY PAIN IN PARAPLEGIA

As upper extremity (UE) function is critical to those with decreased function of the lower extremities, this study investigated the prevalence and patterns of pain in the UE among individuals with spinal cord injury (SCI).

A university healthcare system database was searched for patients with accident related paraplegia, during a period spanning 17 years. Information regarding the level of injury was obtained. A questionnaire was sent with queries regarding medical status, demographics and pain. The data were reviewed to determine relationships of pain with age, gender, time since injury, completeness of injury and neurologic level of injury (NLI).

Participants were 322 men and 129 women with an average age of 49.4 years. The average age at injury was 29.1 years. Pain was reported by 81%, with 61% reporting shoulder pain, 33% reporting elbow pain and 43% reporting wrist pain (of whom 25% had carpal tunnel syndrome). A multivariate analysis revealed that the risk of developing shoulder pain increased by three percent with each year of life, and by 2.4% for each year after injury. The rate of shoulder and elbow pain was higher among those with higher levels of injury ( $p=0.005$  and  $p=0.022$ , respectively), while the rate of wrist pain was related to a longer time since injury ( $p<0.0007$ ).

**Conclusion:** This study of patients with paraplegia found that upper extremity joint pain is more prevalent the longer the time since, and the higher the level of, the injury to the spine.

Kentar, Y., et Al. Prevalence of Upper Extremity Pain in a Population of People with Paraplegia. **Spinal Cord.** 2018; 56(7): 695-703.

### LEVEL OF SPINAL CORD INJURY PREDICTIVE OF ALTERATIONS IN ACUTE RENAL FUNCTION

As many organs, including the kidneys, are partially controlled by sympathetic innervations, some have suggested that the level of spinal cord injury (SCI) should play a role in alterations of renal function. This study explored the relationship between SCI level and renal function.

Three groups of rats were studied, including sham-injured rats, rats injured at the T-1 level and rats injured at the T-8 level. All animals demonstrated complete paraplegia at 24 hours post-injury. Tubular secretion (TS) and glomerular filtration rate (GFR) were calculated by measuring the pharmacokinetics of iopamidol, a radiopaque contrast excreted by the kidneys, and P-aminohippuric acid (PAH), with a known renal extraction ratio.

Both groups of injured rats demonstrated decreased GFR and TS. However, only the T-1 injured group showed statistically significant differences in pharmacokinetics, as compared with the sham-injured group. In the T1-injured group, iopamidol clearance was decreased by 90% ( $p<0.5$ ) and iopamidol AUC and half-life were increased by 10.7 and 6.5-fold, respectively ( $p<0.01$ ). In the T-8 injured group, the iopamidol clearance dropped by 67% ( $p<0.01$ ) and the AUC and half-life increased by three- and 1.5-fold, respectively ( $p<0.01$ ). PAH clearance was reduced in the T1 group by 75% ( $p<0.01$ ), and in the T8 group by 41% ( $p<0.01$ ).

**Conclusion:** This animal study found that the level of spinal cord injury may be a prognostic factor for the severity of loss of kidney function following that injury.

Rodriguez-Romero V., et al. Early Systemic Alterations in Severe Spinal Cord Injury. **Spine.** 2018, August 1; 43(15): E885-E890.

### NEUROMUSCULAR ELECTRICAL STIMULATION IN SPINAL CORD INJURY

Although high intensity strength training can enhance the hypertrophic response and generate optimal muscle strength gains, strength training may not be feasible in patients with a spinal cord injury (SCI). This study assessed the effect of neuromuscular electrical stimulation (NMES) high-intensity training in patients with SCI.

Subjects were five adults with chronic SCI at levels T3-T12, with

American Spinal Injury Association Impairment Scale (AIS) scores of B, B, D, A and A. Training included high intensity electrical stimulation, delivered by a high-voltage, constant-current electrical stimulator, placed at the rectus femoris, vastus lateralis and vastus medialis with five sets of 10 repetitions for each leg, twice per week for 12 weeks. Assessments, completed at baseline and at 12-week follow-up, included knee extension torque measurements, muscle cross-sectional area of the quadriceps, as assessed by ultrasound, blood biomarkers for lipid profiles and inflammation as well as measures of spasticity and quality of life.

Compared with baseline, the quadriceps extension torque increased by a mean of 35%, with the cross-sectional area of this muscle group increasing by 47%. In addition, the LDL concentration was reduced by 1.8 ( $p=0.06$ ), with a significant increase in the HDL/LDL ratio ( $p=0.04$ ) and a near significant decrease in cholesterol/HDL ratio ( $p=0.08$ ). Quality of life measures did not significantly increase, while scores on the spinal cord injury spasticity evaluation tool improved by five percent ( $p=0.04$ ).

**Conclusion:** This study of patients with chronic spinal cord injury found that 12 weeks of high intensity neuromuscular electrical stimulation training can increase knee extensor torque and muscle mass, as well as lipid profiles, though with no significant improvement in quality of life.

Bochkezanian, V., et al. Effects of Neuromuscular Electrical Stimulation in People with Spinal Cord Injury. **Med Sci Sports Exer.** 2018, September; 50(9): 1733-1739.

### POSTOPERATIVE BLOOD GLUCOSE AND INFECTION AFTER JOINT ARTHROPLASTY

Hyperglycemia, independent of diabetes, is a known risk factor for postoperative complications in orthopedic procedures. However, the influence of perioperative hyperglycemia on periprosthetic joint infections is not yet clear. This study was designed to better clarify this relationship.

This single-center, retrospective, case-controlled trial included 24,857, elective, primary total joint arthroplasties performed over 14 years. Post-operative day one blood glucose levels were obtained before breakfast and compared with

outcomes for a minimum of one year. Demographic, medical and surgical variables were collected during hospitalization. All participants received standardized perioperative management for infection prophylaxis. Intravenous antibiotics were given within one hour before the incision, and for 24 hours postoperatively.

The periprosthetic joint infection rate of the entire cohort was 1.59%. A significant and linear increase in the rate of periprosthetic joint infections was noted beginning at glucose levels of 115 mg/dL ( $p=0.028$ ). Those with blood glucose levels of 280 mg/dL had 2.05 greater odds of developing periprosthetic joint infection, as compared to those with a blood glucose level of 100 mg/dL.

**Conclusion:** This study found that postoperative hyperglycemia, with blood sugars of above 115, was associated with an increased risk of periprosthetic joint infection.

Khair, M., et al. Postoperative Blood Glucose Levels Predict Infection after Total Joint Arthroplasty. *J Bone Joint Surg Am.* 2018, August; 100 (16): 1423-1431.

#### RISK OF MYOCARDIAL INFARCTION WITH NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

Inflammatory spondyloarthritis (SpA) has been associated with an increased risk of myocardial infarction (MI). Additionally, non-steroidal anti-inflammatory drugs (NSAIDs) have been associated with an increased risk of cardiovascular events. This study examined the effect of NSAIDs use on the risk of MI in patients with inflammatory arthritis or osteoarthritis (OA).

This case-control study was performed using data from The Health Improvement Network (THIN), a UK-based database of medical records. Data were reviewed for adults with SpA or OA who were taking one or more NSAID prescriptions and who had no history of MI. Within each cohort, each MI case was matched to four controls without MI. Records were reviewed for NSAID use and categorized as current (prescription zero to 180 days prior), recent (181 to 365 days prior) or remote (over 365 days prior).

Within the SpA cohort, current diclofenac use was associated with an increased odds ratio (OR) of 3.32 for MI, with no increased risk found with naproxen use in either the OA or the SpA cohort. The ratio of ORs for

SpA /diclofenac compared to osteoarthritis/diclofenac was 2.64 (95% CI 1.24 to 5.58).

**Conclusion:** The risk of myocardial infarction in spondyloarthritis is increased in current users of diclofenac, but not naproxen.

Dubreuil, M., et al. Risk of Myocardial Infarction with use of Selected Non-Steroidal Anti-Inflammatory Drugs in Patients with Spondyloarthritis and Osteoarthritis. *Ann Rheum Dis.* 2018, 77: 1137-1142.

#### DIRECT CURRENT STIMULATION FOR MINIMALLY CONSCIOUS STATE

Previous studies using transcranial direct current stimulation (tDCS) have demonstrated a transient improvement in consciousness with tDCS applied to the left dorsolateral prefrontal cortex (DLPFC). This study assessed the effects of an extended, home-based program of tDCS stimulation in patients in a minimally consciousness state (MCS).

This prospective study included patients with a severe traumatic brain injury (TBI) in an MCS, 16 years of age or older and greater than three months post-injury. Participants were involved in both active and sham tDCS conditions in a crossover, randomized order. During the active tDCS condition, subjects received anodal stimulation positioned over the left DLPFC, for 20 minutes. The primary outcome measures were safety, as assessed by an adverse events questionnaire, adherence to the treatment protocol and change on the Coma Recovery Scale-Revised (CRS-R) total score after four weeks of stimulation.

Of the 22 people included in the analysis, one patient experienced an epileptic seizure on day four of the study (sham group) and was withdrawn. All subjects tolerated the procedure, with redness reported by five in the sham group and five in the active session group. At four weeks, the effect size was greater in the treatment than in the sham group ( $p=0.043$ ). At the individual level, 22% showed a new sign of consciousness after 20 active sessions which was not present after the sham sessions.

**Conclusion:** This study of patients in a minimally conscious state after a traumatic brain injury found that a home-based treatment with transcranial direct current stimulation resulted in moderate

improvements in consciousness, with minimal side effects.

Martens, G., et al. Randomized, Controlled Trial of Home-Based, Four-Week tDCS in Chronic Minimally Conscious State. *Brain Stimul.* 2018, Sept-Oct; 11(5): 982-990.

#### VACUUM WOUND CARE EFFECT ON METHICILLIN-RESISTANT STAPHYLOCOCCUS

Biofilm-associated methicillin-resistant staphylococcus aureus (MRSA) wound infections have an enhanced resistance to antimicrobial agents. As vacuum-assisted closure (VAC) therapy has been suggested as a tool to reduce wound bioburden, this study assessed the effect of VAC therapy on MRSA infected wounds.

This trial used MRSA strains obtained from chronic wounds of patients admitted to the Department of Vascular Surgery, Institute of Cardiovascular Diseases, in Belgrade, Serbia, from January of 2011 to December of 2014. Strains were identified using a number of genotyping methods and clustered into five clonal complexes. Prepared bacterial suspensions were treated with VAC therapy for three or six days to mimic once or twice weekly dressing changes. Biofilm formation was assessed quantitatively. Control bacterial suspensions were treated under equal conditions while at atmospheric pressure.

Biofilm production was reduced in all observed MRSA strains with VAC therapy. During three-day VAC therapy, biofilm formation was reduced in CC ( $p < 0.01$ ), SCCmec ( $p < 0.01$ ) and agr ( $p < 0.05$ ) types. Relative to the control condition, VAC therapy of MRSA strains diminished biofilm formation capacity after three-day ( $p < 0.01$ ) and six-day ( $p < 0.05$ ) intervals between dressing changes, with three days more effective than six ( $p < 0.01$ ).

**Conclusion:** Results from this *in-vitro* study suggest that vacuum-assisted closure therapy, using twice weekly bandage changes, can produce additional benefit in the treatment of biofilm-associated methicillin-resistant staphylococcus aureus wound infections.

Ćirković, I., et. al. The Effect of Vacuum-Assisted Closure Therapy on Methicillin-Resistant Staphylococcus Aureus Wound Biofilms. *Adv Skin Wound Care.* 2018, August; 31(8): 361-364.

## VERTEBROPLASTY FOR VERTEBRAL FRACTURES

Percutaneous vertebroplasty is widely used to treat osteoporotic vertebral compression fractures. Prior research has produced conflicting data concerning the utility of vertebroplasty for reducing pain, disability, and improving quality of life. This study was designed to help clarify the efficacy of this procedure.

This randomized, double-blind trial included patients at least 50 years of age with one to three osteoporotic compression fractures. The subjects were randomized to receive polymethylmethacrylate cement injections or to undergo a sham procedure with periosteal needle placement, but no cement injection. The primary outcome measure was a ten-point visual analogue scale (VAS) for pain. Secondary outcome measures included the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) and the Roland-Morris Disability Questionnaire (RMDQ). Assessments were made at one day, one week, and one, three, six and 12 months after the procedure.

Both the vertebroplasty (n=90) and sham (n=86) groups showed a significant reduction in VAS scores at all times, with no significant difference between the groups at any follow-up. Statistically significant pain reduction began one day post-procedure in both groups. Similar patterns were found for QUALEFFO and RMDQ scores. A *post hoc* analysis did reveal more patients in the sham group with VAS scores of above five after 12 months.

**Conclusion:** This study of patients with painful osteoporotic vertebral fractures found no significant difference in pain reduction between groups treated with vertebroplasty and those treated with a sham procedure.

Firanesco C., et al. Vertebroplasty versus Sham Procedure for Painful, Acute, Osteoporotic, Vertebral, Compression Fractures (VERTOS IV): Randomized, Sham Controlled, Clinical Trial. *BMJ*. 2018; 361:k1551.

## OVERUSE RUNNING INJURIES

Among the over 20 million regular runners in the United States, 65% report running injuries each year. This study investigated the factors associated with overuse injuries.

This prospective, longitudinal trial, The Runners and Injury Longitudinal

Study (TRAILS), involved 300, injury free runners, 18 to 60 years of age. All reported running a minimum of five miles per week and were free of injury for the prior six months. Questionnaires were administered at baseline and at six and 12 months' follow-up. The patients were contacted every two weeks for a period of two years to inquire about injuries. Overuse injuries were graded as "maintaining full activity despite symptoms" (grade I), "reducing weekly mileage" (grade II) or "interrupted all training for at least two weeks" (grade III).

Of the 290 participants, 66% sustained at least one overuse running injury, including 73% of the women and 62% of the men. Most of the initial injuries occurred during the first year, with approximately half characterized as grade I. A univariate analysis revealed that factors at baseline which were significantly associated with an increased chance of injury were lower mental health-related quality of life, more negative emotions endorsed on the Positive and Negative Affect Scale, female gender and greater knee stiffness. A multivariable analysis found only knee stiffness to be predictive of injury (odds ratio 1.18).

**Conclusion:** This prospective study of adult runners found that overuse injuries are greater among women and among those with greater knee stiffness.

Messier, S., et al. A Two-Year, Prospective, Cohort Study of Overuse Running Injuries: The Runners and Injury Longitudinal Study (TRAILS). *Am J Sport Med*. 2018, July; 46 (9): 2211-2221.

## MAGNETIC RESONANCE IMAGING AFTER HYALURONIC ACID INJECTION

Hip osteoarthritis (OA) leads to approximately 200,000 annual total hip replacements in the United States. As magnetic resonance imaging (MRI) is sensitive to early, subtle tissue abnormalities, this study used MRI to assess the response of hip OA to hyaluronic acid (HA) injections, using the hip MRI inflammatory scoring system (HIMRISS).

Subjects were 60 adults with symptomatic hip OA, with an inadequate response to NSAIDs or oral analgesics, each of whom had undergone a pelvic MRI before a HA hip injection. Pain, stiffness, and function were assessed with the Western Ontario and McMaster

(WOMAC) questionnaire with global health assessed using a Visual Analogic Scale (VAS) at baseline and at three months post-HA injection. Inflammation was assessed with the Hip MRI Inflammatory Scoring System (HIMRISS), before and after the injection. A positive response to the injections was defined as an improvement of WOMAC pain and/or WOMAC function scores by more than 50% (WOMAC50%).

At baseline, WOMAC function scores were found to be significantly related to HIMRISS synovitis scores (p= 0.03). At three months, 45.5% of the patients achieved a WOMAC50%. No baseline WOMAC values or clinical parameters were associated with a WOMAC 50% response at three months. A multivariate analysis revealed that patients who had low HIMRISS-bone marrow lesion femoral scores and low HIMRISS total scores were more likely to achieve a WOMAC50% response to HA (p=0.02 and p=0.016, respectively).

**Conclusion:** This study suggests that inflammation, as measured by magnetic resonance imaging, may be useful in predicting the response to hyaluronic acid injection in patients with symptomatic hip osteoarthritis.

Deseyne, N., et al. Hip Inflammation MRI Scoring System (HIMRISS) to Predict Response to Hyaluronic Acid Injection in Hip Osteoarthritis. *Joint Bone Spine*. 2018, Jul; 85(4): 475-480.

## CEREBRAL MICROBLEEDS AND INTENSIVE BLOOD PRESSURE REDUCTION

Cerebral microbleeds (CMB) are remnants of prior cerebral microhemorrhages at the level of the arterioles and capillaries and have evolved as radiological markers of underlying cerebral small vessel disease (CSVD). This study of patients with acute intracerebral hemorrhage (ICH) investigated the effect of CMBs on the clinical outcomes of patients undergoing acute blood pressure lowering.

This open label, international, randomized, clinical trial (The Antihypertensive Treatment of Acute Cerebral Hemorrhage 2 (ATACH-2)) included 1,000 adult patients with acute ICH volumes of less than 60 mL on CT and a Glasgow Coma Scale score of at least five. The subjects were randomly assigned to either a target systolic blood pressure of 110-130mmHg (low) or to a target of 140-179 mmHg (high). Poor

(Continued from page 2)

\* Marine Dididze, M.D.  
University of Miami, Miami, FL

\*Kenton Hagan, M.D.  
Alyssa Marulli, M.D.  
Tulsi Singh, M.D.  
Univ. of Pennsylvania, Philadelphia, PA

\*Anna Coles, M.D.  
University of Washington, Seattle, WA

\*Michael Sookochoff, M.D.  
Adem Aktas, D.O.  
Sheyna Gifford, M.D.  
Washington U in St. Louis, St. Louis, MO

**Executive Editor Emeritus**

Donald F. Langenbeck, Jr., M.D.

**Subscription Manager**

Michael P. Burke, M.S.

**\*Regional Managing Editors have attested that they have no financial conflict of interest when choosing articles that appear in Rehab in Review.**

outcome was defined as death or disability (disability defined as a modified Rankin scale score of four or more), with secondary outcomes including hematoma volume expansion.

During a mean follow-up period of 92.3 days, 29.3% of the patients had a poor outcome, with a similar risk of poor outcome in both blood pressure groups (p=0.61). In addition, the rates of ICH at 24 hours were similar between those with CMBs and those without CMBs, with the effects of BP lowering no different based on CMBs. However, a strong association was found between CMBs and renal dysfunction.

**Conclusion:** This study of patients with acute ICH found that the presence of cerebral microbleeds at the initial evaluation did not influence the clinical response to acute intensive blood pressure treatment.

Shoamanesh, A., et al. Cerebral Microbleeds and the Effect of Intensive Blood Pressure Reduction on Hematoma Expansion and Functional Outcomes: A Secondary Analysis of the ATACH-2 Randomized, Clinical Trial. **JAMA Neurol.** 2018 Jul; 75(7): 850-859.

*Rehab in Review (RIR)* is produced monthly by physicians in the field of Physical Medicine and Rehabilitation (PM&R), with the cooperation and assistance of Emory University School of Medicine, Department of Rehabilitation Medicine. The summaries appearing in this publication are intended as an aid in reviewing the broad base of literature relevant to this field. These summaries are not intended for use as the sole basis for clinical treatment, or as a substitute for the reading of the original research.

The Emory University School of Medicine designates this journal based activity for a maximum of 3 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. The Emory University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

*RIR* is affiliated with the Association of Academic Physiatrists, the World Health Organization, and the Chinese and Indian Societies of PM&R and endorsed by the International Society of Physical and Rehabilitation Medicine.

Private subscriptions are available by email at [rehabinreview@aol.com](mailto:rehabinreview@aol.com) or by fax or phone at (800) 850-7388.

ISSN # 1081-1303  
[www.rehabinreview.com](http://www.rehabinreview.com)



**REHAB IN REVIEW**

Produced by the Department of Rehabilitation Medicine, Emory University School of Medicine

This issue sponsored by an Allergan Educational Grant



**EMORY**  
UNIVERSITY  
SCHOOL OF  
MEDICINE

Department of  
Rehabilitation  
Medicine

*Expanding the frontier of rehabilitation sciences in research, teaching, and patient care*