

# REHAB IN REVIEW

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Volume 25 Number 7

Published by Physicians  
In Physical Medicine and Rehabilitation

July 5, 2017

## COST AND OUTCOMES OF POSTACUTE CARE AFTER PRIMARY HIP AND KNEE ARTHROPLASTY

With the aging of the population of the United States, significant increases are expected in cases of total hip arthroplasty (THA) and total knee arthroplasty (TKA). Joint arthroplasty is now the largest Medicare procedural cost, at 6.3%. This study examined the duration of care, charges and readmission rates after primary THA or TKA.

Data were obtained from the Medicare Provider Analysis and Review (medPAR) database for individuals undergoing primary TKA (n=136,842) or THA (n=329,233) in 2008. Data collected included subsequent inpatient rehabilitation, extended-care facility stays, home healthcare and outpatient encounters, costs and readmissions within 90 days of discharge.

Those discharged to post-acute care facilities had longer hospitalizations and higher charges than those discharged to home, with or without home health care. Admission to inpatient rehabilitation was associated with a 30% increase in total charges for patients with THA and a 26% increase for patients with TKA. Mortality and readmission within 90 days were both significantly higher for patients discharged to extended care facilities and inpatient rehabilitation, than for those discharged to home ( $p < 0.001$  for both). The number of comorbidities was associated with increased cost and length of stay.

**Conclusion:** This study of patients undergoing elective total knee or total hip arthroplasty found that inpatient post-acute care results in increased costs and an increased risk of 90-day readmission and mortality.

Karthikeyan, P., et al. Post-Discharge Care Duration, Charges and

Outcomes among Medicare Patients after Primary Total Hip and Knee Arthroplasty. *J Bone Joint Surg.* 2017, June; 99(11): e55.

## METHYLPHENIDATE, GRIP FORCE AND BRAIN CONNECTIVITY

The central fatigue theory proposes that force output during fatiguing exercise is limited in order to maintaining homeostasis in advance of tissue damage. As methylphenidate (MPH) has been shown to enhance physical performance, it has been proposed that this medication alters the central fatigue mechanisms of the motor cortex. This study evaluated the neural underpinnings related to the ergogenic effects of MPH.

This double-blind, crossover study involved 15 right-handed subjects, randomized to receive 20 mg of MPH or placebo. The participants were asked to perform 40 grip trials with a visual display of their grip strength. The subjects began the task at a target force of 70% of their maximum voluntary contraction. Test failure was defined as falling below the target force by more than 10% after having reached the target. All sessions were conducted with concurrent functional magnetic resonance imaging (fMRI). Also assessed were a measurement of task-dependent change in neural coupling (PPI), and a key region implicated in mental fatigue (OFC).

The mean forces achieved in all trials were significantly higher in the MPH group than in the placebo group ( $p = 0.032$ ). The MPH condition resulted in an increase in left IC-left hand motor cortex coupling (PPI) and a decrease in bilateral OFC-left IC coupling during grip.

**Conclusion:** This study found that methylphenidate improved force production and brain connectivity during a fatiguing handgrip task.

King, M., et al. Methylphenidate Enhances Grip Force and Alters Brain Connectivity. *Med Sci Sports Exer.* 2017, July; 49(7): 1443-1451.

## VIRTUAL REALITY AND MOTOR PERFORMANCE

When using virtual reality (VR), observation of an action, even simulated, allows recruitment of stored motor programs. These processes are expressed by changes in  $\alpha$  and  $\beta$  oscillation magnitude on electroencephalography across brain areas belonging to the mirror neuron system. This study investigated the neurophysiological underpinning of gait recovery induced by the observation of an animated avatar while performing robot-assisted gait training.

This pilot study included patients at least 55 years of age with spasticity secondary to a first ever ischemic stroke of at least six months' duration. All subjects received Locomat training, either with or without an animated avatar, in a two-dimensional VR. The participants were assessed for clinical, kinematic and electroencephalogram changes. The primary outcome variable was the proportion of patients achieving 20% improvement in lower limb gait and balance, as measured with the Rivermead Mobility Index (RMI), the Tinetti Performance of Oriented Mobility Assessment (POMA) and the gait cycle-related Event-Related-Spectral-Perturbations (ERSPs).

The RMI improved significantly more in the VR group than in the control group ( $p < 0.001$ ), while the POMA improved only in the VR group ( $p = 0.001$ ). In addition, hip force and knee force improved significantly more in the VR group ( $p = 0.02$  for both comparisons). Significant relationships were found between RMI and POMA score improvements and EEG measures of central ERSPs ( $p = 0.001$  and  $p = 0.04$ , respectively)

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and frontal Hy-ERD magnitude ( $p = 0.003$ ). Improvement in hip force was significantly related to frontal Hy-ERD magnitude ( $p=0.004$ ).

**Conclusion:** This study found that virtual reality during gait training can elicit stronger correlations in the fronto-parietaloccipital areas involved in motor intention and planning.

Calabro, R., et al. The Role of Virtual Reality in Improving Motor Performance as Revealed by EEG: A Randomized, Clinical Trial. **J Neuroeng Rehabil.** 2017, June; 14: 53.

### **SPHENOPALATINE BLOCK FOR CLUSTER HEADACHES**

Cluster headaches (CHs) are among the most painful of primary headaches, with unilateral pain occurring up to eight times per day. Sphenopalatine ganglion neuromodulation is a minimally invasive option for treatment, which may involve targeted pharmacologic blocks or acute electrical stimulation with an implantable stimulator. This study evaluated the long-term effects of a treatment with an implanted micro-stimulator.

Participants were 33 patients with chronic cluster headache (cCH), all of whom reported a minimum of four attacks per week. Each underwent implantation of a micro-stimulator which could communicate with a hand-held controller. The patients were asked to activate the stimulator at the onset of a CH. The subjects used an electronic diary to record their acute response to the stimulation, as rated on the Categorical Pain Scale (zero to four).

Among the 33 patients, 5,956 attacks were treated, with 50% of the subjects becoming pain free. The average duration of stimulation was 11.2 minutes. At 24 months, 61% of the patients reported acute effectiveness and/or frequency reduction of at least 50%.

**Conclusion:** This study of patients with cCHs found that the use of an implantable sphenopalatine ganglion stimulator can reduce headache pain acutely, reduce headache disability, and allow patients to reduce or eliminate preventative medications.

Jurgens, T., et al. Long-Term Effectiveness of Sphenopalatine

Ganglion Stimulation for Cluster Headache. **Cephalgia.** 2017, April; 37(5): 423-434.

### **ASSOCIATION BETWEEN MIGRAINE AND CERVICAL ARTERY DISSECTION**

Spontaneous cervical artery dissection (CEAD) is a frequent cause of ischemic stroke (IS) in young and middle-aged adults. Some studies have reported a higher prevalence of migraines in patients with CEAD. This study evaluated the association between migraine and spontaneous CEAD.

Data were derived from the Italian Project on Stroke at Young Age, a countrywide network of neurologic centers. The subjects were patients with first-ever acute stroke, 18 to 45 years of age, consecutively admitted to 126 hospitals between January 1, 2000, and June 30, 2015. Risk factors for premature cerebral ischemia were documented, including hypertension, diabetes, cigarette smoking, hypercholesterolemia and migraine. The CEAD was categorized as traumatic or nontraumatic.

Of the 2,485 targeted individuals, 13.4% had a diagnosis of IS secondary to CEAD (CEAD IS) and 86.6% had a diagnosis of IS due to other causes (non-CEAD IS). Migraine was found to be more common in the subgroup of patients with CEAD IS ( $p=0.01$ ). After adjusting for other risk factors, migraine without aura was significantly associated with CEAD IS, with no such association found in patients with migraine with aura.

**Conclusion:** This large cohort study of patients with ischemic stroke, ages 18 to 45 years, found an association between migraine headaches, especially those without aura, and spontaneous cervical artery dissection.

De Giuli, V., et al. Association between Migraine and Cervical Artery Dissection: The Italian Project on Stroke in Young Adults. **JAMA Neurol.** 2017, May; 74(5): 512-518.

### **PROTEIN INTAKE AND RISK OF STROKE**

As several epidemiological studies have demonstrated that

higher protein intake may reduce the risk of stroke, this prospective, cohort study was designed to further explore this association.

In 1988, a screening survey was performed in Hisayama, Japan. Subjects were 2,587 residents, ages 40 to 79 years, with a comprehensive assessment including a dietary survey. The subjects were followed prospectively for 19 years, with health examinations performed every one to two years. A daily monitoring system was used to identify stroke events. At baseline, stroke risk factors were also determined, with measures taken of body mass index, physical activity, blood pressure, lipid profiles and renal function. The intake of animal and vegetable protein were compared with the risk of stroke.

Age and gender adjusted incidence of total stroke decreased significantly with higher amounts of total protein intake ( $p=0.03$ ). The adjusted incidence of intracerebral hemorrhage decreased significantly with increased protein ( $p=0.008$ ), with no such association for subarachnoid hemorrhage. Multi-variable adjusted analysis revealed that, for every 10 g per day increment increase in total protein intake, a 15% lower risk of stroke was realized. Elevated levels of vegetable protein intake were associated with a lower incidence of total stroke and ischemic stroke ( $p<0.05$ ). Elevated levels of animal protein were associated with a lower incidence of intracerebral hemorrhage ( $p=0.01$ ).

**Conclusion:** This study found that higher protein intake is associated with a lower risk of total stroke, with vegetable protein associated with lower risk of an ischemic stroke and animal protein associated with a lower risk of intracerebral hemorrhage.

Ozawa, M., et al. Dietary Protein Intake and Stroke Risk in the General Japanese Population: The Hisayama Study. *Stroke*, June; 48(6): 1478-1486.

### FUNCTIONAL ELECTRICAL STIMULATION FOR WRIST AND FINGER SPASTICITY

Functional electrical stimulation (FES) has been used to treat patients with central nervous system dysfunctions and intact peripheral innervation. This study investigated

the efficacy of FES for patients with stroke-related hemiplegia and spasticity.

Subjects were 30 patients with at least a three-month history of stroke and spasticity, assessed with the Modified Ashworth Scale (MAS). Those randomized to the treatment group underwent FES, applied to the motor points of the extensor carpi radialis longus, extensor carpi radialis brevis, extensor carpi ulnaris and extensor digitorum communis. The FES was applied 30 minutes per day for five days per week for total of 20 sessions. Both the study group and the conventional treatment group underwent range of motion exercises, stretching and wrist-hand static splint use. Assessments of wrist tone were made with the Modified Ashworth Scale (MAS). Motor function was assessed by the Rivermead Motor Assessment (RMA), Brunnstrom (BS) hand neurophysiological staging, with functional status evaluated with the Barthel Index (BI) and Upper Extremity Function Test (UEFT).

The patients in the FES group experienced significantly greater improvement in BI scores ( $p<0.05$ ) passive range of motion ( $p<0.05$ ), active range of motion ( $p<0.05$ ), and RMA scores ( $p<0.05$ ) as compared with the control group.

**Conclusion:** This study of patients with chronic stroke found that functional electrical stimulation can be an effective method to reduce spasticity and improve range of motion in patients with wrist and finger flexor spasticity.

Yuzer, G., et al. A Randomized, Controlled Study: Effectiveness of Functional Electrical Stimulation on Wrist and Finger Flexor Spasticity in Hemiplegia. *J Stroke Cerebrovasc Dis.* 2017, July; 26 (7): 1467-1471.

### CANNABIDIOL FOR SEIZURES IN DRAVET SYNDROME

The Dravet syndrome is a rare genetic form of epileptic encephalopathy. Small studies have reported a positive effect on seizure frequency of patients with Dravet through the use of cannabidiol. This study was designed to better understand the efficacy of this drug for the treatment of drug resistant epilepsy among patients with Dravet.

Eligible subjects had a diagnosis of Dravet syndrome and were taking

one or more antiepileptic drugs. They had experienced four or more seizures during a 28-day baseline period. After a four-week baseline, during which a daily seizure record was maintained, the subjects were randomized to receive cannabidiol or a matching placebo. The cannabidiol group received doses escalated up to 20 mg/kg per day. Clinical and laboratory assessments were performed at baseline and after two, four, eight and 14 weeks. The primary endpoint was the percentage change in seizure frequency from baseline.

Compared to baseline, the median reduction in convulsive seizures between the treatment and the placebo group was 22.8 percentage points ( $p=0.01$ ). Among the secondary endpoints, a reduction in seizure frequency by 50% or more was more often seen in the cannabidiol group ( $p=0.08$ ) although that finding was not statistically significant. Freedom from seizures was achieved by three in the treatment group and zero in the placebo group. There was no significant difference between groups in sleep disruption scores or Epworth Sleepiness Scale Scores.

**Conclusion:** This study of patients diagnosed with Dravet syndrome found that treatment with cannabidiol resulted in a significant reduction in seizure frequency.

Devinsky, O., et al. Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome. *N Eng J Med.* 2017, May 25; 376 (21): 2011-2020.

### QUADRICEPS STRENGTHENING WITH BLOOD FLOW RESTRICTION FOR PATELLOFEMORAL PAIN

Patellofemoral pain (PFP) is a common source of anterior knee pain among active adolescents. Those with PFP have pain-limited difficulty with resistance exercises at the recommended load of 60-70% one rep maximum (1RM). As blood flow restriction at the targeted muscle has been found to allow for strengthening at 20-30% of 1RM, this study compared the effects of these two types of strength training.

Subjects were between 18 and 40 years of age, with atraumatic PFP. Those randomized to a BFR group were assessed with an arterial

occlusion pressure cuff placed at the proximal thigh in a standing position. The cuff pressure was then increased until the pedal pulse was no longer palpable. The BFR restriction exercise was performed at 60% of this pressure. This group exercised at 30% of the 1RM. Those randomized to a standard group exercised at 70% 1RM. Exercises included leg press, leg extension and knee flexion. The primary outcome variable was PFP at eight weeks.

Over eight weeks, those in the BFR group had a 93% greater reduction in pain with activities of daily living, as compared with the standard treatment group ( $p=0.022$ ), with no significant difference in worst pain scores. A 49% greater improvement in the extensor torque was found in the BFR group, although this finding did not reach statistical significance ( $p=0.073$ ).

**Conclusion:** This study of patients with patellofemoral pain found that blood flow resistance training can reduce pain with activities of daily living more than can traditional strengthening exercise.

Giles, L., et al. Quadriceps Strengthening with and without Blood Flow Restriction in the Treatment of Patellofemoral Pain: A Double-Blind, Randomized Trial. *Br J Sports Med.* 2017; 0: 1-8.

### INCIDENCE OF SECOND ANTERIOR CRUCIATE LIGAMENT TEAR

The risk of anterior cruciate ligament (ACL) injury after an ACL reconstruction has been reported to be as high as one third. This study was designed to better understand the incidence of second ACL injuries in a population-based cohort, and to determined risk factors associated with these injuries.

Data were obtained through the Rochester Epidemiology Project, a medical record linkage system with access to complete medical records for all residents of Olmsted County, Minnesota. This database was reviewed for all occurrences of ACL tears between January, 1990, and December, 2000. Second ACL tears were defined as any that occurred after the primary injury, and until December 2015.

Between 1990 and 2000, of the 1,107 acute tears, six percent were

second tears. Of these, 33.3% involved the ipsilateral graft and 66.7% involved the contralateral ACL. Among individuals less than 20 years of age, the graft failure rate was 5.9%, while the failure rate for those under 16 years of age was 1.8%. Of the failures, the allograft had the highest rate of second tears, accounting for 26.9%, followed by hamstring autografts at 11.4%, and patella autografts at 6.3%. Multivariate regression analysis revealed that use of an allograft was the single significant independent variable predicting second ACL injuries ( $p<0.001$ ). The probability of a second ACL injury was highest among those 17 to 25 years of age, followed by those 26 to 35 years of age.

**Conclusion:** This observational cohort study of citizens of Olmsted County, Minnesota, found that six percent of ACL repairs were second repairs, with 66.7% of these occurring on the side contralateral to the initial surgery.

Schilaty, N., et al. Incidence of Second Anterior Cruciate Ligament Tears (1990 to 2000) and Associated Factors in a Specific Geographic Locale. *Am J Sport Med.* 2017, July; 45(7): 1567-1573.

### PREOPERATIVE OPIOID USE AND TOTAL KNEE ARTHROPLASTY

While total knee arthroplasty (TKA) is an effective treatment to relieve pain, patients are treated for an average of 13 years before undergoing a surgical procedure. This study explored whether the postoperative outcomes of patients are affected by their preoperative opioid use.

Subjects were patients undergoing primary, unilateral TKA, all of whom were at least 40 years of age. The participants completed questionnaires consisting of clinical outcomes, including the Western Ontario and McMaster universities osteoarthritis index (WOMAC), the Pain Catastrophizing Scale and questions about comorbidities. Records were reviewed to determine opioid utilization from two years before, to one year after, surgery. In addition, the authors conducted a literature search to identify published studies regarding the effect of preoperative opioids on postoperative

orthopedic outcomes, to use as a comparison with this study.

Data were obtained for 156 patients with a mean age at the time of surgery of 65.7 years, and a mean body mass index of 31.1 kg/m<sup>2</sup>. Of these, 23% had had at least one opioid prescription within the two years prior to surgery, and 93.6% had multiple opioid prescriptions after surgery. In an adjusted analysis, those who had not used opioids before surgery were found to have a six-month WOMAC pain score of 10.5 points, compared to 17.1 points for those who had used opioids. A multivariate analysis revealed that the opioid group had a mean six-month WOMAC pain score reduction of 27.0 points, as compared with 33.6 points for the non-opioid use group.

**Conclusion:** This study of patients undergoing total knee arthroplasty found that those who used opioids before surgery had less pain relief after surgery than did those who had not used opioids.

Smith, S., et al. Impact of Preoperative Opioid Use on Total Knee Arthroplasty Outcomes. *J Bone Joint Surg.* 2017, May 17; 99 (10): 803-808.

### KINESIOLOGY TAPE IMMEDIATELY AFTER ACL SURGERY

Despite a lack of clinical evidence to support its use, kinesiology taping (KT) is becoming increasingly popular. This study examined the efficacy of this taping technique after arthroscopic knee surgery.

This randomized, controlled trial included 68 patients with elective, primary, anterior cruciate ligament (ACL) repair. Two groups underwent standardized physical therapy, with the groups randomized to receive no taping or KT, applied at the first and second weekly postoperative physiotherapy sessions. Subjects were asked to remove the KT on the fifth day. All participants were assessed with a pain visual analog scale (VAS), the Lysholm-Tegner scale, measures of mid-patellar girth and for knee range of motion.

Changes in pain levels were better in the KT group than in the control group between the first and second weeks post-surgery. No significant difference in changes in pain scores were noted between

groups after the second week. In addition, no significant differences were noted between the two groups in Lysholm-Tegner scores, mid-patella girth or knee range of motion.

**Conclusion:** This study found that kinesiology taping after anterior cruciate ligament repair reduced pain intensity early after surgery, with no effect on swelling, range of motion or knee function.

Chan, M., et al. Does Kinesiology Taping Improve the Early Postoperative Outcomes in Anterior Cruciate Ligament Reconstruction? A Randomized, Controlled Study. *Clin J Sport Med.* 2017, May; 27(3): 260-265.

### BRACING OF RECONSTRUCTED AND OSTEOARTHRITIC KNEES

Radiographic knee osteoarthritis (OA) is evident in more than 50% of people at 10-20 years after anterior cruciate ligament (ACL) reconstruction. This study compared the efficacy of an unloader brace, either with or without varus realignment for patients after ACL reconstruction.

Subjects were 19 patients with a primary ACL reconstruction 5-20 years prior to recruitment who demonstrated valgus malalignment as well as symptomatic and radiographic OA of the knee. Subjects performed hopping, stair ascent and stair descent tasks under three conditions including; no brace, unadjusted brace with a sagittal plane support and no varus alignment, and an adjusted brace with sagittal plane support and varus realignment. Quantitative motion analysis was performed during each examination, with kinematic and external joint movements computed.

There was no difference in pain during hopping or stair climbing between any of the three test conditions. Compared with no brace, the brace conditions increased the maximum knee flexion angle occurring at initial ground contact ( $p < 0.001$ ). The adjusted brace condition increased the maximum external knee flexion moment ( $p = 0.001$ ). There were no significant differences in kinetics or moments between the adjusted and unadjusted brace conditions.

**Conclusion:** This study of patients with ACL reconstruction and

osteoarthritis of the knee found that, compared with no bracing, an unloader brace can positively modulate the kinematics and external joint moments during activity, with no additional positive effect found with the use of varus realignment.

Hart, H et al. Bracing of the Reconstructed and Osteoarthritic Knee during High Dynamic Load Tasks. *Med Sci Sports Exerc.* 2017, June; 49 (6):1086–1096.

### SEQUELAE OF LONG-TERM OPIOID THERAPY IN PATIENTS WITH POLYNEUROPATHY

Polyneuropathy is a common condition, with related impairments including neuropathic pain. This study examined the prevalence of long-term opioid therapy among patients with polyneuropathy and the association between the duration of opioid therapy and functional status, adverse outcome rates and mortality.

Data were obtained from the Rochester Epidemiology Project (REP) database. This database was queried for opioid and other medication prescriptions, as well as for the indication for opioid prescriptions among those receiving 90 or more consecutive days of opioid therapy (defined as long-term use). Patients with polyneuropathy and matched controls were compared by functional status and adverse outcomes, including mortality.

Compared with controls, those receiving chronic opioids were more likely to have a medical comorbidity, with the exception of paralysis, cancer and AIDS. By specialty, the most likely prescribers of long-term opioid therapy were internal medicine 69.5% and family medicine 13.2% physicians. Only 3.7% of the patients received their prescriptions for long-term opioid therapy from pain physicians. After adjusting for confounding variables, those with long-term opioid therapy were found to be at significantly higher risk for depression (hazard ratio (HR) 1.53), opioid overdose (HR 5.12), opioid dependence (HR 2.85) and other chemical dependence (HR 1.7). The adjusted HR for mortality was not statistically significant.

**Conclusion:** This population based study of patients with polyneuropathy found that 18.8% received long-term opioids, with long-

term use associated with depression, opioid dependence and opioid overdose.

Hoffman, E., et al. Association of Long-Term Opioid Therapy with Functional Status, Adverse Outcomes and Mortality among Patients with Polyneuropathy. *JAMA Neurol.* 2017. doi:10.1001/jamaneurol.2017.0486.

### HIP FRACTURE MORTALITY IN EASTERN EUROPE

Data describing excess mortality after hip fracture is well established in developed countries in Western Europe and North America. However, estimates of hip fracture mortality in Eastern Europe are scarce. This study estimated the impact of hip fracture on 10-year, all-cause mortality among the Estonians 50 years of age or older.

This population-based, retrospective, cohort study used data from the Estonian Health Insurance Fund, which contains a complete record of inpatient and outpatient healthcare services. This record was reviewed for all patients hospitalized with incident hip fractures between January 1, 2005, and December 31, 2013. The patients were followed until the study's closure in 2016 or the date of death. The hip fracture patients were compared with matched controls.

During follow-up, the cumulative risks of death at three months were 17.5% for the hip fracture group and 2.0% for the control group. At one, five and 10 years' follow-up, the crude cumulative risks of death in the hip fracture group, as compared with the control group, were 28.3%, and 7.8%, 54.4% and 29.8% and 78.2% and 55.6%, respectively. The adjusted, cumulative, ten-year risks of all-cause death were 77.6% in the fracture group and 56.5% in the control group. At 10 years from fracture, one of four deaths in the hip fracture group was attributable to the patient's hip fracture.

**Conclusion:** This Eastern Europe study found that, 10 years after hip fracture, adjusted all-cause mortality was 77.6%, as compared with 56.5% for the general population.

Jurisson, M., et al. The Impact of Hip Fracture on Mortality in Estonia: A Retrospective, Population-Based,

## PROBIOTICS AND DEPRESSION

A growing body of evidence suggests that an abnormal composition and metabolic activity of gut microbes may play a role in Irritable bowel syndrome (IBS). As alterations in the gut microbiota have also been shown to improve affective disorders, this study examined the effect of microbiota supplementation on the anxiety and depression scores of patients with IBS.

Subjects were 44 adult patients with a diagnosis of IBS with mild to moderate anxiety and/or depression scores as assessed with the Hospital Anxiety and Depression (HAD) scale. At the screening visit, a clinical history was taken, with a physical exam including bloodwork and a functional MRI (fMRI). The subjects were randomized to receive 42 doses of dried Bifidobacterium longum (BL) or a placebo. The patients were assessed by physical exam and repeat laboratory/fMRI assessments through week 10. The primary endpoint was a reduction in HAD scores by two or more points at six weeks.

At week six, 64% of the patients in the treatment group and 32% in the placebo group had significant improvement in HAD depression scores ( $p=0.04$ ). This improvement was sustained at 10-week follow-up. No significant difference was noted between the groups in anxiety scores. For IBS symptoms, a benefit of the treatment was seen, as compared to the placebo, at six, but not at 10, weeks. The fMRI analysis found that the BL group had a reduced response to negative emotional stimuli, at the amygdala and the fronto-limbic regions, with this change significantly related to the improvement in depression scores ( $p=0.004$ ).

**Conclusion:** This study of patients with irritable bowel syndrome and anxiety/depression found that oral supplementation with Bifidobacterium longum results in improved depression scores, with this finding significantly related to changes in the function of the amygdala.

Pinto-Sanchez, M., et al. Probiotic Bifidobacterium Longum NCC3001 Reduces Depression Scores and

Alters Brain Activity: A Pilot Study in Patients with Irritable Bowel Syndrome. **Gastroenterol.** 2017; 10.1053/j.gastro.2017.05.003.

## SPINE FRACTURE PREVALENCE AT 40 YEARS AND OLDER

Approximately two million Americans experienced osteoporosis related fracture in 2005. This study investigated the prevalence of spine fractures in American adults 40 years of age or older.

Data were obtained from the National Health and Nutrition Examination Survey (NHANES), using data collected from a vertebral fracture assessment (VFA) in 2013 to 2014. The VFA was graded by semiquantitative measurement, bone mineral density (BMD) and an osteoporosis questionnaire. The BMDs of the lumbar spine, total hip and femoral neck were determined.

Data were obtained for 1,602 males and 1,728 females. Overall, 5.4% had spine fractures, including 6.2% of the males and 4.6% of the females. The prevalence of fractures was 2.1% among those 40 to 49, 4.2% among those 50 to 59, 5.4% among those 60 to 69, 10.5% among those 70 to 79 years and 18% among those 80 years of age or older. Of those with fractures, the proportion with moderate/severe fracture was higher among those 65 years of age or older ( $p=0.03$ ). Those with fractures had lower BMIs and BMDs at all sites.

**Conclusion:** This cross-sectional analysis of U.S. adults ages 40 years or greater found that the overall prevalence of fractures was 5.4%, with the risk increased among those with a lower body mass index and a lower bone mineral density.

Cosman, F., et al. Spine Fracture Prevalence in a Nationally Representative Sample of U.S. Women and Men Age Greater than 40 Years: Results from the National Health and Nutrition Examination Survey (NHANES) 2013 to 2014. **Osteoporos Intern.** 2017, June; 28 (6): 1857-1866.

## EARLY VERTEBROPLASTY IN ELDERLY PATIENTS

For patients with painful vertebral compression fractures, vertebroplasty

(VP) is often considered after the failure of conservative treatment. As previous studies have suggested better functional outcomes in elderly patients who undergo early VP, this study was designed to better understand the benefits of early VP in patients with a painful vertebral compression fracture (PVCF).

Data were harvested from the Taiwan National Health Insurance Research Database, which includes nearly 99% of the residents of Taiwan. From this database, patients 70 years of age and older were included if they had a PVCF admission between 2000 and 2013. Those who received a VP within three months of symptom onset were compared to those who received later procedures. The primary outcome measures were mortality and hospitalization due to pneumonia or respiratory failure.

Subjects were 1,773 patients with early VP and 5,324 non-VP patients with similar baseline characteristics. Death at one year occurred more frequently in the non-VP group than in the VP group ( $p=0.008$ ). Benefits in the VP group compared to the non-VP group were seen in reduced respiratory failure ( $p=0.028$ ), but not pneumonia.

**Conclusion:** This study of patients 70 years of age or older found that early vertebroplasty (within three months of symptom onset) resulted in improved mortality and a decreased risk of respiratory failure.

Lin, J., et al. Early Vertebroplasty Associated with a Lower Risk of Mortality and Respiratory Failure in Aged Patients with Painful Vertebral Compression Fractures: A Population-Based Cohort Study in Taiwan. **Spine J.** 2017. doi.org/10.1016/j.spinee.2017.05.001.

## STATINS AFTER COLON CANCER IMPROVE SURVIVAL

While colorectal cancer survival has doubled over the past 40 years, the five-year survival rate remains only 65%. Previous studies have suggested that statins may inhibit the proliferation of, and induce apoptosis in, colorectal cancer cells, although the exact mechanism of this phenomenon is unknown. Some have suggested that, as statins activate the bone morphogenetic protein (BMP) signaling pathway, this

mechanism may explain their efficacy. This study evaluated the effect of statins as an adjunctive therapy in colon cancer.

All subjects were diagnosed with colon cancer between 2002 and 2007, selected from the Eindhoven Cancer Registry in the Southern region of the Netherlands. Data were collected concerning the use of statins, as well as the cause of death. Tissue was retrieved from 1,026 colon cancer patients who had undergone surgical resection to determine BMP status. Those subjects considered statin users had been prescribed statins for 14 days or more after colon cancer diagnosis. Survival was compared with statin use.

During follow-up, 465 deaths were recorded. The five-year, overall survival rate for nonusers was 54.6%, while that for statin users was 65.7% ( $p=0.001$ ). Statin use after diagnosis was associated with a reduced risk of death from any cause ( $p=0.003$ ), and a reduced risk of death from cancer ( $p=0.007$ ). The reduced risk of death associated with statin use after diagnosis was more prominent in those with tumors that exhibited intact BMP signaling than for those with nonintact BMP expression.

**Conclusion:** This study of patients with colorectal cancer found that the use of statins after diagnosis improves survival.

Voorneveld, P., et al. Statin Use after Diagnosis of Colon Cancer: Inpatient Survival. 2017; *Gastroent*. DOI: 10.1053/j.gastro.2017.05.011.

### PAIN RECURRENCE AFTER DISCECTOMY

Lumbar discectomy is commonly performed for patients with symptomatic lumbar disc herniation (SLDH). As estimates of pain after surgery include individuals whose pain never resolved, counseling of patients with good pain resolution after surgery is somewhat difficult. This study was designed to identify the cumulative risks of recurrent leg and low back pain following discectomy for SLDH.

This study was a secondary analysis of data from the Spine Patient Outcomes Research Trial (SPORT), a randomized trial of adults with chronic radicular pain, with MRI findings corresponding with clinical

presentation. Patient reported outcomes were evaluated at baseline, at three months and then at one, two, three and four years post-surgery. Outcome measures included the Sciatica Bothersomeness Index (SBI). Pain resolution was defined as having a SBI index score of two or greater before surgery and less than two following surgery.

Of the 788 patients who received surgery, 71% had a resolution of leg pain and 52% a resolution of low back pain. The cumulative risks of leg pain recurrence were 20% at one year and 45% at three years. The cumulative risk of low back pain recurrence was 29% at one year and 65% at three years.

Multivariate analysis revealed that complete leg pain resolution after surgery predicted a lower risk of recurrence, while depression and smoking predicted a greater risk of recurrent leg pain. For recurrence of low back, greater age and current employment predicted a lower risk of recurrence, while being divorced or widowed, as well as having joint problems, predicted a greater risk.

**Conclusion:** This study of patients undergoing discectomy found the cumulative risks of recurrent leg pain and back pain were 20% and 29%, respectively, at one year post-surgery.

Suri, P., et al. Pain Recurrence after Discectomy for Symptomatic Lumbar Disc Radiation. *Spine*. 2017, May 15; 42(10): 755-763.

### MINOCYCLINE AND MULTIPLE SCLEROSIS

Studies have shown that, after a first, focal, clinical demyelinating event (clinically isolated syndrome (CIS), the risk of conversion to multiple sclerosis (MS) is high. In previous trials, minocycline therapy reduced the number of lesions detected on MRI. This study explored the effect of minocycline on the risk of conversion from CIS to MS.

Eligible subjects were patients with a first demyelinating symptom between January, 2009, and July, 2013. The subjects were randomized to receive either 100 mg of minocycline twice per day or a matching placebo for up to 24 months. The subjects were assessed by a physician held blind to the

condition, and underwent blood testing and clinical assessments, including the Expanded Disability Status Scale (EDSS), at screening, baseline and months one through 24. Relapses and adverse events were recorded. MRIs were obtained at baseline and months three, six, 12, and 24. The primary outcome measure was conversion to MS.

The intention to treat analysis included 142 participants. Of these, 23 in the minocycline group and 41 in the placebo group were diagnosed with MS within six months ( $p=0.001$ ). A post-hoc analysis revealed that the differences remained significant at 12 months, but not at 24 months. Adverse events occurred in 86.1% of the minocycline and 61.4% of the placebo group ( $p=0.001$ ), including rash, dental discoloration and dizziness.

**Conclusion:** This study found that 100 mg of minocycline twice a day may delay the conversion of clinically isolated syndrome to multiple sclerosis.

Metz, L., et al. Trial of Minocycline in a Clinically Isolated Syndrome of Multiple Sclerosis. *N Eng J Med*. 2017, June; 376(22): 2122-2133.

### MIGRAINE TREATMENT WITH OXYGEN THERAPY

Current antimigraine therapy may include triptans, though their use may be limited by their cost and cardiovascular risk factors. As oxygen therapy has shown been shown to be effective for cluster headaches (CH), this study explored the effect of this therapy for the treatment of migraines.

Subjects were adult patients with migraines occurring at least once per month. The subjects were randomly assigned to use canisters containing either oxygen or medical air. They were instructed to use the canisters at the onset of a migraine, in a specified order, at a rate of 10–15 l/minute for 30 minutes. The primary endpoint analysis was a comparison of the mean change in pain scores from baseline to 30 minutes between groups. Secondary endpoints were the mean change in pain, nausea, and visual symptom scores from baseline to 15 and 60 minutes, and the percentage of attacks achieving symptom relief.

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

The changes in pain scores were not significantly different between groups at 15, 30 or 60 minutes. Of the secondary endpoints, the percentage of patients achieving a complete resolution of headache were higher among the oxygen group than the medical air group (24% versus 6%,  $p=0.05$ ). The proportion of attacks in which pain scores improved by  $\geq 3$  points, tended to be higher with oxygen (42% versus 23%,  $p=0.08$ ). Significant headache relief, defined as a final pain score 0–1 or an improvement by  $\geq 3$  points, was also higher in the oxygen group (45% versus 23%,  $p=0.05$ ).

**Conclusion:** This randomized, blinded, crossover pilot clinical trial of patients with migraine headaches suggests that oxygen therapy may be an effective treatment.

Singhal, A et al. High-Flow Oxygen Therapy for Treatment of Acute Migraine: A Randomized Crossover Trial: **Cephalgia**. 2017, July: 37 (8):730-736.

*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.

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



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



Department of  
Rehabilitation  
Medicine

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