## MUSCULOSKELETAL

#### IN REVIEW

TM

Volume 4, Number 2

Published by Physicians Specializing In Musculoskeletal Medicine March 5, 2017

## ABALOPARATIDE FOR VERTEBRAL FRACTURES IN POSTMENOPAUSAL WOMEN

Osteoporosis is associated with substantial economic and public health costs. Osteoanabolic therapy is often recommended for women at risk for future fracture, although the evidence of rapid fracture protection with this treatment is lacking. Abaloparatide is a peptide that binds selectively to the conformation of the parathyroid hormone type I receptor. This study was designed to determine the efficacy of this medication for the prevention of new vertebral fractures in postmenopausal women.

This international, randomized, placebo and active controlled trial included postmenopausal women, 49 to 86 years of age with osteoporosis. The participants were randomized to receive subcutaneous injections abaloparatide 80 µg, a matching placebo, or teriparatide 20 Radiographs of the lumbar and thoracic spine were obtained at baseline and at the end of treatment. The primary outcome measure was the percentage of participants with one or more incidents of new morphometric vertebral fracture.

Subjects were 2,463 women with 33.5%, randomized to receive abaloparatide, 33.3% to receive placebo and 33.2% to receive open label teriparatide. New morphometric vertebral fractures occurred in 0.58% of those in the abaloparatide group and 4.22% in the placebo group (p<0.001). In the teriparatide group, fractures occur in 0.84% (p<0.001). At 18 months, compared to placebo,

the abaloparatide group demonstrated significant changes from baseline bone mineral density (BMD) at the total hip, femoral neck and lumbar spine (p<0.001 for all comparisons). The BMD increases from baseline to six months in the abaloparatide group were greater than for those in the teriparatide group for total hip and femoral neck (p<0.001 for all comparisons). The incidence of hypercalcemia was lower in the abaloparatide group teriparatide group than in the (p=0.006).

**Conclusion:** This study of postmenopausal women with osteoporosis found that the use of abaloparatide reduced the incidence of fractures over 18 months.

P., et al. Abaloparatide versus Placebo οn Vertebral Fractures in Postmenopausal Women with Osteoporosis. Α Randomized, Clinical Trial. J Amer Med Assoc. 2016, August 16; 316(7): 722-733.

#### NECK PAIN AND CERVICAL DYSTONIA TREATED WITH BOTULINUM TOXIN A

For cervical dystonia (CD), botulinum toxin injections in selected muscles is the treatment of choice. This study was designed to identify clinical outcomes related to pain in patients with CD treated with botulinum toxin (BoNT).

Data were obtained from an open label, prospective, multicenter clinical registry of patients with CD treated with BoNT. All subjects had a diagnosis of CD, were new to BoNT treatment or had not received such treatment for at least 16 weeks.

Dosing in the muscles injected was at the discretion of the treating physician. Patients were assessed with the Pain Numeric Rating Scale, the Pain subscale of the Toronto Western Spasmodic Torticollis Rating Scale, the Pain subscale of the Toronto Western Spasmodic Torticollis Rating Scale and the Pain and Discomfort subscales of the Cervical Dystonia Impact Profile.

The study enrolled 1,046 subjects, of whom 95% reported neck pain or discomfort prior to the injections. Post-injection pain relief ranged from 67.1% after the first treatment to 76.4% after the third treatment. The average time to pain relief ranged from 7.6 days after the first and 7.1 days after the third treatment. For those reporting moderate to severe neck pain at baseline, all pain scales demonstrated significant reductions in pain levels between baseline and final follow-up (p<0.0001).

Conclusion: This study of patients with pain related to cervical dystonia found that those with moderate to severe neck pain experienced significant pain relief after BoNT injections.

Charles, P., et al. Neck Pain and Cervical Dystonia: Treatment Outcomes from CD PROBE (Cervical Dystonia Patient Registry for Observation of OnabotulinumtoxinA Efficacy). Pain Pract. 2016, November; 16(8): 1073-1082.

### ACETABULAR LABRAL TEAR IN BALLET DANCERS

Ballet dancers are believed to be at an increased risk of acetabular labral tears as a result of the repetitive

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

Daniel Burke, B.S. Georgia College & State University, Milledgeville, GA

#### **Content Editor**

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

#### **Executive Editor**

Di Cui, M.D. Emory University, Atlanta, GA

#### **Copy Editor**

Tracie E. McCargo, EMBA Harvard University Extension School, Cambridge, MA

#### **Distribution Manager**

Michael P. Burke, M.S.

torsional loading of the hip joints in extremes of range of motion. This study, using improved magnetic resonance imaging techniques, was designed to determine whether professional ballet dancers have an increased prevalence of labral tears, as compared to a matched sporting population.

This case-control study engaged ballet dancers and a sporting control group with an average age of 30 years. Dancers included 66 current and 32 retired professional ballet dancers. The 49 controls were matched with dancers by gender and age. The controls who had sport participation including tennis, netball or basketball more than three times a week from at least 10 years of age. All subjects were assessed questionnaire for years of activity and medical/injury history. Questionnaires were used to determine energy expenditure per week and perception of hip pain or dysfunction. Range of motion of the hip and MRI evaluation of the hip were completed for all subjects.

The MRIs demonstrated that 61% of the participants had a labral tear in at least one hip. There was no significant difference in the frequency of labral tears between ballet dancers and controls (p = 0.41). No significant relationship was found between pain and the presence of a labral tear.

Among patients with pain, internal rotation of the hip while in  $90^{\circ}$  of flexion was associated with a labral tear in the left hip but not in the right hip.

**Conclusion:** This study of professional ballet dancers found that these athletes have a high incidence of labral tears, which is similar to that of other age and gender matched sporting participants.

Mayes, S., et al. Similar Prevalence of Acetabular Label Tear in Professional Ballet Dancers and Sporting Participants. **Clin J Sp Med.** 2016, July; 26(4): 307-313.

## CHONDROITIN SULFATE AND GLUCOSAMINE SULFATE FOR KNEE OSTEOARTHRITIS

Results from the glucosamine/ chondroitin arthritis intervention trial (GAIT) failed to demonstrate that this intervention could reduce joint pain among patients with osteoarthritis (OA) of the knee. A subsequent analysis, however, suggested that this intervention might be effective in a subset of patients with moderate to severe knee pain. This study was designed to better assess this treatment as compared with placebo for painful knee OA.

This phase three, multicenter, randomized, double-blind, placebo controlled, parallel group trial included patients with primary symptomatic knee OA. **Participants** radiographic grade 2 or grade 3 knee OA according to the Kellgren/ Lawrence scale. The 164 participants were randomly assigned to receive a placebo or oral glucosamine/ chondroitin sulfate (CS/GS) 1,200 /1,500 mg daily for six months. All subjects were assessed for pain using a visual analog scale, with secondary outcomes including investigators' global assessments of disease activity and Western Ontario McMaster and Universities Osteoarthritis Index (WOMAC) scores.

A modified intent to treat analysis revealed that the treatment group had significantly less reduction in pain scores than did the placebo group (p=0.029). Both groups improved on

total WOMAC scores, as well as on the Pain and Function subscales of the WOMAC, with no significant difference between the groups.

Conclusion: This study of patients with osteoarthritis of the knee did not find that the oral combination of chondroitin sulfate and glucosamine sulfate is effective for reducing pain and improving function over six months.

Roman-Blas, J., et al. Combined Treatment with Chondroitin Sulfate and Glucosamine Sulfate Shows No Superiority Placebo over for of Joint Pain Reduction and Functional Impairment in Patients with Knee Osteoarthritis: A Six- Month Multicenter, Randomized, Double-Blind. Placebo Controlled Trial. Arthritis Rheumatol. 2017, January; 69(1): 77-85.

### BOTOX IN THE MASSETER FOR TENSION HEADACHES

Tension-type headaches are among the most common spontaneous, primary headaches. These are often accompanied by temporomandibular joint (TMJ) dysfunction and masseter pain. This study was designed to assess the efficacy of botulinum toxin type A (BTXA) injections in patients with masseter muscle pain, TMJ dysfunction and tension-type headache.

This prospective study included 42 adults with TMJ dysfunction and tension-type headaches. The patients received 21 units of BTXA in the masseters, at the area of the greatest cross-section surface. The subjects were assessed for pain at one week before treatment and 24 weeks after treatment with a VAS (Visual Analogue Scale) and a VNRS (Verbal Numerical Rating Scale).

At 24 weeks, headache intensity, as measured by both pain scales, had significantly decreased (p=0.0000). After treatment, the patients reported a decrease in the use of analgesic drugs, as well as a decrease in pain duration with headaches (p=0.0000 for all comparisons).

Conclusion: This study of patients with temporomandibular joint

dysfunction and tension-type headaches found that botulinum toxin injections into the masseter muscle could decrease the frequency and intensity of headaches.

Pihut, M., et al. The Efficiency of Botulinum Toxin Type A for the Treatment of Masseter Muscle Pain in Patients with Temporomandibular Joint Dysfunction and Tension-Type Headache. J Headache Pain. 2016; 17: 29.

### COGNITIVE AND PHYSICAL REST AFTER CONCUSSION

The Fourth International Consensus Statement on Concussion in Sport suggested that cognitive and physical rest are important for treatment during acute concussion. While clinical expertise supports this rest period, the external clinical evidence is limited and largely derived from animal research. This study evaluated the effectiveness of cognitive and physical rest on the traditional concussion recovery metrics among college-age student- athletes with concussion.

Participants were drawn from a prospective study on concussion management. As part of a revised concussion management protocol, all student-athletes diagnosed concussion were withheld from all activities for the remainder of the day and were provided one additional day of cognitive and physical rest. Outcomes of these individuals were those compared with of 25 consecutive students treated in the two academic years prior to this policy change, who had not had their activities restricted.

graded symptom checklist, Immediate Post-Concussion Assessment Cognitive Testing (ImPACT), the Balance Error Scoring System (BESS) and the Standard Assessment of Concussion (SAC) test. Both groups

All subjects were assessed with a

and the Standard Assessment of Concussion (SAC) test. Both groups were withheld from team-related physical activity until they self-reported being asymptomatic

and achieved baseline values on the clinical battery of tests.

The rest group was symptomatic for 5.2 days and the no rest group for 3.9

days (p=0.047). There was no significant difference between the two groups in time to return to baseline as assessed with the BESS, the SAC, and computerized neuropsychological testing, or the time to clinical recovery.

**Conclusion:** This study of college students with concussions found that those given a day of rest after concussion had significantly longer time to recovery from symptoms, than did those without such a period of rest, with no difference in time to clinical recovery.

Buckley, T., et al. Acute Cognitive and Physical Rest May Not Improve Concussion Recovery Time. **J Head Trauma Rehabil**. 2016, July/August; 31(4): 233-241.

### DETERMINANTS OF PAIN AND FUNCTION IN OSTEOARTHRITIS

Among patients with osteoarthritis (OA), studies have shown that pain does not always accompany radiologic findings. This study assessed whether disease specific, demographic and psychological factors at baseline may be used to predict pain and function at one-year follow-up.

Subjects were 111 patients with radiologically diagnosed OA of the knee and associated pain symptoms. All participated in a randomized, controlled trial with a group-based cognitive-behavioral intervention to treat pain. Each subject was assessed at baseline and at 12- month follow-up with questions concerning knee pain and physical function, as well as demographic, socioeconomic and psychological variables. Outcome measures included The Western Ontario and McMaster University Osteoarthritis Index (WOMAC), the SF -36 item Health Survey and RAND-36 subscales. Psychological variables were assessed with questions focusing on psychological resources, fear and catastrophizing. Depressive symptoms were assessed with the Beck Depression Inventory (BDI), and anxiety symptoms with the Beck Anxiety Inventory (BAI).

A multivariate, linear, mixed model analysis revealed that a normal mood

at baseline, measured with the BAI, predicted significantly better results at one-year follow-up for pain (WOMAC p=0.02) and function (WOMAC p=0.002, RAND-36 p=0.002). High scores on the Pain Catastrophizing Scale predicted significantly higher WOMAC pain levels at one year. Low kinesiophobia scores predicted significantly lower impairment in WOMAC measured function. Conclusion: This study of patients with osteoarthritis of the knee found anxiety symptoms, catastrophizing and kinesiophobia are predictive of pain and function at one

Helminen, E., et al. Determinants of Pain and Function in Osteoarthritis: A One-Year, Prospective Study. **Clin Rehabil**. 2016, September; 30(9): 890-900.

### HOME EXERCISES FOR KNEE OSTEOARTHRITIS

Knee osteoarthritis (OA) is a major cause of musculoskeletal disability. The aims of treatment include decreased pain and improved function. A number of studies have suggested that home exercise programs are effective in improving strength, reducing pain and improving function among patients with OA. systematic review and meta- analysis designed clarify the to effectiveness of home exercise programs for this disease.

A literature review was conducted for comparing home exercise programs with inpatient or outpatient physical therapy for patients with knee OA. Outcome measures of interest were pain and function. After review, 16 studies were selected for inclusion. Interventions used as home exercise programs included a combination of open and closed kinetic chain exercises. Three studies used muscle stretching and range of motion exercises, while four studies used balance exercises. One study used proprioception, cold compression, electrical stimulation and tai chi.

A meta-analysis demonstrated that most treatments resulted in significant

improvement in pain compared with no intervention. In addition, most studies demonstrated significant improvement in function with intervention, as compared with no treatment (p<0.001).

Conclusion: This literature review and meta-analysis concluded that home exercise programs can reduce pain and improve function among patients with knee osteoarthritis.

Anwer, S., et al. Effect of Home E xercise Program in Patients with Knee Osteoarthritis: A Systematic Review and Meta-Analysis. **J Geriatr Phys Ther**. 2016, January/March; 39

(1): 38-48.

#### INTRA-ARTICULAR STEROID INJECTION BEFORE HIP REPLACEMENT SURGERY

Among patients with osteoarthritis those who oral (OA), medications may benefit from an intra-articular injection. Data suggest that surgeons often refrain from these injections prior to hip replacement surgery for fear of increasing the risk of infection. This study employed a literature review and meta-analysis to further explore this question.

A literature review was completed of articles published between 1992 and 2013. Studies were chosen involving patients with OA of the hip who underwent total hip arthroplasty, comparing those who did with those who did not receive a steroid injection prior to the surgery.

A total of eight pertinent studies were identified, with a mean time elapsed between the most recent steroid injection and surgery ranging from 3.7 months to 18 months. Of these, one was a prospective, observational, cohort design, while the remaining were retrospective cohort studies. The definition of infection was not described in five studies. The rate of infection varied from 0% to 30%. In one study, infection occurred in 30% of those in the injection group and 7.5% in the

non-injection group. Overall, the data were found to be insufficient to conclude whether intra-articular corticosteroid injections increased the risk of postsurgical infections.

**Conclusion:** This systematic literature review failed to demonstrate that preoperative intra-articular injections, prior to total hip arthroplasty, increase the risk of postoperative infection.

Pereira, L., et al. Intra-Articular Steroid Injection for Osteoarthritis Prior to Total Hip Arthroplasty. **Bone Joint J.** 2016, August; 98-B (8): 1027-1035.

### LATITUDE AND AGE OF ONSET IN MULTIPLE SCLEROSIS

Multiple sclerosis (MS) has been found to have a higher prevalence as latitude increases. Some have suggested that lower ultraviolet radiation levels and vitamin D deficiency may predispose those genetically at risk. This study examined whether there is a latitude variation of the place of residence at the age of onset of MS, and whether ultraviolet ray levels play a role.

Data were collected from the MSBase registry, a worldwide data set for patients diagnosed with MS. From this registry, 30,415 patients with clinically diagnosed MS were identified, of whom 22,162 were of European descent. The age at onset was compared to the latitude at which the patient lived at the time.

Patients living in a higher latitude were found to be diagnosed with MS at a younger age. For every 10° of latitude increase, the age of onset was found to be 10 months earlier (p=0.000). Those in the lowest latitude had an onset at almost two years later than those in the highest latitude. In addition, the data revealed a significant association between lower winter ultraviolet radiation levels and earlier onset of MS (p<0.001).

Conclusion: This study of patients of European descent with a diagnosis of MS found that those living at higher latitudes have an

earlier age of onset than do those living at lower latitudes.

Tao, C., et al. Higher Latitude Is Significantly Associated with an Earlier Age of Disease Onset in Multiple Sclerosis. J Neurol Neurosurg Psychiatry. 2016, November; 87: 1343-1349.

### LONG-TERM OPIOID USE AND REPRODUCTIVE DYSFUNCTION

Chronic noncancer pain (CNCP) is defined as any painful condition lasting for three months or longer that is not associated with neoplastic disease. Among patients with CNCP, 12-13% are prescribed opioids. As chronic opioid use in men has been found to be associated with hypogonadism and reproductive dysfunction, this literature review was designed to CNCPbetter clarify related dysfunction among women with long -term prescription opioid use.

Databases were reviewed for studies including women 18 to 55 years of age, involving opioids and genetic and reproductive side effects. From this review, six studies involving oral, five studies involving intrathecal and one study involving transdermal opioids were identified for inclusion.

Of the 10 studies reviewing menstrual cycle changes, 23% to 81% of women taking oral or intrathecal opioids had menstrual cycle abnormalities. This was not true in a study of women using transdermal buprenorphine. Of the three articles reviewing libido, reduced libido was found in 61% to 100% of patients taking opioids, although a reduction was also noted among controls. Only two of the ten studies reviewing hormone levels found a significant decrease in levels.

Conclusion: This literature review of premenopausal adult women taking oral or intrathecal long- term opioids found that these women were more likely to have clinical symptoms of hypogonadism with reduced levels of hormones.

Wersocki, E., et al. Comprehensive Systematic Review of Long-Term Opioids in Women with Chronic Noncancer Pain and Associated Reproductive Dysfunction (Hypothalamic-Pituitary-Gonadal Axis Disruption). **Pain.** 2017, January; 158(1): 8-16.

### MENISCUS TRANSPLANTATION SURVIVAL

Meniscus transplantation has been performed for more than 20 years, with the goal of decreasing pain and improving function. This study was designed to determine the long-term functional outcomes and survivorship rates in a consecutive series of patients receiving meniscal transplants.

Subjects were 69 consecutive patients, 50 years of age or younger, seen between 1995 and 2005, receiving a total of 72 meniscus transplants. Of these isolated surgeries, 44% were meniscus transplantations, and 56% involved a concurrent or staged operative procedure. Outcomes determined at follow-up examinations included physical exam findings, ratings using the International Knee Documentation Committee (IKDC) and Cincinnati Knee Rating System. Postoperative imaging included radiographs and MRI.

For all transplants, the combined probability of survival was 85% at two years, 77% at five years, 45% at 10 years and 19% at 15 years. Repeat surgeries related to the failure of transplants performed in 37 cases, ranging in time from 0.2 to 3.5 years postoperatively. Of the transplants available for long-term functional outcome, at 11.2 years, 26 failed and required later surgery. For all 58 survivors, significant improvements were found in pain, swelling, patient perception of overall knee condition, walking and stair climbing.

**Conclusion:** This study of 69 patients undergoing meniscus transplant found the survival rates at

10 and 15 years to be 45% to 19%, respectively.

Noyes, F., et al. Long-Term Survivorship and Function of Meniscus Transplantation. **Amer J Sports Med.** 2016, September; 44 (9): 2330-2338.

### METABOLIC SYNDROME AND POLYNEUROPATHY

Polyneuropathy is thought to affect two to seven percent of the population. The most common etiology is diabetes. This study was designed to better understand the prevalence of polyneuropathy as it relates to glycemic status in obese and lean populations.

Between November of 2010 and December of 2014, adult patients with a body mass index of 35 kg/m2 or greater, each seen at the University of Michigan Weight Management Program, were invited to participate in this study. At baseline all subjects underwent a workup, including a history and physical examination, with testing including glucose tolerance tests, lipid panels and morphometric evaluation. Diabetic status and metabolic profiles were also recorded. Polyneuropathy was identified by the Toronto consensus definition of probable polyneuropathy. То clarify peripheral nerve function, various nerve conduction studies were completed. The primary analysis involved the presence οf polyneuropathy compared with components of the metabolic syndrome.

Data were obtained from 102 obese patients and 79 lean controls. The prevalence of polyneuropathy among those with normoglycemia was 3.8% in the lean control group and 11.1% in the obese group, 29% obese participants prediabetes and 34.6% in obese patients with diabetes (p<0.01). In multivariable logistic regression analysis, age and waist circumference were significantly associated with polyneuropathy.

Conclusion: This study found a high prevalence of polyneuropathy among obese patients, even among those with normoglycemia.

Callahan, B., et al. Association between Metabolic Syndrome Components and Polyneuropathy in an Obese Population. JAMA Neurol. 2016, December; 73(12): 1468-1476.

#### **OSTEOPOROSIS**

Even after fracture, fewer than 25% of patients receive pharmacologic treatment for osteoporosis. After the discovery that sclerostin deficiency causes rare genetic conditions that are characterized by high bone mass and resistance to fracture, sclerostin has become a therapeutic target for the treatment of this disease. This study assessed the effect of romosozumab, а monoclonal antibody that binds and inhibits sclerostin with the dual effect of increasing bone formation and decreasing bone resorption.

Subjects were ambulatory. postmenopausal women, 55 to 90 years of age, with T scores at the total hip or femoral neck of -2.5 to -3.5. All patients received daily calcium at 500 to 1000 mg and daily vitamin  $D_3$  or  $D_2$  at 600 to 800 IU. participants were then randomly assigned to receive subcutaneous injections of 210 mg of romosozumab or placebo once per month for 12 months. The subjects then received open label denosumab, 60mg milligrams, every six months for an additional 12 months. The primary endpoints were new vertebral fracture at 12 months and 24 months.

Of the patients who underwent randomization, 6,006 completed the 24 month study. At 12 months, the romosozumab group had a risk of new vertebral fracture that was 73% lower than that of the placebo group (p<0.0001). The treatment group also had a 36% lower risk of clinical fractures at 12 months, as compared with placebo (p=0.008). At 24 months, the cumulative

incidence of new vertebral fracture was lower in the group that had originally received romosozumab, as compared to those who had originally received placebo (p<0.001).

**Conclusion:** This study of women with postmenopausal osteoporosis found that treatment with romosozumab, a sclerosin inhibitor, resulted in a significantly lower risk of vertebral fracture and clinical fracture at 12 months.

Cosman, F., et al. Romosozumab Treatment in Postmenopausal Women with Osteoporosis. **N Engl J Med**. 2016, September. DOI: 10.1056/NEJMoa1607948

### PHENYTOIN FOR ACUTE OPTIC NEURITIS

Multiple sclerosis (MS) is an antiinflammatory, demyelinating disorder of the central nervous system. Acute optic neuritis is a common feature of MS, which can damage vision through neurodegeneration of the optic nerve. As phenytoin has been found to be neuroprotective in preclinical models, this study was designed to determine whether this medication can be neuroprotective for patients with acute optic neuritis.

This randomized, double-blind, placebo-controlled trial included patients 18-60 years of age with MS and acute demyelinating optic neuritis. Participants were randomized to receive either phenytoin achieve serum to concentrations appropriate for epilepsy, or placebo. The patients were assessed by the treating physician at one and three months from baseline. The primary outcome measure was the change in retinal nerve fiber layer thickness (RNFL) in the affected eye at six months compared to the unaffected eye.

Of the 81 patients available for follow-up, the mean RNFL thickness remained stable in the unaffected eye. In the modified intention-to-treat population, the adjusted mean difference in six-month RNFL in the

affected eye (phenytoin group minus placebo group) was  $7.15 \mu m$  (p=0.021). This represents a 30% reduction in the extent of RNFL loss with phenytoin as compared with placebo.

**Conclusion:** This study of patients with multiple sclerosis and acute demyelinating optic neuritis, found that phenytoin can be neuroprotective, reducing the loss of RNFL thickness.

Raftopoulos, R., et al. Phenytoin for Neuroprotection in Patients with Acute Optic Neuritis: A Randomized, Placebo-Controlled, Phase 2 Trial. **Lancet Neurol.** 2016, March: 15(3):259-269.

### ROMOSOZUMAB FOR OSTEOPOROSIS

Even after fracture, fewer than 25% of patients receive pharmacologic treatment osteoporosis. After the discovery that sclerostin deficiency causes rare genetic conditions that are characterized by high bone mass and resistance to fracture, sclerostin has become a therapeutic target for the treatment of this disease. This study assessed the effect of romosozumab. а monoclonal antibody that binds and inhibits sclerostin with the dual effect of increasing bone formation and decreasing bone resorption.

Subjects were ambulatory, postmenopausal women, 55 to 90 vears of age, with T scores at the total hip or femoral neck of -2.5 to -3.5. All patients received daily calcium at 500 to 1000 mg and daily vitamin D<sub>3</sub> or D<sub>2</sub> at 600 to 800 IU. participants were randomly assigned to receive subcutaneous injections of 210 mg of romosozumab or placebo once per month for 12 months. The subjects then received open label denosumab, 60mg milligrams, every six months for an additional 12 months. The primary endpoints were new vertebral fracture at 12 months and 24 months.

Of the patients who underwent randomization, 6,006 completed the 24 month study. At 12 months, the romosozumab group had a risk of new vertebral fracture that was 73% lower than that of the placebo group (p<0.0001). The treatment group also had a 36% lower risk of clinical fractures at 12 months, compared with placebo (p=0.008). At 24 months, the cumulative incidence of new vertebral fracture was lower in the group that had originally received romosozumab. as compared to those who had originally received placebo (p<0.001).

**Conclusion:** This study of women with postmenopausal osteoporosis found that treatment with romosozumab, a sclerosin inhibitor, resulted in a significantly lower risk of vertebral fracture and clinical fracture at 12 months.

Cosman, F., et al. Romosozumab Treatment in Postmenopausal Women with Osteoporosis. **N Engl J Med**. 2016, September. DOI: 10.1056/NEJMoa1607948

#### SUBACROMIAL STEROID INJECTION AFTER ROTATOR CUFF REPAIR

Patients frequently experience severe postoperative pain after rotator cuff repair, despite improvements in surgical technique. Few studies have investigated the methods for controlling the pain which persists during the period of rehabilitation. This study was designed to determine the effectiveness and of safety subacromial steroid injections for pain control after rotator cuff repair.

This retrospective review included 458 patients who underwent arthroscopic rotator cuff repair with a minimum two-year follow-up. After surgery, the patients received oral nonsteroidal anti-inflammatory drugs once a day for two weeks, and engaged in a standard rehabilitation program. Shoulder function was evaluated using the American Shoulder and Elbow

Surgeons (ASES) score and the Constant score.

In addition, a postoperative visual analogue scale for pain (pVAS) was administered, and patient satisfaction was assessed. Those patients with painful postoperative shoulders received a subacromial corticosteroid injection of 40 mg triamcinolone and 4mL of 2% lidocaine. An independent examiner measured and recorded the pain scores and shoulder function at the first and third months after the injection, and every three months thereafter. Outcomes were compared between those with and those without injections.

The pVAS scores of patients administered injections averaged 7.7 (0 to 10) at the time of the injection, 2.3 at the end of the first month (p<0.01) and 1.2 after three months. The final outcome functional scores did not differ between those receiving and those not receiving injections. The re-tear rate was 6.8% among those with an injection and 18.4% among those without an injection.

**Conclusion:** This study of patients undergoing rotator cuff repair found that a single corticosteroid injection is a safe and effective method for reducing pain during the recovery period.

Shin, S., et al. Efficacy of a Subacromial Corticosteroid Injection for Persistent Pain after Arthroscopic Rotator Cuff Repair. **Am J Sports Medicine.** 2016, September; 44 (9):2231-2237.

### VITAMIN D AND FRACTURE COMPLICATIONS

Research has shown that vitamin D regulates several areas of human physiology, including the cardiac, immune, digestive and musculoskeletal systems

musculoskeletal systems.

Orthopedic surgeons frequently prescribe calcium and vitamin D supplementation for patients with fractures to promote fracture healing. This study was designed to better understand the relationship

between serum 25(OH) D levels and the likelihood of postoperative complications after fracture related surgery.

This retrospective review was performed for all adult orthopedic trauma patients seen at a level I trauma center for a fracture between 2009 and 2010. The patients had available serum 25(OH) D levels drawn within two weeks of injury and repeat levels drawn at a minimum of eight weeks later. All patients received 100 IU of vitamin D<sub>3</sub> and 1,500 mg of calcium daily. Those with a serum 25(OH) D deficiency or insufficiency also received regimen of 50.000 IU ergocalciferol weekly until 25(OH)D levels were normalized (>32 ng/mL). Standard clinical follow- up was performed at two, six and 12 week visits, and every two to three months until fracture healing. Among the 201 patients included in this study, 15 had fracture healing complications, including infection (6%), nonunion (3%), osteomyelitis (1.5%), wound dehiscence (1.5%), malunion (0.5%) and joint contracture (0.5%). There was no significant difference in the likelihood of fracture healing complications based upon the initial or repeat levels of 25(OH) D (p>0.5 and p>0.6, respectively).

**Conclusion:** This retrospective study of patients with traumatic fractures found that vitamin D supplementation does not appear to have a large impact on fracture healing.

Bodendorfer, B., et al. Do 25-Hydroxyvitamin D Levels Correlate with Fracture Complications? **J Ortho Trauma.** 2016, September; 30(9): e312 – e317.

### MODIFIED FLIP-FLOPS AND FOOT PAIN

Recent studies have estimated that one in five people over 45 years of age experience frequent foot pain. This study reviewed the efficacy of flip-flop style footwear, with a molded foot bed, for reducing pain and improving function among adults with disabling foot pain.

Adult subjects were recruited who reported disabling foot pain, defined as pain with restriction of at least one normal activity. Exclusion criteria included peripheral artery disease, venous insufficiency or neuropathy. peripheral Those randomized to an intervention group were fitted with flip-flops with a molded foot bed, heel cup and wide straps. They were asked to wear this footwear as much as possible for the next 12 weeks. Those in a control group were asked to wear their usual footwear. The primary outcome measure was the foot pain domain of the Foot Health Status Questionnaire (FHSQ). Secondary outcome measures included current foot pain (VAS) as well as the FHSQ domains of foot function and general foot health.

Of the subjects recruited, 54 were allocated to the treatment and 54 to the control group. Compared to the control group, the treatment group had significant improvement in pain at 12 weeks, as measured by the foot pain domain of the FHSQ (p<0.01). In addition, the treatment group obtained significantly better scores on the pain VAS (p<0.01), the FHSQ domain of function (p<0.01) and the FHSQ domain of general foot health (p<0.01).

Conclusion: This study of patients with disabling foot pain found that the use of flip-flops, with a contoured bed, resulted in significant improvement in pain and function.

Chuter, V., et al. Flip-Flop Footwear with a Molded Foot Bed for the Treatment of Foot Pain: A Randomized, Controlled Trial. BMC Musculoskelet Disord. 2016, Nov 11; 17: 468.

# IMMEDIATE AND DELAYED LOWER LIMB AMPUTATION COMPARED TO SALVAGE

Functional outcomes of amputees are often comparable with those in the age matched general population. This study compared the outcomes of patients who underwent immediate unilateral amputation to

those of patients who underwent delayed unilateral amputation and those who underwent lower limb salvage.

This retrospective analysis involved a cohort of military patients undergoing posttraumatic lower limb salvage or amputation between January 2013 and January 2015. The majority were soldiers involved in the wars in Iraq or Afghanistan. Injury severity was determined at the time of injury, with demographics, of hospitalization, comorbidities also recorded. Patients assessed for functional outcome and mental health outcome measures.

Of the 100 military personnel included in the study, 11 underwent immediate below knee amputation. delayed below knee 15 amputation. 10 immediate above knee amputation, 43 bilateral amputation and 21 limb salvage. The mean time between injury and amputation in the delayed was 10 months. immediate above knee and below knee amputation group required a significantly greater number of months of rehabilitation than did the delayed below knee amputation and the limb salvage group (p<0.05). At completion of rehabilitation, those with unilateral amputation could walk significantly farther in the 6 minute walk test than those with limb salvage and those with bilateral amputation (p<0.05).

Conclusion: This study of British military veterans found that those electing for delayed amputation after limb salvage attempts achieved superior functional gains than did those who underwent limb salvage only, with equivalent outcomes to those with immediate amputation.

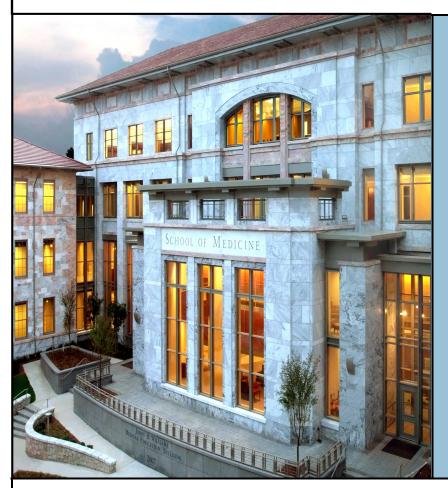
Ladlow, P., et al. Influence of Immediate and Delayed Lower Limb Amputation Compared with Lower Limb Salvage on Functional and Mental Health Outcomes Post-Rehabilitation in the UK Military. J Bone Joint Sur. 2016, Dec 7; 98 (23): 1996-2005.

Musculoskeletal in Review (MSK) produced physicians specializing in musculoskeletal and neurological medicine, with the cooperation and assistance Emory University School of Medicine. Summaries appearing in this publication are intended as an aid in reviewing the literature relevant to the practice of clinical musculoskeletal medicine. summaries appearing 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.

MSK is affiliated with the World Health Organization and multiple national medical societies worldwide.

Private subscriptions are available by email at mskinreview@aol.com or by phone at (417) 779-9101.



### MUSCULOSKELETAL IN REVIEW

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

Expanding the frontier of medicine in research, teaching, and patient care