MUSCULOSKELETAL

IN REVIEW

TM

Volume 4, Number 1 | Published by Physicians Specializing In Musculoskeletal Medicine | January 5, 2017

ACETYLCHOLINESTERASE INHIBITORS AND WEIGHT LOSS

Malnutrition and cognitive decline are geriatric syndromes associated with an increased risk of premature mortality in the elderly. As cognitive deterioration often alters oral intake, this meta- analysis was designed to better understand how acetylcholinesterase inhibitors affect nutritional status.

This systematic review and meta-analysis included studiespublished through 10/14/15. Pub Med was searched for randomized, controlled and open label trials involving acetylcholinesterase inhibitors for patients with dementia that reported nutritional status data. The primary outcome variables were changes between baseline and follow-up in the parameters of weight, body mass index and nutritional status.

The final analysis involved 12 open label trials, nine randomized, controlled trials and four longitudinal studies, including 10,792 patients with dementia. A significant, cumulative incidence of weight loss was noted, among those using acetylcholinesterase inhibitors in the longitudinal studies ($p<0.0001$). Similar results were found in the open label and randomized, controlled trials ($p<0.0001$ for both).

Conclusion: This literature review and meta-analysis found that, among patients with dementia, the use of acetylcholinesterase inhibitors is associated with an increased risk of weight loss.

Soysal, P., et al. Acetylcholinesterase Inhibitors Are Associated with Weight Loss in Older People with Dementia: a Meta-Analysis. **J Neurol, Neurosurg Psychiatr.** 2016, December; 87: 1368-1374.

ACUPUNCTURE VERSUS IV MORPHINE FOR ACUTE PAIN

While acupuncture has been introduced to a number of health systems throughout the world, its use in the (ED) is rare. This study evaluated the efficacy and safety of acupuncture compared with that of morphine for adults presenting to the ED with acute pain.

This prospective, randomized, non-blinded trial included adult patients presenting to the ED of a university hospital in Tunisia with acute pain syndromes. All patients reported a pain intensity of at least 40 on a 100-point visual analogue scale (VAS). In the group randomized to receive acupuncture (n=150), protocols were selected from a pool of predetermined acupuncture points for each condition. Those randomized to the morphine group (n=150) received IV morphine, titrated from an initial dose of 0.1 mg per kilogram, adding a dose of 0.05 mg per kilogram every five minutes, until reaching sufficient pain relief, to a maximum of 15 mg. The primary outcome measure was pain severity at baseline and five, 10, 20, 30, 45,and 60 minutes.

Success, defined as a reduction of at least 50% in pain severity from baseline, was achieved in 92% of the acupuncture group and 78% of the morphine group ($p<0.01$). Pain resolution time averaged 16 minutes in the acupuncture group and 28 minutes in the morphine group ($p<0.01$). Minor adverse events were experienced by 56.6% of those in the morphine group and 2.6% in the acupuncture group.

Conclusion: This randomized trial of patients presenting with acute pain in the emergency department found that acupuncture could provide better and quicker relief than could IV morphine.

Grissa, M., et al. Acupuncture versus Intravenous Morphine in the Management of Acute Pain in the E.D. **Am J Emerg Med.** 2016, November; 34 (11): 2112-2116.

CIGARETTE SMOKING AND CUBITAL TUNNEL SYNDROME

Studies have demonstrated that gender, age, body mass index and workers' compensation status contribute to the development of cubital tunnel syndrome (CubTS). As conflicting results have been found for the association between tobacco abuse and CubTS, this study was designed to better understand this relationship.

Subjects included 100 patients with CubTS who underwent surgical repair, compared with 100 individuals who underwent surgical correction for ulnar abutment syndrome (UAS). The latter were chosen, as the pathogenesis of UAS has not been shown to be associated with cigarette smoking. Smoking history was assessed by patient self-report, with subjects classified as current smokers, past smokers or never smokers.

A significantly greater proportion of the controls had never smoked cigarettes ($p<0.001$), while a significantly greater proportion of patients with CubTS were past smokers ($p=0.001$). There was no difference between groups in current smokers. There was a dose dependent association between pack years smoked and the odds ratio for CubTS, ranging from 2.9 among those with 1-15 pack years to 29.93 among those with more than 30 pack years.

Conclusion: This retrospective study suggests an association between cubital tunnel syndrome and a history of cigarette smoking.

Suzuki, T., et al. Cigarette Smoking Is Associated with Cubital Tunnel Syndrome. **Muscle Nerve.** 2016, December; 54(6): 1136-1138.

DIURETIC USE AND THE RISK OF VERTEBRAL FRACTURES

It has been estimated that 25% of postmenopausal women in the United States will sustain a vertebral fracture, with the prevalence increasing with advancing age. Among older adults in the United States, hydrochlorothiazide, a diuretic, is the second most commonly used prescription or over- the-counter drug. Thiazides have been shown to decrease urinary calcium excretion, improve calcium balance, but can also cause hyponatremia, a condition associated with an increased risk of fractures. Loop diuretics increase urinary calcium excretion and lower bone mineral density, but rarely cause hyponatremia. This prospective study compared the association between thiazide and loop diuretic use and vertebral fractures.

Data were obtained from the Nurses' Health Study, an ongoing, prospective, cohort study begun in 1976, and enrolling 121,700 female registered nurses, 30 to 55 years of age. Data from this study included 55,780 women who completed both the 2002 questionnaire including questions of diuretic use, and the 2012 questionnaire which included questions about vertebral fractures. Potential confounders for fracture risk were also recorded.

During 543,209 person-years of follow-up, there were 420 confirmed cases of incident vertebral fracture. In the multivariable-adjusted analysis, thiazide diuretic as well as loop diuretic use were both associated with a significantly increased risk of vertebral fracture (relative risk 1.47 and 1.59, respectively) compared to nonusers.

Conclusion: This study found that both thiazide diuretics and loop diuretics are independently associated with an increased risk of vertebral fracture in women.

Paik, J., et al. Diuretic Use and Risk of Vertebral Fracture in Women. **Am J Med.** 2016, December; 129(12): 1299-1306.

HELMET USE AND THE RISK OF HEAD INJURY IN SNOWBOARDERS AND ALPINE SKIERS

Previous studies have suggested that helmet use can reduce the risk of head injury for Alpine skiers and snowboarders. According to the National Ski Areas Association National Demographics Study, helmet

use has increased from 25% in 2003 to 70% in 2013. This study examined the effect of this change in behavior on the risk of head injury.

Six ski patrols at major Norwegian ski resorts registered injuries during the 2002, 2010 and 2011 seasons. Those with injuries to the head were compared to those with injuries to areas other than the head. The data were compared by year collected.

In 2002, 17.6% of the injuries among skiers were injuries to the head. In 2010, this percentage was 15.3%, while in 2011, it was 15.4%. During the same decade, helmet use increased among injured skiers and snowboarders, from 23.8% in 2002,

to 68.1% in 2010, and 77.1% in 2011. Head injuries were less common among those wearing a helmet than among those who did not, with odds ratios of 0.57, in 2003, 0.82 in 2010 and 0.9 in 2011.

Conclusion: This study of injuries among skiers and snowboarders found that the use of helmets has increased dramatically over the past 10 years, with a significantly reduced risk of head injury among those wearing helmets.

Sulheim, S., et al. Helmet Use and the Risk of Head Injuries in Alpine Skiers and Snowboarders: Changes after an Interval of One Decade. Br J Sports Med. 2017, January; 51(1): 44-50.

EPIDURAL STEROIDS AND BONE MINERAL DENSITY

Lumbar epidural steroid injections (ESI) are widely used to treat back pain. Previous studies have demonstrated that glucocorticoids have multiple side effects, including glucocorticoid-induced osteoporosis. This study assessed the relationship between ESIs and changes in bone mineral density (BMD) in postmenopausal women with low back pain (LBP).

This retrospective analysis included 126 postmenopausal patients who underwent ESI for the treatment of LBP, who had received dual-energy x -ray absorptiometry (DEXA) scans before and after treatment. Body mass index was calculated with BMD determined using DEXA. Of those included, group one comprised 74 patients who received injections with dexamethasone while taking an anti- osteoporotic medication, while group two comprised 52 patients who underwent these injections while not taking an anti-osteoporotic medication.

The mean changes between baseline and post-treatment BMD in group one were 1.25% in the lumbar spine and 0.45% in the femoral neck, 0.39% in the femoral trochanter and 0.21% in the total femoral region, with none reaching statistical significance. The mean changes in group two, were 0.69% in the lumbar spine, -1.48% in the femoral neck ($p=0.003$), -2.8% in the femoral trochanter ($p=0.008$) and -2.23% in the total femoral region ($p<0.001$).

Conclusion: This study of postmenopausal women undergoing epidural steroid injections found that these injections are associated with worsening osteoporosis, an effect that seems mitigated by the use of anti-osteoporotic medication.

Kim, Y., et al. Effect of Epidural Steroid Injection on Bone Mineral Density in Postmenopausal Women According to Anti-Osteoporotic Medication Use. **Pain Physician.** 2016, July/August; 19 (6): 389-396.

FRACTURE HEALING AND OSTEOPOROTIC DRUGS

The two major categories of pharmacologic treatment for osteoporosis are antiresorptive and bone anabolic medications. Teriperatide is the only currently approved anabolic medication for the treatment of osteoporosis. This study compared the effects of this medication with that of a bisphosphonate, risondronate, on the functional and radiographic outcomes after a hip fracture.

This multinational, randomized active controlled trial included patients with peritrochanteric hip fractures and bone mineral density T- scores of -2.0 or less, and 25-OH- vitamin D levels of 9.2 ng/mL or greater. The patients were randomized to receive teriperatide 20µg per day subcutaneously, or risondronate 35 mg per week. At screening, both groups began oral supplements of calcium and vitamin D and discontinued any ongoing osteoporotic drugs. Patients were assessed for functional mobility at six, 12, 18 and 26 weeks, with outcome measures including the SF – 36 survey, Timed up and Go (TUG) test, a visual analogue pain scale, the modified Charnley hip pain score, as well as the ability to walk.

Of the patients randomized, 171 contributed to the efficacy analysis. The time required to complete the TUG test was shorter in the teriperatide group compared with the risondronate group at six, 12, 18, and 26 weeks (p=0.021 for the overall between-treatment effect). The self- reported pain was reduced more in the teriperatide group than the risondronate group (p=0.032). There was no difference between groups in the domains of the SF – 36, radiographic healing, or the ability to walk at 26 weeks.

Conclusion: This prospective randomized trial of patients with peritrochanteric hip fractures found that teriperatide treatment after fracture is associated with better functional outcome compared with risondronate.

Aspenberg, P et al. Effects of Teriperatide Compared with Risondronate on Recovery after Peritrochanteric Hip Fracture: Results of a Randomized, Active Control, Double-Blind Clinical Trial at 26 Weeks. **J Bone Joint Surg Am.** 2016, Nov 16; 98 (22):1868 – 1878.

OCRELIZUMAB FOR PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS

As B cells are thought to influence the pathogenesis of multiple sclerosis (MS), through antigen presentation, auto antibody production or cytokine secretion, a number of treatment options have focused on manipulating the function of B cells. This study explored the efficacy and safety of Ocrelizumab, a humanized monoclonal antibody that selectively depletes CD20-expressing B cells.

Subjects were 18 to 55 years of age with a diagnosis of primary, progressive MS. The patients were randomized to receive Ocrelizumab, 600 mg every 24 weeks, or a placebo for a minimum of five doses (120 weeks). All patients received IV methylprednisolone at 100 mg before infusion.

The primary endpoint was the percentage of patients with disability progression, using the Expanded Disability Status Scale (EDSS). Secondary endpoints included change from baseline to week 120 in performance on the timed 25-foot walk, change in the total volume of brain lesions on T_2-weighted MRI, change in the Physical Component Summary score of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF -36), Version 2, and change in brain volume from week 24 to week 120.

The percentages of patients with 24-week confirmed disability progression were 29.6% in the treatment group and 35.7% in the placebo group (p=0.04). Significant improvement was noted in the treatment group as compared with the placebo group on the timed 25 foot walk (p=0.04), with no difference between groups on the SF-36 Physical Component score (p=0.6). The total volume of hyperintense lesions on T_2-weighted images decreased in the treatment group and increased in the placebo group (p<0.001).

Conclusion: This study of patients with primary progressive multiple sclerosis found that Ocrelizumab is associated with lower rates of clinical and MRI progression.

Montalban, X., et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. **N Engl J Med.** 2016. DOI: 10.1056/ NEJMoa1606468.

INTRANASAL KETAMINE FOR ACUTE TRAUMATIC PAIN

Opiates are the current mainstay of severe pain relief. Ketamine, an NMDA -antagonist, has been studied for its efficacy in analgesia and anesthesia. This study was designed to better understand the efficacy and safety of intranasal (IN) ketamine for use in the emergency department.

This single center, randomized, prospective, clinical trial recruited patients ages 18 to 70 years presenting to the ER with orthopaedic pain rated as $\geq$ 80/100 on a visual analogue scale (VAS). Eligible subjects were randomized to receive IN ketamine (1mg/kg), IM morphine (0.15 mg/kg IM) or IV morphine (0.1 mg/kg) in a 1:1:1 ratio. Vital signs and VAS measurements were recorded at five minute intervals. The primary outcome measure was the effectiveness of the drug in reducing pain intensity. The "time to onset" (TTO) was defined as the time until the patient reached a 15 mm VAS pain score reduction.

In the 90 patients recruited, the TTO for IN ketamine was 14.3 minutes, for IV morphine was 8.9 minutes (p=0.30) and for IM morphine was 26 minutes (p = 0.003). The maximal VAS pain score reduction was 56 mm, 59 mm and 48 mm pain for the IN ketamine, IV morphine and IM morphine groups,respectively (p = 0.3). The time to maximum pain reduction was 40.4 minutes for IN ketamine, 33.4 minutes for IV morphine, and 46.7 minutes for IM morphine (significant at p = 0.019 comparing IM and IV morphine). No significant difference was seen between groups in patient satisfaction.

Conclusion: This emergency room study of patients with moderate to severe orthopedic pain found that intranasal ketamine may have similar efficacy as IM or IV morphine.

Shimonovich, S., et al. Intranasal Ketamine for Acute Traumatic Pain in the Emergency Department: A Prospective, Randomized, Clinical Trial of Efficacy and Safety**. BMC Emerg Med.** 2016, November; 16:43.

SUSTAINED HEAT TREATMENT FOR DELAYED-ONSET MUSCLE SORENESS

Muscle soreness after exercise is

common, and can reduce the ability to perform in the days following. While cold is the most commonly recommended modality after exercise, both heat and cold have been prescribed. This study assessed the effect of sustained heat treatment on both objective and subjective measures of delayed -onset muscle soreness (DOMS).

The 20 subjects were randomized to one of three groups, including heat wraps applied immediately after exercise (group 1), heat wraps applied 24 hours after exercise (group 2) or a control. To provoke DOMS, subjects were engaged in squatting exercises for 15 minutes. Patients were assessed for muscle soreness with a visual analogue (VAS) scale, for strength and range of motion, and for changes in plasma biomarker measurements at baseline and 48 hours after exercise. Heat therapy was applied by placing a ThermaCare heat wrap on each leg over the quadriceps for eight hours.

At 24 hours post-exercise, the control group demonstrated a 23.8% loss of muscle strength as compared with baseline, with group 2 demonstrating similar results. In group 1, no significant reduction in strength was noted on any post-exercise day. An increase in pain was found after exercise for all three groups, peaking by post-exercise day two. Significantly less pain was noted by group 1 on the first and second days after exercise ($p<0.001$), but not day three. Greater pain-free passive range of motion was noted in group 1 than in the other two groups.

Conclusion: This study found that, after intense exercise, immediate, low level heat wraps applied for eight hours can reduce delayed-onset muscle soreness and post-exercise strength reductions.

Petrofsky, J., et al. The Efficacy of Sustained Heat Treatment on Delayed-Onset Muscle Soreness. **Clin J Sports Med.** 2016; DOI: 10.1097/JSM.0000000000000375.

PHYSICAL EXERCISE AND MYASTHENIA GRAVIS

Myasthenia gravis (MG) is a neuromuscular disease with weakness as a cardinal symptom. Little research exists concerning aerobic or muscular resistance training in patients with MG. This study examined the effects of exercise in this population.

This prospective study included patients diagnosed with chronic MG, recruited from three outpatient neurology clinics in Sweden. The participants underwent supervised exercise sessions lasting 75 minutes and consisting of aerobic, resistance and balance training two times per week for 12 weeks. The patients were assessed before and after training with nerve conduction studies, strength and performance measures and with blood tests of serum for serum specific microRNAs, interleukin-6, muscle enzymes, CRP, and creatinine, as well as the MG Composite Score, and peak expiratory flow.

Among the 10 participants, there was no evidence of increased disease activity during the study. In the nerve conduction studies, the CMAP amplitude increased significantly in the biceps and quadriceps ($p=0.002$ and $p=0.037$, respectively). Proximal muscle strength significantly improved in both arm and leg muscles. Performance on the Six-Minute Walk Test and 30- Second Walk Test improved significantly ($p=0.002$ and $p=0.0039$, respectively). While BMI did not significantly change, body composition did, with increased muscle mass and reduced fat mass ($p=0.02$). All patients scored much higher in physical activity after the study ($p=0.008$). The disease-specific microRNAs, miR150-5p ($p=0.048$) and miR21-5p ($p=0.0020$), were significantly reduced after the training period, while muscle enzymes remained normal.

Conclusion: This small study of patients with chronic myasthenia gravis found that exercise training, twice per week, increased aerobic capacity, improved body composition, improved motor action potential amplitudes, and improved disease specific biomarkers.

Westerberg, E., et al. Physical Exercise in Myasthenia Gravis Is Safe and Improves Neuromuscular Parameters and Physical Performance-Based Measures: A Pilot Study. Muscle Nerve: DOI: 10.1002/mus.25493.

SHOCKWAVE THERAPY VERSUS BOTOX FOR PLANTAR FASCIITIS

Plantar fasciitis (PF) is very common in the general population, often persisting for many months. As extracorporeal shockwave therapy (ESWT) has been used in the management of tendinopathies and botulinum toxin A (BoNT-A) has been used to treat pain, this study compared the effects of those two interventions for the treatment of PF.

This open label, prospective, randomized study included patients with PF who had not responded to physiotherapy and electrotherapy. The participants were randomly assigned to receive either ESWT, focused at the area of maximum tenderness for 15 minutes per session, or 100 units of BoNT-A, with injections divided between the insertion of the plantar fascia in the calcaneus and the area of maximal tenderness. The subjects were assessed for pain in the affected foot on a 10-point visual analogue scale (VAS), when taking the first steps in the morning, during daily activity, and while performing exercises. Each patient was also assessed with the Quality of Life Health Status Questionnaire.

Data for 72 patients were included in the analysis. The median pain score when taking the first steps in the morning was significantly better in the ESWT group than in the BoNT-A group ($p=0.009$). Better improvement was also noted in the ESWT group than in the BoNT-A group on the Roles and Maudsley Scale of Pain between the first and second visit, as well as in the percentage of patients who noted improvement in pain on at least one of three modalities of VAS pain scores ($p=0.006$ and $p=0.029$, respectively). A regression analysis revealed that ESWT and low body weight were independently associated with improvement in pain.

Conclusion: This study of patients with recalcitrant plantar fasciitis found that shockwave therapy was superior to botulinum toxin A for reducing pain.

Roca, B., et al. Comparison of Extracorporeal Shockwave Therapy

with Botulinum Toxin Type A in the Treatment of Plantar Fasciitis. **Disabil Rehab.** 2016, October. 38 (21); 2114-2121.

WEIGHT CHANGE AFTER SPINAL CORD INJURY

Individuals with disabilities have a higher prevalence of obesity than do the general population. However, literature concerning weight change after spinal cord injury (SCI), as well as factors associated with patterns of weight loss or gain, is limited. This study evaluated the patterns weight change one year post-SCI, in an effort to identify factors associated with weight change.

Data were retrieved from 16 SCI model systems, with information obtained for 1,094 individuals ranging in age from 17 to 88 years, all with traumatic SCI. All patients were discharged from rehabilitation between October of 2006 and November of 2012. Body mass index (BMI) was compared at the time of discharge and at one-year follow-up. Patient characteristics were compared between those with and those without significant weight changes.

The baseline BMI of the participants averaged 26.3 kg/m², while that at one year post-injury averaged 25.8 kg/m². In the first year, 19.1% maintained their weight, 33.4% gained over two kg and 47.5% lost over two kg. Those classified as overweight or obese during rehabilitation demonstrated an average decrease in BMI at one-year of 1.4 kg/m², while those classified as underweight or normal weight demonstrated an average increase of 0.5 kg/m². Gender, education, neurologic level of injury, ethnicity, mental status, age and education were all significant contributors to change in BMI.

Conclusion: This study of patients with traumatic spinal cord injury found that, on average the mean BMI decreases slightly during the first year post-injury. Those who were overweight at injury tend to lose weight, and those were underweight at injury tend to increase weight.

Powell, D., et al. Weight Change after Spinal Cord Injury. **J Spinal Cord Med.** 2016, 10.1179/2045772314Y.0000000264

WIRELESS NERVE STIMULATORS TO ASSESS FUNCTIONAL RECOVERY

Peripheral nerve injuries are among the most common causes of sensory deficits, with great interest in surgical rehabilitative strategies to treat these injuries. This animal study assessed a wireless implantable stimulator to map the recovery of nerve and muscle function following a peripheral nerve injury.

Fifteen adult rats were divided into three groups. All groups underwent surgical exposure of the sciatic nerve, with group one undergoing no nerve injury, group two undergoing crush injury of the sciatic nerve and group three undergoing transection of the sciatic nerve with repair. All groups underwent implantation of a wireless nerve stimulator. Each week for 14 weeks, functional recovery was assessed by wireless stimulation of the sciatic nerve, with EMG recording at distal muscles. After the study, the animals were euthanized and distal muscles were harvested.

All implanted devices remained operational throughout the study. The EMG responses in muscles distal to the site of the injury demonstrated progressive recovery of function over six weeks. The change in EMG measured amplitude from week one to week 14 ranged from 6.4% to 69.1% measured in the plantaris of group three to 77.5% to 104.3% measured in the gluteal muscle of group two.

Conclusion: This animal study demonstrated that wireless nerve stimulators at the site of the injured nerve can be used to assess the course of recovery in both crush and transection injuries.

Gamble, T., et al. Serial Assessment of Functional Recovery following Nerve Injury Using Implantable Thin- Film Wireless Nerve Stimulators. Muscle Nerve. 2016, December; 54(6):1114-1119.

TOOTH LOSS AND FUNCTIONAL CAPACITY

Many studies have reported on the relationship between oral health and general health. This study was designed to determine whether an association exists between dental health and a decline in higher-level functional capacity.

Data were derived from the Japan Gerontological Evaluation Study (JAGES), involving community dwelling adults, 65 years of age or older, who were cognitively independent. A baseline survey was conducted between August of 2010 and January of 2012, with a follow-up conducted between January of 2013 and December of 2013. Subjects were asked about the status of their dental health, including the number of natural teeth that they currently possessed. Higher-level functional capacity was assessed using the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC), with covariates including health, and health behavior variables that might be related to the TMIG-IC.

Of the respondents, 62,333 were included in the final analysis, with a median follow-up of 707 days. In the adjusted analysis, a multiple linear regression model found a dose response association between tooth loss and decline in TMIG-IC scores.

Conclusion: This large, population-based, prospective cohort study indicates a dose response association between tooth loss and a decline in higher-level functional capacity over two years.

Sato, Y., et al. Tooth Loss and Declining Functional Capacity: A Prospective Cohort Study from the Japan Gerontological Evaluation Study. **J Am Geriatr Soc**. 2016, November; 64(11): 2336-2342.

PRECUT KINESIOLOGY TAPE FOR SUBACROMIAL IMPINGEMENT

Subacromial impingement is among the most frequently diagnosed shoulder disorders in adults, with its lifetime prevalence estimated to be as high as 36%. While the initial management is most often with physical/exercise therapy, some studies have suggested that kinesiology tape may be effective. This prospective study examined the effectiveness of precut kinesiology tape as

compared with that of nonsteroidal anti-inflammatory drugs for reducing shoulder pain among patients with subacromial impingement.

This prospective, parallel group, randomized, controlled trial included patients with a primary complaint of shoulder pain, further diagnosed with subacromial impingement syndrome. The subjects were randomized to receive precut kinesiology tape and exercise (K), Naprosyn 500 mg twice daily and exercise (N), or exercise alone(E) for a total of four sessions over two weeks. The primary outcome measure was the numeric pain rating scale (NPRS), with secondary measures including the Simple Shoulder Test (SST) and the Constant Score.

Of the 100 individuals who completed the study, all three groups had a significant decrease in pain by all measures. Between group differences on all outcome measures were not statistically significant or clinically meaningful.

Conclusion: This study of patients with subacromial impingement who underwent exercise therapy found no clinically meaningful difference in outcomes between patients who received additional treatment with Naprosyn or precut kinesioolgy tape.

Devereaux, M., et al. Short-Term Effectiveness of Precut Kinesiology Tape Versus an NSAID as Adjuvant Treatment to Exercise for Subacromial Impingement: A Randomized, Controlled Trial. **Clin J Sports Med.** 2016, January; 26(1): 24-32.

PHARMACOTHERAPIES FOR FRACTURE PREVENTION AFTER GLUCOCORTICOID USE

Oral glucocorticoids are crucial for the management of chronic inflammatory and autoimmune diseases. However, the use of oral glucocorticoids is a common cause of iatrogenic osteoporotic fractures. This study assessed the efficacy of different interventions for the prevention of osteoporosis among glucocorticoid users.

Data were reviewed from published data through March of 2015. Eligible studies were double-blinded, randomized, controlled trials including patients with continuous oral glucocorticoid use during the study timeframe, with a follow-up of at least six months.

The studies selected for analysis included a total of 3,286 patients with 12 agents examined, including placebo, calcium, calcium plus vitamin D, alendronate, etidronate, ibandronate, risedronate, zoledronic acid, calcitonin, raloxifene, denosumab, and teriparatide. The mean glucocorticoid dose ranged from five to 25 mg per day, with a duration ranging from six to 102 months.

Those treated with etidronate, risedronate and teriparatide had reduced vertebral fractures, although no studies were found to have significant effects for the treatment of non-vertebral fractures. Teriparatide was ranked as the best for preventing vertebral and nonvertebral fractures.

Conclusion: This meta-analysis of studies reviewing the efficacy of pharmacotherapies for preventing fractures among glucocorticosteroid effective in preventing osteoporotic fractures.

Amiche, M., et al. Efficacy of Osteoporosis Pharmacotherapies in Preventing Fracture among Oral Glucocorticoid Users: A Network Meta-Analysis. **Osteoporosis Intern.**DOI 10.1007/s00198-015-3476-4.

ULTRASOUND GUIDANCE FOR SUBACROMIAL INJECTIONS

Subacromial impingement is one of the most common causes of shoulder pain in adults, with corticosteroid injections one of the most common management tools for this condition. Ultrasound (US) guidance has been recommended for these injections due to the increased accuracy provided by its use. This study compared the clinical effectiveness of US-guided subacromial injections with that of blind subacromial injections.

This prospective, double-blind, randomized, controlled trial included 51 patients with a diagnosis of subacromial impingement with 28 shoulders undergoing US-guided injections and 28 receiving a landmark guided injection. Examiners held blind to group assignment performed clinical evaluations before and after the procedures.

Both groups realized significant improvement at week six in visual analog scale scores for pain with overhead activities, decreasing from 59 to 33 in the US group ($p<0.001$), and from 63 to 39 in the landmark guided group ($p<0.001$). American Shoulder and Elbow Surgeons (ASES) scores improved from 57 to 68 at week six in the US group ($p<0.01$) and from 54 to 65 in the landmark guided group ($p<0.01$). No significant difference was seen between groups in either measurement.

Conclusion: This study found no significant difference in clinical outcomes for ultrasound guided versus landmark guided subacromial injections for the treatment of subacromial impingement syndrome.

Cole, B., et al. Ultrasound-Guided versus Blind Subacromial Corticosteroid Injections for Subacromial Impingement Syndrome. Randomized, Double-Blind, Clinical Trial. **Am J Sports Med**. 2016, March; 44(3): 702-707.

SHORT-TERM, LOW INTENSITY, BLOOD FLOW RESTRICTED INTERVAL TRAINING

While research has demonstrated that both strength training and aerobic fitness training contribute significantly to health, there is interest in identifying efficient training methods which can simultaneously improve both cardiovascular and neuromuscular performance. Given the research concerning blood flow restricted (BFR) training, this study was designed to determine the aerobic and strengthening effects of intermittent, BFR exercise.

Thirty-seven adults, with an average age of 23.8 years, were randomly assigned to one of four training groups: high intensity (HIT) interval training, low intensity interval training with BFR, low intensity interval training without BFR or HIT interval training with BFR (every session performed 50% as BFR and 50% as HIT). At baseline and after four weeks of training (three sessions per week), subjects were assessed for maximal

oxygen uptake, maximal power output, onset blood lactate accumulation (OBLA) and muscle strength. The training power was 30% of P_{Max} for low and BFR training groups, and began with 110% in the HIT group. The BFR group wore pressure cuff belts inflated to 140 mmHg, progressing by 20 mmHg after three complete sessions up to 200 mmHg in the last session.

After 12 sessions, low intensity interval BFR training resulted in significant improvements in all selected variables, including $VO2_{Max}$, P_{Max}, OBLA and muscle strength. Those in the HIT and BFR + HIT training groups only produced improvements in aerobic variables, although HIT provided a higher effect size compared with BFR and ~~BFR+HIT~~ training. The low-intensity interval training on its own without occlusion (LOW) was not sufficient to improve VO_{2max}, P_{max} or muscular strength, but did improve OBLA.

Conclusion: This study demonstrated the advantage of short- term, low intensity, interval blood flow restricted training as a method to concurrently improve aerobic parameters and muscle strength.

Oliveira, M., et al. Short-Term, Low Intensity, Blood Flow Restricted Interval Training Improves Both Aerobic Fitness and Muscle Strength. **Scand J Med Sci Sports**. 2016, September; 26(9): 1017-1025.

ANTI-IL-17 THERAPY FOR RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a chronic, autoimmune disease which causes synovitis and cartilage damage. The recent identification of a subset of CD4 + T helper cells has expanded the target of therapy for this disease. As IL-17 is a pro-inflammatory cytokine thought to be involved in both the induction and expansion of the cytokine cascade in (RA), this systemic review and meta- analysis was designed to better understand the effectiveness of anti- IL-17 agents for the treatment of RA.

This literature search included multiple databases reviewed through September of 2015 for studies involving adult patients with RA, randomly selected for treatment with anti-IL-17 therapy compared with placebo. The efficacy outcomes were measured with ACR20/50/70 response to anti-IL-17 therapy.

Of the 244 citations discovered, seven were chosen for full text review, with these studies involving 1,226 patients. Combining these results, anti-IL-17 agents were found to be more effective than placebo in achieving ACR 20 response ($p = 0.006$), as well as ACR 50 response ($p=0.005$). Compared with placebo, treatment with anti-IL agents did not increase the risk of adverse events.

Conclusion: This literature review and meta-analysis of randomized, controlled trials found that, for patients with rheumatoid arthritis, anti-IL-17 treatment is effective, without an increase in the risk of serious, adverse events.

Kunwar, S., et al. Anti-IL-17 Therapy in Treatment of Rheumatoid Arthritis: a Systematic Literature Review and Meta-Analysis of Randomized, Controlled Trials. **Rheumatol Int**. 2016, August; 36 (8):1065-1075.

CHANGE IN BONE MINERAL DENSITY AS AN INDICATOR OF ANTI-FRACTURE EFFECT OF INTERVENTION

Osteoporosis related fractures result in a significant individual and societal burden. This diagnosis is usually based on finding low bone mineral density (BMD) using dual energy x-ray absorptiometry (DXA). This study assessed the effectiveness of repeated BMD testing in routine clinical practice as a predictor of treatment related fracture risk.

Since 1997, routine DXA baseline screening has been completed for women in Manitoba, Canada, at the age of 65 years, as well as younger women with additional risk factors. This program's recommended interval for follow-up is three years for most patients and at least five years for those reported as low risk. From this database, women 40 years or older were identified, each of whom had undergone at least one follow-up examination. Using a linkage with a province-wide retail pharmacy network, women were identified who had not been receiving osteoporosis treatment during the year before baseline testing, who had then initiated. The DXA scans were reviewed to determine whether subsequent scans revealed stable, decreased or increased BMD. Incident fractures were recorded and compared to the DXA data.

The final sample were 6,629 women, with an average age of 64.3 years at baseline. Of these, 57.2% met the BMD criteria for osteoporosis at one or more sites. Biphosphonates were prescribed in 84.9% of the women. The mean interval between the first and second BMD tests was 4.5 years. For the total hip, a detectable increase was seen in 30.4% of the women and a detectable decrease in 18.8%.

As compared with stable total hip BMD, a decrease in total hip BMD was associated with a greater risk of fracture ($p < 0.001$), while an increase was associated with lower risk of fracture ($p = 0.004$). A one standard deviation increase in total hip BMD was associated with 19% relative reduction in the fracture hazard rate.

Conclusion: This Canadian study found that treatment related increases in total hip BMD are associated with a reduction of fracture risk, while decreases in BMD are associated with an increased risk of fracture.

Leslie, W., et al. Change in Bone Mineral Density Is an Indicator of Treatment-Related Anti-Fracture Effect in Routine Clinical Practice. **Ann Int Med**. 2016 doi:10.7326/ M15- 2937.

CONTRALATERAL FUNCTIONAL ELECTRICAL STIMULATION IN CHRONIC HEMIPARESIS

Data suggest that cyclic neuromuscular electrical stimulation (cNMES) of the paretic wrist and finger extensors can improve upper extremity function in patients with subacute and chronic stroke. Contralateral controlled functional electrical stimulation (CCFES) is a new modality that enables the patient to actively open the paretic hand. The patient controls the stimulus in real-time by opening and closing the unaffected hand. This

study compared the efficacy of CCFES to that of cNMES.

This parallel group study included patients at least six months out from a hemorrhagic or ischemic stroke, each of whom had unilateral finger extensor paresis. For each participant in the CCFES group, surface electrodes were positioned over the forearm finger and thumb extensors to produce hand opening. Using electrodes, pulses of electric current with a frequency of 35 Hz and amplitude of 40 mA were applied. The stimulus was programmed to increase the pulse duration for each electrode in proportion to the amount of opening of an instrumented glove worn on the contralateral nonparetic hand. The cNMES group was treated with the stimulator automatically and repetitively applying stimulus. A total of 20 sessions of therapist-guided, and 10 sessions of self-administered therapy were administered at 60 minutes per session over 12 weeks. The primary outcome measure was the Box and Block Test, a measure of manual dexterity.

During the study, 72 patients completed the treatment. By six months, both groups had realized significant improvement in BBT scores, with the gain significantly greater in the CCFES group than in the cNMES group (p=0.045). Both groups improved on the upper extremity Fugl-Meyer, with no significant difference between groups. Those with the greatest gains were less than two years post-stroke.

Conclusion: This study of patients with chronic, moderate to severe hand impairment after stroke found that 12 weeks of CCFES therapy improves manual dexterity more than does an equivalent dose of cNMES.

Knutson, J., et al. Contralaterally Controlled Functional Electrical Stimulation Improves Hand Dexterity in Chronic Hemiparesis. A Randomized Trial. **Stroke.** 2016; 47:00-00. DOI: 10.1161/ STROKEAHA.116.013791.

***Musculoskeletal in Review* (*MSK*) is produced by physicians specializing in musculoskeletal and neurological medicine, with the cooperation and assistance of 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. 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.

***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