

MUSCULOSKELETAL

IN REVIEW

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Volume 1, Number 1

Published by Physicians Specializing In
Musculoskeletal Medicine

January 5, 2014

ARTHROSCOPIC PARTIAL MENISCECTOMY VERSUS SHAM SURGERY

Arthroscopic partial meniscectomy is the most common orthopedic procedure performed in the United States. A recent, randomized trial demonstrated that this surgery, combined with physical therapy, provides no better relief than does physical therapy alone. This multicenter, randomized, double-blind, sham controlled trial was designed to better understand the efficacy of arthroscopic partial meniscectomy for patients with a degenerative tear of the medial meniscus.

Patients 35 to 65 years of age were enrolled who had knee pain for at least three months that was unresponsive to conventional conservative treatment. All had clinical findings consistent with a tear of the medial meniscus. Arthroscopy examination was first performed in all patients for a visual assessment of the meniscus. The patients were then randomized to receive either arthroscopic partial meniscectomy or sham surgery. Assessments were obtained at baseline and at two, six and 12 months after surgery. The primary outcome measures included knee pain after exercise, the Lysholm knee score, and the Western Ontario Meniscal Evaluation Tool, as assessed at 12 months after surgery.

Of the 146 patients undergoing randomization, 70 underwent partial meniscectomy and 76 underwent sham surgery. Significant improvement from baseline to 12 months was seen on the primary outcome measures in both groups. However, no significant differences occurred between the groups in the primary outcome measures. In addition, no significant group differences were seen in any of the secondary outcome measures nor in the frequency of the need for subsequent knee surgery or serious adverse events.

Conclusion: This randomized, sham controlled study of patients with degenerative medial meniscal tears found that arthroscopic partial meniscectomy is not superior to sham surgery for relieving pain or improving function.

Sihvonen, R., et al. Arthroscopic Partial Meniscectomy versus Sham Surgery for a Degenerative Meniscal Tear. *N Eng J Med.* 2013, December 26; 369(6): 2515–2524.

BETROOT JUICE AND ALTITUDE CYCLING PERFORMANCE

Dietary nitrate supplementation has been shown to reduce systolic blood pressure, attenuate the oxygen demand of submaximal exercise and improve cycling, running and rowing performance. This study investigated the effects of a single dose of nitrate rich beetroot (BR) juice on the oxygen cost, peripheral oxygen saturation and time trial performance in simulated moderate altitude conditions.

Nine competitive cyclists, all training at least three sessions per week, were studied. All were tested at baseline for determination of $V\cdot O_{2peak}$ and maximum work rate WR_{max} in a simulated altitude of approximately 2,500 m (15% O₂). The participants then underwent four separate performance trials at 60% WR_{max} and a 16.1 km timed trial. Second and third trials were completed after ingestion of either 70 mL of BR juice or a nitrate depleted BR placebo.

Systolic blood pressure was reduced more after BR juice ingestion than after placebo ingestion ($p=0.041$). $V\cdot O_2$ during steady state exercise was lower in the BR juice trial than in the placebo trial ($p=0.049$). $V\cdot O_2$ was significantly reduced in both the 12 minute and 15 minute intervals. Time trial performance improved by 2.9% in the BR juice group compared with baseline ($p=0.006$), improving

significantly more in the treatment group than in the placebo group ($p=0.021$).

Conclusion: This study of competitive bicyclists found that a single dose of beetroot juice reduces the oxygen cost of steady-state exercise and enhances time trial performance at simulated altitude.

Muggerridge, D., et al. A Single Dose of Beetroot Juice Enhances Cycling Performance in Simulated Altitude. *Med Sci Sports Exer.* 2014, January; 46(1): 143–150.

BICYCLE TRAINING IN BOYS WITH DUCHENNE MUSCULAR DYSTROPHY

Functional decline in patients with Duchenne muscular dystrophy (DMD) is thought to primarily result from progressive loss of muscle strength and endurance. The resultant decrease in activity leads to secondary deterioration of the musculoskeletal and cardiovascular systems, further accelerating the decline. This trial evaluated whether dynamic exercises could safely counteract the secondary functional decline of patients with DMD.

Subjects were boys between seven and 13 years of age, all diagnosed with DMD. The participants were divided into an intervention group and a control group. The intervention group received assisted bicycle training of the arms and legs for 15 minutes a day, five days a week, for 24 weeks. The control group received the usual care during the same period, followed by the training regimen. Primary outcome measures were the Motor Function Measure (MFM) and the Assisted Six-Minute Cycling Test (A6MCT). Secondary outcome measures included the Pediatric Evaluation of Disability Inventory (PEDI), timed tests (rise from floor, 10-meter run, nine-hole peg test), muscle strength, passive joint range of motion, and quantitative muscle ultrasound (QMUS).

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At follow-up evaluation, the mean, total MFM score remained stable in the intervention group and was significantly decreased in the control group. No differences between the groups were noted in the A6MCT for the legs ($p=0.06$) or the arms ($p=0.71$). Finally, no significant between group differences were found on the secondary outcome measures.

Conclusion: This study of patients with Duchenne muscular dystrophy found that assisted bicycle training can delay functional decline.

Jansen, J., et al. Assisted Bicycle Training Delays Functional Deterioration in Boys with Duchenne Muscular Dystrophy: A Randomized, Controlled Trial "No Use is Disuse". *Neurorehab Neural Repair*. 2013, Nov/Dec; 27(9): 816-827.

BIOLOGIC THERAPY AND FUNCTION IN RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a systemic autoimmune disease causing inflammation and pain, with a potential serious loss of function. In recent years, new biologically engineered medications have been introduced, which either block tumor necrosis factor-A (TNF) or otherwise influence the system. This meta-analysis investigated the magnitude of the benefits of these biologic agents on the functional capacity of

patients diagnosed with RA.

A systematic literature search was performed to identify studies involving adult patients with a diagnosis of RA, treated with biologic agents including abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab or rituximab. The primary outcome measure was the standardized mean difference (SMD) in change from baseline on the Health Assessment Questionnaires (HAQ), comparing biologic and non- biologic disease-modifying anti- rheumatic drugs (nbDMARDs).

Of the studies reviewed, 35, randomized, controlled trials were included, involving 8,733 individuals in the treatment groups and 4,664 in the control groups. Taking all RCTs together, a mean superiority of biologic treatment compared with MTX/nbDMARD treatment was found. On the SMD of the HAQ scale, biologics led to a 0.32 greater improvement in functional capacity in early RA patients who were DMARD naive and to a 0.48 greater improvement in DMARD inadequate responders.

Conclusion: This meta-analysis of studies involving patients with rheumatoid arthritis found that biologics are superior to nbDMARDs, with likely minor differences between them.

Callhoff, 2013; 52(12) Impact Of Biologic Therapy on Functional Status in Patients with Rheumatoid Arthritis—A Meta-Analysis. *J Rheum*. 2013, December; 52(12): 2127-2135.

DIET PATTERNS IN MIDLIFE AND AGING

Maintaining health in an aging population is a major challenge. While literature has demonstrated the role of diet in mortality, there is a relative lack of data concerning the role of dietary patterns and their effect on overall healthy aging. This study examined the association between dietary patterns in midlife and healthy aging.

Data were obtained from the Nurses Health Study, begun in 1976 with a cohort of female nurses, ages 30 to 55 years. In 1980, the participants completed a semi- quantitative food frequency questionnaire, which was repeated in 1984, 1986 and every four years thereafter. Dietary quality was assessed using the Alternative Healthy Eating index-2010 (AHEI-2010), and the Alternate Mediterranean Diet Scores (a-MeDi). Healthy aging was assessed at 15

years' follow-up, defined as survival to 70 years without one of 11 major chronic diseases, no major impairments in cognition, no physical disabilities and intact mental health.

At follow-up, 11% were considered healthy agers and 89% were considered usual agers. Compared with usual agers, healthy agers had a lower prevalence of obesity and tobacco abuse, and exercised more at midlife. Multivariable analysis revealed that greater adherence at midlife to AHEI- 2010 and a-MeDi diets were both strongly associated with greater odds of healthy aging ($p<0.001$ and $p=0.002$ respectively).

Conclusion: This study demonstrates that adherence to better dietary patterns in midlife is associated with better health and function among those surviving to an older age.

Samieri, C., et al. Association between Dietary Patterns at Midlife and Health in Aging. *Ann Intern Med*. 2013, Nov; 159(9): 584-591.

EARLY MORTALITY AFTER HIP FRACTURE REPAIR

Despite improvements in perioperative care, the 30 day mortality rate after hip fracture surgery is estimated to be over 13%. This excess mortality is highest in the immediate period following the fracture, and appears to decrease with time thereafter. This study further assessed the 30-day mortality rate after hip fracture surgery and reviewed the causes and risk factors of early mortality.

Consecutive patients admitted to the authors' institution with a hip fracture between April of 2009 and March of 2010 were included in this study. Primary and secondary causes of death were noted from death certificates and coroners' reports. The records were reviewed to collect data on comorbidities, age, gender, the American Society of Anesthesiologists (ASA) grading, source of admission and pre-injury walking ability. Those undergoing surgery within 48 hours (group 1) were compared with those undergoing surgery later than 48 hours (group 2), a time frame based upon recommendations of the British Orthopedic Association. The overall, 30-day mortality rate was 7.5%. The mortality rate of group 1 was four percent, and that of group 2 was 11% ($p=0.006$). Over two thirds of 30-day mortality occurrences were due to

pneumonia or acute myocardial infarction. In a multivariate analysis, risk factors for early death included time to surgery ($p=0.051$) history of cardiac disease ($p=0.001$) and admission source other than own home ($p=0.001$).

Conclusion: This retrospective study of 467 consecutive individuals undergoing hip fracture surgery found that patients at greater risk of dying within 30 days of surgery are care dependent prior to injury, have a history of cardiovascular disease and have a delay of over 48 hours from admission to surgery.

Khan, M., et al. Predictors of Early Mortality after Hip Fracture Surgery. *Intern Orthop.* 2013, November; 37: 2119-2124.

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FIBROMYALGIA VERSUS SMALL FIBER POLYNEUROPATHY

Fibromyalgia syndrome (FMS) is believed to have a one to five percent prevalence in Western countries. Despite this, the biologic causes of FMS remain poorly understood. As small fiber polyneuropathy (SFPN) is a neurologic cause of chronic, widespread pain, and is often undiagnosed, this study was designed to determine whether some patients diagnosed with FMS have unrecognized SFPN.

The subjects were 27 patients diagnosed with FMS and 30 matched normal controls. All subjects completed the Michigan Neuropathy Screening Instrument (MNSI) and underwent a targeted neurologic examination, which was codified using the Utah Early Neuropathy Scale (UENS). In addition, all completed the Beck Depression Inventory and the Medical Outcomes Study Short Form Health Survey (SF-36). Finally, all underwent nerve neurodiagnostic skin biopsies to assess SFPN, as well as autonomic function testing.

Of the patients with FMS, 41% had skin biopsies diagnostic for SFPN, in contrast to three percent in the control group. Subjects with FMS also scored higher on the MNSI and the UENS than did the controls. No significant difference was seen between groups on autonomic function testing.

Conclusion: This prospective study found that some patients diagnosed with fibromyalgia have symptoms that may be attributable to small fiber polyneuropathy.

Oaklander, A., et al. Objective Evidence that Small Fiber Polyneuropathy Underlies Some

Illnesses Currently Labeled as Fibromyalgia. *Pain.* 2013, November; 154(11): 2310-2316.

JOGGING AFTER TOTAL HIP ARTHROPLASTY

Total hip arthroplasty (THA) is often sought by patients who wish to return to a more active lifestyle. This study investigated the number of patients who participate in jogging after THA, the parameters surrounding this decision, and the short-term clinical and radiographic results of those who chose to jog.

Subjects were patients undergoing THA between January of 2005 and May of 2011. Those who did jog after surgery answered questions regarding jogging frequency, distance, velocity, and symptoms. Those who did not jog were asked to give reasons why they did not participate. The subjects were administered the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) self-assessment questionnaire and the University of California – Los Angeles (UCLA) activity scales. Radiographs were reviewed to identify implant loosening, wear or osteolysis.

Of the 608 patients undergoing surgery, 33 were habitual preoperative joggers and 23 continued after surgery. The mean frequency of postoperative jogging was four times per week, with a mean distance per session of 3.6 km. Joggers had significantly lower mean scores for pain ($p = 0.03$) and physical function ($p = 0.02$) compared with non-joggers. For the postoperative UCLA activity score, joggers had a significantly higher scores ($p < 0.0001$). No joggers showed hardware loosening, abnormal migration or excessive wear at a mean of five years' follow-up. Of the patients who did not participate in post-operative jogging, 511 responded that they had no interest, while 74 reported they had an interest but did not participate. Most of them cited anxiety as the reason.

Conclusion: This study of patients undergoing total hip arthroplasty found that only 3.8% participated in jogging following surgery. No excessive wear was found among joggers at five-year follow-up.

Abe, H., et al. Jogging after Total Hip Arthroplasty. *Amer J Sports Med.* 2014, January; 42(1): 131–137.

LOW BACK PAIN AND ABNORMAL FOOT FUNCTION

While abnormal foot posture has

been proposed as a mechanism for low back pain (LBP), this relationship has not been well studied. This study analyzed data from the Framingham Foot Study cohort to further investigate this relationship.

The Framingham Foot Study cohort was derived from members of the Framingham Study's original cohort, and the Framingham offspring cohort. Participants underwent a physical examination of the foot between 2002 and 2005. Foot posture and function were both assessed using the Matscan system. In addition, LBP was documented with a structured questionnaire. Asymmetry of foot posture and foot function was assessed. Covariates in the analysis included age, sex, weight, smoking status and depressive symptoms.

Of the 3,370 participants, 1,930 had LBP and foot pressure data at the time of the analysis. The mean age of the participants was 64 years, with 55% female. Overall, neither foot posture nor function was associated with increased risk of LBP. However, among women, compared to the normal foot function reference group, those with pronated foot function had an increased likelihood of LBP ($p=0.011$).

Conclusion: This study found an association between foot posture and low back pain, but only among women.

Menz, H, et al. Foot Posture, Foot Function and Low Back Pain: The Framingham Foot Study. *Rheum.* 2013, December; 52(12): 2275-2282

MEDITERRANEAN DIET AND PERIPHERAL ARTERY DISEASE

Adherence to a Mediterranean diet is thought to reduce the risk of myocardial infarction and stroke. Thus, some have hypothesized that this diet could be effective in reducing the risk of peripheral artery disease (PAD). This study explored the association between adherence to a Mediterranean diet and symptomatic PAD.

This randomized, primary prevention trial included men ages 55 to 80 years of age and women 60 to 80 years of age, all without clinical PAD. All had diabetes mellitus or at least three cardiovascular risk factors. The patients were randomized to one of three groups, a Mediterranean diet supplemented with extra virgin olive oil, a

Mediterranean diet supplemented with nuts, or counseling concerning a low-fat diet. All participants received comprehensive dietary education on a quarterly basis. A confirmed diagnosis of PAD in symptomatic patients served as the primary endpoint.

Of the 8,713 eligible candidates, 7,477 were initially randomized. At five-year follow-up, both intervention groups had a lower risk of PAD, as compared to the control group. While the risk of PAD was slightly lower in the olive oil supplementation group than in the nut supplementation group, no significant difference was found between the two Mediterranean diet groups.

Conclusion: This randomized, primary prevention trial targeting individuals with diabetes and/or cardiovascular risk factors, found that a Mediterranean diet can reduce the risk of peripheral artery disease.

Ruiz-Canela, M., et al. Association of Mediterranean Diet with Peripheral Artery Disease: The PREDIMED Randomized Trial. *JAMA.* 2014, January 22/29; 311(4): 415-417.

MEMANTINE AND GAIT SAFETY IN ALZHEIMER'S DISEASE

A limited number of studies have suggested that, among patients with dementia, both memantine and donepezil use may reduce gait variability. This study compared these medications with regard to their ability to affect gait in patients with Alzheimer's disease (AD).

This prospective, nonrandomized, case-control trial included patients with mild to moderate AD and related disorders (ADRD), treated with an acetylcholinesterase inhibitor (donepezil), a NMDA receptor antagonist (memantine), or no medication. All subjects underwent gait analysis, with measurements including the coefficient of variation of stride time and walking speed.

Stride time decreased significantly after medication, with this change due to memantine ($p=0.01$) more than to donepezil ($p=0.084$).

Conclusion: This pilot study of patients with Alzheimer's disease suggests that treatment with memantine may result in improvement in gait, with no such findings seen for those treated with acetylcholinesterase inhibitors.

Beauchet, O., et al. Anti-Dementia Drugs and Changes in Gait: A Pre-Post, Quasi Experimental, Pilot Study. *BMC Neurol.* 2013, 13: 184.

NONSTEROIDAL ANTI-INFLAMMATORY DRUG USE WITH STABLE ATHEROTHROMBOTIC DISEASE

Previous studies have outlined the risk of prescribing nonsteroidal anti-inflammatory drugs (NSAIDs) to patients with a history of myocardial infarction. The American Heart Association update for clinicians has issued a consensus statement concerning the cautious use of these agents in patients with a history of cardiovascular disease. This study further evaluated this risk in patients with stable atherothrombotic disease. Subjects were obtained from the Reduction of Atherothrombosis for Continued Health (REACH) registry, a large, multi-national registry of outpatients with stable atherothrombotic disease. The patients were 45 years of age, all with established atherothrombotic disease or at least three risk factors for

atherothrombotic disease. The use of aspirin and other antiplatelet agents, including NSAIDs, was assessed at the baseline visit, as well as at annual follow-up visits. Cardiovascular outcomes were recorded, including the composite of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke and ischemic hospitalization. The use of medications was compared with subsequent myocardial events.

Of the 44,095 patients in the database, 4,420 used NSAIDs at baseline. Univariate analysis revealed significantly higher rates of cardiovascular death/myocardial infarction/stroke/hospitalization, hospitalization for heart failure and hospitalization for ischemic events among those who used NSAIDs ($p<0.001$ for all). After adjustment, NSAID use was associated with a 1.16 higher risk of cardiac vascular death, myocardial infarction or stroke, and a 1.12 higher risk of cardiovascular death, myocardial infarction, stroke, ischemic hospitalizations. Patients taking NSAIDs also had a higher risk of nonfatal myocardial infarction, nonfatal stroke, heart failure hospitalization and ischemic hospitalization, as compared to

nonusers.

Conclusion: This observational study found that, among patients with stable atherosclerotic disease, the use of NSAIDs is associated with a significantly increased risk of major adverse cardiovascular outcomes.

Kohli, P., et al. NSAID Use and Association with Cardiovascular Outcomes in Patients with Stable Atherothrombotic Disease. *Am J Med.* 2014, January; 127(1): 53-60.

NSAIDS AND DEPRESSION IN OSTEOARTHRITIS

Recent studies have indicated that depression is two to three times more prevalent among patients with osteoarthritis (OA) than among patients without. A recent hypothesis has emerged attributing aspects of depression to chronic systemic inflammation. The association between cytokine release and prostaglandin synthesis and depression has led to an exploration of the benefits of anti-inflammatory agents for the treatment of depression. This study was designed to better understand whether NSAID therapy among patients with OA is associated with reduced depressive symptoms.

length, with subjects at least 40 years of age and diagnosed with symptomatic OA. The participants were randomized to one of three regimens, including ibuprofen, 800 mg three times per day, naproxen, 500 mg twice per day, Celebrex, 200 mg per day or a placebo. All subjects were screened for major depression with the Patient Health Questionnaire-Nine (PHQ-9) at baseline and at six weeks follow-up.

A total of 1,497 patients were included in the analysis. After six weeks of treatment, nine percent of the subjects in the ibuprofen or naproxen group, and nine percent in the Celebrex group, compared to 14% in the placebo group, were classified as depressed. Multivariable regression analysis demonstrated a detectable effect in lowering PHQ-9 scores in the ibuprofen/ naproxen group and Celebrex group ($p=0.039$). Logistic regression analysis revealed a trend toward a treatment effect for those treated with NSAIDs as compared with placebo ($p=0.087$).

Conclusion: This pooled analysis of patients with osteoarthritis found that NSAID

usage may reduce depressive symptoms.

Iyengar, R., et al. NSAIDs Are Associated with Lower Depression Scores in Patients with Osteoarthritis. *Am J Med.* 2013, November; 126 (11): 1017. e11-1017.e18.

NUT CONSUMPTION AND MORTALITY

Observational studies and clinical trials have suggested that nut consumption may have beneficial effects on coronary heart disease. Other studies have noted reductions in various mediators of chronic diseases with nut consumption. This study investigated nut consumption in relation to total mortality.

Data were obtained from two, large, independent cohort studies of nurses and other health professionals. The Nurses Health Study (NHS) is a prospective cohort of 121,700 female nurses from the United States, enrolled in 1976. The Health Professionals Follow-up Study (HPFS) is a cohort of 51,529, male health professionals, enrolled in 1986. For this paper's analysis, the baseline year was defined as the year of the first validated food frequency questionnaire in each study. Dietary intake was measured every two to four years. The primary endpoint was death from any cause. The final analysis included 76,464 women in the NHS and 42,498 men in the HPFS.

During 30 years of follow-up, age-adjusted and multivariate adjusted analyses revealed a significant, inverse association between frequency of nut consumption and total mortality among both men and women. The pooled multivariate hazard ratios for death for those who ate nuts as compared to those who did not were 0.93 for consumption less than once per week, 0.89 for once per week, 0.87 for two to four times per week, 0.85 for five or six times per week and 0.8 for seven or more times per week ($p<0.001$). Multivariate analyses indicated that nut consumption was inversely associated with the risk of most major causes of death in both men and women, including cancer, heart disease and respiratory disease.

Conclusion: This study found a significant, inverse association between the frequency of nut consumption and total mortality

among both men and women.

Bao, Y., et al. Association of Nut Consumption with Total and Cause Specific Mortality. *N Eng J Med.* 2013, November 21; 369(21): 2001-2011.

OBESITY AND LATE AGE SURVIVAL AND MORBIDITY AMONG OLDER WOMEN

As obesity is thought to be a modifiable risk factor for physical disability, this study investigated whether obesity in older women is related to survival to 85 years of age without major disease or disability.

The sample was taken from the Women's Health Initiative observational study and clinical trial programs which studied postmenopausal women 50 to 79 years of age, recruited from 40 U.S. clinical centers. At enrollment, the participants completed questionnaires concerning demographic characteristics, health behaviors and medical history. All patients were measured for body mass index and waist circumference (WC). Major chronic diseases were recorded, with disabilities documented.

A total of 27,532 women lived to 85 years of age. At 85 years of age, 12.0% of healthy-weight women were classified as mobility disabled, while for women in the obese I, II, and III groups at baseline, the proportions were 25.5%, 33.3%, and 34.1%, respectively. Of women with a baseline WC greater than 88 cm 24.8% were mobility disabled compared with 14.2% of women with a baseline WC of 88 cm or less. In addition, the risk of earlier death was higher among obese women than among normal weight women.

Conclusion: This study of women with a baseline age range of 66 to 81 years found that obesity and higher waist circumference are associated with increased risk of mortality and of developing mobility disability by the age of 85 years.

Rillamas-Sun, E., et al. Obesity and Late-Age Survival without Major Disease or Disability in Older Women. *JAMA Intern Med.* 2014, January; 174(1): 98-106.

PHYSICAL ACTIVITY AND ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) is a

common, inflammatory rheumatic disease which causes characteristic inflammatory back pain. Treatment guidelines recommend exercise as important for disease management. This study compared physical activity levels and exercise habits of patients with AS with high disease activity versus those with low disease activity.

This cross-sectional study included patients diagnosed with AS who were 70 years of age or younger. The AS disease activity score (ASDAS) was used to assess disease activity, and the Bath Ankylosing Spondylitis Functional Index (BASFI) was used to assess physical function.

Physical activity was measured with the International Physical Activity Questionnaire-Long. Data were included for 149 patients with AS and 133 controls. Patients with high disease activity had significantly lower energy expenditure than those with low disease activity ($p=0.02$) or controls ($p=0.01$). No differences were found between patients with low disease activity and controls. Patients with high disease activity were less likely to achieve predefined health enhancing physical activity levels than were the low disease activity patients ($p=0.02$). A larger proportion of patients with high disease activity reported participating in swimming ($p=0.04$) and fewer reported participating in hiking ($p=0.02$) as compared to patients with low disease activity.

Conclusion: This study of patients with ankylosing spondylitis activity are less physically active and perform less vigorous activities than those with low disease activity.

Fongen, C., et al. High Disease Activity is Related to Low Levels of Physical Activity in Patients with Ankylosing Spondylitis. *Clin Rheum.* 2013, December; 32(12): 1719-1725.

PROLONGED RELEASE OXYCODONE-NALOXONE FOR RESTLESS LEG SYNDROME

Dopaminergic drugs are recommended as a first-line treatment for restless leg syndrome (RLS). However, some studies have shown that prolonged use of these medications can result in lost efficacy and problems with tolerability. As an off-label use, opioids are thought to be an

effective second line treatment. This study investigated the efficacy of prolonged release oxycodone-naloxone in the treatment of severe RLS.

This 12-week, double-blind, placebo-controlled trial included patients diagnosed with RLS, with at least six months of symptoms. Those in the treatment group received a starting dose of oxycodone 5 mg and naloxone 2.5 mg, twice per day, which could be titrated up to oxycodone 40 mg and naloxone 20 mg. Once stabilized, treatment was maintained for a further six weeks. The primary endpoint was the International Restless Leg Syndrome Study Group Severity Rating Scale, measured as change from baseline to 12 weeks.

A total of 306 patients were included in the randomization, with 154 assigned to a placebo group and 150 assigned to the treatment group. The change in international RLS Study Group Severity Rating Scale sum scores at 12 weeks was significantly greater for the treatment than the placebo group ($p<0.0001$). During the treatment phase, treatment related adverse events were reported by 73% of the treatment group and by 43% of the placebo group.

Conclusion: This study of patients with restless leg syndrome suggests that prolonged release oxycodone-naloxone may be effective in reducing symptoms.

Trenkwalder, C., et al. Prolonged Release Oxycodone-Naloxone for Treatment of Severe Restless Leg Syndrome after Failure of Previous Treatment: A Double-Blind, Randomized, Placebo-Controlled Trial with an Open Label Extension. *Lancet-Neurol.* 2013, December; 12:1141-1150.

QUALITY-OF-LIFE AFTER SCOLIOSIS SURGERY

Scoliosis is often treated surgically when the Cobb's angle exceeds 45° to 50°. The success of this surgery is traditionally measured by radiographic changes, although these changes only weakly predict patient satisfaction. This study was designed to better understand the changes in quality-of-life experienced by patients treated for scoliosis with surgery.

This study included data collected from the Swe-Spine registry, beginning in 1993 with registration

of surgery in the lumbar spine. All patients were diagnosed with idiopathic, congenital or neuromuscular scoliosis. Before surgery the Cobb angles of the primary curves were obtained. In addition, the EuroQol (EQ-5D) and the Scoliosis Research Society 22r instrument (SRS-22r) were answered by the patients after surgery and at one and two years postoperatively.

A total of 211 patients were included. The EQ-5D scores improved at two-year follow-up in the idiopathic group ($p=0.001$), in the congenital group ($p=0.07$) and in the neuromuscular group ($p=0.06$). By examining specific domains, at two years, pain and anxiety scores were improved in all groups. Improvements were also found for all groups in scores on the SRS-22r for pain function and quality of life, with the least improvement noted in the congenital group.

Conclusion: This study of patients undergoing surgery for scoliosis found that pain and quality-of-life significantly improved in those with idiopathic or neuromuscular scoliosis, with the least effect seen in those with congenital scoliosis.

Ersberg, G., et al. Pre-and Postoperative Quality-of-Life in Patients Treated for Scoliosis. *Acta Orthopædica.* 2013, December; 84 (6): 537-543.

REFORMULATION IN EXTENDED-RELEASE OXYCODONE AND ABUSE

Misuse of prescription opioid analgesics is of growing concern. Those who abuse long-acting opioid medications often alter the tablets by crushing, dissolving or chewing the medication to bypass the controlled release delivery system. To counter this problem, the makers of OxyContin reformulated the medication to counter tampering. This study assessed the effect of this reformulation.

Data were obtained from the poison center and drug diversion programs of the Research Abuse Diversion and Addiction Related Surveillance System (RADARS). Data were reviewed for the two years before and the two years after the release of reformulated extended-release OxyContin. Data were reviewed for the number of abuse exposures, therapeutic error exposures and diversion into illegal

markets.

The average extended release opioid (ERO) abuse exposure in the post-reformulated period was 38% less than that of the period prior to the introduction of this medication ($p < 0.001$). The average abuse exposure population rates for the other prescription opioids did not significantly differ during the same time periods. Therapeutic error exposures declined 24% in the general population. The average ERO diversion rate was 53% less than the average rate before the introduction of reformulated ERO.

Conclusion: This study suggests that tamper-resistant extended-release oxycodone may be effective in reducing the misuse of this medication.

Severtson, S., et al. Reduced Abuse, Therapeutic Errors, and Diversion following Reformulation of Extended-Release Oxycodone in 2010. *J Pain*. 2013, October; 14(10): 1122-1130.

SUPRASCAPULAR NERVE BLOCK FOR POST-STROKE SHOULDER PAIN

Population-based studies suggest that approximately one fourth of stroke survivors develop hemiplegic shoulder pain. This pain is associated with reduced functional ability, a higher incidence of depression, interference with rehabilitation and an increased length of hospitalization. This randomized, controlled trial investigated the efficacy of a suprascapular nerve block for the treatment of hemiplegic shoulder pain.

Adult subjects with post-stroke hemiplegic shoulder pain were recruited from acute stroke and rehabilitation wards across Adelaide, South Australia. The patients were randomized to receive either a suprascapular nerve block (1 ml of 40 mg/ml methylprednisolone and 10 ml of 0.5% bupivacaine) or a placebo subcutaneous injection with normal saline. The participants were assessed before randomization and at one, four and 12 weeks post-injection. The primary outcome variable was pain, as measured with a visual analogue scale (VAS).

The reduction in pain was significantly greater in the treatment group than in the normal saline group at weeks one, four and 12 ($p = 0.02$, $p = 0.01$ and $p = 0.02$, respectively). At four weeks, 78% of

the treatment group reported an improvement in symptoms, with 80% of those responders demonstrating at least a 20 mm improvement on a 100 mm VAS. Despite this pain reduction, no significant impact was noted on the secondary outcomes of function and quality of life.

Conclusion: This study of patients with post-stroke shoulder pain found that a suprascapular nerve block can provide significant pain relief in the first year after stroke.

Adey-Wakeling, Z., et al. Suprascapular Nerve Block for Shoulder Pain in the First Year after Stroke: A Randomized, Controlled Trial. *Stroke*. 2013, Nov; 44(11): 3136-3141.

ULTRASOUND TO DIFFERENTIATE BETWEEN POLYNEUROPATHIES

In acquired and inherited peripheral polyneuropathy, ultrasound (US) can detect nerve enlargement. Recently, patterns of enlargement, determined at different locations along the nerve length, have been proposed as a way to characterize types of neuropathy. This US study was designed to describe and compare patterns and degrees of nerve size changes in acquired and inherited demyelinating polyneuropathy. This retrospective study compared US findings of patients with demyelinating Charcot Marie Tooth type 1 (CMT-1), chronic inflammatory demyelinating polyneuropathy (CIDP), Guillain-Barré Syndrome (GBS) and multifocal motor neuropathy (MMN). Images were obtained at four standard sites in one arm for each subject. As nerve sizes can vary by height, measured nerve sizes were translated to a nerve size index (NSI), comparing the measured to the expected nerve size. A nerve with an NSI of above two standard deviations of the mean was considered enlarged. Enlargement patterns were classified as mild, regional or diffuse.

Nerves in both CMT-1 and acquired demyelinating polyneuropathy were larger than those in controls. Nerves were enlarged at one or more sites in 100% of subjects with CMT-1, 80% with CIDP, and 65% with MMN. A diffuse enlargement pattern was more common in CMT-1 than CIDP, GBS, or MMN ($p < 0.001$). In addition nerve enlargement to more

than twice normal size was more common in CMT-1 ($p < 0.001$) than in acquired neuropathies.

Conclusion: This ultrasound study found that median and ulnar enlargement in CMT-1 is nearly always present, and is typically diffuse.

Zaidman, C., et al. Ultrasound of Inherited versus Acquired Demyelinating Polyneuropathies. *J Neur*. 2013, Dec; 260(12): 3115-3121.

ULNAR NERVE MORBIDITY AFTER HUMERAL FRACTURE

Supracondylar humeral fracture is one of the most common elbow fractures in children, representing two to seven percent of all pediatric fractures. The incidence of primary nerve injury in dislocated supracondylar fractures is as high as 20%. This study evaluated the long-term morbidity of the ulnar nerve after a supracondylar humeral fracture.

This retrospective study reviewed a cohort of 91 patients under 16 years of age from two centers in Finland. All subjects were hospitalized with a supracondylar humeral fracture between 1992 and 2000. Half of the patients underwent surgery. These cases were re-examined at follow-up, averaging 12 years after the primary injury.

At 12-year follow-up, seven cases had ulnar nerve symptoms, with four of those demonstrating pure sensory ulnar neuropathy. One case demonstrated diminished control over the muscles innervated by the ulnar nerve. The four cases with ulnar neuropathy had undergone surgery, with three of those initially fixed by wire. All of the cases with secondary ulnar neuropathy presented with diminished axial angles of the elbow, as compared to uninjured side. All with secondary neuropathy had a good result, with no symptoms at three-month follow-up.

Conclusion: This study of patients with pediatric supracondylar humeral fractures found that 4.4% had ulnar neuropathy at 12-year follow-up.

Sinikumpu, J., et al. Ulnar Nerve Morbidity as a Long-term Complication of Pediatric Supracondylar Humeral Fracture.

Musculoskel Surg. 2013, 10.1007/s12306-013-0291-4.

WEIGHT-BEARING AFTER MENISCAL REPAIR

Rehabilitation is an important factor for meniscal healing after surgical repair. However, the optimal rehabilitation regimen has not been previously established. This study investigated the outcome of isolated meniscal repair using either a free or a restricted rehabilitation regimen.

This prospective, randomized, controlled trial included 60 young adults with isolated meniscal injury. All underwent surgical repair and were randomized to either a free rehabilitation group, in which free range of motion and weightbearing were allowed, beginning on the second postoperative day, or to a restricted group, in which range of motion and weight bearing were restricted for six weeks postoperatively. The participants were assessed at three, 12 and 24 months postoperatively with the Knee Osteoarthritis Outcome Score (KOOS) and the Tegner Function Score. The primary outcome variable was surgery failure, as evaluated at repeat arthroscopy, in patients with

continuous symptoms, or recurrence of symptoms within the two-year study.

At 24-month follow-up, nine patients in the free, and ten in the restricted rehabilitation groups had non-healed menisci identified at arthroscopy. At two-year follow-up, KOOS pain scores were 82 in the restricted group and 87 in the free range group, while Tegner scores were 4.1 in the restricted group and 4.5 in the free range group. Neither difference was significant.

Conclusion: This prospective study suggests that free rehabilitation after meniscus repair is safe and does not result in increased failure rates as compared with a weight and range of motion restricted rehabilitation protocol.

Lind, M., et al. Free Rehabilitation Is Safe after Isolated Meniscus Repair: A Prospective, Randomized Trial Comparing Free with Restricted Rehabilitation Regimens. **Am J Sports Med.** 2013, December; 41 (12): 2753-2758.

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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