

# REHAB IN REVIEW

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## BISPHOSPHONATE USE AND IMPLANT SURVIVAL AFTER ARTHROPLASTY

With an increase in the elderly population, the number of individuals undergoing total knee or total hip arthroplasty is increasing. Some randomized, clinical trials have suggested a potential benefit of bisphosphonate treatment for implant survival, although results have been mixed. This study tested whether bisphosphonate use is associated with increased survival of implants after primary arthroplasty.

This British study included data from the United Kingdom's General Practice Research Database. Data included medical prescriptions, clinical events, specialist referrals and hospital admissions from a sample of 6.5 million patients. From among these, the authors identified 41,995 patients who underwent hip arthroplasty (23,269) or knee arthroplasty (18,726). The patients were followed for a maximum of 15 years after surgery with revision rates compared between those who did and those who did not use bisphosphonates.

At five years' follow-up, 1.2% of the participants had a revision surgery, 1.3% for hips and 1.2% for knees. The rate of revision was lower among bisphosphonate users than among non-users. After stratifying for the type of joint replacement, among those using bisphosphonates, the time to revision more than doubled after knee arthroplasty, and increased by 70% after hip arthroplasty as compared to non-users.

**Conclusion:** This study of patients undergoing total hip or total knee arthroplasty demonstrates that the use of bisphosphonates significantly improves the implant survival time.

Prieto-Alhambra, D., et al. Association between Bisphosphonates Use and Implant

Survival after Primary Total Arthroplasty of the Knee or Hip: Population Based, Retrospective Cohort Study. **BMJ.** 2011; 343:d7222.

## RISEDRONATE AND HIP FRACTURES AMONG WOMEN WITH PARKINSON'S DISEASE

Previous studies have demonstrated a high incidence of hip fractures among patients with Parkinson's Disease (PD). Recent studies have shown the effectiveness of once weekly risedronate in women with postmenopausal osteoporosis. This study was designed to determine the effect of once weekly risedronate for the reduction of hip fractures among older women with PD.

Participants were 272 female outpatients diagnosed with PD. These subjects were randomized to receive either risedronate at 17.5 mg once per week or a placebo. The patients were followed for changes in biochemical markers, bone mineral density (BMD) and the incidence of hip fractures for two years.

During the two-year period, hip fractures occurred in 15 patients in the placebo group and three in the treatment group. BMD was enhanced by 3.4% in the treatment group and decreased by 3.2% in the placebo group ( $p=0.001$ ). Serum ionized calcium and urinary D-pyr decreased in the treatment group and increased in the placebo group. Serum parathyroid hormone and 1,25-[OH]<sub>2</sub>D were decreased in the placebo group, with a trend toward increasing in the treatment group.

**Conclusion:** This study demonstrates that once weekly risedronate treatment may reduce the risk of hip fracture among women with Parkinson's disease.

Sato, Y., et al. Once Weekly Risedronate for Prevention of Hip Fracture in Women with Parkinson's

Disease: A Randomized, Controlled Trial. **J Neurol Neurosurg Psychiatry.** 2011, December; 82(11): 1390-1393.

## CHRONIC OPIOID USE PRIOR TO KNEE REPLACEMENT

Osteoarthritis of the knee may ultimately result in total knee arthroplasty (TKA). Before this decision is made, however, many reports recommend that mild analgesics such as acetaminophen be used, followed by nonsteroidal anti-inflammatory drugs and opioids. This study reviewed the outcomes of patients who had been treated chronically with opioids.

This retrospective study included patients who were identified as having undergone a primary TKA to address end-stage degenerative joint disease. Charts were reviewed to identify individuals who had received opioid medications for knee pain for a minimum of six weeks prior to the surgical procedure. These patients were matched with a group who had not been treated with opioids.

Those with a history of opioid medication use had a significantly longer duration of postoperative hospitalization than did non-users ( $p=0.013$ ). A significantly higher number of subjects in the opioid group required additional surgical procedures over the course of the study period for unexplained knee stiffness or pain ( $p < 0.001$ ). In addition, a greater number of patients in the opioid group were referred for specialized management of intractable pain. Clinical outcomes, as measured with the Knee Society objective knee score, were significantly worse in the opioid group ( $p<0.001$ ).

**Conclusion:** This study of patients undergoing a total knee arthroplasty for degenerative joint disease of the knee found that the chronic use of opioid medications

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prior to knee surgery is associated with an increased rate of complications and worse clinical outcome.

Zywiell, M., et al. Chronic Opioid Use Prior to Total Knee Arthroplasty. **J Bone Joint Surg (Am)**. 2011, November 2; 93: 1988-1993.

### **MORTALITY AND MORBIDITY OF LOWERING CHOLESTEROL WITH SIMVASTATIN**

In observational, epidemiological studies, lower blood cholesterol concentrations have been found to be associated with higher rates of particular types of cancer and other non-vascular causes of morbidity and mortality. Some have suggested therefore, that medications that lower low-density lipoprotein cholesterol might produce increases in the rates of cancers and other adverse effects that take longer than five years to emerge. This study further explored this possibility.

Between July of 1994 in May of 1997, 20,536 men and women, ages 40 to 80 years, were randomly allocated to receive 40 mg of simvastatin daily or a matched placebo. Routine follow-up in study clinics occurred at four, eight and 12 months, and then every six months thereafter. Data collected included suspected heart attacks, strokes, vascular procedures, cancers and other serious, adverse events. The mean in-trial follow-up period was 5.3 years, with post-trial follow up of surviving patients continued for an average of 11 years. The primary outcome measure was the first major vascular event, with secondary outcomes including other vascular events and cancers.

During the trial period, a first major vascular event occurred in 21% of the simvastatin group and in 26.4% of the placebo group ( $p < 0.0001$ ). No significant difference was noted in the first year, but reductions of approximately one quarter were seen during each subsequent year. Similar patterns were seen for each component of major vascular events. During the combined in-trial and post-trial periods, no significant differences were noted in the incidence of cancer or in mortality attributed to cancer or nonvascular causes.

**Conclusion:** This randomized trial demonstrated that major vascular

events can be reduced with the use of simvastatin, with no increase in nonvascular events, including cancer.

Heart Protection Study Collaborative Group. Effects on 11-year Mortality and Morbidity of Lowering LDL Cholesterol with Simvastatin for about 5 years in 20,536 high-risk Individuals: A Randomized, Controlled Trial. **Lancet**. 2011, December; 378(9808): 2013-2020.

### **OBESITY AND RECURRENT VASCULAR EVENT RISK**

Obesity has been established as a risk factor for primary stroke. However, obesity has not been associated with poor outcomes among patients with vascular disease. In fact, among patients with known cardiac disease, an "obesity paradox," has been described, whereby a paradoxical decrease in morbidity and mortality has been found with increasing body mass index (BMI). This study assessed whether baseline obesity is associated with recurrent vascular risk after stroke.

Data were obtained from the Prevention Regimen for Effectively Avoiding Second Strokes Trial, including 20,246 patients with a recent stroke. The subjects were divided into three groups, based on BMI. Those categories included obese, defined as a BMI of at least 30, overweight, defined as a BMI of at least 25, and lean, defined as a BMI of less than 25. The primary outcome variable was a recurrent stroke of any type with secondary outcomes including time to recurrent stroke, myocardial infarction or vascular death. The average patient follow-up time was 2.5 years.

A first recurrent stroke occurred in 9.06% of lean patients, 8.82% of overweight patients and 8.89% of obese patients. Secondary outcomes were identified in 14.47% of lean patients, 12.25% of overweight patients and 12.74% of obese patients. The occurrence of a first major vascular event after ischemic stroke was higher in the lean patients when compared to the other two categories.

**Conclusion:** This study of patients with a recent ischemic stroke found that baseline obesity was not an independent predictor of recurrent

stroke risk over 2.5-year follow-up period.

Ovbiagele, B., et al. Obesity and Recurrent Vascular Risk after a Recent Ischemic Stroke. **Stroke**. 2011, December; 42(12): 3397-3402.

### PHYSICAL ACTIVITY AND FUNCTIONAL OUTCOME AFTER STROKE

Meta-analyses have demonstrated a relationship between occupational or leisure time physical activity and the risk of total, ischemic and hemorrhagic stroke. This study investigated the association between physical activity and functional outcome after a stroke.

This prospective cohort study included data analysis from 21,794 men enrolled in the Physician's Health Study. Participants were free of any history of stroke, transient ischemic attack (TIA), myocardial infarction or other major diseases at baseline. Baseline activity levels were defined as vigorous exercise (enough to "work up a sweat") either less than one time per week, once per week, two to four times per week or more than five times per week. Participants were followed for a mean of 20.2 years, with new medical conditions recorded, including stroke and transient ischemic attack. Functional outcomes were obtained from those with confirmed strokes and were assessed with a modified Rankin Scale (mRS).

During the study, 761 TIAs, 1,146 ischemic strokes, 221 hemorrhagic strokes and 11 strokes of unknown type were recorded. Men who exercised at least five times per week had a significantly reduced risk of TIA as compared to those who exercised less than one time per week ( $p < 0.01$ ). Men who exercised two to four times per week had a significantly reduced risk of stroke as compared to those who exercised less than one time per week ( $p < 0.02$ ). In addition, those who exercised at least five times per week had a decrease risk of TIA and milder strokes. The data did not show a strong association between higher levels of physical activity before the stroke and better functional outcome after the stroke.

**Conclusion:** This study demonstrates that, while physical activity has a protective effect against the occurrence of stroke, pre-stroke

activity does not affect functional outcome after the occurrence of a stroke.

Rist, P., et al. Physical Activity and Functional Outcomes from Cerebral Vascular Events in Men. **Stroke**. 2011, December; 42(12): 3352-3356.

### YOGA FOR CHRONIC LOW BACK PAIN

Studies of the effects of exercise treatments for low back pain (LBP) have produced mixed results. Recent evidence suggests that yoga may be an effective treatment of chronic LBP, although these studies have had significant limitations. This investigation further tested the efficacy of yoga for the treatment of chronic LBP.

Patients were obtained from 39 general medical practices. All were 18 to 65 years of age and had a clinical presentation of LBP within the prior 18 months. From these practices and from media recruitment, 313 patients were randomly assigned to either participate in yoga or to receive only usual care. All participants received a back pain education booklet and usual care. The intervention group also received yoga, delivered in 12, 75-minute classes. Home practice sheets were distributed to the class at four intervals over 12 weeks. The yoga program introduced foundational elements of yoga, adapted appropriately for LBP. The subjects were encouraged to practice yoga for 30 minutes per day. The primary outcome variable was back function at three months, assessed with the Roland-Morris Disability Questionnaire (RMDQ). Secondary outcomes included physical/mental health, evaluated using the 12-item Short Form Survey and measures of back pain, self-efficacy and class attendance.

The yoga group had better back function (RMDQ scores) at three, six and 12 months than did the usual care group ( $p = 0.001$ ,  $p = 0.011$  and  $p < 0.007$ , respectively). Pain and general health scores at three, six and 12 months were similar between the two groups. The yoga group had higher scores in pain self-efficacy at three and six months, but not at 12 months. Yoga subjects reported 12 adverse events, with most involving increased pain.

**Conclusion:** This study of patients with chronic low back pain found yoga to be a safe activity that can lead to greater improvement in back function for up to 12 months as compared with usual care.

Tilbrook, H., et al. Yoga for Chronic Low Back Pain. **Ann Intern Med**. 2011, November 1; 155(9): 569-578.

### TAI CHI FOR LOW BACK PAIN

Low back pain (LBP) is one of the most common reasons for presenting to a general practitioner. The majority of nonpharmacologic interventions for LBP have produced disappointing results. Exercise therapy is among the most effective interventions, although the most effective exercise approach remains uncertain. Tai chi has been found to have positive effects on other musculoskeletal disorders. This study investigated the effects of a 10-week tai chi intervention for patients with LBP.

Eighty patients were randomized to either a usual care or a tai chi group. The tai chi group participated in 18, 40 minute sessions over a 10-week period. The primary outcome measure was bothersomeness of pain symptoms, as measured using a numerical rating scale from 0 to 10. Secondary outcomes included pain intensity, assessed with a numeric rating scale, disability assessed with the Roland Morris Disability Questionnaire, and scores on the Pain Disability Index, the Québec Back Pain Disability Scale, and the Patient Specific Functional Scale. Perception of overall recovery was assessed with the 11-point Global Perceived Effect Scale.

Compared to the control group, patients who participated in tai chi reported a 1.7 point decrease in bothersomeness of symptoms. Secondary outcome measures showed similar reductions in pain intensity and disability, as evidenced by a 2.6 point decrease on the Roland Morris Disability Questionnaire and a 6.6 point decrease on the Québec Back Pain Disability Scale.

**Conclusion:** This randomized, controlled trial found that tai chi can be an appropriate, nonpharmacologic therapy for persistent, nonspecific low back pain.

Hall, A., et al. Tai Chi Exercise for Treatment of Pain and Disability in People with Persistent Low Back Pain: A Randomized, Controlled Trial. *Arthritis Care Res.* 2011, November; 1576-1583.

### ADJACENT SEGMENTAL DEGENERATION AFTER SPINAL FUSION

Posterior lumbar interbody fusion (PLIF) is increasingly popular as a treatment for degenerative disorders of the lumbar spine. After such fusions, compensatory and chemical changes have been demonstrated at adjacent segments. Explanations for adjacent segmental degeneration have varied from the natural course of aging, to abnormal intradiscal pressures and excess motion. This study compared risk factors, instrumentation configurations, radiologic findings and clinical outcomes following lumbar spine fusion.

This prospective study included 68 patients scheduled to undergo PLIF for degenerative disease. Baseline and interval postoperative radiological assessments were performed for each patient with a minimum of five years' follow-up. Using established criteria, participants were divided into groups based on the degree of radiographic evidence of adjacent segment degeneration (ASD). The patients were divided into two groups according to progression of L3-L4 degeneration at the final follow-up, with Group A demonstrating no progression and Group B demonstrating progression in degeneration. A visual analogue scale for clinical outcomes and the Oswestry Disability Index were used to assess functional outcomes.

At an average of 39.3 months of follow-up, radiographic evidence for ASD was found in 22% of the patients. The only significant risk factor identified for ASD was preoperative disc degeneration at an adjacent segment. Gender, age at the time of surgery, preoperative diagnosis, length of fusion, instrumentation configuration and alignment were not found to be significant risk factors. No significant relationship was seen between the development of ASD and clinical outcome.

**Conclusion:** This study of patients undergoing lumbar fusion found that the only risk factor for developing adjacent segment degeneration was evidence of preoperative degeneration.

Anandjiwala, J., et al. Adjacent Segment Degeneration after Single-Segment PLIF: The Risk Factor for Degeneration and Its Impact on Clinical Outcomes. *Eur Spine J.* 2011, November; 20: 1951-1960.

### AGMATINE FOR SPINAL CORD INJURY

The failure of regeneration after a spinal cord injury is attributed to non-permissive environmental factors in the adult mammal. These factors include astrocyte derived inhibitory molecules in scar tissue and myelin components of oligodendrocytes that interfere with the regeneration of axons. As agmatine has been found to be neuroprotective in central nervous system injuries, this animal study sought to determine its effects on the sequelae of spinal cord injury.

Subjects were 60 mice, undergoing surgical spinal cord injury, and divided into two groups. One group received agmatine, while a control group received saline five minutes after the transaction, and then daily for four weeks. Half the mice were assessed for survival rate and behavioral outcome, while the other half was assessed for immunohistochemical changes.

At four weeks, the treatment group had a survival rate of 61.5%, as compared to 54.5% in the control group ( $p=0.076$ ). The agmatine-treated mice performed better on the surface righting reflex test by more quickly overturning their bodies, as compared with the saline-treated mice ( $p=0.030$ ). The agmatine-treated mice had an increase in protein expression of BMP-7, reduced scar formation and a decrease in the number of TGF [beta]-2 positive cells after complete transection.

**Conclusion:** This animal study of spinal cord injury found that agmatine can support neuroregeneration by reducing collagen scar formation through a decrease in the expression of TGF [beta]-2 and by increasing the overexpression of BMP-7.

Kim, J., et al. Agmatine-Reduced Collagen Scar Area Accompanied

with Surface Righting Reflex Recovery after Complete Transection Spinal Cord Injury. *Spine.* 2011, December 1; 36(25): 2130-2138.

### CORTICAL AFFERENT INHIBITION AND STROKE RECOVERY

Inhibitory circuits of human cerebral cortex can be measured by several methods. Different receptor subtypes are involved in short interval intracortical inhibition (SICI) and short latency afferent inhibition (SAI). This study investigated SICI and SAI in acute stroke, in order to study the correlation between the level of cortical inhibition and functional outcome at six months.

Sixteen patients with first-ever acute stroke were recruited. Outcome at six months was assessed using a modified Rankin scale. All patients underwent acute assessment using brain magnetic resonance imaging, as well as measurement of active motor threshold and resting motor threshold amplitude of motor-evoked potentials, SICI at 2 ms interstimulus interval and SAI at interstimulus intervals from N20 latency plus two, three and four milliseconds. Data obtained for the patients were compared with those obtained for 13 healthy subjects.

No evidence was found of an association between electrophysiological parameters and stroke severity in the acute phase ( $p>0.05$ ). The affected hemisphere's SAI was significantly reduced in patients, as compared to controls. The SAI correlated with functional outcome at six months ( $p=0.03$ ).

**Conclusion:** This study demonstrates that suppression of afferent inhibition in acute stroke is correlated with recovery at six months.

Lazzaro, V., et al. The Level of Cortical Afferent Inhibition in Acute Stroke Correlates with Long-Term Functional Recovery in Humans. *Stroke;* 2012, January; 43: 250-252.

### ANTIGANGLIOSIDE ANTIBODIES AND AXONAL GUILLAIN-BARRÉ SYNDROME

Guillain-Barré Syndrome (GBS) is an acute, immune mediated polyneuropathy. The two major subtypes of this disorder are acute

inflammatory demyelinating polyneuropathy (AIDP) and acute motor axonal neuropathy (AMAN), an axon subtype. In certain patients, AMAN is caused by molecular mimicry of human gangliosides by the *Campylobacter jejuni* lipooligosaccharide. This study was designed to better understand the relationship between anti-ganglioside antibodies and the GBS electrodiagnosis.

A total of 156 patients with GBS were identified from two cohorts. Clinical and electrophysiological data were identified for each cohort. Based upon results of those studies, patients were classified as having AIDP or AMAN. The participants were further classified as having acute motor and sensory axonal neuropathy (AMSAN) when motor conduction studies showed the AMAN pattern and sensory nerve action potential amplitudes were less than 50% of the lower limit of normal in at least two nerves. In addition, IgG antibodies against gangliosides were measured by ELISA testing.

After combining the two cohorts, 36% of the patients were found to be positive for antiganglioside antibodies. This positivity was significantly associated with electrodiagnosis of AMAN. Those who were seropositive more frequently had a clinical history of antecedent diarrhea and pure motor neuropathy.

**Conclusion:** This study of patients with Guillain-Barré' syndrome found that antiganglioside positive patients predominately have motor polyneuropathy.

Sekiguchi, Y., et al. Antiganglioside Antibodies Are Associated with Axonal Guillain-Barré Syndrome: A Japanese-Italian Collaborative Study. *J Neurol Neurosurg Psychiatry*. 2012, January; 83: 23-28.

### SEIZURE RECURRENCE AFTER DISCONTINUING ANTIPILEPTICS

Approximately 60 to 70% of people with epilepsy enter remission from seizures on antiepileptic drug treatment. This study sought to clarify the risk of seizures after medication withdrawal.

Data were collected by the Medical Research Council Antiepileptic Drug Withdrawal Study, a prospective, multicenter,

randomized study of 1,013 patients with epilepsy, conducted between 1984 and 1989. All participants had a history of two or more definite unprovoked seizures, were taking seizure medication and had been seizure free for at least two years. Two outcomes were examined; the risk of seizure recurrence following drug withdrawal and the risk of seizure following a recurrent seizure followed by a resumption of antiepileptic drug treatment.

The 12-month, recurrent seizure risk immediately following medication withdrawal was 30%. After three months without seizures, this risk dropped to 15%. At three months, after reinstating antiepileptic drug treatment following a seizure recurrence, the 12-month risk of seizure was 26%. In this group, this risk dropped to 18% after six months without seizure activity.

**Conclusion:** This study of patients with a history of unprovoked seizures found that the risk of seizure recurrence after medication withdrawal is 30%, with this risk cut in half if the patient remains seizure free for three months.

Bonnett, L., et al. Seizure Recurrence after Antiepileptic Drug Withdrawal and the Implications for Driving: Further Results from the MRC Antiepileptic Drug Withdrawal Study and a Systematic Review. *J Neurol Neurosurg Psychiatry*. 2011, December; 82(12): 1328-1333.

### EPILEPSY AFTER SUBARACHNOID HEMORRHAGE

Recent studies have suggested that the incidence of late epilepsy, developing the year after surgical treatment for subarachnoid hemorrhage (SAH), is approximately five to seven percent. This study sought to better understand the influence of treatment type, the time of onset of seizures after treatment and the effect of interventions on the risk of late onset seizures.

The subjects were 2,143 patients with ruptured intracranial aneurysms, randomly assigned to treatment by neurosurgical clip occlusion or endovascular coil embolization. The occurrence of seizures was recorded at hospital discharge, at two months, at one year, and then annually thereafter. Data collected included history of seizures, antiepileptic

medications, time and nature of seizures and complications of medications.

The mean follow-up time was nine years. Of the 2,143 patients, 235 (10.9%) reported seizures, with 8.3% in the endovascular group and 13.6% in the neurosurgical clip group ( $p < 0.014$ ). The cumulative risks of first seizure at one, two and five years were 3.3% and 5.2%, 4.5% and 7.3%, 6.4% and 9.6% in the endovascular and neurosurgical groups, respectively. The risk of seizure was significantly greater in the neurosurgical group at two years and at up to 14 years ( $p = 0.005$  and  $p = 0.013$ , respectively).

**Conclusion:** This study of patients with subarachnoid hemorrhage demonstrates that the risk of seizures after coil embolization is significantly lower than that after neurosurgical clip occlusion.

Hart, Y., et al. Epilepsy after Subarachnoid Hemorrhage: The Frequency of Seizures after Clip Occlusion or Coil Embolization of a Ruptured Cerebral Aneurysm. *J Neurosurg*. 2011, December; 115(6): 1159-1168.

### CRANIOCERVICAL ARTERIAL DISSECTION AFTER CHIROPRACTIC MANIPULATION

Chiropractic manipulation of the cervical spine can injure vessels of the head and neck, producing stroke and other significant injuries. Studies have suggested that their incidence ranges between 1 in 100,000 and 1 in 6,000,000 manipulations. In these cases, stroke is produced by propagation of a thrombus from a dissected arterial segment, or by severe dissection induced stenosis and secondary ischemia. This study was designed to describe the patterns of injury and their management.

The authors reviewed a prospectively maintained endovascular database, in order to identify patients who experienced craniocervical arterial dissections after chiropractic manipulation. A history of chiropractic cervical manipulation was obtained through interview with either the patient or a family member. The interval of symptomatic presentation, the location of the injured arterial segment, neurological symptoms,

treatments and outcomes were recorded.

The authors identified thirteen patients who presented within hours to days of chiropractic manipulation of the cervical spine. The longest interval between manipulation and presentation was 14 days. Of these patients, 12 presented with acute neurological deficits or complaints. The remaining patient complained of only neck and suboccipital pain. Twelve of the patients demonstrated vertebral artery dissections, most often involving the V2 and V3 segments. Six were treated using endovascular interventions. Three underwent an emergency craniotomy for cerebellar decompression. At presentation, 10 of the 13 patients demonstrated infarctions on diffusion weighted imaging. Of those, three were left with debilitating neurological deficits, and one died.

**Conclusion:** This study identified patients with injuries to the vertebral and carotid arteries after chiropractic manipulation of the cervical spine. In this series, 31% were permanently disabled or died.

Albuquerque, F., et al. Craniocervical Arterial Dissections as Sequelae of Chiropractic Manipulation: Patterns of Injury and Management. *J Neurosurg.* 2011; 115(6), December: 1197-1205.

#### **BLOOD BIOMARKERS TO PREDICT OUTCOME AFTER STROKE**

Many studies have examined the association between blood marker levels and poor outcome after stroke. This study sought to determine whether such markers can improve outcome prediction after stroke.

Between March of 2007 and February of 2009, consecutive patients with ischemic stroke or transient ischemic attack were eligible for inclusion. Each subject underwent a blood draw to measure markers of inflammation, thrombosis, cardiac strain and neural and glial damage. The associations between these values were compared to outcomes at three months, with outcome measured using the modified Rankin's score.

Of the 270 patients recruited, 40 demonstrated symptom resolution within 24 hours. At three months,

11% had died and 42% had a poor outcome. The risk of poor outcome doubled per decade of patient's age. Although higher levels of most of the markers were positively associated with poor outcome, after adjustment for age and the baseline NIHSS, the only associations that reached statistical significance were IL-6 and NT pro-BNP. However, neither of these markers had sufficient predictive power to be of clinical use to predict poor outcome.

**Conclusion:** This study of patients with acute stroke found that, among markers of inflammation, thrombosis, cardiac strain and cerebral damage, interleukin six and NT pro-BNP were correlated with poorer outcome. However, these factors were not found to be helpful in clinically predicting poor outcome.

Whiteley, W., et al. The Use of Blood Biomarkers to Predict Poor Outcome after Acute Transient Ischemic Attack or Ischemic Stroke. *Stroke.* 2012, January; 43: 86-91.

#### **EFFECTS OF HORMONAL CHANGES AND ORAL CONTRACEPTIVE USE ON MUSCLE PROPERTIES**

Prior research suggests that lower extremity stiffness and hamstring neuromuscular control may be influenced by hormonal changes that occur across the menstrual cycle. This study investigated the effect of oral contraceptives on lower extremity stiffness and hamstring neuromechanics across the menstrual cycle.

This study included 30, physically active women, who were randomized to receive either monophasic oral contraceptives or a placebo. In the placebo group, testing occurred three to five days after self-reported menstruation, corresponding to low levels of estrogen, and within two to four days after ovulation, corresponding to high levels of estrogen. The contraception group testing occurred within the days associated with pill numbers three to five (placebo pills) and 15 to 17 (ovulation). The subjects performed three separate tests to assess lower extremity stiffness, hamstring stiffness and hamstring neuromechanical function, with

comparisons made within and between groups.

No differences in hamstring or lower extremity stiffness were observed across the menstrual cycle or between the two groups. In addition, no changes were noted in the hamstring neuromechanics, including electromechanical delay, rate of force production and time to 50% peak force.

**Conclusion:** This study suggests that muscle properties are not influenced by hormone fluctuations across the menstrual cycle or by oral contraceptive use.

Bell, D., et al. The Effects of Oral Contraceptive Use on Muscle Stiffness across the Menstrual Cycle. *Clinical J Sports Med.* 2011, November; 21(6): 467-473.

#### **ETANERCEPT IN JUVENILE ARTHRITIS**

Since the introduction of biologic therapies such as etanercept, the treatment of juvenile idiopathic arthritis (JIA) has changed significantly. Etanercept is a tumor necrosis factor alpha antagonist which was approved 10 years ago by the Federal Drug Administration and the European Medicines Agency for the treatment of JIA. This study evaluated disease activity after etanercept initiation and identified baseline characteristics associated with treatment response.

This prospective study included 262 biologically naïve patients who had started etanercept prior to October of 2009. Patient and disease characteristics were collected at baseline, and then at three months and yearly thereafter. Response to therapy was assessed as excellent, (defined as an active disease or discontinuation due to disease remission), intermediate (defined as more than a 50% improvement from baseline) or poor (defined as less than 50% improvement). The subjects were evaluated for at least 15 months after the initiation of the medication.

Among patients with JRI who initiated treatment with etanercept, one third achieved an excellent response, one third an intermediate response and one third a poor response. Those with an excellent response tended to have a low

baseline disability score, DMARD use prior to the initiation of etanercept and a younger age at onset of disease. A poor response was associated with systemic JIA and female gender.

**Conclusion:** This study of patients with juvenile idiopathic arthritis found that etanercept treatment may have variable effects, based on the baseline characteristics of the patient.

Otten, M., et al. Factors Associated with Treatment Response to Etanercept in Juvenile Idiopathic Arthritis. *JAMA*. 2011, December 7; 306(21): 1671-1678.

### REHABILITATION DURATION AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

The anterior cruciate ligament (ACL) is one of the most commonly injured ligaments of the knee. However, little is known about the amount of activity that promotes rehabilitation without risking an elongation of the graft or producing abnormal laxity of the knee. This study sought to determine the effect of accelerated rehabilitation on knee laxity and outcome after ACL reconstruction.

This prospective trial included 42 patients undergoing bone patella tendon bone reconstruction after an ACL tear. The subjects were randomized to receive either accelerated rehabilitation over 19 weeks or standard rehabilitation over 32 weeks. Crutch use was discontinued on day eight in the accelerated group and on day 22 in the non-accelerated group. The exercises performed by the two groups were identical. During the program, the patients visited the rehabilitation center three times per week to perform exercises under supervision. The participants were evaluated preoperatively and then at three, six, 12 and 24 months for knee laxity and functional recovery.

Patients in both arms of the study had similar increases in laxity in all planes tested at two-year follow-up. No significant differences were seen between the treatments, with no treatment-time interactions for the Knee Injury and Osteoarthritis Outcome Scores, outcomes of pain, symptoms, activities of daily living,

sports and recreation participation or knee-related quality of life .

**Conclusion:** This study of patients undergoing anterior cruciate ligament reconstruction found that rehabilitation over 19 weeks provided a long-term outcome equal to that of 32 weeks of rehabilitation.

Benyonn, B., et al. Accelerated versus Non-Accelerated Rehabilitation after Anterior Cruciate Ligament Reconstruction. A Prospective, Randomized, Double-Blind Investigation of Evaluating Knee Joint Laxity Using Roentgen Stereo Stereophotogrammetric Analysis. *Am J Sports Med*. 2011, December; 39 (12): 2536-2548.

### RISK FACTORS FOR DANCE INJURY

The practice of dance often requires adopting non-anatomic positions that place stress on the musculoskeletal system. Studies concerning dance have reported a high frequency of musculoskeletal injuries. Different dance styles produce different musculoskeletal stresses. This study sought to identify the characteristics of injuries among dancers and to investigate risk factors for injury.

The study included 500 dancers participating in the 26th Festival of Joinville in 2008. In this retrospective investigation, data were collected through interviews addressing the occurrence of injuries and respective characteristics over the prior 12 months. Personal data collected included gender, age, weight, height, duration of practice (in years), number of practices (hours per week), specific technique (classical ballet, jazz, contemporary, tap, street dance or folk dance) and body mass index. A dance injury was considered any pain or musculoskeletal condition resulting from training and competition sufficient to alter the dancer's normal training routine.

Among the dancers, 377 (75%) reported at least one injury. Jazz/contemporary dancers who suffered injuries had higher age and height values. Jazz/contemporary dancers who suffered injuries had higher age and weight values. Classical ballet dancers who suffered injury had higher mean height values, and tap/folk dancers who suffered injury had

lower height values. The most affected anatomic regions were the ankle/foot and thigh/leg in classical ballet, the thigh/leg in jazz/contemporary dance and the knee in tap/folk dance. Dynamic overload and excessive use were the most often reported causal mechanisms.

**Conclusion:** This study of dancers demonstrates a high risk of injury per participant, with the most affected sites including the ankle/foot and the thigh/leg.

Campoy, F., et al. Investigation of Risk Factors and Characteristics of Dance Injuries. *Clin J Sport Med*. 2011, November ; 21(6): 493-498.

### AEROBIC TRAINING AND GLUCOSE TOLERANCE IN PRE-DIABETICS

Regular physical activity and the adoption of other healthy lifestyle habits may prevent or delay the onset of type II diabetes mellitus. Several large scale prospective trials have examined the role of physical activity in preventing or delaying the transition to overt diabetes. This study was designed to determine whether training adaptations in the glucose and insulin response to an oral glucose tolerance test(OGTT) differ between prediabetic and normoglycemic patients.

The subjects were sedentary, normotensive or hypertension-controlled, nondiabetic, nonsmoking men and women ages 50 to 75 years. Analysis of fasting OGTT plasma data from the participants who originally completed the screening, dietary stabilization, and baseline testing phases of the study identified a total of 116 normoglycemic subjects and 47 who were able to complete the study. None had a prior history of cardiovascular disease, use of lipid or glucose-lowering medications and all had a body mass index of <37 kg/m<sup>2</sup>. All participants completed a six-week American Heart Association dietary stabilization program. Glucose and insulin responses to an oral glucose tolerance test were assessed for all subjects. These tests were completed before and after a six-month, standardized endurance exercise training program. Exercise training was gradually increased in frequency and intensity over the course of the study.

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Prediabetic subjects experienced a greater training-induced change in BMI than did normoglycemic subjects ( $p < 0.05$ ). Prediabetic subjects had greater insulin and glucose responses than did control subjects, both before and after training. The training induced changes in response to the glucose tolerance test at zero, 60, 90 and 120 minutes were greater in the prediabetic than in the normoglycemic subjects. These changes were not sufficient on average to normalize the baseline difference between the two groups.

**Conclusion:** This study demonstrates that aerobic training produces greater changes in glucose tolerance test results among prediabetic than in normoglycemic patients. However, this training does not completely reverse the difference between the two groups.

Jenkins, N., et al. Aerobic Training Effects on Glucose Tolerance in Prediabetic and Normoglycemic Humans. *Med Sci Sports Exer.* 2011, December; 43(12): 2231-2240.

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