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PHYSICAL ACTIVITY AND MENTAL HEALTH

Mental illness is a known risk factor for mortality and morbidity, and is becoming an increasing health concern. Previous studies have shown an inverse association between physical activity and incident depression, although others have produced conflicting results. This study sought to examine the association of different types and amounts of physical activity with current mental health.

The Scottish Health Survey is a periodic survey that draws a nationally representative sample from the general population. Data for this study were collected in two household visits. During the first visit, interviewers collected self-reported data and measured height and weight. In the second visit, nurses inquired about medical history. Risk estimates per category of physical activity per week were calculated using regression models.

A total of 3,200 participants with psychological distress were identified. Any form of daily physical activity was associated with a lower risk of psychological distress. Different types of activities, including housework, gardening, walking and sports, were all associated with lower odds of psychological distress. The strongest relationship was noted with sports.

Conclusion: This study of Scottish households demonstrates an inverse dose response relationship between physical activity and mental health that is evident with as little as 20 minutes of activity per week

Hamer, M., et al. Dose Response Relationship between Physical Activity and Mental Health: The Scottish Health Survey. **British Journal of Sports Medicine** 2009, December; 43: 1111-1114.

EXERCISE VERSUS BODY WEIGHT AND HEALTH

The obesity epidemic throughout the world is now well acknowledged. It is thought that preventing weight gain can contribute to improved health. Exercise is widely promoted as a method of weight management. This study sought to determine to what extent exercise-induced improvements in health are influenced by changes in body weight.

Fifty-eight, sedentary, overweight men and women completed a 12-week, supervised aerobic exercise program. Each exercise session was designed to expend approximately 500 kcal. Body composition, blood-pressure, resting heart rate and acute affective response to exercise were measured at weeks zero and 12. Subjects were instructed not to modify their energy intake during the study.

The mean reduction in body weight over the course of the study was 3.3 kg ($p < 0.01$). The subjects were divided into two groups. The non-responders were those who lost less weight than predicted based on their individual, total exercise-induced energy expenditure. This group's mean weight loss was 0.9 kg ($p < 0.01$). The remaining participants lost an average of 5.2 kg ($p < 0.01$). The non-responders experienced a significant increase in aerobic capacity ($p < 0.01$), reductions in waist circumference ($p < 0.01$), and decreases in systolic ($p < 0.05$) and diastolic ($p < 0.01$) blood pressure and resting heart rate ($p < 0.01$). The reduction in both systolic and diastolic blood pressure was more marked when examining the individuals classified as hypertensive at baseline.

Conclusion: This study demonstrates that aerobic exercise, even without significant weight loss, still results in significant health benefits.

King, N., et al. Beneficial Effects of Exercise: Shifting the Focus from Body Weight to Other Markers of Health. **British Journal of Sports Medicine** 2009, November; 43(12): 924-927.

BODY MASS INDEX AND RISK OF SUICIDE

Obesity and depression have a complex relationship. While obesity has been associated with depressive symptoms in several studies, others have suggested exactly the opposite, particularly among men. This study sought to determine the association between body mass index (BMI) and the risk of suicide.

This study used data gathered for the American Cancer Society Cancer Prevention Study II. This prospective study enrolled 1,184,657 men and women in 1982. Participants were asked to provide information on demographic characteristics, personal history, family history of diseases, various aspects of behavior, environmental and occupational exposures, and diet. In addition all were asked for their height and weight with a BMI calculated. Deaths that occurred between enrollment and December 2004, were reviewed for cause of death and were obtained in 99% of the cases. The data for suicides was compared to BMI.

A total of 2,231 participants died of suicide during over 21 million person-years of follow-up. The median age at death from suicide was 69 years. In age and sex adjusted analyses, there was a lower suicide mortality with increasing BMI. Exclusion of those with extreme BMI did not influence the linear association of BMI with the risk. Interestingly, BMI appeared to be inversely associated with risk only among married adults. The unmarried subgroup represented less than 20% of the cohort.

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(Continued on page 8)

Conclusion: This prospective study involving participants in all 50 states demonstrates an inverse relationship between body mass index and the risk of suicide.

Makamal, K., et al. Body Mass Index and Risk of Suicide among One Million U.S. Adults. **Epidemiology**. 2010, January; 21(1): 82-86.

MEDITERRANEAN DIET AND RISK OF CHD

Cardiovascular disease is the main cause of death worldwide, accounting for approximately 30% of global mortality. Nearly half of these deaths are attributable to coronary heart disease (CHD). A large proportion of premature CHD events are believed to be preventable by modifiable lifestyle behaviors, including diet. This study sought to prospectively investigate the relationship between adherence to a Mediterranean diet and incident CHD events.

EPIC is a large prospective study conducted in 10 European countries. The present study uses data from the Spanish cohort of EPIC-heart, the cardiovascular branch of EPIC. The EPIC Spain cohort was recruited between 1992 and 1996 with participants followed until the summer of 2004. Included were 41,438 healthy volunteers, ages 29 to 69 years. Participants were interviewed concerning usual food intake over the previous 12 months. The proportion of each food consumed was quantified. Total energy and ethanol intakes were estimated using a food consumption table. A lifestyle questionnaire was used to collect information concerning sociodemographic characteristics, lifestyle factors, medical history and reproductive indicators. Anthropometric measures were taken at recruitment. During the follow up period, confirmed fatal and nonfatal CHD events were compared to diet adherence, as measured by a Mediterranean diet score.

At a mean follow-up of 10.4 years, 609 participants were identified with a definite incident CHD event. Adherence to a Mediterranean diet was associated with a significant reduction in the risk of CHD. High, compared to low adherence to the diet corresponded to a 40% reduced risk of CHD. A significant inverse

trend for CHD was observed from low to high adherence ($p < 0.001$). Similar results were obtained for men and women. Overall, intakes of vegetables, olive oil and alcohol were associated with a significantly reduced risk of CHD, while intake of dairy products was associated with an increased risk of CHD.

Conclusion: This large sample of healthy adults followed for more than 10 years found that adherence to a Mediterranean diet is associated with up to a 40% reduced risk of a first CHD event.

Buckland, G., et al. Adherence to the Mediterranean Diet and Risk of Coronary Heart Disease in the Spanish EPIC Cohort Study. **American Journal of Epidemiology** 2009, December; 170(12):1518-1529.

GOUT AS A RISK FACTOR FOR CARDIOVASCULAR MORTALITY

The relationship between gout and hyperuricemia and cardiovascular disease has been well documented. Recent studies have closely linked gout with diabetes and chronic kidney disease. These conditions are related to atherosclerosis and to reduced long-term survival. This study examined the relationship of gout or hyperuricemia to all causes of cardiovascular mortality.

The sample included individuals involved in the health screening program conducted at Chang Gung Memorial Hospital in Taiwan from the years 2000 through 2006. Demographic data and disease history were recorded in a structured questionnaire. Serum urate levels were determined with individuals categorized as normouricemic or hyperuricemic based on the level of serum urate, or as gout by a predetermined definition. The National Death Registry in Taiwan was used to determine survival status and the causes of death through December of 2007. All cause mortality and cardiovascular mortality were compared between the groups.

Among the subjects 78.1% were normouricaemic, 19.8% were hyperuricaemic and 2.1% had gout. The metabolic syndrome and hypertension were significantly more prevalent among those with gout or hyperuricaemia as compared to those who were normouricaemic. Among

the 61,527 study cohorts, there were 1383 deaths. Of these, 198 were cardiovascular. All cause and cardiovascular mortality rates were highest in the gout group, followed by the hyperuricaemic group and then the normouracemic group.

Compared with subjects with normouricaemia, individuals with gout had a significantly higher risk of all cause mortality ($p=0.005$) or cardiovascular mortality ($p=0.027$), with this relationship still significant after adjusting for explanatory variables. Hyperuricemia was not, however, significantly associated with all cause or cardiovascular mortality after adjusting for explanatory variables.

Conclusion: This large population based study demonstrates that gout is associated with a higher risk of cardiovascular and all cause mortality, independent of age, gender, metabolic syndrome and proteinuria.

Chang-fu, K., et al. Gout: An Independent Risk Factor for All Cause and Cardiovascular Mortality. **Rheumatology**. 2010, January; 49: 141-146.

MODAFINIL FOR MS FATIGUE

Fatigue is a complaint in 70-90% of patients with multiple sclerosis (MS). Modafinil, initially licensed for narcolepsy, has been studied in patients with MS, with mixed results. This study sought to further explore the benefits and the long-term usefulness of the treatment of MS-related fatigue with this medication.

All patients receiving Modafinil at the Oxford MS clinic over a five-year period were included in this study. All were diagnosed with MS-related fatigue by a single neurologist. The diagnosis required that fatigue reduced physical or cognitive function, worsened towards the end of the day or with physical activity, and improved with rest or sleep. Treatment was only initiated when fatigue seriously limited daily activities. Modafinil was prescribed initially at 200 mg per day, with dose escalation permitted. Patients were instructed to take the drug for one month and then report to their general practitioner. The perceived benefit, side effects and decision on continuation of therapy at one month was obtained retrospectively from

medical notes. Additionally, all patients were interviewed at a median of two years. At this interview the patients were asked to judge the effect of Modafinil on symptoms over time.

Forty-two patients received Modafinil, three of whom could not be contacted. At the interview, the remaining 39 recalled notable fatigue prior to treatment. Forty-six percent of the patients perceived a useful benefit from Modafinil and continued with treatment. Among the patients with fatigue and excessive daytime sleepiness, the fatigue response rate was 56%, and the number reporting an improvement in daytime sleepiness was even greater at 78%. Among those without sleepiness, the fatigue response rate was only 25%. Adverse effects were reported by 19 of the 39 treated patients, occurring at 100 to 200 mg daily doses in all but one case. Insomnia was the most frequent symptom, followed by nausea, lightheadedness, headache and lack of concentration.

Conclusion: This small retrospective study found that Modafinil may be useful for patients with MS related fatigue and daytime sleepiness.

Littleton, E., et al. Modafinil for Multiple Sclerosis Fatigue: Does It Work? **Clinical Neurology and Neurosurgery**. 2010, January: 112 (1):29-31.

PREDICTING STROKE RISK AFTER TIA

Ischemic strokes are often preceded by a transient ischemic attack (TIA). Hospital and population-based cohort studies have reported a wide variation in the seven-day risk of stroke after TIA, ranging from 0% to 12.8%. Scores have been devised to help clinicians with the prediction of very early stroke risk after TIA. One such score is the ABCD², is based on five factors. These include age of at least 60(1 point), blood pressure of at least 140/90mm/Hg(1 point), clinical features such as unilateral weakness (2 points), speech impairment alone(1 point), duration of symptoms for at least 60 minutes(2 points), or less(1 point), and diabetes (1 point). This study sought to validate the use of ABCD² for predicting stroke after TIA.

This retrospective observational study included all patients presenting over a two-year period to an emergency department with TIA. Patients with a clinical diagnosis of stroke were excluded. The gold standard for diagnosis of stroke was a clinical diagnosis supported by a computed tomography scan or magnetic resonance imaging scan within 48 hours of admission. All patients were followed in outpatient clinics up to 90 days after admission. The main outcome measure was the occurrence of stroke after TIA up to 90 days post-presentation.

During the study period, 470 patients were admitted with a diagnosis of TIA. Follow-up data revealed that age, unilateral weakness and duration of symptoms of more than 60 minutes were significantly associated with the occurrence of stroke within two days. The data revealed that an admission rule based on an ABCD² score of at least four points showed a sensitivity of 86.4% and a negative predictive value of 91.7% for stroke at seven days. Admissions based on the ABCD² score of at least three showed a sensitivity of 96.6% and a negative predictive value of 96.1%.

Conclusion: This study demonstrates that the ABCD² rule has a good sensitivity and a high negative predictive value for stroke within seven days.

Ong, M., et al. Validating the ABCD² Score for Predicting Stroke Risk after Transient Ischemic Attack in the ED. **The American Journal of Emergency Medicine**. 2010, January 28 (1): 44-48.

CANNABIS EXTRACT AND SPASTICITY

Spasticity can be a painful and problematic issue for patients with multiple sclerosis (MS). Cannabis, a psychotropic drug known for its analgesic properties, has a long history as a treatment for spasticity. Although several clinical studies have reported a therapeutic benefit, clinical reports of symptom reduction among patients with MS describe mixed results. This study provides a systematic review of studies that used a combination of delta tetrahydrocannabinol (THC) and cannabidiol (CBD) for the treatment of MS related spasticity.

Six, randomized, placebo controlled trials were included in the analysis. The studies were reviewed to evaluate for treatment dosage, duration, subjective/objective measures of spasticity, and reports of adverse events.

Five of the six studies found a reduction of spasticity and improved mobility in patients with MS. One study reported no reduction in spasticity. Adverse events were reported in each study combined extracts were generally well tolerated. Of the three studies that reported visual analogue scores for pain, two reported a reduction with treatment.

Conclusion: This literature review found that a combination of THC and CBD extracts are effective in providing subjective, symptomatic relief in patients with spasticity due to multiple sclerosis.

Lakhan, S., et al. Whole Plant Cannabis Extracts in the Treatment of Spasticity in Multiple Sclerosis: A Systematic Review. **BMC Neurology**. 2009, 9; 59 (December 2009).

ACECLOFENAC –TIZANIDINE VS ACECLOFENAC FOR LBP

Acute low back pain (LBP) is among the most common conditions requiring a consultation with a physician. While early mobilization is important, effective analgesia may be helpful in achieving that goal. Both aceclofenac, a non-steroidal anti-inflammatory drug, and tizanidine, a central acting skeletal muscle relaxant, have been effective in reducing low back pain. This study sought to evaluate the efficacy of the combination of aceclofenac and tizanidine as compared to aceclofenac alone for the treatment of acute LBP.

One hundred ninety-seven patients with uncomplicated acute lumbosacral pain, who were between 18 and 70 years of age, were recruited for this study. All reported a pain intensity of at least six on a 10 point visual analogue scale. Patients were randomized to receive either seven days of aceclofenac, 100 mg twice per day, or a combination of aceclofenac and tizanidine, 2 mg twice per day. The primary outcome measures were pain intensity on movement, at rest, and at night, and pain relief scores using a ten point visual analogue scale. Pain was

assessed on days three and seven. Secondary outcome measures include functional impairment and overall treatment efficacy.

Both treatment groups showed significant improvement on pain intensity and pain relief, with the combination group showing significantly better improvement as compared to the monotherapy group ($p<0.05$). Seventy six percent of the combination group rated their overall efficacy of treatment as good as compared with 34% of the monotherapy group.

Conclusion: This study suggests that tizanidine may be a useful adjunct to aceclofenac for the treatment of acute low back pain.

Pareek, S., et al. Aceclofenac-Tizanidine in the Treatment of Acute Low Back Pain: a Double-Blind, Double-Dummy, Randomized, Multicentric, Comparative Study against Aceclofenac Alone. **European Spine Journal**. 2009, December; 181; 1836-1842:

ARE CORTICOSTEROID INJECTIONS EFFECTIVE FOR PATIENTS UNDERGOING TKA

Periarticular injections during total knee arthroplasty (TKA) have been reported to significantly decrease pain and the use of pain controlled analgesia, while significantly improving patient satisfaction. It remains unclear whether the addition of a corticosteroid to this intraarticular analgesia is important to the efficacy of these injections. This study sought to determine whether corticosteroids injected after TKA could help improve outcome without an increased risk of complications.

Subjects included patients ages 18 to 95 years who were scheduled to undergo a unilateral primary TKA. Of the 333 eligible patients, 76 were randomized to one of two treatment groups. One group received a periarticular injection containing bupivacaine, morphine, epinephrine, clonidine, cefuroxime and normal saline. The study group received the same injections with the addition of depomedrol. The sites of the injections included the periarticular ligament attachments, synovium, posterior capsule, and arthrotomy sites. Pain, narcotic consumption, length of inpatient stay, Knee Society Scores, range of motion and the

occurrence of complications were compared between groups postoperatively and at six and 12 weeks follow-up.

The length of hospital stay for the study group was nearly one day shorter than that of the control group ($p<0.001$). The other outcome measures did not differ between the groups. The study group had three complications including decreased range of motion requiring manipulation under anesthesia, and one patient who developed septic arthritis and eventually died.

Conclusion: This blinded study, involving patients undergoing total knee arthroplasty, found that injections with corticosteroid at the time of surgery significantly reduce the length of hospitalization with no change in pain control, motion or function. There was also a greater risk of infection with the use of steroids.

Christian, C., et al. Effect of Periarticular Corticosteroid Injections During Total Knee Arthroplasty: A Double-Blind Randomized Trial. **Journal of Bone and Joint Surgery**. 2009, November; 91(11): 2550-2555.

AUTOLOGOUS CHONDROCYTE IMPLANTATION FOR EARLY OA

Osteoarthritis (OA) is expected to become symptomatic in almost half of the United States population within their lifetime. The presence of even asymptomatic chondral defects doubles the rate at which cartilage is lost when compared to intact knees. Autologous chondrocyte implantation (ACI) produces hyaline like tissue in full thickness cartilage defects, and functional improvement with up to 10 years of follow-up. This study investigated the efficacy of ACI for intervention in early stage OA.

This cohort study included patients who underwent ACI for full thickness chondral defects. Inclusion criteria were a minimum of two years follow-up, and evidence of early OA as defined by radiographic and clinical criteria. There were no exclusion criteria. Of the knees treated, 155 had been classified as having early OA and were included in the data analysis. Patient pain and function were followed using the WOMAC, modified Cincinnati, SF-36, Knee Society score, and a satisfaction questionnaire.

One hundred forty seven knees demonstrated improvements in all scores from baseline to final follow-up ($p < 0.001$). Twelve of the 155 knees were considered treatment failures and revised to partial or total joint arthroplasty. The proportion of patients who experience extreme or severe pain while walking on a flat surface decreased by 73%. The proportion of those who experienced similar pain walking up and down stairs decreased by 76%.

Conclusion: This study of patients with early OA suggests that ACI may result in clinically relevant reductions in pain and improvement in function. At five years postoperatively, 92% of the patients were functioning well and able to delay joint replacement.

Minas, T., et al. Autologous Chondrocyte Implantation for Joint Preservation in Patients with Early Osteoarthritis. **Clinical Orthopedics and Related Research**. 2010; 468: 147-157.

UNDERSTANDING OF ONLINE EDUCATIONAL INFORMATION ABOUT ARTHRITIS

Written material has been produced to improve patients' knowledge about rheumatoid arthritis and other similar disorders. Patients with limited literacy skills often do not read this information. This study sought to assess the readability and lexical density of online material designed for physicians to distribute to patients with arthritic disorders.

The Colorado Multiple Institutional Review Board evaluated online information designed for patient education about rheumatoid arthritis, lupus and fibromyalgia from three websites commonly used by physicians. These included the arthritis foundation, Up to Date, and M. D. consult. Readability was determined by using the Simplified Measure of Gobbledygook Formula (SMOG). The results were verified using an online literacy calculator.

The readability of material available online ranged from 11th to 16th grade level. The average educational handout was written at the 14th grade level. The lexical density of the educational handouts ranged from 5.7 to 7.2, with an average of 6.3. All materials reviewed had a lexical density greater

than the recommended four contact words per clause. Noting the reading levels of adults in the United States, the study found that the reading materials were inappropriate for 86.2% of patients seen at the Denver Health Medical Center, and for 65.5% of the residents of the county where treatment was received (Denver County).

Conclusion: This study found that much of the educational information about common rheumatologic illnesses available on the internet was inappropriate for most rheumatology patients at a public health urban hospital and for two thirds of the residents of a large urban county.

Hirsh, J., et al. A Pilot Study to Determine Whether Patients Are Likely to Understand the Educational Information Available Online about Arthritic Disorders. **Journal of Clinical Rheumatology**. 2009, October; 15(7) 367-368.

EARLY HYALURONIC ACID DELIVERY AFTER CARTILAGE LESION

Partial thickness articular cartilage lesions often occur with knee trauma, and are commonly encountered in orthopedic surgery. After knee trauma, the normal physiologic joint homeostasis is disrupted, and catabolic agents exceed anabolic agents, causing a degradation of cartilage. Nonsurgical options for partial thickness articular lesions involve symptomatic agents, while surgical options include stabilizing the lesion edges. As hyaluronic acid has been shown to increase the synthesis of extracellular matrix proteins, this study sought to assess the effectiveness of hyaluronic acid for cartilage healing after acute knee injury.

This controlled animal study involved a 10 x 10 mm partial thickness cartilage lesion created at the medial condyle of 16 adult sheep. Eight sheep received intra-articular hyaluronic acid injections at days 0, 8 and 15. The eight controls received saline on the same days. The contralateral limb served as the nonoperative control. The sheep were sacrificed at 12 weeks after surgery. Synovial fluid was drawn before surgery and after euthanasia for analysis of collagen II, nitric oxide

and interleukin one beta. The medial condyle was assessed by gross appearance, for cell viability, histologic analysis for cartilage morphology, and dimethylene blue analysis for proteoglycans.

At 12 weeks, histologic analysis revealed that the treatment group had significantly better scores than did the saline group ($p = 0.001$). The hyaluronic acid group also had significantly greater glycosaminoglycan content ($p = 0.011$) and showed a trend toward reduced chondrocyte death as compared with the saline group ($p = 0.07$). Synovial fluid analysis showed no significant differences between the groups for collagen II, nitric oxide, and interleukin 1 beta levels.

Conclusion: This animal study reveals that the early administration of hyaluronic acid results in better cartilage health after acute traumatic cartilage injury. These findings suggest that early hyaluronic acid treatment may decrease or delay articular degeneration.

Kaplan, L., et al. The Effect of Early Hyaluronic Acid Delivery in the Development of an Acute Particular Cartilage Lesion in a Sheep Model. **American Journal of Sports Medicine**. 2009, December; 37:2323-2327.

CHRONIC PAIN AND FALLS IN THE ELDERLY

Falls rank among the 10 leading causes of death in older adults in the United States. Despite a growing body of evidence supporting associations between the number of risk factors and falls, efforts to translate these into effective fall prevention have been limited. This study sought to explore a set of risk factors for falls in the elderly in order to better identify targets for fall prevention.

Study participants included 749 women and men, aged 70 years and older and living in the community in Boston and in nearby suburbs. Initial eligibility was based on age 70 years or older, ability to walk 20 feet without personal assistance and the expectation to stay in the area for two years. Participants were screened for cognition and excluded for moderate or severe cognitive impairment. Patients were also assessed for pain,

by location and severity, sociodemographic characteristics including age, sex, race, and years of education, and for body mass index, visual deficits, physical activity, and medication use.

At baseline, 40% of participants reported chronic, polyarticular pain and 24% reported pain in one joint. A total of 1029 falls were reported over the 18 months of the study. Polyarticular pain was associated with a greater occurrence of falls, having an age-related adjusted rate for falls per person year of 1.18. Participants with single site pain had an adjusted rate of falls per person of 0.9 and those with no joint pain had a rate of falls of 0.78. More severe pain was associated with a greater risk of falls.

Conclusion: This study found that chronic musculoskeletal pain, regardless of the measure used, is associated with increased risk of falls in community living older adults.

Leveille, S., et al. Chronic Musculoskeletal Pain in the Occurrence of Falls in Older Population. *JAMA*. 2009, November 25; 302(20):2214-2221.

TERIPARATIDE VERSUS ALENDRONATE FOR STEROID INDUCED OSTEOPOROSIS

Glucocorticoids are often a mainstay of treatment for chronic conditions such as rheumatoid arthritis, asthma and lupus. Bone loss is a common complication of chronic glucocorticoid use, which can lead to an increased risk of fracture. Current treatments for glucocorticoid induced osteoporosis include biphosphates with supplemental calcium and vitamin D. Teriperatide is an anabolic agent which has been shown to increase bone mineral density in postmenopausal women and hypogonadal men with osteoporosis. This study sought to determine the usefulness of treating glucocorticoid induced osteoporosis with teriperatide.

This multi-centered, multinational double-blind controlled study included 428 patients with glucocorticoid induced osteoporosis. The subjects were randomized to teriperatide at 20 mcg per day or alendronate at 10 mg per day, and followed over 36 months. The primary outcome measure was changes in lumbar

spine and hip bone mineral density. Other measures included changes in bone turnover markers and fracture incidence.

Although both groups experienced increases in bone mineral density, the teriperatide group improved significantly more than did the alendronate group (11% versus 5.3% in the lumbar spine and 5.2% versus 2.7% at the hip). In addition, bone formation markers were increased and a bone resorptive markers were decreased in both groups as compared to baseline. The teriperatide group also had a significantly lower vertebral fracture rate when compared to the alendronate group.

Conclusion: This study shows that, for patients with glucocorticoid induced osteoporosis, teriperatide may be more effective in increasing bone mineral density and preventing fractures than alendronate.

Saag, K., et al. Effects of Teriperatide Versus Alendronate for Treating Glucocorticoid Induced Osteoporosis: 36-Month Results of a Randomized, Double-Blind, Controlled Trial. *Arthritis and Rheumatism*. 2009, November; 60(11):3346-3355.

PELVIC FRACTURE AND MORTALITY AFTER TRAUMA

Pelvic fractures are associated with substantial mortality and morbidity. This study sought to compare the mortality risk posed by pelvic fracture with the risk conferred by other injuries, as well as to determine whether the association of a pelvic fracture with mortality varies when combined with other known risk factors for mortality.

Trauma registry records from two level one trauma centers were retrospectively examined with information on 67,826 trauma patients. Patients with pelvic fracture were identified by ICD-9 code. Patients with penetrating mechanisms of injury were excluded. A logistic regression analysis was performed on 63,033 patients with complete data. A total of 3,296 pelvic fractures were identified. The odds ratio of mortality for pelvic fractures was compared with other variables. A second analysis explored whether the mortality risk of pelvic fractures varied when combined with other known mortality risk factors.

At both centers, when the trauma patient sample was analyzed as a whole, the presence of a pelvic fracture was significantly associated with mortality ($p < 0.001$). At both centers, the odds ratio of mortality associated with a pelvic fracture was roughly equivalent to that posed by an abdominal injury. Hemodynamic shock, severe head injury and age of 60 years or more all carried a risk of mortality greater than that noted with a pelvic fracture.

Conclusion: This analysis of trauma patients found that pelvic fracture is associated with a mortality risk essentially equivalent to that of an abdominal injury. However, among patients with a severe head injury or shock, a pelvic fracture did little to change the risk of death.

Sathy, A., et al. Effect of Pelvic Fracture on Mortality after Trauma: An Analysis of 63,000 Trauma Patients. *Journal of Bone and Joint Surgery*. 2009, December; 91-A: 2803-2810.

POST-THROMBOTIC SYNDROME AFTER TKA

Post-thrombotic syndrome is a chronic condition in the lower extremity that develops after a deep venous thrombosis (DVT). The syndrome consists of edema, skin induration, hyperpigmentation, venous ectasia, redness, pain with compression, and venous ulceration. While much has been written about the prevention of DVT and pulmonary emboli, little has been written about the morbidity caused by post-thrombotic syndrome after DVT. This study sought to determine whether the incidence of post-thrombotic syndrome is greater in patients with DVT than in patients without DVT.

This retrospective study reviewed all of the records of patients undergoing a total knee arthroplasty (TKA) for all admissions from 2001 through 2004. All patients were treated with a combination of mechanical devices and adjusted dose warfarin. All patients underwent screening with bilateral lower extremity ultrasound on postoperative day three. If no DVT, four weeks of warfarin was prescribed. If a DVT was diagnosed, patients received 12 weeks of warfarin. Each patient, regardless of treatment group, was followed as an outpatient in the

orthopedic surgeon's office at six weeks, three months, six months, one year, three years and every two years thereafter. The incidence of PTS in both groups was calculated and tested using logistic regression.

The overall rate of DVT was 4.7% (66 of 1,406). Of the 50 patients with at least one year of follow-up, three had a least two signs of PTS. The most common sign was edema, followed by skin induration, venous ectasia, erythema and pain with calf compression. Of the 88 patients without DVT and at least one year of follow-up, eight percent had at least two signs of PTS. The most common sign was edema with hyperpigmentation of the skin and venous ectasia.

Conclusion: This study of patients undergoing total knee arthroplasty for osteoarthritis found that post-thrombotic syndrome does not seem to be a major sequelae of DVT.

McAndrew, C., et al. Incidence of Post-Thrombotic Syndrome in Patients Undergoing Primary Total Knee Arthroplasty for Osteoarthritis **Clinical Orthopedics and Related Research**. 2010, January ;468 (1): 178-181.

RISK OF THROMBOVASCULAR EVENTS WITH EPOETIN ALPHA IN SPINE SURGERY

Recombinant human erythropoietin is indicated for the reduction of allogenic blood transfusion in anemic patients scheduled to undergo elective, noncardiac, nonvascular surgery with significant anticipated blood loss. This trial sought to compare the risks of thrombovascular events with the use of Epoetin alpha versus standard care in spine surgery without prophylactic anticoagulation.

This multicenter trial included 80 centers in the United States, with data collected between April 1998 and May 2006. Patients were included if they were older than 18 years of age, and were a minimum of three weeks prior to elective spinal surgery, with a surgical blood loss estimated at two to four units and a hemoglobin ranging from 10 to 13 g/dl. Participants were randomly assigned to a treatment or usual care group. There were 680 patients total, with 340 assigned to each treatment

group. Patients randomized to the treatment group were given once weekly epoetin injections for three weeks prior to surgery. Both groups were followed for serious adverse events for 30 days after surgery. Mechanical DVT prophylaxis was permitted, although no perioperative anticoagulation was given.

Overall, deep venous thrombosis was diagnosed in 4.7% of the people in the treatment group and 2.1% in the standard of care group. This finding exceeded the preset boundaries of four percent to establish noninferiority. Other thrombovascular events and all adverse events occurred with similar frequency in both groups.

Conclusion: This randomized, open label, parallel group study found a higher level of deep vein thrombosis among those patients receiving preoperative epoetin, suggesting the need for ant-thrombotic prophylaxis among these patients.

Stowell, C., et al. An Open Label Randomized Parallel Group Study of Perioperative Epoetin Alpha versus Standard of Care for Blood Conservation in Major Elective Spinal Surgery. **Spine**. 2009, November; 34: 2479-2485.

EFFICACY AND SAFETY OF WARFARIN VERSUS DABIGATRAN IN ACUTE VTE

Venous thromboembolism (VTE) is the third most common cause of vascular death in the United States. Treatment with vitamin K antagonists requires frequent serum monitoring, with levels influenced by multiple interactions with foods and other drugs. Dabigatran is an orally available, direct inhibitor of thrombin which does not need regular monitoring. This study compared dabigatran with warfarin for the treatment of acute VTE.

This double-blind, double dummy, randomized trial included 2,548 people with a radiologic diagnosis of proximal deep vein thrombosis (DVT) or pulmonary embolism (PE). The patients were randomized to receive six months of dose adjusted warfarin or dabigatran at 150 mg twice per day. The subjects were followed at seven days and then monthly for six months for outcome measures including death from VTE,

symptomatic DVT or PE, major bleeding events, minor bleeding events, acute coronary syndrome, liver function tests, and side effects including headache, nausea, diarrhea, back pain, dyspnea, and dyspepsia.

At follow-up, a similar percentage of patients in both the dabigatran and warfarin groups developed recurrent DVT (2.4% versus 2.1%, respectively), major bleeding events (1.6% versus 1.9% respectively), any bleeding events (16% versus 21.0% respectively), or ACS (0.4% versus 0.2% respectively). The only difference was a symptom of dyspepsia which was higher in the dabigatran group than in the warfarin group (P<0.001).

Conclusion: This study of patients with VTE demonstrates that dabigatran, a direct thrombin inhibitor, is as effective as warfarin for the prevention of recurrent VTE. The authors note that the doses are fixed and do not require laboratory monitoring, improving its ease of use.

Schulman, S., et al. Dabigatran Versus Warfarin in the Treatment of Acute Venous Thromboembolism. **N Eng J Med**. 2009, December 10; 361 (24): 2342-2352.

FALLS, PD AND CHOLINERGIC ACTIVITY

There are two major sources of cholinergic projections in the brain. These include the nucleus basalis of Meynert, which provides the principal cholinergic input to the entire cortical mantle, and the pedunculo pontine nucleus, a brainstem locomotor center which provides cholinergic inputs to the basal ganglia, thalamus, cerebellum, several brainstem nuclei and the spinal cord. Both degenerate in Parkinson's disease (PD). This study sought to investigate the impact of cholinergic function on falls in individuals with PD and to compare this to the degree of nigrostriatal dopaminergic denervation.

This cross-sectional study involved 44 patients with PD without dementia and 15 control subjects. The patients with PD were assessed and staged according to the Unified Parkinson's Disease Rating Scale. Dopaminergic drugs were withheld overnight in patients with PD. Every subject underwent brain PET imaging using tracers relevant to the

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assessment of cholinergic and dopaminergic function. MRI was performed to manually trace volumes of interest of the thalamus, caudate nucleus, and putamen.

Seventeen of the patients with PD reported a history of falls, while 27 had no falls. Analysis of covariance of the cortical acetylcholine hydrolysis rates demonstrated reduced cortical acetylcholine in PD fallers when compared with controls ($p=0.0004$). Thalamic acetylcholine activity was lower only in the PD fallers ($p=0.008$). No significant difference occurred in the nigrostriatal dopaminergic activity between PD fallers and non-fallers.

Conclusion: This study examined the relationship between a history of falls and cholinergic activity in patients with PD, finding that thalamic cholinergic hypofunction is associated with increased falls

Bohnen, N., et al. History of Falls and Parkinson's Diseases Associated with Reduced Cholinergic Activity **Neurology** 2009, November; 73(20): 1670-1676.

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