REHAB IN REVIEW™

WWW.REHABINREVIEW.COM

Volume 22 Number 4 | Published by Physicians In Physical Medicine and Rehabilitation | April 5, 2014

THIRTY DAY READMISSION AFTER ACUTE REHABILITATION

The Patient Protection and Affordable Care Act has created a hospital readmission reduction program to decrease readmissions and improve transitions from acute care. In 2010, 12% of patients discharged from inpatient rehabilitation facilities to the community were readmitted to acute care hospitals within 30 days. This study reviewed the readmission records for patients from the six largest impairment categories, in order to assess current readmission rates in the Medicare population.

Data were obtained from the Centers for Medicare & Medicaid Services's (CMS) files of Medicare fee-for-service patients discharged from acute-care hospitals to inpatient rehabilitation facilities. Six impairment categories were selected, based upon the 2013 MedPac report of the most common impairment groups. Hospital readmission within 30 days was tracked and reviewed by sociodemographic characteristics, functional status, comorbidities as well as clinical and facility factors.

The sample's mean age was 78 years, with 62.5% women. The mean rehabilitation length of stay was 12.4 days, with lower extremity joint replacement the largest impairment category (25%). The 30-day readmission rate was 11.8%, ranging from 5.8% for those with lower extremity joint replacements to 18.8% for those with debility. Common reasons for readmission included kidney and urinary tract infection, pneumonia and pleurisy, heart failure and shock, esophagitis, gastroenteritis and other digestive disorders and nutritional and miscellaneous metabolic disorders. Approximately half of those readmitted were readmitted within 11 days of discharge.

Conclusion: This study of Medicare patients found that, after hospitalization in an acute rehabilitation hospital, the 30-day readmission rate among those with the six most common impairment categories was 11.8%.

Ottenbacher, K., et al. Thirty- Day Hospital Readmission following Discharge from Post-Acute Rehabilitation in Fee for Service Medicare Patients. **JAMA.** 2014, February 12; 311(6): 604-614.

ADVERSE EVENTS IN SKILLED NURSING FACILITIES

The Office of Inspector General (OIG) of the United States conducted a series of studies concerning adverse events in hospitals from 2008 to 2012, finding that 27% of hospitalized Medicare beneficiaries experience adverse and temporary harm events. As Medicare expenditures for skilled nursing facilities (SNFs) have more than doubled in the past decade, the OIG chose to continue this assessment by reviewing the adverse events occurring in these SNFs.

The sample included records from a selected group of 655 Medicare beneficiaries with Medicare paid SNF stays. From these, adverse, temporary harm events were identified. The levels of harm included a) events that might contribute to or resulted in death, b)events that require intervention to sustain life, c) events that contribute to or result in permanent resident harm and d) events that prolong the stay in SNFs or led to a transfer to another medical facility. These data were used for the adverse event incidence analysis, preventability analysis and a Medicare cost analysis.

Approximately 22% of the patients experienced at least one adverse event during the stay. The majority (79%) of adverse events were sufficiently severe to result in a prolonged stay or transfer to another medical facility. Of the remaining, 14% required intervention to save the resident's life, and six percent contributed to or resulted in the death of the patient. Of the total events, 37% were related to medication, 37% to ongoing resident care and 26% to infection. The physician reviewers determined that 59% of the adverse and temporary harm events were clearly or likely preventable.

Conclusion: According to this report, 22% of Medicare beneficiaries experienced adverse events during skilled nursing facility stays, which resulted in prolonged stays or hospitalization, permanent harm, life-sustaining intervention or death.

Levinson, D. Adverse Events in Skilled Nursing Facilities: National Incidence among Medicare Beneficiaries. **U.S. Department of Health and Human Services**, **Office of the Inspector General.** February, 2014. Report No. OEI-06-11-00370.

STATINS REDUCE NEW ONSET ATRIAL FIBRILLATION AFTER MYOCARDIAL INFARCTION

Atrial fibrillation (AF) is a common complication after myocardial infarction (MI). New onset AF is associated with adverse outcomes and a large, excess risk of death in this setting. Current guidelines suggest that the use of statins is an auxiliary means of preventing AF. This study was designed to examine the effect of statins in reducing new onset AF in the post-MI population.

Data were obtained from the Danish National Patient Registry. All patients 30 years of age or older, hospitalized with an acute MI between 1997 and 2009, were identified. Patients with a prior history of AF were excluded. From the registry, all patients with new onset AF and atrial flutter were then identified. Prescription use was reviewed, with all statin prescriptions

© Rehab in Review

Editor-in-Chief
David T. Burke, M.D., M.A.
Emory University, Atlanta, GA

Executive Editor
Randolph L. Roig, M.D.
Emory University, Atlanta, GA

Copy Editor
Roberta Alysoun Bell, Ph.D.
Emory University, Atlanta, GA

Contributing Editors
*Amy Cao, M.D.
Erika Moody, M.D.
BCM/UT Alliance, Houston, TX

*Jennifer Knowlton, M.D.
East Carolina University, Greenville, NC

*Mikhail Zhukalin, D.O.
Anna Cruz, M.D.
Chukwuemeka Ibekwe, M.D.
Mitchel Leavitt, M.D.
Cleo D. Stafford II, M.D., M.S.
Donnie Staggs, M.D.
Christopher Williams, M.D.
Emory University, Atlanta, GA

*Cyrus Kao, M.D.
*Pablo Vazquez, M.D.
Georgetown/MedStar National Rehab, Washington, DC

*Alexander Drakh, D.O.
Christine Cao, M.D.
LSU Medical Center, New Orleans, LA

*Bryndon Hatch, M.D.
*Katie Nanos, M.D.
Mayo Clinic, Rochester, MN

*Eric Leung, M.D.
Mount Sinai Med. Ctr., New York, NY

*Arpit A. Patel, D.O.
Nassau University Med Center

*Christina Marciniak, M.D.
Ashwin Babu, M.D.
Zack McCormick, M.D.
N.W.U../R.I.C., Chicago, IL

*David Woznica, M.D.
NYP, Columbia-Cornell, NY, NY

*Samaira Khan, D.O.
NYU/Rusk Inst. of Rehab Med, NY, NY

*Craig Best, D.O.
*Kashif Saeed, M.D.
Daniel Buzol, M.D.
Stephanie Kim, D.O.
Rush University Medical Center, Chicago, IL

*Alice Hon, M.D.
*Leroy Lindsay, M.D.
Lawrence P. Lai, M.D., MS
Jay Panchal, BA
Rutgers/Kessler Rehab, Newark, NJ

*Alan Vo, D.O.
Sinai Hospital, UMD, Baltimore, MD

*Vikram Arora, D.O.
*Anthony A. Cuneo, M.D., PhD
Christopher Connor, D.O.
Temple Univ./UPenn., Philadelphia, PA

*Anupam Sinha, D.O.
Thomas Jefferson Univ/Rothman Inst., Philadelphia, PA

*Deep Garg, M.D.
Angie Lastra, M.D.
University of Miami, Miami, FL

*Seth Swank, D.O.
University of Michigan, Ann Arbor, MI

*Peter Hwang, M.D.
University of Missouri, Columbia MO

identified, isolating those subjects with post-MI statin therapy. From these data, dosages and compliance were documented. Rates of new onset AF were compared with statin use.

A total of 97,499 patients were treated for a first-time MI, with 92% alive at follow-up. After discharge, 62.5% had at least one prescription of statin therapy, with the other subjects serving as controls. During follow-up, 14% in the statin group and 21.2% in the non-statin group had re-infarction ($p<0.001$). Of the statins identified, simvastatin and atorvastatin were more effective than pravastatin in reducing new onset AF ($p<0.001$for both comparisons).

Conclusion: This study of patients with myocardial infarction found that the use of statins reduces the chance of new onset atrial fibrillation.

Bang, C., et al. Statins Reduce New Onset Atrial Fibrillation in a First-Time Myocardial Infarction Population: A Nationwide Propensity Score Matched Study. **Euro J Preventive Cardiol**. 2014, March; 21(3): 330-338.

DOPAMINERGIC ALTERNATIVES FOR RESTLESS LEG SYNDROME

Restless leg syndrome (RLS) affects two to three percent of the European and United States populations. Currently, the mainstay of treatment is the use of dopaminergic medications. Among patients treated with dopamine agonists, RLS augmentation can occur, with symptoms becoming more pervasive and intense than before. This study assessed the efficacy of pregabalin, as an alternative to the dopaminergic drug, pramipexole, for the treatment of RLS.

This randomized, double-blind, placebo-controlled trial enrolled 731 patients over 52 weeks. The subjects were randomized to receive either pregabalin, 300 mg, pramipexole, at a dose of 0.25 or 0.5 mg per day or a placebo over 12 weeks. The participants were followed at set intervals to assess RLS severity with the International RLS (IRLS) Study Group criteria, with augmentation scales completed including the Structured Interview for the Diagnosis of Augmentation (SIDA) and the Augmentation Severity Rating Scale (ASRS). Self-report measurements of sleep and adverse events were also recorded.

A total of 719 patients received treatment. At 12 weeks, those receiving pregabalin enjoyed a significantly greater improvement in IRLS scores than did those receiving pramipexole or placebo ($p<0.001$). As compared with placebo, the 0.5-mg dose of pramipexole, but not the 0.25 -mg dose, was associated with a significant reduction in the IRLS score. The rate of augmentation at 12 weeks was significantly lower among those receiving pregabalin than among those receiving 0.5 mg of pramipexole, but not among those receiving 0.25 mg of pramipexole ($p=0.001$,and $p= 0.08$, respectively). Discontinuation due to adverse events was lower among those receiving pramipexole.

Conclusion: This randomized, controlled trial involving patients with restless leg syndrome demonstrates that pregabalin may be an appropriate alternative to dopaminergic drugs, with significant symptom improvement and a lower rate of augmentation.

Alan, R., et al. Comparison of Pregabalin with Pramipexole for Restless Leg Syndrome. **N Eng J Med.** 2014, February 13; 370(7): 621-631.

TRANSFUSIONS AND WOUND INFECTION AFTER TOTAL KNEE AND TOTAL HIP ARTHROPLASTY

Previous studies have demonstrated that perioperative transfusions may increase the morbidity and mortality associated with surgery. This study compared the effects of perioperative allogenic and autologous transfusions on the risk of reoperation for suspected infection after primary total hip or total knee arthroplasty.

This retrospective study reviewed the cases of 3,352 patients undergoing primary total knee arthroplasty or total hip arthroplasty, performed between 1997 and 2007. Outcomes were compared between those receiving no transfusions, those receiving allogenic transfusions and those receiving autologous transfusions. The groups were compared by the number of repeat surgeries within three months for

suspected acute joint space or extra-capsular tissue infection.

Of the patients studied, 1,746 perioperative transfusions were received, with 836 patients having allogenic exposure and 910 autologous-only exposure. The rate of reoperations for suspected infection was higher among patients with allogeneic exposure (1.67%) as compared with all others (0.72%, p = 0.014). Autologous transfusion was not associated with a higher reoperation rate. A multivariable regression analysis revealed that the total number of units transfused (p = 0.011) and American Society of Anesthesiologists scores of >2 (p = 0.008) were significant predictors of reoperation.

Conclusion: This retrospective study of patients undergoing total knee or total hip arthroplasty found that the total number of blood units transfused was a significant risk factor for reoperation for acute infection, although allogenic exposure itself was not significantly predictive.

Newman, E. Impact of Perioperative Allogenic and Autologous Blood Transfusion on Acute Wound Infection following Total Knee and Total Hip Arthroplasty. **J Bone Joint Surg.** 2014, February; 96(4): 279-284.

SOCCER BOOTS AND PLANTAR PRESSURE

Foot and ankle injuries are common among soccer players, with footwear and playing surface thought to impact these injuries. This study assessed plantar pressures in elite soccer players, comparing differences in these pressures in soccer boots versus running shoes.

Seventeen, elite, German, male soccer players were equipped with sensor loaded insoles designed to measure pressure and force. In a first trial, all players ran at 3.3 m/s in a straight line in running shoes. In a second trial, the players ran with soccer boots equipped with a 12-stud profile. The preferred and nonpreferred feet were identified for each player. Changes in peak plantar pressure between soccer boots and running shoes were compared for nine, predefined foot locations for each foot.

The subjects had an average age of 23 years and a mean weight of 81 kg. Significantly increased plantar pressures were noted with the use of soccer boots, as compared to the running shoes at the lateral midfoot, first metatarsal head, fourth and fifth metatarsal heads and great toe, for both the preferred and nonpreferred foot. The greatest differences were noted at the lateral midfoot and great toe.

Conclusion: This study of elite soccer players found that, compared with running shoes, running in soccer boots results in significant loading, particularly at the lateral midfoot.

Hands – Dieter, C., et al. Soccer Boots Elevate Plantar Pressures in Elite Male Soccer Professionals. **Clin J Sports Med**. 2014, January; 24(1): 58-61.

RETURN TO PITCHING AFTER TOMMY JOHN SURGERY IN MAJOR LEAGUE PITCHERS

The medial ulnar collateral ligament (UCL) of the elbow provides stability to valgus stress during throwing sports. The outcome of UCL reconstruction surgery, often referred to as the Tommy John surgery, has enjoyed increased use over the years. This study was designed to determine the rate of return to pitching and to clarify the performance of those pitchers after this reconstructive procedure.

Major League Baseball (MLB) pitchers with symptomatic UCL injury, who underwent reconstruction were included in the study. Data were obtained from the MLB database. A player was deemed to have returned to pitching if he pitched in any MLB game after the surgery. Controls were matched by age, body mass index, position, handedness, and MLB experience and performance.

A total of 179 pitchers with UCL tears who underwent reconstruction were included in the analysis. Of these 148 were able to return to play in the major leagues and 174 in the major or minor leagues combined. The pitchers returned at a mean of 20 months after reconstruction. After surgery, pitchers had significantly fewer innings pitched per season and had both fewer wins and losses per season as compared to before surgery. Pitchers who had undergone the surgery had lower earned-run averages and walks plus hits per inning, had significantly lower losing percentages and gave up fewer hits per inning as compared with controls. Two years after surgery there were no significant differences between cases and controls.

Conclusion: This study of Major League Baseball pitchers with ulnar collateral ligament injury reconstruction found that the majority return to major-league baseball, and were successful as measured by multiple performance variables.

EricsKon, B et al. Rate of Return to Pitching and Performance after Tommy John Surgery in Major League Baseball Pitchers. **Am J Sports Med** 2014, March; 42(3): 536 – 543

HOME-BASED EXERCISE AFTER HIP FRACTURE

Hip fractures occur in more than 250,000 people in the United States each year. Two years after these fractures, more than half of men and 39% of women are dead or living in long-term care facilities. This study was designed to determine the efficacy of a six-month, functionally oriented rehabilitation program, designed to extend the benefits of the initial hip fracture rehabilitation.

This randomized, clinical trial included two parallel groups, 60 years of age or older, with a primary diagnosis of hip fracture. All patients were discharged from rehabilitation services within 20 months of the baseline assessment. An intervention group was instructed to perform a home exercise program three times per week for six months, initially taught by physical therapists. A control group received dietary nutritional education during a single home visit, followed by telephone calls and mailings. The frequency of contact with dietitians was matched to that of the physical therapists in the treatment group. Function was measured with the Short Physical Performance Battery (SPPB) and the Active Measure for Post-Acute Care (AM-PAC).

Of the 232 randomized patients, 195 were followed up at six months. The treatment group showed significant improvement relative to the control group on the SPPB in both the adjusted and the unadjusted analyses (p<0.001 for both analyses). Significant differences were also noted at six months in favor of the

treatment group on the mean AM-PAC mobility scores (p=0.01), and mean AM-PAC daily activity scores (p=0.01). The benefits persisted at nine month follow up.

Conclusion: This study demonstrates that, among patients who had undergone a standard rehabilitation program after hip fracture, home-based, functionally oriented exercise significantly improved physical function at six and nine months after initiation.

Latham, N., et al. Effect of a Home-Based Exercise Program on Functional Recovery following Rehabilitation after Hip Fracture. A Randomized Clinical Trial. **JAMA**. 2014, February; 311(7): 707-709.

TRANSCRIPTION FACTOR DECOY AYX1 PREVENTS ACUTE AND CHRONIC PAIN

As Early Growth Response 1 (ERG1) is a transcription factor essential for the early response to noxious injury, it is thought that its immediate activation after injury triggers the delayed, long-term transcription and neuronal excitability changes necessary for the development of chronic pain and mechanical hypersensitivity. A DNA decoy, AYX1, with high affinity and specificity for EGR1, was developed to block ERG1 function. This study examined the effect of the intrathecal administration of this molecule on the development of postoperative pain.

This placebo controlled, animal incisional knee pain model used the vehicle only, or AYX1, injected via a single intrathecal bolus, one hour before surgery for the incisional and knee surgery models, once at the time of surgery for the chronic neuropathic (SNI) model and at −24 hours, −1 hour, +24 hours, and +72 hours relative to injury for the inflammatory (CFA) model. The animals were tested for mechanical hypersensitivity and functional recovery after surgery.

In the mechanical hypersensitivity model, the treatment group was noted to have significantly less response to light and robust mechanical stimuli, suggesting an effect on allodynia and hyperalgesia. In addition, greater spontaneous activity was noted, as compared with the control groups, demonstrating the ability of AYX1 to suppress reduced function post-surgery.

Conclusion: This animal study demonstrates that a DNA decoy drug, administered by a single intrathecal injection, can significantly reduce mechanical and neuropathic pain after surgery.

Mamet, J., et al. Single Intrathecal Administration of the Transcription Factor Decoy AYX1 Prevents Acute and Chronic Pain after Incisional, Inflammatory or Neuropathic Injury. **Pain.** 2014, February; 155(2): 322-333.

TREATMENT OF PHANTOM LIMB PAIN WITH AUGMENTED REALITY

Phantom limb pain is experienced by up to 70% of amputees, with multiple medical and nonmedical interventions proposed. Virtual reality mirror therapy has been introduced as an upgrade to a previously introduced mirror therapy. This study investigated whether a higher degree of realism provided by augmented reality (AR) could improve the efficacy of this therapy.

A patient with chronic, phantom limb pain, 48 years in duration, was studied after failing a variety of treatments. For this patient, myoelectric activity at the residual limb was used to assess the intended phantom limb motions. Using this input a virtual arm was superimposed on his residual limb. The patient was then instructed to perform specified movements. The protocol was applied once weekly for 18 weeks and then twice weekly. Pain was recorded at baseline and throughout the training period.

After four weeks of training, the patient reported episodes of lower pain intensity. At 10 weeks, episodes of near absent pain began to occur, developing into completely pain free episodes, which were new to the patient since amputation.

Conclusion: This case study of a patient with chronic, phantom limb pain found that pain levels can be significantly reduced by using augmented reality and gaming, controlled by myoelectric pattern recognition.

Ortiz-Catalan, M., et al. Treatment of Phantom Limb Pain (PLP) Based on Augmented Reality and Gaming Controlled by Myoelectric Pattern Recognition: A Case Study of Chronic PLP Patient. **Frontiers in Neurosci.** 2014, February; 8 doi: 10.3389/fnins.2014.00024

PLATELET RICH PLASMA FOR PATELLAR TENDINOPATHY

Patellar tendinopathy (PT) is a degenerative disease of the patella tendon, resulting in anterior knee pain. Among the newer therapies introduced to address PT, platelet rich plasma (PRP) has been suggested as a potential intervention. This study investigated whether the combination of the eccentric exercise and PRP may be effective for the treatment of PT.

This double-blind, randomized, controlled trial included 23 patients with PT who had failed conservative treatment. The subjects underwent either a single injection of PRP or a placebo dry needling (DN) technique. These treatments were combined with a standardized, five-phase program of eccentric exercise. For the primary outcome measure, patients were assessed at baseline and at three, six, nine, 12 and >26 weeks with the Victorian Institute of Sport Assessment (VISA) score for patella tendinopathy. Secondary outcome measures included the Tegner Activity Scale, the Lysholm Knee Scale and the Short Form (SF-12) Questionnaire.

A total of 13 patients were randomized to the DN group and ten to the PRP group. At 12 weeks, the PRP group demonstrated significantly more improvement, as measured by the VISA, than did the DN group (p=0.02). However, the significance of that difference had dissipated by week 26 (p=0.66). Measurement of activity using Tegner scores revealed no significant difference between the groups at 26 weeks. Measurement of function and stability using Lysoholm scores demonstrated better function at 26 weeks in the DN group (p=0.006). No significant differences were noted between the groups in measures of pain (VAS) or of health-related quality of life (SF-12).

Conclusion: This study of patients with patella tendinopathy demonstrates that combining eccentric exercise and platelet rich plasma injection accelerates the recovery from patella tendinopathy relative to exercise alone. However,

this benefit seems to dissipate over time.

Dragoo, J., et al. Platelet Rich Plasma as a Treatment for Patellar Tendinopathy: A Double-Blind, Randomized, Controlled Trial. **Am J Sports Med.** 2014, March; 42: 610-619.

TESTOSTERONE LEVELS IN MEN WITH RHEUMATOID ARTHRITIS

Risk factors for rheumatoid arthritis (RA) include genetic, environmental and hormonal factors. In cross-sectional studies, lower levels of serum testosterone have been found in both male and female patients with RA. This study investigated the significance of hormonal concentrations among men who subsequently develop RA.

This population-based, case-control study screened 22,444 males born between 1921 and 1949, and 10,902 females born between 1925 and 1938. A health survey was designed to screen large strata of the adult population to identify individuals for preventive intervention. All subjects underwent physical examination, including laboratory tests and self-administered questionnaires focusing on health and lifestyle factors. From laboratory tests, serum total free testosterone, sex hormone binding globulin (SHBG), luteinizing hormone (LH) and follicle stimulating hormone (FSH) concentrations were quantified. All medical records were reviewed to determine individuals who developed RA. Two matched controls were found for each validated case.

From the cohort, 104 cases with RA were identified. After adjustments for confounding factors of tobacco abuse and body mass index, low testosterone levels were found to be weakly associated with the development of rheumatoid factor-negative RA (odds ratio 0.31), with a weaker association with rheumatoid factor-positive RA. Those who developed RA had lower mean concentrations of all measured hormones except SHBG, as compared with controls. Serum levels of FSH were positively associated with the development of rheumatoid factor-negative RA, and negatively associated with the development of rheumatoid factor-positive RA.

Conclusion: This study demonstrates that low levels of testosterone are associated with the subsequent development of rheumatoid factor-negative RA.

Pikwer, M., et al. Association between Testosterone Levels and Risk of Future Rheumatoid Arthritis in Men: A Population-Based, Case-Control Study. **Ann Rheum Disease.** 2014, March 1; 73(3): 573-579.

PLATELET RICH PLASMA VERSUS WHOLE BLOOD FOR CHRONIC TENNIS ELBOW

Lateral elbow epicondyle tendinosis (tennis elbow) is a common condition, occurring at the common extensor tendon. Newer treatment options have included platelet rich plasma (PRP), autologous blood, prolotherapy and extracorporeal shockwave therapy. Both PRP and autologous blood contain platelets with strong growth factors which may help the healing process from chronic injuries. Given the high cost of autologous PRP therapy, this study compared the efficacy of whole blood injections with that of PRP.

Patients diagnosed with chronic lateral epicondylitis with a duration of more than three months and a pain severity of at least five on a 10-point scale were included in the sample. Those subjects were randomized to receive 2 mL of autologous PRP into a maximal tenderness point at the elbow under aseptic techniques, or 2 mL of autologous peripheral whole blood using the same technique. Pain severity was assessed before injection and at four weeks, eight weeks, and six and 12 months post-injection. Additional outcome measures included the Modified Mayo Clinic Performance Index and the Pressure Pain Threshold (PPT).

Sixty-one patients completed this study. The mean pain score decreased significantly in both treatment groups at each follow-up evaluation ($p<0.001$). Mayo and PPT scores significantly improved in both treatment groups at 12 months ($p<0.001$ and $p<0.002$, respectively). No significant differences were noted between the groups in pain scores and function scores at any follow-up examination.

Conclusion: This study of patients with chronic lateral epicondylitis found that both platelet rich plasma and autologous whole blood injections are effective treatments, both for reducing pain and increasing function.

Raeissadat, S., et al. Is Platelet Rich Plasma Superior to Whole Blood in the Management of Chronic Tennis Elbow: One-Year, Randomized Clinical Trial. **BMC Sports Sci, Med Rehab**. 2014; 6: 12.

COMPARISON OF PLATELET RICH PLASMA FORMULATIONS FOR CARTILAGE HEALING

Although platelet rich plasma (PRP) has been studied as a means to deliver autologous growth factors, the optimal method of preparing PRP for cartilage repair is not known. This study investigated the mechanisms of action of different PRP formulations on human chondrocytes.

Platelet rich plasma and platelet poor plasma (PPP) were obtained from 10, healthy, male volunteers. In this one-step method, 45 mL of venous blood was divided into five tubes. From these, three formulations were prepared, including PRP with a low concentration of platelets and very few leukocytes (L-PRP), pure PRP with high concentrations of both platelets and leukocytes (P-PRP) and platelet poor plasma (PPP). These different formulations were applied to cartilage samples from patients undergoing knee replacement surgery. Chondrocyte growth in the presence of each formulation was evaluated after zero, three and seven days of culture.

The five percent, 10% and 20% concentrations of each formulation induced a dose-dependent enhancement of chondrocyte proliferation, with the only difference between the formulations being greater cell growth on day seven with P-PRP as compared to the other formulations ($p<0.05$). At each concentration, P-PRP induced greater cell proliferation on day seven when compared with L-PRP and PPP ($p < 0.05$).

Conclusion: This study of cartilage response to different platelet rich plasma (PRP) formulations found that PRP with a low concentration of platelets and very few leukocytes had superior effects on cell growth and resulted in higher levels of growth

factors and cytokines than did other formulations.

Cavallo, C., et al. Comparison of Platelet Rich Plasma Formulations for Cartilage Healing: An *In Vitro* Study. **J Bone Joint Surg.** 2014, March 5; 96(5): 423-429.

C-REACTIVE PROTEIN AND LACUNAR STROKE

Inflammation plays a major role in atherosclerosis and cardiovascular disease. However, relatively little information is available concerning serum markers of inflammation as indicators of post-stroke prognosis. This study assessed the efficacy of inflammatory biomarkers to predict recurrence after lacunar stroke.

This study was nested within the ongoing Secondary Prevention of Small Subcortical Strokes Study, a multicenter study focusing on secondary prevention of stroke recurrence in patients with small vessel ischemic stroke or lacunar strokes. Patients with MRI-demonstrated lacunar stroke were eligible for inclusion. Blood samples were collected at enrollment with high sensitivity C-reactive protein (hsCRP) assay analysis. Primary outcomes were recurrent, ischemic stroke and the combined outcome of a major cardiovascular event, including recurrent, ischemic stroke, myocardial infarction or vascular death.

A total of 1,244 patients were included, with a mean age of 63.3 years, and with 63.4% of the sample men. At three-year follow-up, 83 recurrent strokes were documented, including 45 lacunar strokes, 16 hemorrhagic strokes and 115 other major vascular events. Compared to those in the bottom quartile of hsCRP, those in the top quartile had an increased risk of recurrent ischemic stroke, with an unadjusted hazard ration (HR) of 2.54. There was an insignificant trend toward increased risk in those in the second and third quartiles. HsCRP was associated with increased risk of major vascular events, with an HR of 2.04 for those in the top quartile, as compared to the bottom quartile.

Conclusion: This study found that, after lacunar stroke, the risk of recurrent ischemic stroke, total stroke and major vascular events is over double among those with high levels of hsCRP.

Elkind, M., et al. C-Reactive Protein as a Prognostic Marker after Lacunar Stroke. **Stroke.** 2014, March; 45(3): 707-716.

CRANBERRY CAPSULES FOR URINARY TRACT INFECTION PROPHYLAXIS

Urinary tract infections (UTIs) are common among long-term care facility residents, accounting for nearly 25% of all infections. The use of prophylactic antibiotics remains controversial because of potential side effects, as well as antibiotic resistance. Previous studies have demonstrated that cranberry capsules may be effective as a prophylactic against UTIs, although the protective effect of these capsules in vulnerable older adults in long-term care facilities has not been previously studied.

This randomized, double-blind, placebo-controlled, multicenter trial included residents 65 years of age or older from 21, long-term care facilities in the Netherlands. Participants were stratified according to UTI risk, and were randomized to receive either cranberry or a placebo. A total of 928 participants were assigned to take either cranberry or placebo capsules orally twice per day for a total of 12 months. The primary outcome variable was the incidence of UTI, compared by groups.

For the high-risk group, those taking cranberry capsules had a 26% reduced incidence of clinically defined UTI as compared with placebo (p=0.04). However, the incidence of UTI following the strict definition did not significantly differ between groups. In the low risk group, no significant difference was seen in clinical UTIs between groups.

Conclusion: This study of patients in long-term care facilities found that twice daily cranberry capsules can reduce the incidence of clinically defined urinary tract infections, although this difference was not significant for strictly defined urinary tract infections.

Caljouw, M., et al. Effectiveness of Cranberry Capsules to Prevent Urinary Tract Infections in Vulnerable Older Persons: A Double-Blind, Randomized, Placebo-Controlled Trial in Long-Term Care Facilities. J **Am Geriatr Soc.** 2014, January; 62 (1): 103-110.

REVIEW OF OPIOID PRESCRIPTION GUIDELINES

Currently, 8 to 30% of patients with chronic non-cancer pain received opioids. Given the current rates of opioid overdose, a number of organizations have created guidelines for opioid prescribing. This review paper was designed to summarize the current guidelines for the treatment of chronic pain

Several medical databases were searched for guidelines addressing the use of opioids in the treatment of chronic pain published between 2007 2013. The content of the guidelines meeting selection criteria were reviewed and appraised.

Thirteen guidelines met the selection criteria and were screened for quality. Ten received poor to fair scores and two received high scores according to standardized assessment tools. Most guidelines were based on observational data or expert consensus. In describing the guideline content, the authors note that the majority of guidelines recommend that physicians avoid prescribing greater than 90-200 morphine equivalents per day, reduce doses by 25 to 50% when rotating opioids, acquire additional knowledge before prescribing methadone, and recognize the risks of fentanyl patches. Most guidelines recommend the use of opioid risk assessment tools, written treatment agreements, and urine drug screen.

Conclusion: This review of current guidelines for chronic pain found agreement on upper dosing thresholds, cautions with certain medications and the use of risk assessment tools, treatment agreements and urine testing

Nuckols, T et al. Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain. **Ann Intern Med.** 2014, January 7: 38 – 47

PHYSICAL ACTIVITY, LOW BACK PAIN, AND OBESITY

Combined, obesity and back pain are thought to be associated with 30% of United States healthcare expenditures. While studies of back

pain often list obesity as a confounding factor, research has failed to consistently establish this association. This study examined the interrelationships among physical activity, obesity and low back pain (LBP).

Data were obtained from the 2003 -2004 survey of the National Health and Nutrition Examination Survey (NHANES). From these data, LBP was determined by a questionnaire. Body mass index (BMI) was calculated during the physical examination and divided into four groups: normal weight (BMI<25kg/ m^2), overweight (BMI 25- 30kg/m^2), obese (BMI 31-35kg/m^2) and morbidly obese (BMI 36kg/m^2 and above). Physical activity was reviewed and characterized by intensity, frequency and duration.

The risks of LBP were 2.9% for normal weight, 5.2% for overweight, 7.7% for obese and 11.6% for morbidly obese subjects. Tobacco abuse was the strongest predictor of LBP across the BMI spectrum. The best physical activity predictors of LBP were found in the moderate- and high-intensity ranges with small predictive effects. For the average overweight American, a modest increase in moderate activity time (17.6 minutes each day) reduced the LBP risk by 32%. For the average morbidly obese American, an increase in moderate activity average bout duration from 1.3 minutes to 2.1 minutes reduced the risk of back pain risk by 38%.

Conclusion: This study found that an elevated body mass index is a risk factor for low back pain, and that increases in the total amount and time per bout of moderate physical activity decreases this risk.

Smuck, M., et al. Does Physical Activity Influence Relationship between Low Back Pain and Obesity. **Spine J.** 2014, February; 14(2): 209-216.

STROKE AND VASCULOPATHY ASSOCIATED WITH ADA2

Hereditary or acquired vascular disorders may be caused by a mutation in a single gene. This study used whole exome sequencing to screen for common genetic causes of disease among patients with early onset stroke.

Whole exome sequencing was completed in three patients who had experienced a stroke before the age of five years, each with a history of intermittent fevers, recurrent lacunar strokes, elevated levels of acute-phase reactants, livedoid rash, hepatosplenomegaly and hypogammaglobulinemia. In addition, candidate-gene sequencing was completed in three patients with a similar phenotype, as well as two young siblings, one with polyarteritis nodosa and one with small-vessel vasculitis.

Whole gene exome sequencing was performed on patients as well as their unaffected parents. A single, common candidate gene, CECR1, was identified in all patients. Subsequently, candidate gene sequencing was performed on samples from four additional patients from other centers. All encoded adenosine deaminase 2 (ADA2), which was absent or rare in healthy controls.

Conclusion: This study describes a disorder characterized by recurrent fevers and a spectrum of vascular pathology among patients with early onset stroke. The data implicate mutations in CECR1, encoding the ADA2 protein.

Zhou, Q., et al. Early-Onset Stroke and Vasculopathy Associated with Mutations in ADA2. **N Eng J Med**. 2014, March 6; 370(10): 911-920.

ORAL TERIFLUNOMIDE FOR RELAPSING MULTIPLE SCLEROSIS

Teriflunomide is the principal, active metabolite of lefonomide, a drug approved for the treatment of rheumatoid arthritis. This study was designed to further understand the safety and efficacy of teriflunomide as a treatment for patients with relapsing multiple sclerosis (MS).

This randomized, double-blind, placebo-controlled trial included patients 18 to 55 years of age, each diagnosed with relapsing MS. All patients were assessed with the Expanded Disability Status Scale (EDSS), completed at screening, at the time of randomization and every 12 weeks thereafter. The primary endpoint was the annualized relapse rate. The secondary endpoints included time to sustained accumulation of disability, defined as an increase from baseline of at least one EDSS point, sustained for at least 12 weeks.

Of the patients randomized, 821 completed the study, with a median duration of treatment of 581 days. In the primary analysis, both the seven mg and 14 mg dosages of teriflunomide significantly reduced the annualized relapse rate, as compared with placebo (p=0.0183 and p=0.0001, respectively). Teriflunomide was associated with a significantly longer time to first relapse, by 30.2% for the seven mg and 36.9% for the 14 mg dosage (p=0.0016 and p<0.0001 respectively). Further, a reduction in the risk of sustained accumulation of disability was observed in the 14 mg group, although not in the seven mg group.

Conclusion: This study of patients with relapsing MS found that teriflunomide, at 14 mg, was associated with a lower relapse rate and less disability accumulation as compared with placebo.

Confavreux, C., et al. Oral Teriflunomide for Patients with Relapsing Multiple Sclerosis (TOWER): A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial. **Lancet Neurol**. 2014, March; 13(3): 247-256.

DIABETES AND CERVICAL LAMINOPLASTY

Cervical spondylotic myelopathy (CSM) is an increasingly common condition in the geriatric population. Treatment for this condition includes cervical laminoplasty. As diabetes mellitus is a frequent comorbidity, this study was designed to better understand the impact of diabetes on the outcome of this surgical procedure.

Between January of 2007 and March of 2011, 700 patients underwent laminoplasty for the treatment of CSM. Of the 528 eligible patients, 505 were followed for over 12 months, and were included in this study. All patients were followed for clinical outcomes, with measures including the Japanese Orthopedic Association (JOA) score for cervical myelopathy, as well as radiographic and functional assessments. These outcomes were compared between those with, versus those without, a diagnosis of diabetes at the time of

(Continued from page 2)

diagnosis of diabetes at the time of the surgery.

The mean JOA scores before surgery were similar between the two groups. The pre-and post-operative JOA scores at the final follow-up of the nondiabetic group were significantly lower than those of the diabetic group. The diabetic group showed a significantly lower relative risk (defined as post-operative – preoperative JOA score x100%) than did the diabetic group (p=0.047). However, the mean JOA scores were similar between the two groups (p=0.343). No significant difference was seen in surgical site infection or postoperative complication rates between the two groups.

Conclusion: This study of patients diagnosed with cervical spondylotic myelopathy and treated with laminoplasty found that diabetic patients and non-diabetic patients experience similar benefits from the surgery.

Machino, M., et al. Impact of Diabetes on the Outcome of Cervical Laminoplasty. **Spine.** 2014; 39(3): 220-227.

*Peter Hwang, M.D.
University of Missouri, Columbia MO

*Chulhyun Ahn, M.D., MS
*Alexis Tingan, M.D.
UPenn Health System, Philadelphia, PA

*Thiru Annaswamy, M.D.
Trixy Syu, M.D.
UTSW Medical Center, Dallas TX

*Rachel Hallmark, M.D., Ph.D.
UVA, Charlottesville, VA

*Ryan Solinsky, M.D.
Sarah Wittry, D.O.
University of Washington, Seattle, WA

*Bonnie Weigert, M.D.
University of Wisconsin, Madison, WI

*William Robbins, M.D.
VCU, Richmond, VA

*Adam J. Schulte, M.D.
Mark F. Adderley, D.O.
Laura Giganti, M.D.
Joey Malbrough, M.D.
Washington University, St. Louis, MO

Executive Editor Emeritus
Donald F. Langenbeck, Jr., M.D.

Subscription Manager
Michael P. Burke, M.S.

***Regional Managing Editors have attested that they have no financial conflict of interest when choosing articles that appear in Rehab in Review.**

Rehab in Review (RIR) **is produced monthly by physicians in the field of Physical Medicine and Rehabilitation (PM&R), with the cooperation and assistance of Emory University School of Medicine, Department of Rehabilitation Medicine. The summaries appearing in this publication are intended as an aid in reviewing the broad base of literature relevant to this field. These summaries are not intended for use as the sole basis for clinical treatment, or as a substitute for the reading of the original research.**

The Emory University School of Medicine designates this journal based activity for a maximum of 3 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. The Emory University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

RIR **is affiliated with the Association of Academic Physiatrists, the World Health Organization, and the Chinese and Indian Societies of PM&R and endorsed by the International Society of Physical and Rehabilitation Medicine.**

Private subscriptions are available by email at rehabinreview@aol.com or by fax or phone at (800) 850-7388.

ISSN # 1081-1303

www.rehabinreview.com

REHAB IN REVIEW

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

EMORY UNIVERSITY SCHOOL OF MEDICINE | Department of Rehabilitation Medicine

Expanding the frontier of rehabilitation sciences in research, teaching, and patient care