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STROKE AMONG OLDER ANTIDEPRESSANT USERS AFTER TBI

Previous studies of Medicare beneficiaries 65 years of age or older have demonstrated that, following traumatic brain injury (TBI), the risk of ischemic and hemorrhagic stroke dramatically increases. As depression is common among elderly patients with TBI, this study assessed whether the risk of stroke is associated with the use of antidepressants.

Using Medicare administrative claims data from January of 2006 through December of 2010, patients who began antidepressant medication use following the TBI were identified. The primary outcome variable was hemorrhagic or ischemic stroke.

During the study period, 64,214 patients were hospitalized for a TBI, all of whom had no previous history of antidepressant use. Of these, 68% had no antidepressant use post-injury and 38% were prescribed antidepressants at least once following the injury. Among the antidepressant users, 4.6% had a hemorrhagic stroke and 11.7% had an ischemic stroke.

An adjusted analysis revealed that the new use of serotonin norepinephrine reuptake inhibitors (SNRIs) and phenylpiperazine antidepressants (PPAs) was associated with an increased risk of composite stroke, as well as ischemic stroke. New use of selective serotonin reuptake inhibitors was associated with an increased risk of hemorrhagic stroke.

Conclusion: This study, using a national sample of older Medicare beneficiaries hospitalized for traumatic brain injury, found that the new use of some antidepressants is associated with an increased risk of stroke.

Khokhar, B., et al. Risk of Stroke among Older Medicare Antidepressant Users with Traumatic Brain Injury. **J Head Trauma Rehab.** 2017, Jan/Feb; 32(1): E42-E49.

HIP STRENGTH AND RISK OF ANKLE SPRAIN IN YOUTH SOCCER

Soccer is currently the most popular sport played in the world. The high incidence of injury in youth soccer is a growing concern. Ankle sprains account for approximately 20% of all injuries in youth soccer players. This study examined whether hip muscle strength is a risk factor for sustaining a lateral ankle sprain among youth soccer players.

This prospective study included youth soccer players who played in the national league of their respective age category. Data collected including demographic, anthropometric and hip strength. Isometric hip strength was measured for the flexors, extensors, abductors, adductors and external/internal rotators. Injuries were monitored by the team's medical staff, and defined as that which prohibited the player from participating in practices or games for at least 48 hours.

Of the 133 players followed, 12 sustained a lateral ankle sprain, representing 18% of all injuries. These injuries resulted in a mean time lost of 22.4 days. An adjusted multivariate regression model revealed that players with greater hip extension muscle forces had a lower risk of lateral ankle sprain (p=0.028).

Conclusion: This prospective study of youth soccer players found that hip muscle extension force was significantly associated with a reduced risk of lateral ankle sprain.

De Ridder, R., et al. Hip Strength as an Intrinsic Risk Factor for Lateral Ankle Sprains in Youth Soccer Players: A 3-Season. Prospective Study. **Am J Sports Med.** 2017, February; 45(2): 410-416.

ANTI-INFLAMMATORY TREATMENT AFTER ACL INJURY

More than 50% of patients with anterior cruciate ligament (ACL) rupture develop radiographic abnormalities and post-traumatic osteoarthritis within five to 15 years post-injury. This study was designed to determine whether steroid injections affect the inflammatory biomarkers evident in the joint after such injuries.

Patients with ACL tears received intra-articular injections at four days and two weeks post-injury. Group one received a corticosteroid injection (triamcinolone, 40 mg) at four days and a placebo at two weeks. Group two received a placebo saline injection at four days and a corticosteroid injection at two weeks. Group 3 received corticosteroid injections at both time intervals. Group four received placebo injections at both intervals.

Arthrocentesis was performed on the day of initial presentation, between six and 10 days after the initial visit and on the day of surgery. Patient-reported outcomes were collected at the initial visit and at the time of surgery, with outcome scores obtained from the 5 KOOS subscales, the International Knee Documentation Committee Measure, visual analog scale pain scale and the Pain Catastrophizing Scale.

Both chondrodegenerative and inflammatory markers worsened over the first five weeks, while all patient-reported outcomes improved during this time. Patient-reported outcomes did not differ between those of patients in the corticosteroid group and those in the placebo group. Increases in CTX-II, associated with greater type II collagen breakdown, were significantly greater in the

placebo group than either of the two groups receiving steroids within the first several days post-injury.

Conclusion: This study of patients with ACL ruptures found that biochemical indicators of early osteoarthritis were evident before surgery, with intra-articular steroids able to suppress some of these.

Latterman, C., et al. A Multicentered Study of Early Anti-Inflammatory Treatment in Patients with Acute Anterior Cruciate Ligament Tear. **Am J Sports Med.** 2017, February; 45 (2): 325-333.

CILOSTAZOL FOR ALZHEIMER'S DISEASE

More than 35 million people worldwide suffer from Alzheimer's disease (AD). No cure currently exists for this disorder. While acetylcholinesterase inhibitors (AChEIs) are frequently prescribed, the benefit is often minor. Cilostazol is a selective inhibitor of cyclic nucleotide phosphodiesterase 3 (PDE3), with multiple activities in the brain including anti-inflammatory, antioxidative, and antiapoptotic. This study examined the therapeutic response of this medication as an add-on in patients with stable AD.

Subjects were 30 patients with stable AD, all receiving Cilostazol 50 mg twice per day as an add-on therapy with AChEIs. Each subject was matched with one patient with stable AD receiving only AChEIs for at least 12 months. The participants were tested at baseline and every six months thereafter with various neuropsychological assessments, including the Mini-Mental State Examination, the Cognitive Assessment Screening Instrument (CASI) Neuropsychiatric Inventory and Clinical Dementia Rating Sum of Boxes (CDR-SB). In addition, all patients underwent ApoE genotyping.

For the primary outcome measure of change in the Mini-Mental State Examination, a favorable response was noted in 50% of those in the Cilostazol group. A logistic regression analysis demonstrated that Cilostazol use was significantly associated with change in MMSE (p=0.024).

Conclusion: This study of patients with stable Alzheimer's disease taking an acetylcholinesterase inhibitor found that an antiplatelet drug, Cilostazol may reduce the odds of deterioration of cognitive function.

Tai, S et al. Cilostazol as An Add-On Therapy for Patients with Alzheimer's disease In Taiwan: A Case Control Study. **BMC Neurology**. 2017, February 23; 17:40.

ACUPUNCTURE FOR POST-TRAUMATIC STRESS DISORDER

Post-traumatic stress disorder (PTSD) may develop when a person witnesses or experiences a traumatic event. Among treatment options for PTSD, complementary and alternative medicine (CAM) approaches are becoming more widespread. As a number of studies have reviewed the effects of acupuncture on the symptoms of posttraumatic stress disorder, this literature review and meta-analysis was completed to better understand the effects of this intervention.

Medical electronic databases were searched through January of 2016 for studies including acupuncture for PTSD. From the literature review, seven studies, with a combined total of 719 participants, were selected. Acupuncture treatment ranged from 30 to 60 minutes per session, two to four times per week, three to 12 weeks in duration. Outcomes were measured up to six months after treatment.

The meta-analysis revealed a large effect in favor of acupuncture for improving symptoms of PTSD, versus any comparison group at short -term follow up (p=0.05), and a medium effect in favor of acupuncture versus any comparison group at longer-term follow-up (p=0.04). No significant difference was found between traditional Chinese medicine and auricular acupuncture. Further, no significant difference was identified between acupuncture and the control condition for the short term relief of physical and mental health related quality of life, symptoms of depression, anxiety or sleep quality. A significant effect of acupuncture was noted for depression at long-term follow-up (p=0.01)

Conclusion: This meta-analysis of published, randomized, controlled trials involving patients with post-traumatic stress disorder found that acupuncture may have significant, positive effects on the symptoms of

that syndrome, although the authors note that that the analysis was hampered by the quality of the studies.

Grant, S., et al. Acupuncture for the Treatment of Adults with Posttraumatic Stress Disorder: A Systematic Review and Meta-Analysis. **J Trauma and Dissociation**. 2017,doi.org.proxy.library.emory.edu/10.1080/15299732.2017.1289493

ACUTE TRANSIENT VESTIBULAR SYNDROME

Acute transient vestibular syndrome (ATVS) is characterized by a rapid onset of vertigo, nausea/ vomiting and gait unsteadiness in association with head motion. While isolated vertigo is not considered a symptom of transient ischemic attack, involving the vertebrobasilar territory (VB-TIA), ATVS may occur in VB-TIA. This study was designed to determine the prevalence of stroke among patients with acute, transient (less than 24 hours) vestibular syndrome.

This prospective, single center study included patients presenting with ATVS between January and December of 2014. Inclusion criteria were a rapid onset of vertigo/ dizziness, gait unsteadiness and head motion intolerance, resolution of vestibular symptoms within 24 hours and no history of recurrent vertigo. All patients underwent brain imaging after a structured neurologic and neuro-otologic examination, including a HINTs examination (head impulse, nystagmus patterns, test of skew, and finger rubbing).

Of the 86 patients studied, stroke was diagnosed in 27% of the patients with ATVS, 13 with completed cerebral infarction and 10 with only cerebellar hypoperfusion on PWI. The most common site of lesion among the 13 patients with cerebral infarction was the cerebellum. Multivariate logistic regression analysis revealed craniocervical pain (odds ratio 9.6), focal neurologic symptoms /signs pain (odds ratio 15.2), and VA stenosis/hypoplasia pain (odds ratio 7.0), to be risk factors for stroke among those with ATVS.

Conclusion: This single site study found that, among patients presenting with Acute Transient Vestibular Syndrome, 27% had a stroke that was often not apparent with conventional bedside exam and MRI. Associated craniocervical pain and focal neurological symptoms/ signs are useful clues in identifying those with stroke.

Choi, J., et al. Acute Transient Vestibular Syndrome. Prevalence of Stroke and Efficacy of Bedside Evaluation. **Stroke.** 2017, March; 48 (3): 556-562.

IVIG TREATMENT OF MILD COGNITIVE IMPAIRMENT DUE TO ALZHEIMER'S DISEASE

Open label studies of patients with Alzheimer's disease (AD) dementia treated with IVIG therapy have found evidence of modest cognitive improvement. This study was designed to determine whether a short treatment course of IVIG, given at the mild cognitive impairment (MCI) stage of AD, can reduce rates of brain atrophy, cognitive decline and/or conversion to AD dementia.

Subjects were patients 50 to 84 years of age diagnosed with amnesic MCI. At baseline, the patients underwent physical and neurologic evaluation with laboratory testing, cognitive testing and MRI. The subjects were randomized to receive either 0.4 g/kg IVIG or 0.9% IV saline placebo once every two weeks for eight weeks. Patients were reassessed with the Mini-Mental State Exam (MMSE), the Clinical Dementia Rating (CDR) scale and the ADAS-Cog at four-month intervals. Brain imaging was completed at 12 and 24 months. The primary endpoint was the annualized percent change in ventricular volume (APCV).

The ventricular APCV percentages were 8.14% at 12 months and 7.08% at 24 months in the placebo group and 5.87% and 6.26% in the IVIG group, respectively. The unadjusted analysis of APCV between groups at 12 months demonstrated a 28% reduction in the rate of atrophy in the treatment group compared with the placebo subjects. This effect was statistically significant when adjusted for MCI status (p=0.037). At both 12 months and 24 months, patients in the treatment group had higher scores on the MMSE than did those in the placebo group (p=0.004 and p=0.012, respectively). At both 12 and 24 months, the ADAS-Cog scores were more favorable in the treatment group than in the placebo group (p=0.01 and p=0.027, respectively). Conversion to AD dementia occurred in 33.3% of the treatment group and 58.3% of the control group.

Conclusion: This study found that IVIG, administered over eight weeks, a can reduce brain atrophy and cognitive decline for the first year after administration.

Kile, S., et al. IVIG Treatment of Mild Cognitive Impairment Due to Alzheimer's Disease: A Randomized, Double-Blind, Exploratory Study of the Effect on Brain Atrophy, Cognition and Conversion to Dementia. **J Neurol Neurosurg Psychiatry**. 2017, Feb; 88(2): 106-112.

VISUAL REACTION TIMES POST-CONCUSSION

Visual symptoms may develop after a concussion. Some have noted that visual dysfunction has been associated with patient reports of feeling slower than normal. This study was designed to determine whether central vision reaction time (CVRT) and peripheral vision reaction time (PVRT) are prolonged among patients with post-concussive visual symptoms.

This study included 23 patients with concussion who complained of new visual symptoms. All underwent prospective evaluations of CVRT and PVRT. A control group included 30, healthy subjects with no previous history of concussion.

The mean CVRT for the post-concussion group was 0.375 seconds, which was 0.063 seconds longer than that for the control group (p=0.000). The mean PVRT for the concussion group was 0.477 seconds, 0.13 seconds longer than that for the control group (p=0.000). The difference between CVRT and PVRT was 15.6% greater in the concussion group than in the control group (p=0.000).

Conclusion: This study of patients with concussion found that central and peripheral vision reaction times are both prolonged in patients with concussion, and that the difference between central and peripheral reaction times are significantly greater among those with concussion.

Clark, J., et al. Analysis of Central and Peripheral Vision Reaction Times

in Patients with Post-Concussion Visual Dysfunction. **Clin J Sports Med.** 2017 DOI: 10.1097/ JSM.0000000000000381.

EMERGENCY ROOM OPIOID PRESCRIBING AND RISK OF LONG-TERM USE

Rates of opioid prescribing and opioid related overdoses have quadrupled in the past three decades. This study examined a national sample of Medicare beneficiaries in an effort to understand how the initial exposure to an opioid relates to subsequent outcomes.

Data were retrieved using the Centers for Medicare and Medicaid Services carrier files. From these, a 20% random sample of beneficiaries from January of 2008 through December of 2011 was used to identify those who were assessed and treated in emergency rooms (ERs). From these visits were identified new prescription claims corresponding to an opioid. For this and subsequent opioid prescriptions, the number of days for which opioids were supplied was determined. The primary outcome was long-term opioid use, defined as 180 days or more of opioid supplied in the 12 months after the emergency room visit. The secondary outcome variable was the rate of hospital encounters. Physicians within the same ER were categorized by their rate of opioid prescribing.

The sample consisted of 215,678 patients treated by low intensity opioid prescribers and 161,951 treated by high-intensity opioid prescribers. Long-term opiate use at 12 months was significantly higher among those treated by high-intensity prescribers than among those treated by low intensity prescribers. Rates of opioid-related hospital encounters and encounters for fall or fracture were significantly higher in the 12 months after the index emergency department visit among patients treated by high-intensity opioid prescribers than among those treated by low intensity opioid prescribers ($p=0.02$).

Conclusion: This study of elderly patients seen in the same emergency department found that long-term opioid use was significantly higher among those treated by physicians who were high-intensity opioid prescribers than among those treated by low intensity prescribers.

Barnett, M., et al. Opioid-Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use**. N Engl J of Med.** 2017, February 16; 376: 663-673.

AUTOLOGOUS WHOLE BLOOD VERSUS STEROIDS FOR PLANTAR FASCIITIS

Plantar fasciitis is the most common cause of heel pain, with typical, conservative treatments including orthoses, stretching, taping and nonsteroidal anti-inflammatory drugs. When conservative treatment fails, corticosteroid injections are often used. This study compared the outcomes of treatment with autologous whole blood (AWB) with those of corticosteroids for patients with chronic plantar fasciitis.

Patients diagnosed with chronic plantar fasciitis were randomized to a control group or to receive treatment by injection with either 1 mL of autologous whole blood combined with 1 mL of 1% lidocaine or 40 mg of methylprednisolone combined with 1 mL of 1% lidocaine. The subjects returned for evaluation at four and 12 weeks after therapy. The assessment included the plantar fasciitis pain/disability scale (PFPS), a visual analog scale (VAS) and pressure pain threshold.

Both the steroid and AWB groups improved significantly on all pain measures at each of the measurement intervals ($p<0.05$ for all measures). At four weeks after treatment, the steroid group had significantly greater improvement than the AWB group on the VAS, PFPS and PPT ($p<0.05$). At 12 weeks, both treatment groups had better pain scores than the control group, with no differences between the two treatment groups.

Conclusion: This study of patients with chronic plantar fasciitis found that both steroids and autologous whole blood injections are effective for reducing pain, with steroids demonstrating better outcomes at four weeks, but equal in outcome to autologous whole blood at 12 weeks post-injection.

Karimzadeh, A., et al. Autologous Whole Blood versus Corticosteroid Local Injection in Treatment of Plantar Fasciitis: A Randomized, Controlled, Multi-Center Clinical Trial. **Clin Rheum.** 2017, March; 36 (3): 661-669.

THROMBOPROPHYLAXIS AFTER KNEE ARTHROSCOPY

The use of pharmacologic thromboprophylaxis after most orthopedic interventions is well established. Whether such prophylaxis is effective after arthroscopic knee surgery is less certain. The Prevention of Thrombosis after Knee Arthroscopically (POT-KAST) and the Prevention of Thrombosis after Lower Leg Plaster Cast (POT-CAST) trials were designed to assess the effect of low molecular weight heparin for the prevention of symptomatic venous thromboembolism (VTE).

Subjects 18 years of age or older who were scheduled to undergo knee arthroscopy were enrolled in the POT -KAST study and those treated for at least one week with casting of the lower leg with or without surgery were enrolled in the POT-CAST study. Eligible patients in the two trials were randomly assigned to receive either a prophylactic dose of low molecular weight heparin or no anticoagulant therapy. In the POT-KAST study, heparin was administered once daily for eight days, while in the POT-CAST study, heparin was administered for the full period of immobilization. The primary outcome measure was the cumulative incidence of symptomatic VTE within three months of the procedure.

Subjects were 1,543 patients, with 773 assigned to receive low molecular weight heparin and 770 to a control group. In the intention to treat analysis, in the POT-CAST trial, the cumulative incidences of symptomatic VTE within three months were 0.7% in the treatment group and 0.4% in the control group. This finding represented a relative risk of 1.6. One patient in each group had a major hemorrhagic event. The POT-KAST study revealed that the cumulative incidence of symptomatic venous thromboembolism was 1.6% in the treatment group and 1.8% in the control group. In neither study was the prophylaxis found to be effective.

Conclusion: This study found that administering low molecular weight heparin for eight days

following knee surgery performed arthroscopically or during immobilization due to casting was not significantly effective for preventing symptomatic venous thromboembolism.

Adrichem, R., et al. Thromboprophylaxis after Knee Arthroscopically and Lower Leg Casting. **N Engl J Med.** 2017, February 9; 376(6): 515-525.

LOW INTENSITY PULSED ULTRASOUND FOR BONE HEALING

The U.S. Food and Drug Administration has approved Low Intensity Pulsed Ultrasound (LIPUS) to accelerate fracture healing. This systematic review further assessed the efficacy of LIPUS for radiographic healing and clinical efficacy.

Medical databases were searched for controlled studies concerning the efficacy of LIPUS for the healing of fractures, published through November of 2016.The outcomes included time to return to work, full weight bearing, pain reduction, bone healing and subsequent fractures.

The search identified 42 studies, of which 26 were randomized, controlled trials. The authors found significant heterogeneity in the studies and found that, among those with a low risk of bias, treatment with LIPUS did not significantly reduce pain, days to weight bearing, or days to radiographic healing.

Conclusion: This literature review, focusing on those with a "low risk of bias", failed to identify low intensity pulsed ultrasound as an effective treatment to accelerate healing, pain or functional outcome in patients with fractures.

Schandelmaier, S., et al. Low Intensity Pulsed Ultrasound for Bone Healing: Systematic Review of Randomized, Controlled Trials. **BMJ:** 2017; 356: j656.

SEDENTARY BEHAVIOR AND LOW BACK PAIN

Low back pain (LBP) is among highest causes of disability in the world. Previous studies have assessed the association between sedentary behavior and LBP, although no prior study has explored the influence of sedentary behavior on the occurrence of LBP. This study was designed to better understand the association between sedentary behavior and the occurrence of LBP.

Data were collected from a population based registry of monozygotic (MZ) and dizygotic (DZ) twins, registered in a population-based twin registry of adult multiples born between 1940 and 1966. Data were collected between 2009 and 2011, including demographic information and self-reported health-related questionnaires. The main outcomes in the longitudinal analysis were the occurrence of new cases of LBP, with data on sedentary behavior collected using a categorical self-report questionnaire. The data were reviewed for an association between sedentary behavior and LBP outcome for both the cross-sectional and the longitudinal analysis.

Data were collected from 2,148 twins, with an overall lifetime prevalence of persistent LBP of 32%. A multivariate analysis revealed that sedentary behavior was weakly associated with a lifetime prevalence of persistent LBP (p=0.06). Further analysis found that, among DZ twins, sedentary behavior was associated with an increased prevalence of persistent LBP in females, but not males. The MZ twins analysis found no significant difference between males and females.

Conclusion: This study of twins found that sedentary behavior is only weakly associated with low back pain, with this relationship more evident in females than in males.

Amorim, A., et al. Sedentary Behavior Increases the Risk of Low Back Pain? A Population Based, Co-Twin Study of Spanish Twins. **Spine J.** 2017.doi.org/10.1016/ j.spine.2017.02.004.

CONCUSSED ATHLETES MORE PRONE TO INJURY

Previous studies have demonstrated that athletes who sustain a concussion have a higher risk of sustaining another serious injury during the 21 days after return to play. This study employed a large database of patients who had presented to the emergency department with concussion, to better understand the rate of subsequent injuries.

Patient data were collected from the Umea Injury Data Base in northern Sweden, the only hospital within a 120km radius. Data were collected concerning participants in four contact sports, (ice hockey, soccer, handball and floorball), who were treated for concussion between 1995 and 2009. Data were reviewed for injuries treated 24 months before through 24 months after the index concussion. A control group of athletes with an ankle sprain, but no concussion, was used for comparison.

Between 1995 and 2009, 4,961 concussions were documented, of which 699 occurred during the participation in the sports identified. These athletes were compared to 1,259 athletes without concussion. Compared to the control group, those with concussion had a higher risk of injury in the 24 months after the index concussion (OR 1.72), as well as in the 24 months before the injury (OR 1.98). This was not true for the athletes with ankle injury.

Conclusion: This study found that, while athletes who suffer a concussion are more likely to sustain injuries during the two years after the concussion, this risk is no greater than during the two years before the concussion.

Burman, E., et al. Concussed Athletes Are More Prone To Injury both Before and After Their Index Concussion: A Data Base Analysis of 699 Concussed Contact Sports Athletes. **BMJ Open Sport Exer Med.** 2016; 2(1).

BARICITINIB VERSUS ADALIMUMAB FOR RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a systemic autoimmune disease associated with severe disability and increased mortality. Activated Janus Kinases (JAK) are known to play a pivotal role in intracellular signaling for multiple cytokines that have been implicated in the pathological processes of RA. Baricitinib is an orally available small molecule that provides a reversible inhibition of JAK1 and JAK2. This study compared the effects of baricitinib with a tumor necrosis factor alpha inhibitor, adalimumab, for the treatment of RA.

Adult patients with active RA, with inadequate response to methotrexate were randomized to receive baricitinib, 4 mg once daily, adalimumab, 40 mg subcutaneous every other week or oral placebo. For the primary endpoint, baricitinib was compared with placebo and adalimumab for the proportion of patients at week 12 with a 20% response according to the criteria of the American College of Rheumatology (ACR20 response).

Subjects were 1,305 patients, with 488 in the placebo group, 487 in the baricitinib group and 330 in the adalimumab group. At week 12, the ACR20 responses were 70% for baricitinib and 61% for adalimumab ($p=0.01$). In addition, baricitinib was superior to adalimumab in reducing disease activity at week 12, as assessed with the Disease Activity Score for 28 Joints (DAS28) with the use of high-sensitivity c-reactive protein ($p<0.001$). A reduction in radiographic progression was observed for both treatment groups as compared to placebo at weeks 24 and 52.

Conclusion: This study of patients with rheumatoid arthritis and inadequate response to methotrexate found that an oral dose of baricitinib resulted in significantly greater clinical improvement than placebo or adalimumab.

Taylor, P., et al. Baricitinib versus Placebo or Adalimumab in Rheumatoid Arthritis**. N Engl J Med.** 2017, February 16; 376(7): 652-662.

RHEUMATOID ARTHRITIS TRIPLE THERAPY COMPARED WITH ETANERCEPT

Among patients with rheumatoid arthritis (RA) treated with methyltrexate (MTX), it is estimated that 70% will need additional therapy. Previous studies have demonstrated that triple therapy (SSZ and HCQ added to MTX) was non-inferior to MTX, and that TNF inhibition produces similar results, to triple therapy. This study examined the difference in infectious disease and GI adverse events (AEs) between patients treated with triple therapy and those treated with a tumor necrosis factor inhibitor (etanercept).

Subjects were 353 patients with active RA despite treatment with MTX. The participants were randomized to triple therapy (T) with SSZ and HCQ added to MTX, or Etanercept added to MTX therapy (E). Those without improvement of 1.2 or greater on the DAS28-ESR at 24 weeks were switched in a blinded fashion to the other therapy. Both GI and infectious disease adverse events (AEs) were recorded for both groups.

For both therapies, the majority of infectious AEs were non-serious, with a greater number occurring in the E group than in the T group ($p=0.02$), remaining significant after adjusting for comorbidities ($p=0.01$). No significant difference was found between groups for serious infectious disease AEs. For non-serious GI AEs, T therapy had a higher incidence ($p=0.02$), with no significant difference between the groups in serious GI AEs. Further, there was no significant difference between the treatment groups in the number of patients who switched treatment groups due to poor improvement in RA symptoms.

Conclusion: This study of patients with active RA, treated with methyltrexate, found that there is no difference in treatment outcome, or serious adverse outcomes among those treated with triple therapy (SSZ + HCQ + MTX) and those treated with TNF-inhibitor therapy (MTX+ Etanercept).

Quach, L., et al. Rheumatoid Arthritis Triple Therapy Compared with Etanercept: Difference in Infectious and Gastrointestinal Adverse Events. **Rheum**. 2017, March; 56 (3): 378-383.

OUTCOME OF FEMOROACETABULAR IMPINGEMENT SURGERY

Femoroacetabular impingement (FAI) is a common cause of hip pain and dysfunction. This study was designed to better understand the functional outcome of patients at least two years after arthroscopic surgical treatment of FAI.

This prospective study included 289 patients with FAI who had failed nonsurgical intervention. At baseline, the subjects underwent physical exams, including radiologic evaluation. All participants completed web-based, patient reported outcome measures at baseline and at 24 months postoperatively. These included the International Hip Outcome Tool (iHOT-12), the Copenhagen Hip and Groin Outcome Score (HAGOS) the Hip Sports Activity Scale (HSAS), a visual analog scale for overall hip function and a standardized instrument for the measurement of health (ED-5Q). In addition, the subjects were asked whether they were satisfied with the surgery. Postoperatively, the patients were allowed free range of motion and full weight bearing during the early rehabilitation phase, with crutches recommended for one month for outdoor and longer ambulation.

The subjects' average age was 37 years, with an average symptom duration prior to surgery of 3.8 years. At two-year follow-up, significant improvements were found for all measured outcomes ($p<0.05$). Satisfaction with surgery was endorsed by 82%, with 13% expressing dissatisfaction. Symptom duration was significantly and negatively related to both the iHOT-12 and the HAGOS-QoL.

Conclusion: This study of patients with femoral acetabular impingement found that surgical intervention resulted in statistically and clinically significant improvement in patient outcome.

Sansone, M., et al. Outcome after Hip Arthroscopic for Femoral Acetabular Impingement in 289 Patients with Minimum Two-Year Follow-Up. **Scand J Med Sci Sports.** 2017, February: 27(2); 230-235.

HYALURONIC ACID FOR HEMIPLEGIC SHOULDER IN STROKE

Hemiplegic shoulder pain (HSP) is a common complication of stroke. While steroid injections have been prescribed to alleviate pain, some have expressed concerns about the long-term effects of steroids, including tissue degeneration and tendon rupture. This study was designed to determine the effects of hyaluronic acid for the treatment of HSP.

This double-blind, randomized trial included 26 patients with stroke and hemiplegic shoulder, admitted to a rehabilitation unit. All participants were receiving one hour per day of occupational therapy and physical therapy. The subjects were randomly

divided to receive an injection of either 2.5 mL of sodium hyaluronate or 0.9% of sodium chloride into the subdeltoid bursa once per week for three weeks under ultrasound guidance. Before and after treatment the patients were assessed for shoulder spasticity using the modified Ashworth scale, shoulder subluxation, pain-free range of motion, Fugl-Meyer assessment of the upper extremity (FMA-UE) and the severity of HSP measured by a visual analog scale (VAS) for pain.

Significant improvement on the VAS was achieved for patients in the control group (p=0.007) as well as the treatment group (p=0.003) with better pain reduction in the treatment group (p=0.001). In addition, significant improvement in the FMA-UE was noted in the control group (p=0.042), as well as the treatment group (p=0.09), with a trend toward better improvement in the treatment group (p=0.09).

Conclusion: This double-blind, randomized, controlled trial found that hyaluronic acid may improve pain and function in the shoulders of patients with hemiplegic shoulder pain secondary to stroke.

Huang, Y., et al. The Effects of Hyaluronic Acid on Hemiplegic Shoulder Injury and Pain in Patients with Subacute Stroke. A Randomized, Controlled Pilot Study. **Medicine.** 2016, Dec; 98(45): e5547.

CRIZANLIZUMAB FOR PAIN IN SICKLE CELL

Patients with sickle cell disease experience sickle cell related pain crises. These are thought to be caused by vascular occlusion in the microcirculation, with the process of leukocyte adhesion to the endothelium believed to be initiated by P-selectin. Crizanlizumab is a humanized monoclonal antibody that binds to P-selectin and blocks its interaction with P-selectin glycoprotein ligand 1. This study assessed the efficacy of this medication in reducing the rate of sickle cell related crises.

Patients eligible for study inclusion had sickle cell disease, sickle cell hemoglobin C disease, sickle beta^0 thalassemia or sickle cell beta$^+$ thalassemia, were 16 to 65 years of age and had experienced two to 10 sickle cell related pain crises in the prior 12 months. The participants were randomized to receive Crizanlizumab, 2.5 mg/kg, 4 5 mg/kg or placebo, administered intravenously 14 times over a period of 52 weeks. The primary efficacy endpoint was the yearly rate of sickle cell related pain crises.

At the end of the treatment phase, the median crisis rates in the intention to treat population were 1.63 in the high-dose group, 2.01 in the low dose group and 2.98 in the placebo group. The difference between treatment and placebo was only significant for the high dose group (p=0.01). A crisis rate of zero was achieved by 36% in the high-dose, 18% in the low-dose and 17% in the placebo group.

Conclusion: This study of patients with sickle cell disease found that treatment with Crizanlizumab resulted in a significantly lower rate of sickle cell related pain crises, and was associated with a low incidence of adverse events.

Ataga, K., et al. Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease. **N Engl J Med.** 2017, February 2; 376: 429-439.

ENDOVASCULAR TREATMENT FOR STROKE WITH LARGE MISMATCH IMAGING PROFILE

When assessing patients with ischemic stroke for endovascular therapy or tPA, the ratio of hypoperfused to nonviable ischemic tissue is determined. From previous studies, appropriate candidates for endovascular intervention have a ratio of 1.8 or greater between critically hypoperfused and ischemic core, and a volume of ischemic core of 70mL or less. This study assessed the benefits of treating patients with baseline ischemic cores of up to 150mL.

Data were reviewed from a prospectively collected large vessel occlusion stroke database for patients with intracranial internal carotid artery and/or proximal middle cerebral artery occlusion on CT angiography, with a time from last known normal of less than 12 hours, baseline ischemic cores of greater than 50 mL and an absolute mismatch volume of 40 mL-150mL. Patients undergoing endovascular treatment were compared with matched controls who did not receive this treatment.

Data were included from 28 patients in the intervention group and 41 in the control group. Endovascular therapy was significantly associated with a favorable shift in the 90 day modified Rankin scores ((mRS (p=0.04)), with good outcomes in 0% of the controls and in 25% of the intervention group (p=0.04). The final infarct volumes were smaller in the intervention group (87ml) than in the control group (242 ml). For the subgroup with ischemic volumes of greater than 70ml, a significant improvement in final infarct volume was noted in the intervention group (p<0.001) with an insignificant trend towards better mRS in the treatment group. The 90 day mortality was numerically but not statistically lower in the treatment group.

Conclusion: This study of patients with ischemic stroke found that for properly selected patients, endovascular therapy may benefit those with a large ischemic core and large mismatch profiles.

Rebello, L., et al. Endovascular Treatment for Patients with Acute Stroke Who Have a Large Ischemic Core and Large Mismatch Imaging Profile. **JAMA Neurol.** 2017, January 1; 74;(1): 34-40.

EXERCISES FOR PARKINSON'S DISEASE

While short-term exercise may improve health, well-being and function in patients with Parkinson's disease (PD), there is a lack of evidence of long-term benefits. This study was designed to better understand these benefits.

This phase II, randomized, controlled trial included patients with idiopathic PD, who were able to walk at least 100 m. The subjects were randomized to perform exercises or receive handwriting training, twice per week for six months. Exercise included 30 minutes of aerobic training followed by 30 minutes of resistance training. A control group underwent handwriting exercises, using workbooks at home. Outcome measures were performed at baseline, and at three, six and 12 months. The primary outcome measure was the two-minute walk test. Mobility was also assessed using the Timed Up and Go Test, the Nine Hole Peg Test and global motor function assessed using the Motor

(Continued from page 2)

*Bonnie Weigert, M.D.
Jonathan Carrier, D.O.
Jacob Halvorsen, D.O.
University of Wisconsin, Madison, WI

*Chris Arbonies, M.D.
Randy Jenkins, M.D.
Rondy Michael Lazaro, M.D.
Joe Seahrist, M.D.
VCU, Richmond, VA

*Rucha Kharod, M.D.
Gregory Decker, M.D.
Donel Angelo Sequea, M.D.
Washington University, St. Louis, MO

function assessed using the Motor Examination of the MDS-UPDRS (III).

At 12 months, during the two-minute walk test, the exercise group was able to walk 144.6 m, while the control group walked 137.9 m ($p=0.06$). The largest effect was found on the MDS-UPDRS III at 12 months ($p<0.05$), indicating an improvement in motor symptoms ($p<0.05$). Small, statistically insignificantly better gains were found in the exercise group than in the control group in improvement in leg power, aerobic capacity and perceived health-related quality of life.

Conclusion: This study of patients with Parkinson's disease suggests that twice weekly aerobic and resistance exercise may improve physical function.

Collett, J., et al. Phase II, Randomized, Controlled Trial of a Six -Month Self-Managed Community Exercise Program for People with Parkinson's Disease. **J Neurol Neurosurg Psychiatry**. 2017, March; 88(3): 204-211.

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