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INTRAARTICULAR CAPSAICIN FOR KNEE ARTHRITIS

With an increase in the average age of the population, the incidence of symptomatic knee osteoarthritis (OA) is increasing. This study assessed the long-term analgesic effect of intra-articular capsaicin on moderate to severe pain associated with OA of the knee.

Subjects were patients 45 to 80 years of age with radiographic evidence of chronic OA of the knee. The patients were randomly assigned to one of three treatment groups. These included a single intra-articular injection of; a) four mL of placebo, 2) synthetic trans- capsaicin 0.5 mg, 3) synthetic trans- capsaicin 1.0 mg. The subjects recorded pain during walking, daily from baseline to week 12, and then weekly for weeks 12 through 24.

Data were complete for 157 patients. The reduction in pain scores between baseline and week 12 was greater in the capsaicin 0.5 and 1 mg groups than in the placebo group (p=0.07 and p=0.0001, respectively). At week 24, compared with the placebo group, better pain relief was noted in the 1 mg group, but not in the 0.5 mg capsaicin group.

Conclusion: This study of patients with moderate osteoarthritis of the knee found that an intra-articular injection of capsaicin could significantly reduce pain, with the effects persisting for up to 24 weeks.

Stevens, R., et al. Randomized, Double-Blind, Placebo Controlled Trial of Intra-Articular Trans-Capsaicin for Pain Associated with Osteoarthritis of the Knee. **Arthr Rheum.** 2019, September; 71(9): 1524-1533.

MARATHON RUNNING AND KNEE DAMAGE IN THE MIDDLE-AGED

Few studies have investigated the effects of marathon running on the internal structures of the knee. This study reviewed the effects of marathon running on the knee joints of first-time marathoners.

Subjects were 82 healthy, middle-aged, asymptomatic volunteers registered for their first marathon and 11 controls. All underwent bilateral MRI scans of the knee, six months before and two weeks after the marathon. The Knee Injury and Osteoarthritis Outcome Score (KOOS) was used as a self-report outcome measure.

Data were complete, including follow-up, for 71 subjects. At follow-up, MRI studies revealed decreased damage in the marathon group, including subchondral bone marrow edema in the condyles of the tibia (p=0.011) and femur (p=0.082). In contrast, worsened MRI scores were noted for the cartilage of the lateral patella (p=0.0005), semimembranosus tendon (p=0.016), iliotibial band (p<0.0001) and prepatellar bursa (p=0.016). After the marathon, only one runner obtained a worsened meniscus grade. The menisci of all other scanned knees remained unchanged. No significant changes between pre-marathon and post-marathon KOOS scores were identified in either group.

Conclusion: This study of middle-aged runners found that running a marathon improved MRI evidence of health in the subchondral bone of the tibial and femoral condyles but resulted in asymptomatic worsening of the peri-patella cartilage.

Horga, L., et al. Can Marathon Running Improve Knee Damage of Middle-Aged Adults? A Prospective Cohort Study. **BMJ Open Sport Exer Med.** 2019, October 16; 4-6.

FEVER AND ANTIBIOTIC USE FOLLOWING SUBARACHNOID HEMORRHAGE

Fevers occur in approximately 70% of patients with subarachnoid hemorrhage (SAH). Of these, it is estimated that only 50% have an infectious etiology. This study was designed to better understand the associations among fever burden, antibiotic use and outcomes in patients with SAH.

This retrospective, cohort investigation studied 194 patients, hospitalized with non-traumatic SAH. Data gathered included body temperature through day 13, patient demographics, SAH severity (Hunt and Hess score and Fisher score), antibiotic exposure and infection status.

Of the 194 patients followed, 93 (48%) experienced fever and 133 (68.6%) received antibiotics. The fever burden peaked on day five. Of the 45 patients determined to have a noninfectious fever, 31 received antibiotics, with an average of 32.25 doses per patient. Fever burden was not significantly associated with poor outcome, as measured by the modified Rankin Scale.

Conclusion: This retrospective, cohort study of patients with nontraumatic, subarachnoid hemorrhage found that 48% experienced fever, peaking at day five, with 16% of the patients receiving antibiotics without evidence of an infection.

Magee, C., et al. Fever Burden in Patients with Subarachnoid Hemorrhage and the Increased Use of Antibiotics. **J Stroke Cerebrovasc Dis.** 2019, November; 28 (11):104313.

TRANEXAMIC ACID FOR ACUTE TRAUMATIC BRAIN INJURY

Tranexamic acid reduces bleeding by inhibiting the enzymatic breakdown of fibrin blood clots. This study evaluated efficacy of tranexamic acid on head injury related death and disability.

This international, multicenter, randomized, placebo-controlled trial enrolled patients with traumatic brain injury (TBI) within three hours of injury. Eligibility for study inclusion were, a Glasgow Coma Scale Score (GCS) of 12 or lower, no intracranial bleeding on CT and no major

extracranial bleeding. The participants were randomized to receive one gram of tranexamic acid or a matching placebo by IV. The primary endpoint was in-hospital death within 28 days of injury.

Between July of 2012 and January of 2019, 12,737 patients were enrolled. Head injury related death was noted in 18.5% of the tranexamic acid group and in 19.8% of the placebo group, with a relative risk (RR) of 0.94. Excluding patients with a GCS score of three, and those with bilaterally unreactive pupils at baseline, the risks of head injury related death were 12.5% in the tranexamic acid group and 14.0% in the placebo group (RR 0.89). The rate of head injury-related death was reduced in the treatment group among patients with mild-to-moderate head injury (RR 0.78), but not among patients with severe head injury (RR 0.99).

Conclusion: This multicenter, randomized trial of patients with traumatic brain injury found that those treated with IV tranexamic acid within three hours of the trauma had a reduced risk of head injury related death.

The CRASH-3 Trial Collaborators. Effects of Tranexamic Acid Death, Disability and Vascular Occlusive of Patients with Acute Traumatic Brain Injury (CRASH-3): A Randomized, Placebo Controlled Trial. **Lancet**; 2019; 394(10210): 1713-1723.

HEMORRHAGE WITH MILD HEAD INJURY AND ORAL ANTICOAGULANTS

The past decade has seen an increase in the use of direct oral anticoagulants (DOACS) for the prevention of thromboembolism among patients with atrial fibrillation (AF). This study was designed to better understand the effect of these medications on patients treated for mild head trauma.

This observational study reviewed patients seen in the emergency department for a minor head trauma (Glasgow Coma Score of 14 to 15) who were taking anticoagulants at the time of the trauma. Data collected included medical history and laboratory data, with a hemorrhagic risk score calculated for each patient.

Subjects were 226 patients receiving one of the four DOACs (dabigatran, rivaroxaban, apixaban or edoxaban) and 176 patients taking a vitamin K antagonist (VKA). Most were being treated for AF. Intracranial bleeding was found in 10.2% of the patients in the VKA group and 2.6% of the DOAC group ($p<0.01$). Of interest, 28% of those in the VKA group had INRs of >3, while 40% in the DOAC group were receiving the lowest available dose.

Conclusion: This study of patients seen in the emergency department for mild head injury found that those taking DOACS had less intracranial bleeding complications than did those taking vitamin K antagonists.

Spinola, M., et al., Hemorrhagic Risk and Intracranial Complications in Patients with Minor Head Injury (MHI) Taking Different Oral Anticoagulants. **Am J Emerg Med** 2019, September; 37(9): 1677-1680.

PHONOPHERESIS WITH PHYLLANTHUS AMARUS FOR OSTEOARTHRITIS

Among the treatments for osteoarthritis (OA), ultrasound (US) has been used in combination with the drug therapeutic energy technique referred to as phonophoresis. As previous studies have found antioxidant and anti-inflammatory properties in Phyllanthus Amarus (PA), a rich source of polyphenols, this study assessed the efficacy of PA delivered by phonophoresis for the treatment of patients with OA of the knee.

Subjects were 30 patients, all over 50 years of age, with OA of the knee. The subjects were randomized to a control group or a treatment group. Both received daily sessions of US therapy (1.0W/cm^2 power at 1MHz), with the treatment group also receiving PA. The primary outcome measure was a visual analog scale (VAS) of pain, administered before and after 10 sessions of US treatment. Secondary outcomes included blood serum levels of TNF-Alpha, nitrous oxide (NO), superoxide dismutase (SOD) and serum total antioxidant capacity (TAC).

Compared with baseline values, a significant improvement in VAS pain scores was noted in both groups. The improvement was significantly better in the group receiving PA than in the control group ($p<0.01$). In addition, compared with baseline, the levels of TNF-alpha and NO were significantly more reduced ($p<0.01$ for both), and the SOD and TAC activity more increased, in the PA group than in the control group (both $p<0.01$).

Conclusion: This study of patients with osteoarthritis of the knee

found that phonophoresis delivery of Phyllanthus Amarus resulted in better pain relief than did ultrasound alone. This improvement coincided with improvement on measures of oxidative stress and inflammation.

Pinkaew, D., et al. Phonophoresis Associated with Nanoparticle Gel from Phyllanthus Amarus Relieves Pain by Reducing Oxidative Stress and Pro-Inflammatory Markers in Adults with Knee Osteoarthritis. **Chin J Integr Med**. 2019, September; 25 (9): 691-695.

DULOXETINE AND GABAPENTIN FOR KNEE OSTEOARTHRITIS

Pain is a major symptom among patients with osteoarthritis (OA). As both duloxetine and gabapentin have been found to be useful for the treatment of pain from other conditions, this study compared these two medications for the treatment of OA related pain.

This blinded, randomized, controlled trial included 150 patients with moderate to severe knee OA, all between 45 and 75 years of age. The subjects were randomly allocated to receive duloxetine, gabapentin or acetaminophen, titrated to a maximum of 60mg, 600mg and 2,000mg daily, respectively. The participants were assessed at baseline, two, four and 12 weeks after the intervention. Evaluations included a Visual Analog Scale (VAS) for pain severity and assessment of physical status using the Western Ontario and McMaster University's Osteoarthritis (WOMAC) questionnaire.

Both the gabapentin and duloxetine groups had significantly lower VAS scores as compared to the acetaminophen group in the first ($p<001$) and third months ($p<0.001$), with no significant difference between the two groups. Those in the gabapentin group had significantly better WOMAC total scores than did those in the duloxetine ($p= 0.006$) and acetaminophen ($p= 0.002$) groups, with no significant difference between the duloxetine and acetaminophen groups ($p= 0.77$).

Conclusion: This study of patients with moderate to severe osteoarthritis of the knee found that gabapentin and duloxetine have similar effects in reducing pain, with both superior to acetaminophen.

Enteshari-Moghaddam, A., et al. Efficacy of Duloxetine and Gabapentin in Pain Reduction in Patients with Knee Osteoarthritis. **Clin Rheum.** 2019, October; 38(10): 2873-2880.

ANTIBIOTICS FOR LOW BACK PAIN WITH MODIC CHANGES

Among patients with low back pain (LBP), those who have signal changes in the vertebral bone, extending from the endplate as visualized on magnetic resonance imaging (MRI) are described as having Modic changes. As some have speculated that these indicate a low-grade bacterial discitis, this study examined the efficacy of antibiotic treatment for patients with this finding.

This multicenter, randomized, double blind, placebo controlled Norwegian trial recruited adults 18-65 years of age with chronic LBP, lumbar disc herniation, and type I or type II Modic changes. The patients were randomized to receive amoxicillin 750 mg three times per day or placebo for three months. All patients were assessed with the Norwegian version of the Roland-Morris Disability Questionnaire (RMDQ) as well as the Oswestry Disability Index, low back pain intensity and health-related quality of life.

At one year the mean RMDQ scores had improved by 3.7 points in the amoxicillin group and 2.1 points in the placebo group ($p=0.04$). Among those assigned to the amoxicillin group 12% discontinued or paused treatment because of adverse events compared with 2% in the placebo group.

Conclusion: This study of patients with chronic low back pain and Modic changes on MRI found that those treated with amoxicillin had a statistically significant, though clinically small, improvement in disability scores as compared to those treated with placebo.

Braten, L., et al. Efficacy of Antibiotic Treatment in Patients with Chronic Low Back Pain and Modic Changes (the AIM Study): Double-Blind, Randomized, Placebo Controlled Multicentre Trial. **BMJ**. 2019 doi: 10.1136/bmj.l5654.

PLATELET RICH PLASMA FOR REFRACTORY LATERAL EPICONDYLITIS

Lateral epicondylitis (LE) has a prevalence of one to three percent in the United States. This study reviewed the long-term outcomes of patients with recalcitrant LE who were treated with platelet rich plasma (PRP).

This prospective study included 34 patients with refractory LE. All had received an autologous PRP injection between November of 2011 and May of 2013. Injections were of four to seven mL of PRP, with the shoulders immobilized in a sling for 48 hours post-injection. All were evaluated with the Oxford Elbow Score (OES), from which a minimal clinically important difference (MCID) was calculated.

At a mean long-term follow-up of 5.2 years, 87.1% exhibited a MCID in pain scores, while 90% had a MCID in function. Of the original group, two underwent a repeat injection and one underwent surgery. Significant improvement was noted in OES scores between baseline and post-operative, as well as long term follow up for overall OES scores as well as the three OES domains of Pain, Elbow Function and Psycho-Social ($p<0.001$ for all comparisons).

Conclusion: This study of patients with refractory lateral epicondylitis found that a single injection of autologous platelet rich plasma may be effective in providing long-term pain relief.

Brkljac, M., et al. Long-Term Follow-Up of Platelet Rich Plasma Injections for Refractory Lateral Epicondylitis. **J Ortho.** 2019, Nov-Dec; 16(6): 496-499.

PLATELET RICH PLASMA FOR PLANTAR FASCIITIS

Chronic plantar fasciitis is the most common cause of foot complaints in the United States. This study compared the effect of corticosteroid injections to that of platelet rich plasma (PRP) for patients with chronic plantar fasciitis.

Subjects were adult patients with chronic plantar fasciitis who had failed nonoperative treatment. The patients were randomly assigned to receive a six mL injection with either autologous PRP (n=63) or corticosteroid (n=46) into the plantar fascia. All were assessed at baseline and at follow-up using a visual analog scale for pain, and with the American Orthopedic Foot and Ankle Society Foot Function Index, administered at four, twelve, twenty-six and fifty-two weeks.

Both groups demonstrated decreased pain over time. In the corticosteroid group, pain scores decreased quickly and remained

stable over time. For the PRP group, pain reduction was more modest initially, surpassed by the corticosteroid group at one month, reaching its lowest value at 12-month follow-up. Between baseline and 12-month follow-up, pain was reduced by at least 25% in 84% of the PRP group and in 55.6% of the steroid group.

Conclusion: This study of patients with chronic plantar fasciitis found that injections with corticosteroids resulted in better pain relief at one month, but inferior relief compared to PRP at 12 months.

Peerbooms, J., et al. Positive Effect of Platelet Rich Plasma on Pain in Plantar Fasciitis: A Double-Blind, Multicenter, Randomized, Controlled Trial. **Am J Sports Med**. 2019, November; 47(13): 3238-3246.

ENDOVASCULAR THROMBECTOMY AND IV FIBRINOLYSIS IN LARGE VESSEL STROKE

The combination of intravenous thrombolysis and endovascular thrombectomy (IVT+EVT) is commonly used for the treatment of stroke caused by large vessel occlusion. However, no randomized trial has compared the efficacy of IVT+EVT to that of non-reperfusion therapy for these patients. This study was designed to make that comparison.

This study is a secondary analysis, combining the data from the SWIFT PRIME trial with that of the two NINDS rt-PA trials. This process allowed for a comparison of four different reperfusion treatment strategies: (1) supportive care only (the placebo group of the NINDS rt-PA Study), (2) intravenous alteplase alone (the IVT group of the NINDS rt-PA Study), (3) continued intravenous alteplase alone among patients with an early nonresponse to IVT (the IVT alone group of the SWIFT PRIME trial) and (4) EVT added to intravenous alteplase among patients with early non-response to IVT alone (the IVT+EVT group of the SWIFT PRIME trial). The primary outcome measure was level of disability at 90 days, as measured by the modified Rankin Scale (mRS).

Subjects were 240 patients, including 80 each treated with supportive care, IVT alone or IVT+EVT. At 90 days, IVT+EVT was superior to both IVT alone and supportive care only. However, the benefit of IVT alone over supportive care did not reach statistical significance. Freedom from disability (mRS 0-1) occurred in 48.1% of the IVT+EVT group, 30.0% of the IVT group and 21.3% of the supportive care only group. The odds ratios of better mRS scores, as compared to supportive care, were 3.34 for the IVT+EVT group and 1.14 for the IVT alone group.

Conclusion: This study found that, for every 100 patients treated for ischemic stroke caused by large vessel occlusion, compared with intravenous thrombolysis alone, adding endovascular thrombectomy reduced long-term disability in 55.

Young-Saver, D., et al. Magnitude of Benefit of Combined Endovascular Thrombectomy and Intravenous Fibrinolysis in Large Vessel Occlusion Ischemic Stroke. **Stroke.** 2019, September; 50(9): 2433-2440.

ENDOVASCULAR RECANALIZATION IN CHILDHOOD STROKE

Childhood arterial ischemic stroke is a rare clinical event. As studies of adults have shown the efficacy and safety of endovascular recanalization for large intracranial vessel occlusions, this study evaluated the efficacy of treatment regimens in a pediatric sample.

This retrospective, observational, multicenter, cohort study was conducted from January of 2000 to December of 2018. For each patient, baseline characteristics, imaging and treatment modalities were recorded. All participants underwent MRI or CT imaging before and after intervention. Endovascular recanalization procedures included a combination of distal thrombaspiration and/or clot retrievers. At 24 hours post-treatment, CT or MRI was performed. The primary outcome variable was the change in the Pediatric National Institutes of Health Stroke Scale (PedNIHSS) score from admission to day seven.

Subjects were 73 children from 27 participating centers with a median age of 11.3 years. The median time from onset to recanalization was four hours. Of these subjects, 86% were treated for anterior circulation vessel occlusion and 14% for posterior circulation occlusion. PedNIHSS scores improved from a median of 14.0 on admission to a median of 5.0 at 12-24 hours after thrombectomy and to a median of 4.0 at day seven. A comparison of mRS (at discharge and 180 days) to mRS (at 90 days) in the HERMES (adult) meta-analysis revealed a lower proportion of poor outcomes in this sample.

Conclusion: This multicenter study of endovascular thrombectomy in pediatric patients with ischemic stroke and large vessel occlusion found a high rate of success with a low rate of complications.

Sporns, P., et al. Feasibility, Safety and Outcome of Endovascular Recanalization in Childhood Stroke: The Save ChildS Study. **JAMA Neurol**. 2019, October 14; doi: 10.1001/jamaneurol.2019.3403.

COGNITIVE IMPAIRMENT AND POSTSTROKE OUTCOME

Cognitive impairment is common among stroke survivors. This study investigated the impact of cognitive impairment at six months after the stroke.

The Action on Secondary Prevention Interventions and Rehabilitation in Stroke (ASPIRE-S) study was a prospective, observational, cohort study of ischemic stroke survivors. Subjects were 256 patients hospitalized for acute ischemic stroke. Of the original 256 subjects, 226 underwent cognitive assessments at six months post-stroke. Of these, 101 stroke survivors were followed at a mean of 5.1 years. Data collection included face-to-face assessments and self-report questionnaires, including the Montréal Cognitive Assessment (MoCA), the Nottingham Extended Activities of Daily Living Scale (NEADL), the Stroke Specific Quality of Life Scale (SSQOL) and the Hospital Anxiety Depression Scale, Depression subscale.

At six months post-stroke, 40.7% of the patients had evidence of cognitive impairment (MoCA<24). Of those with cognitive impairment at six months, 80% remained impaired at five years. Additionally, 27.8% without cognitive impairment at six months were found to have cognitive impairment at five years. A multivariable analysis found that cognitive impairment at six months was independently associated with a worse quality of life, lower levels of independence in activities of daily living, a greater likelihood of receiving care from family or friends and an increased likelihood of experiencing depression at five years.

Conclusion: This study of patients with acute ischemic stroke found that over 40% remained cognitively impaired at six months, with an increased risk among these

patients of depression, a worse quality of life and worse ADLs.

Rohde, D., et al. The Impact of Cognitive Impairment on Poststroke Outcomes: A Five-Year Follow-Up. **J Geriatr Psychiatry Neurol.** 2019, September; 32(5): 275-281.

CHOCOLATE CONSUMPTION AND DEPRESSION

Depression affects more than 300 million people worldwide. While previous studies have failed to demonstrate an association between chocolate consumption and depression, the type of chocolate consumed has not been concluded. This study was design to assess the association between dark chocolate consumption and depression.

The National Health and Nutrition Examination Survey (NHANES), was designed to provide estimates of the prevalence of health, nutrition, and potential risk factors among the civilian noninstitutionalized US population. Data for this study were obtained from participants over five NHANES cycles starting in 2007. These included two, 24-hour dietary recalls. Daily chocolate consumption as well type of chocolate consumed were recorded. The primary outcome measure was depressive symptoms as measured by the Patient Health Questionnaire (PHQ-9).

Subjects were 20,125 adults aged ≥20 years with a mean age of 46.5 years. Of these, 11.1% reported any chocolate consumption occurring during their dietary recalls, and of these 12% reported at least some dark chocolate consumption. In an adjusted analysis, there was no association between non-dark chocolate consumption and clinically relevant depressive symptoms. Those who reported any dark chocolate consumption had a 70% lower rate of reporting depressive symptoms than did those who did not report any chocolate consumption (OR 0.30). When reviewing the quantity of chocolate consumed, those reporting chocolate consumption in the highest quartile (104–454 g/day) had 57% lower odds of depressive symptoms than those who reported no chocolate consumption (OR 0.43).

Conclusion: This study provides some evidence that the consumption of chocolate, particularly dark chocolate, may be associated with a reduction in the odds of clinically relevant depressive symptoms.

Jackson, S., et al. Is There a Relationship Between Chocolate Consumption and Symptoms of Depression? A Cross-Sectional Survey Of 13,626 US Adults. **Depress Anxiety.** 2019, October;36 (10):978-995.

BLOOD PRESSURE AND RISK OF DEMENTIA

While some have hypothesized that elevated blood pressure may lead to an increased risk of dementia, confusion exists regarding the associations between blood pressure, and dementia subtypes. This large study was designed to better understand this association.

This historical cohort study was conducted using data (1987-2014) from the United Kingdom primary care data from the Clinical Practice Research Datalink (CPRD). The index date was defined as the date when BP was first measured among those at least 40 years of age. Follow-up occurred until the final CPRD data record or until a diagnosis of dementia. An adjusted analysis was completed to better isolate the association between blood pressure and the risk of dementia.

Subjects were 2,593,629 patients with a mean age of 54 years with a median follow-up of 8.2 years. During follow-up 65,518 cases of dementia were recorded of which 75 were Alzheimer's disease (AD), 21% were vascular dementia and 3.9% were other rare subtypes. Age- and sex-adjusted standardized rates of dementia were lower among individuals with higher systolic BP. During the first five years, systolic blood pressure (SBP) was moderately and inversely associated with the risk of dementia. The association between increased SBP and decreased dementia was stronger with AD (RR 0.83) than with vascular dementia (RR 0.903). During the 5-10-year follow-up, this negative association was less marked than during the first five years. After 10 years, there was only very weak association with SBP, with the association found among those <70 years of age but not those who were older. Among those 85 years of age or older, the association reversed.

Conclusion: This population-based study of 2.6 million adults found that increased systolic blood pressure was associated with a decreased risk of dementia, with this association reversing among those 85 years of age and older.

Gregson, J., et al. Blood Pressure and Risk of Dementia and Its Subtypes: A Historical Cohort Study with Long Term Follow-Up in 2.6 Million People. **Europ J Neurol.** 2019:1479–1487.

ANKLE-BRACHIAL INDEX OVER TIME

When managing venous leg ulcers, compression therapy is often used to assist with the healing and the recurrence of these ulcers. Wound care guidelines suggest that pressure dressings should not be applied to patients with an ankle-brachial index (ABI) of 0.5 or less. Among patients who have had an ABI in the past, there are no data concerning the change in ABI over time and thus no data to inform the decision to recheck the ABI. This study was designed to help determine the change in ABI over time.

A chart review was completed for all patients seen in our healthcare network between April 2005 and April 2013. Eligible patients had at least two ABIs with no revascularization procedures between the two tests. The difference between these two test values was divided by the number of days between tests to determine the average change in ABI per day.

Data were completed for 76 patients, with a mean of 539 days between ABI evaluations. The mean of the initial ABI was 0.881. The mean of the second ABI was 0.885. The mean daily change in ABI was 0.000033. The estimated change in ABI for a 12-month period was 0.0120. Extrapolating from these data, it was determined that a meaningful deterioration in ABI (0.1) would be expected to occur at an average of 8.3 years. There was no significant difference in the change in ABI per day between those who use tobacco and those who do not, those with coronary artery disease, and those without, as well as between those with diabetes and those without.

Conclusion: This study of patients with at least two ankle-brachial index evaluations found that a deterioration of 0.1 in the ABI value could be expected every 8.3 years.

Burke, D., et al. Change over Time of the Ankle Brachial Index. **Wound Med.** 2020;28: March. doi.org/10.1016/j.wndm.2019.100174.

VESTIBULAR DYSFUNCTION IN ACUTE TRAUMATIC BRAIN INJURY

Studies have shown that approximately half of patients with traumatic brain injury (TBI) have vestibular complaints at five years. This study assessed whether the treatment of vestibular diagnoses can accelerate recovery in patients with TBI.

Patients with acute TBI admitted to an adult Major Trauma Ward were included in the study. The work-up included ophthalmoscopy, otoscopy eye movements, the Hallpike maneuver and gait assessment. All subjects were followed for clinical outcome.

Of the 111 patients screened, 96 (87%) had vestibular symptoms, vestibular signs of gait, postural ataxia or ocular motor signs of vestibular dysfunction. Of those who underwent formal testing, gait ataxia was the most common sign. Of note, half of these patients denied a sense of imbalance. Diagnoses included BPPV (38%), acute peripheral unilateral vestibular loss (19%) and migraine phenotype headache (34%).

Conclusion: This study of patients admitted for traumatic brain injury found that the great majority had vestibular signs and symptoms.

Marcus, H., et al. Vestibular Dysfunction in Acute Traumatic Brain Injury. **J Neurol.** 2019, October; 266 (10): 2430-2433.

HIP SURGERY AND ANTICOAGULATION

The incidence of total hip arthroplasty (THA) is expected to continue to rise as the population ages. While the international normalized ratio (INR) has historically been associated with the risk of bleeding, a clear association between that risk and INR level has not yet been established. This study examined the association between INR level and postoperative bleeding and mortality among patients undergoing a primary THA.

This prospective, cohort study included data from the American College of Surgeons' National Surgical Quality Improvement Program. Data were extracted for adults undergoing primary THA between 2005 and 2016. Only patients with a preoperative INR value obtained within two days of surgery were included in the analysis. The subjects were divided into groups by INR level, including; <1, INR 1-≤1.25, INR 1.25-1.5, and INR ≥1.5. The primary outcome measure was bleeding that required a transfusion within 72 hours of surgery. Secondary outcomes included mortality, length of stay, pneumonia and infection.

Data were obtained for 17,567 patients. Mortality increased from 0.3% for INRs of <1 to 4.9% for INRs of ≥1.5 ($p<0.001$). Bleeding requiring transfusion increased from 13.2% for INRs <1, to 29.3% for INRs of 1.5 or greater ($p<0.001$). Independent risk factors for bleeding requiring transfusion included a preoperative INR of 1.25-1.5 (OR 1.55) and an INR of >1.5 (OR 1.55). In the adjusted analysis, the only group with an increased risk of mortality was that with an INR of 1.5 or greater (OR 2.69).

Conclusion: This study of patients undergoing total hip arthroplasty found an increased risk of bleeding with an INR of 1.25 or higher at the time of surgery, as well as an increased risk of death among those with an INR of 1.5 or higher.

Rudasill, S., et al. Revisiting the International Normalized Ratio Threshold for Bleeding Risk and Mortality in Primary Total Hip Arthroplasty. **J Bone Joint Surg.** 2019, Oct 11. doi: 10.2106/ JBJS.19.00160.

PARAVERTEBRAL BLOCK FOR COMPLEX REGIONAL PAIN SYNDROME

For patients with intractable complex regional pain syndrome (CRPS) involving the upper extremities (UEs), a stellate ganglion block (SGB) has been a frequent therapeutic intervention. In clinical practice, this block is performed at the middle sympathetic ganglion located at the level of C6-C7. This study compared the efficacy of a T2 paravertebral block (T2PV) with that of a standard SGB for the treatment of CRPS.

Subjects were adult patients with unilateral CRPS of the upper extremity, randomized to either a T2PV or an SGB group. Those receiving SGB were injected with five mL of one percent lidocaine under ultrasound guidance. Those in the paravertebral group received 10 mL of one percent lidocaine. Temperature was measured at the volar aspect of the index finger in both hands before the procedure and up to 20 minutes after the procedure. The primary outcome variable was the difference in temperature increase between the treated and the contralateral UE. Pain was assessed with the numerical rating scale (NRS).

The change in temperature was 2.37° in the T2PV group, and 0.77° in the SGB group ($p<0.0001$). There was no significant change in temperature in the contralateral hand in either group. A Horner's sign was observed in 53% of those in the SGB group and in 86.7% of those in the T2PV group. At 20 minutes, the NRS pain scores were significantly better in the T2PV patients than in those in the SGB group ($p=0.007$). The duration of pain relief was greater among those in the T2PV group than among those in the SGB group (9.26 versus 37.2 hours; $p=0.015$).

Conclusion: This study of patients with upper extremity, complex regional pain syndrome found that better and longer pain relief was achieved with a paravertebral block at the T2 level than with a standard stellate ganglion block at the C6-7 level.

Kim, Y., et al. A Prospective, Randomized, Crossover Trial of T2 Paravertebral Block as a Sympathetic Block in Complex Regional Pain Syndrome. **Pain Phys.** 2019; 22: E417-E424.

MICROBIOME AND FIBROMYALGIA

Fibromyalgia (FM) is one of the most common forms of chronic, widespread pain. The pathophysiology of this disorder is not well understood. As the microbiome has been implicated in several diseases, this study assessed the contribution of the microbiome in patients with FM.

Subjects were patients 30 to 60 years of age with a diagnosis of FM, and three control groups, including first-degree female relatives (genetic controls), household members (environmental controls) and unrelated, healthy women, ages 30 to 60 years. Stool samples were collected for microbiome analysis, with symptoms and groups compared by the abundance of different taxa. A dietary assessment was performed for all participants, with all subjects completing dietary reports.

The microbiome composition analysis revealed a distinct pattern of the fecal microbiome of the patients with FM. The symptoms of FM were associated with an abundance of several taxa.

Those species that were lower in relative abundance in the FM group included *F.prausnitzii*, *B.uniformis*, *P.copri*, and *B.lautiafaecis*. Those seen in greater abundance in patients with FM included *Intestinimonas butyriciproducens*, *Flavonifractor*

plautii, *Butyricoccus desmolans*, *Eisenbergiella tayi*, and *Eisenbergiella massiliensis*. Using the relative ratios of these bacteria, the authors were able to correctly identify patients with FM, with a prediction accuracy of 87.2%.

Conclusion: This study suggests that patients with fibromyalgia have significantly different intestinal microbiome populations than do controls.

Minerbi, A., et al. Altered Microbiome Composition in Individuals with Fibromyalgia. **Pain.** 2019, November; 160(11): 2589-2602.

MIGRAINE AND ONABOTULINUMTOXINA

Chronic migraine affects up to two percent of the population. As onabotulinumtoxinA is approved for chronic migraine headaches, this study assessed the efficacy of this medication for the treatment of chronic and high-frequency episodic migraine (HFEM) headaches.

This prospective study included consecutive patients treated with onabotulinumtoxinA between 2014 and 2018. Response to the medication was evaluated at six, 12, 18 and 24 months from baseline, with headache frequency and migraine days per month recorded.

A total of 105 patients completed nine cycles of treatment. Headache frequency decreased by 10.5 days per month from baseline. A 50% or greater reduction in headache days was reported by 52% of the patients and a 50% or greater reduction in pain intensity was reported in 64%. A reduction in migraine days from baseline was sustained at month 24, as was improvement in the Migraine Disability Assessment ($p<0.001$).

Conclusion: This study of patients with chronic migraine headaches found onabotulinumtoxinA to be effective in treating chronic migraines and high-frequency episodic migraines.

Alpuente, A., et al. Early Efficacy and Late Gain in Chronic and High-Frequency Episodic Migraine with OnabotulinumtoxinA. **Euro** J **Neurol. 2019,** Dec; 26(12): 1464-1470.

SHOCKWAVE VERSUS STEROID INJECTION FOR CARPAL TUNNEL SYNDROME

For patients with carpal tunnel syndrome (CTS), many will choose conservative treatments before considering surgical intervention. This study compared the clinical efficacy of steroid injection with that of extracorporeal shockwave therapy (ESWT) for patients with CTS.

Subjects were patients 26 years of age or older with CTS verified by electrodiagnostic evaluation. The participants were randomized to receive either ESWT, three times per week, for three consecutive weeks, or 40 mg of betamethasone, injected once into the carpal tunnel, adjacent to the median nerve. The median sensory and motor distal latencies and amplitudes were evaluated at baseline and at follow-up.

The visual analog scale (VAS) for pain and paresthesia, and the Boston Carpal Tunnel Questionnaire (BQ) scores, at both the three- and nine-week follow-ups were improved in both groups. The ESWT group demonstrated better recovery on the visual analog scale (VAS) for pain and paresthesia and the Boston Carpal Tunnel Questionnaire (BQ) at week 12, as compared with the steroid group. The ESWT group had an improvement in the distal latency of the sensory nerve action potential at nine- and 12-week follow-ups, with significantly better improvement than the steroid group at 12 weeks ($p<0.05$).

Conclusion: This study found that nine sessions of extracorporeal shockwave therapy significantly improved symptoms and function in patients with carpal tunnel syndrome, with better recovery as compared to an injection with corticosteroids.

Xu, D., et al. A Randomized, Controlled Trial Comparing Extracorporeal Shockwave Therapy versus Local Corticosteroid Injection for the Treatment of Carpal Tunnel Syndrome. **Intern Ortho.** (SICOT) (2019). https://doi.org/10.1007/s00264-019-04432-9.

INTERVAL VERSUS CONTINUOUS EXERCISE IN CARDIAC REHABILITATION

Exercise based cardiac rehabilitation (CR) has been shown to be effective in reducing cardiovascular as well as all-cause mortality in patients with coronary artery disease (CAD). Currently the best practice in CR involves the prescription of moderate intensity, continuous exercise (MICE), three to five times per week. This study compared the efficacy of aerobic interval training (AIT) to that of MICE on aerobic exercise capacity (VO2peak).

Subjects were 31, post-menopausal females with CAD, 50 years of age or older. Those randomized to a MICE group participated in sessions of walking or jogging for 30-40 minutes at an intensity of 60-80% of VO2 peak. The AIT group began with the MICE treatment through week six. Starting at week seven, MICE was replaced on three days per week by AIT. AIT included five to 10 minutes of warmup, followed by four intervals of four-minute walking/jogging at 90-95% of peak heart rate. Each of the four sessions was separated by three minutes of active recovery at an intensity of 50 -70% of peak heart rate, followed by a cool down period.

Of the 765 women referred, most did not meet the primary disease diagnosis or language requirements. Subjects included 17 women randomized to the treatment group and 14 to the MICE group. Of the treatment group, 59% dropped out before completion, and, of the MICE group, 50% dropped out before completion. Of those who remained, improvement of the VO2 peak was significantly better in the AIT group than in the MICE group.

Conclusion: This study of patients with coronary artery disease, all referred for cardiac rehabilitation, found that intensive interval training improved VO2 peak significantly more than did traditional, continuous exercise. Both groups had a high attrition rate.

Lee, L., et al. Randomized, Controlled Trial in Women with Coronary Artery Disease, Investigating the Effects of Aerobic Interval Training versus Moderate Intensity Continuous Exercise in Cardiac Rehabilitation: AIT versus Mice. **BMJ Open Sport Exer Med.** 2019: doi:10.1136/bmjsem-2019-000589.

MEDICATION CHANGES AT HOSPITAL DISCHARGE

Severe adverse drug events contribute to 20% of all hospitalizations in older adults. In addition, between 11% and 37% of patients suffer an adverse drug event after hospitalization. One third of these are considered preventable. This study assessed the incidence of, and variables associated with, failure to follow newly prescribed medications after hospital discharge.

This prospective study included patients admitted to medical or surgical units between 2014 and 2016 who were covered by the Quebec Province Health Insurance plan. Those with at least one

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medication change from their preadmission medications were eligible for inclusion. Data collected included demographics, health care service use and pharmacy claims data from one year prior to hospital admission, through one year after hospital discharge. Medications were classified as discontinued, new or changed in dose.

Data were collected and analyzed for 2,655 patients with an average age of 69.5 years. Overall, 24% of the changes in medications were not followed in the 30 days post-discharge. These included 27% of new medications that were not filled, 12% of the discontinued medications that were refilled and 30% of dose modifications that were filled at an incorrect dose.

Conclusion: This study of patients hospitalized in medical and surgical wards found that, post-surgery, 24% of medication changes were not followed in the 30 days after discharge.

Weir, D., et al. Challenges at Care Transitions: Failure to Follow Medication Changes Made at Hospital Discharge. **Am J Med**. 2019, October; 132: 1216-1224.

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