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VESSELPLASTY FOR OSTEOPOROTIC VERTEBRAL FRACTURES

Surgical treatment for osteoporotic vertebral compression fractures (OVCF) has included percutaneous vertebroplasty and kyphoplasty. However, these procedures both have a high incidence of bone cement leakage (BCL), with estimates ranging from 19 to 76%. Vesselplasty involves a novel implant device featuring a non-stretchable, controlled pore size container through which cement is introduced to restore the height of the affected vertebral body. This study assessed the clinical effects and the risk of BCL with the vesselplasty procedure.

This retrospective study reviewed the cases of 62 patients (70 vertebrae) who had been treated for OVCF using vesselplasty. Data collection included operation time, volume of bone cement injected, BCL, infection, ectopic embolism, and systemic manifestations. Clinical outcomes were pain and dysfunction, as assessed on a 10-point visual analog scale (VAS) and the Oswestry Disability Index (ODI) to assess motor function. The data were obtained at 24 hours, one month, three months, and final follow-up.

The mean volume of bone cement injected was three to eight milliliters, with BCL detected in three (4.3%) of the 70 vertebrae. Vertebral body height, Cobb angle, VAS, and ODI were all improved as compared with baseline ($p<0.05$).

Conclusion: This study of patients with osteoporotic vertebral fractures found that vesselplasty resulted in a small risk of bone cement leakage, with significant improvements in pain, vertebral height, and function.

Chen, J., et al. Vesselplasty for the Treatment of Osteoporotic Vertebral Compression Fractures with Peripheral Wall Damage: A Retrospective Study. **Br J Neurosurg**. 2024, April; 38(2): 272-276.

METFORMIN IN ELDERLY TYPE 2 DIABETES AND DEMENTIA

Diabetes-associated dementia is a significant public health concern. This study explored the potential for metformin to reduce the risk of dementia among elderly individuals with type 2 diabetes (T2DM).

This population-based, cohort study utilized data from Taiwan's National Health Insurance Research Database. The subjects were 60 years of age or older, each diagnosed with T2DM, and each of whom had used at least one type of anti-diabetic drug between 2008 and 2018. Metformin use was compared to the risk of a diagnosis of dementia. Covariates included age, gender, income level, urbanization level, types of anti-diabetic drug use, diabetes severity, coexisting morbidities, smoking status, alcohol-related liver disease, and Charleston Comorbidity Index scores.

A significant reduction in the risk of dementia was found among those who used metformin, with an adjusted hazard ratio (HR) of 0.34. Cox regression analysis revealed a dose dependent reduction in the risk of dementia, associated with metformin use. After adjusting for all covariates, the adjusted hazard ratio for dementia in this group was 0.52 among metformin users, with the risk lower among those with more than a once per day dose, as compared to those with a dose of once per day or less.

Conclusion: This study of elderly patients with type 2 diabetes found that the use of metformin could significantly reduce the risk of dementia.

Sun, M., et al. Metformin in Elderly Type 2 Diabetes Mellitus: Dose Dependent Dementia Risk Reduction. **Brain**. 2024, April; 147(4): 1474-1482.

POST-TREATMENT LYME DISEASE SYMPTOMS

The prognosis of early Lyme disease after antibiotic treatment is relatively good, with a low rate of residual symptoms. However, some patients report incomplete resolution of symptoms after treatment, termed post-treatment Lyme disease symptoms (PTLDs) or post-treatment Lyme disease syndrome (PTLDS). This systematic review summarizes the available evidence and provides evidence-based guidance for healthcare practitioners faced with patients with residual or unspecific symptoms following Lyme disease.

The authors completed a literature review of studies of patients with PTLDS which contained a control group and five or more patients. From that review, eight randomized, controlled studies met the inclusion criteria and were included in data analysis. The analysis found no significant difference between those treated with a placebo and those treated with antibiotics for outcomes including quality of life, cognition, depression, or fatigue. A meta-analysis revealed significantly more adverse events for those treated with antibiotics than for those treated with placebo.

Conclusion: This study of patients treated for Lyme disease found that post-treatment Lyme disease symptoms did not differ between those treated with antibiotics and those treated with a placebo.

Dersch, R., et al. Treatment of Post Treatment Lyme Disease Symptoms: A Systematic Review. **Euro J Neurol**. 2024: E16293. Online ahead of print.

APPLE CIDER VINEGAR FOR WEIGHT LOSS

Obesity is a growing health concern globally. Recently, interest in alternative remedies to support weight loss management has increased. As animal studies have

demonstrated that apple cider vinegar (ACV) may assist in weight loss, this study was designed to further understand the effect of this nutritional supplement on weight loss in young adults.

Subjects were 120 overweight adolescents and young adults, between 12 and 25 years of age, with a body mass index (BMI) of between 27 kg/m^2 and 30 kg/m^2. The participants were randomized to receive either a morning placebo or ACV at a dose of 5 mL, 10 mL, or 15 mL for 12 weeks. Baseline and follow-up measures included anthropometric measurements, blood glucose, triglycerides, and fasting total cholesterol.

Compared with baseline, all ACV groups realized significant loss of BMI ($p<0.05$). The group receiving 15mL doses had a greater weight loss than those receiving 5ml or 10 ml or a placebo, beginning at week four ($p<0.05$). Significant improvements in fasting blood sugar were also noted in all treatment groups, as compared to baseline and compared to placebo, with the 15ml group realizing greater improvement than all other groups.

Conclusion: This study of overweight adolescents and young adults found that daily morning consumption of apple cider vinegar resulted in significant weight loss.

Abou-Khalil, R, et al. Apple Cider Vinegar for Weight Management in Lebanese Adolescents and Young Adults with Overweight and Obesity: A Randomized, Double-Blind, Placebo-Controlled Study. **BMJ Nutr Public Health**. 2024; 0: E000823. Doi: 10.1136/Bmjnph-2023-000823.

SEMAGLUTIDE FOR PATIENTS WITH OBESITY-RELATED HEART FAILURE AND TYPE 2 DIABETES

Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, has been found to induce substantial weight loss in overweight persons, with favorable effects on cardiometabolic risk factors. This study examined the efficacy and safety of semaglutide, 2.4 mg per week, for patients with obesity-related heart failure and type 2 diabetes (T2DM).

The STEP-HFpEF DM (Semaglutide Treatment Effect in People with Obesity and Heart Failure with Preserved Ejection Fraction and Diabetes Mellitus) trial was a double-blind, randomized, placebo-controlled trial involving adults with documented heart failure and a body mass index of 30 kg/m^2 or more and with a glycated hemoglobin level of no more than 10%. The subjects were randomized to receive once-weekly subcutaneous semaglutide at a dose of 2.4 mg or a placebo for 52 weeks. The primary outcome measures were the change in the Kansas City Cardiomyopathy Questionnaire Clinical Summary score (KCCQ-CSS) and the percentage change in body weight from baseline to week 52.

Of the 616 participants who underwent randomization, the mean changes in the KCCQ-CSS were 13.7 points with semaglutide, and 6.4 points with placebo ($p<0.001$). The mean percentage changes in body weight were −9.8% in the semaglutide group, and −3.4% in the placebo group ($p<0.001$). The semaglutide group also demonstrated greater improvement on the six-minute walk distance ($p=0.008$). Serious adverse events were reported by 55 participants (17.7%) in the semaglutide group and 88 (28.8%) in the placebo group.

Conclusion: This study of patients with obesity related heart failure and type 2 diabetes found that semaglutide led to a reduction in weight, heart failure related symptoms and physical limitations.

Kosiborod, M., et al. Semaglutide in Patients with Obesity-Related Heart Failure and Type 2 Diabetes. **N Eng J Med**. 2024, April 18; 390 :1394-1407.

POLYMYALGIA RHEUMATICA GLUCOCORTICOSTEROID TREATMENT

Glucocorticoids (GC) is the first line drug for treating polymyalgia rheumatica (PMR). This study was designed to better understand the inflammatory parameters and adverse events associated with this treatment.

This retrospective study included two databases maintained by the Health, Clinic, and Education Information Evaluation Institute and the Real-World Data Company, both in Kyoto, Japan. The data were queried for newly diagnosed cases of PMR among patients 50 years of age or older. Exposures of interest were GC prescriptions, with doses converted to prednisolone equivalents. Dosing, clinical responses, and adverse events were recorded.

Data were analyzed for 373 adults with a mean age of 77.3 years. The

mean GC dose was 15 mg/d at baseline, falling to 3.5 mg/d at week 52. The median baseline CRP was 63.3 mg/L, falling to 2.4 mg/L at week two. The median baseline ESR was 77mm/h, falling to 24 mm/h at week two. The median accumulated GC dose at 52 weeks was 2,455 mg. The cumulative rates of adverse events related to GC were 49% for osteoporosis, 30.2% for diabetes, 14.9% for hypertension, 12.2% for peptic ulcer disease, 11.3% for dyslipidemia, 2.9% for glaucoma, and 4.3% for serious infections.

Conclusion: This study of 373 patients with polymyalgia rheumatica found that treatment with glucocorticoids reduced CRP and ESR, although over 30% remained at levels above the upper limits of normal throughout the 52 weeks of follow-up.

Tanaka, Y., et al. Glucocorticoid Treatment and Clinical Outcomes in Patients with Polymyalgia Rheumatica: A Cohort Study Using Routinely Collected Health Data. **Joint Bone Spine**. 2024, May; 91(3): 1055680.

RADIOFREQUENCY ABLATION FOR TREATMENT OF GLOSSOPHARYNGEAL NEURALGIA

Glossopharyngeal neuralgia (GPN) is a rare form of neuropathic facial pain that presents as spasmodic attacks to the posterior tongue, jaw, ears, tonsillar fossa, and other areas of the oropharynx. Radiofrequency ablation (RFA) is a technique that destroys the targeted nerves through heat generated from radio waves. This study was designed to better understand the efficacy of RFA as a minimally invasive procedure for the treatment of GPN.

A literature review was conducted for studies of RFA in the treatment of patients with GPN. From this review, 18 articles were chosen. Using the National Institutes of Health tool and the JBL Appraisal Checklist for Case Reports, 13 of the studies were labeled good quality, four as fair quality, and one as poor quality.

Of the 288 patients treated with RFA, 231 experienced relief or complete resolution of pain, yielding an efficacy of 80.2%. Most of the patients reported immediate relief of pain, with some noting a change in taste sensations.

Conclusion: This study of patients with glossopharyngeal neuralgia found that radiofrequency ablation may be an effective treatment for this condition.

Do, K., et al. Effectiveness of Radiofrequency Ablation for Treatment of Glossopharyngeal Neuralgia: A Systematic Review of the Current Literature. **Pain Physician**. 2024, Mar; 27(3): 97-110.

BOTOX FOR MIGRAINE

OnabotunlinumtoxinA (onabotA) received Food and Drug Administration (FDA) approval for the prevention of chronic migraine in October of 2010. Despite the longstanding use of this treatment, it is still not fully known to what extent patients continue onabotA treatment over an extended period of time.

This retrospective analysis included patients who had received care through the Stanford Headache Clinic. Each had received at least one prescription for onabotA during the years 2011 to 2021. The primary outcome measure was the number of treatments each patient received.

The cohort included 1,551 with chronic migraine, with a mean age of 44.8 years, and a mean of 7.6 treatments. Twenty-six percent continued to receive onabotA at the end of the study, with 72.5% completing at least two treatments, 48.1% completing six treatments, and 26% completing at least 29 treatments. Importantly 72.8% received a prescription for additional preventative medications after initiating onabotA injections.

Conclusion: This study of patients receiving botulinum toxin injections for headaches found that 48.1% received at least six treatments, over 70% completed at least two treatments and 26% completed at least 29 treatments.

Moskatel, L., et al. Long-term Persistence to OnabotulinumtoxinA to Prevent Chronic Migraine: Results from 11 Years of Patient Data from a Tertiary Headache Center. **Pain Med**. 2024 Mar 22: pnae020. doi: 10.1093/pm/pnae020.

BLUNT HEAD INJURY IN THE ELDERLY

Traumatic brain injury (TBI) is particularly prevalent in the elderly population. This study was designed to present prospective information on the demographics, mechanisms, presentations, injuries, interventions, and outcomes of blunt TBI among the elderly.

Data were obtained from the National Emergency X-Radiography Utilization Study (NEXUS) Head Computed Tomography validation study. The patients were classified according to those with no intracranial injuries and those with any intracranial injury. The data were reviewed from patients 65 years of age or older, compared to that of those in the younger cohort.

Significant injuries were identified in 8.9% of the older, and 5.4% of the younger, cohorts. The most frequent types of injuries in the elderly population were subdural hematomas (377 discreet lesions in 299 patients) and subarachnoid hemorrhages (333 discreet instances in 256 patients). Among older patients who required neurosurgical intervention, only 16.4% were able to return home, with 32.1% requiring discharge to an extended care facility, while 41.8% died from their injuries.

Conclusion: This study suggests that older patients are at high risk of sustaining serious intracranial injuries, even with low-risk mechanisms of injury-like ground-level falls.

Mower, W., et al. Blunt Head Injury in the Elderly: Analysis of the NEXUS II Injury Cohort. **Ann Emerg Med**. 2024, May; 83(5): 457-466.

MULTIPLE SCLEROSIS DISEASE MODIFYING THERAPIES

Over the past 20 years, more than 15 disease modifying therapies (DMTs) have been introduced for the treatment of multiple sclerosis (MS). As real-world effectiveness is dependent on compliance, this study describes real world DMT persistence, and the reasons given when patients discontinue DMTs.

As part of the United Kingdom Multiple Sclerosis Trials and Registries Consortium, regional MS centers were invited to provide data regarding people with MS, exposed to DMTs. The eligible patients had relapse-onset MS and had received at least one DMT, with complete records of DMT prescriptions available for the entire duration of their MS.

Data were analyzed for 4,366 patient records, with a mean age at the first prescription of 37.6 years. The median time spent on any single DMT was 4.3 years. The greatest two -year persistence on a DMT was found for alemtuzumab (96.5%) and

cladribine (95.5%). Of 704 recorded first courses of alemtuzumab (n=504) or cladribine (n=200), only 46 (6.5%) people with MS ever received an alternative, subsequent DMT (mean follow-up duration, 4.3 years). The reasons for DMT discontinuation overall were adverse events (1,170 of 3,324 DMT stops; 35.2%) and lack of efficacy (1,012 of 3,324; 30.4%).

Conclusion: This study of patients with multiple sclerosis found that the medication prescription with the highest chances of continued use occurred with alemtuzumab and cladribine.

Tallantyre, E., et al. Real-World Persistence of Multiple Sclerosis Disease-Modifying Therapies. **Euro J Neurol**. 2024; 00: e16289.

NEUROANATOMICAL CORRELATES OF DRIVING PERFORMANCE

Motor vehicle crashes are a leading cause of death in the United States, with an increased risk noted with advanced age. This study combined anatomical magnetic resonance imaging (MRI) with virtual reality to measure correlations between grey matter and driving performance.

The 138 participants, ranging in age from 17 to 85 years, were recruited for a simulated driving task. All were assessed with T1 weighted MRI to quantify gray matter volume and cortical thickness at areas previously noted to affect driving performance (the middle frontal gyrus (MFG), precentral gyrus (PCG), superior temporal cortex (STC), posterior parietal cortex (PPC), and cerebellum). The driving task simulated standard licensing road tests of Ontario, Canada.

During the driving simulation the subjects were assessed under distracted and undistracted conditions. During the distracted driving condition, the subjects were required to answer verbal questions posed by the study staff, which required a response using a handheld button. This was designed to be similar to the use of a handheld mobile device. Measures of driving performance included time elapsed, distance traveled, driving speed, lateral lane position, vehicle heading, angle, crash events, and button responses.

During the DD condition, the drivers exhibited greater speed, slower acceleration, and altered lane position (all $p<0.001$). Those with greater PPC grey matter volume spent less time off center during undistracted driving and had reduced variability in lane position and heading angle in the distracted condition. Cortical thickness measures in the MFG, PCG, PPC, and STG were all associated with at least one driving measure.

Conclusion: This exploratory study of driving performance, with and without distraction, found that grey matter volume/thickness was correlated with position and speed maintenance.

Guan, D., et al. Neuroanatomical Correlates of Distracted Straight Driving Performance: A Driving Simulator MRI Study across the Lifespan. **Front Aging Neurosci**. 2024, April, https://doi.org/10.3389/fnagi.2024.1369179.

OLEZARSEN FOR HYPERTRIGLYCERIDEMIA

Elevated levels of triglycerides and triglyceride-rich lipoproteins remain an unmet clinical need. Olezarsen is an antisense oligonucleotide targeting APOC3 mRNA. This study evaluated the efficacy of olezarsen for treatment of moderate hypertriglyceridemia at elevated cardiovascular risk.

This phase 2b, randomized, double-blind, placebo-controlled trial included adults receiving stable lipid lowering therapy, all with either moderate hypertriglyceridemia plus elevated cardiovascular risk or severe hypertriglyceridemia. The patients were randomized to receive monthly doses of placebo or olezarsen at either 50mg or 80mg. The primary outcome variable was the percent change in triglyceride level.

Subjects were recruited from 24 sites in the United States, with a total of 154 undergoing randomization. Compared to placebo, the olezarsen, 50mg, group had a decrease in triglycerides of 57.1% ($p<0.001$), while the 80mg group had a decrease of 60.9% ($p<0.001$). Adverse events were similar among the three groups.

Conclusion: This phase 2b trial involving patients with hypertriglyceridemia and elevated cardiovascular risk found that monthly dosing of olezarsen could significantly reduce triglyceride levels, with no significant safety concerns.

Bergmark, B., et al. Olezarsen for Hypertriglyceridemia in Patients at High Cardiovascular Risk. **N Eng J Med**. 2024, April 7. DOI: 10.1056/NEJMoa2402309.

LIFESTYLE FACTORS IN LATE MIDLIFE PREDICT FRAILTY

Frailty is characterized by increased vulnerability and reduced physiologic reserves. This study explored the effect of lifestyle on the progression of frailty with older age.

Participants of the Helsinki Birth Cohort Study (HBCS) underwent clinical evaluations for frailty and lifestyle in late midlife and at 57 to 69 years of age, with follow-up for 17 years. Six healthy lifestyle factors were reviewed (exercise, diet, sleep, smoking, alcohol, and body composition), with frailty defined using a 37-Item Frailty Index (FI). Regular exercise was defined as participating in at least 12.5 metabolic equivalent hours of leisure-time physical activity (LTPA). A healthy body composition was defined as a percent body fat of under 25% among men and under 35% among women.

At baseline, more than a quarter (27.4%) were frail at a mean age of 61.5 years. Compared to participants who kept exercising regularly and did not experience disturbed sleep, those who stopped regular exercise and those who continued to or began experiencing disturbances in sleeping showed more rapid increases in frailty. Participants with worsening lifestyle (over 3 points) experienced worsening frailty from late midlife into old age, while those who increased exercise and sleep experienced reduced frailty.

Conclusion: This study of adults, 57 to 69 years of age, found that the risk of frailty over the next 17 years was greater among those with worse lifestyle factors, with the risk reduced among those who increased exercise and sleep.

Haapanen, M., et al. Lifestyle Related Factors in Late Midlife as Predictors of Frailty from Late Midlife into Old Age: A Longitudinal, Birth Cohort Study. **Age Ageing**. 2024; 53. https://doiorg.proxy.library.emory.edu/10.1093/ageing/afae066.

DELIRIUM IN ACUTE STROKE AND SUBSEQUENT COGNITIVE AND PSYCHIATRIC SYMPTOMS

Globally, the lifetime risk of stroke is 25%. Delirium in the acute phase of stroke has been reported at an average of 25% of cases. This study evaluated the relationship between

acute stroke delirium and later symptoms of cognitive and psychiatric decline.

Subjects were 18 years of age or older, admitted to an inpatient stroke unit within seven days of symptom onset. At admission, each patient's health history was collected, with premorbid function registered using the Global Deterioration Scale and the Charleston Comorbidity Index. The patients were assessed at admission for stroke severity using the National Institutes of Health Stroke Scale, with delirium diagnosed using the Confusion Assessment Method. Cognitive function was measured with the Montreal Cognitive Assessment (MoCA) and psychiatric symptoms with the Neuropsychiatric Inventory-Questionnaire (NPI-Q). The Hospital Anxiety and Depression Scale (HADS) was used to assess affective function.

Data were analyzed for 334 patients with a mean hospital length of stay of 6.2 days. The subjects with delirium during hospitalization were compared to those without at three, 18, and 36 months. At three, 18, and 36 months, the NPI-Q scores were worse in the delirium group than in the control group ($p=0.016$, $p=0.035$, and $p=0.003$). In addition, at 18 and 36 months, worse scores on the HADS were noted in the delirium group ($p=0.001$ and $p=0.006$, respectively).

Conclusion: This study of patients admitted for acute stroke found that a diagnosis of delirium was associated with an increased risk of cognitive and psychiatric symptoms in the chronic phase of stroke.

Gjestad, E., et al. Delirium in Acute Stroke Is Associated with Increased Cognitive and Psychiatric Symptoms Over Time: The Nor-COAST Study. **J Stroke Cerebr Dis**. 2024, Feb 27; 33 (6): 107667.

TERIPARATIDE IN VERY ELDERLY PATIENTS WITH PROXIMAL FEMORAL FRACTURE

Fragility fractures in the elderly can result in impaired mobility, independence, and overall quality of life. Teriparatide, a parathyroid hormone analog, has been shown to accelerate recovery of osteoporotic related fractures by improving bone mineral density (BMD) and reducing pain. Some have noted that adherence to teriparatide treatment can be hampered by its cost, side effects, such as leg cramps and hypercalcemia, and injection site discomfort. This study compared the effect of teriparatide with that of denosumab, a human monoclonal antibody, for the treatment of femoral fractures in the elderly.

This retrospective cohort study included 150 ambulatory patients over 75 years of age, treated surgically for proximal femoral fractures between 2016 and 2020. The participants were placed into one of two groups, those who received daily teriparatide injections of 20 micrograms for 18 months and those who received denosumab 60 milligrams every six months for 24 months.

Data were analyzed for 126 patients with a mean age of 85.5 years. Of these, 68 received teriparatide, and 58 received denosumab. Compared to the denosumab group, greater improvements were noted in the teriparatide group on the Visual Analog Scale (VAS) for pain ($p=0.20$) and in bone mineral density at the femur ($p<0.002$) and at L1-L4 ($p=0.003$).

Conclusion: This retrospective study of very elderly patients undergoing surgical intervention for proximal femoral fractures found that those receiving daily injections of teriparatide after surgery enjoyed better outcomes than did those receiving denosumab every six months for 24 months.

Sheng, O., et al. Therapeutic Advantage of Teriparatide in Very Elderly Patients with Proximal Femoral Fractures: A Functional and BMD Analysis. **BMC Musculoskelet Dis**. 2024; 25: 288.

SODIUM CHANNEL AS A REGULATOR OF OSTEOARTHRITIS

Previous studies have implicated voltage gated sodium channels (VGSCs) in the pathophysiology of osteoarthritis (OA). Serial genetic ablation of Nav1.7 in multiple mouse models demonstrates that Nav1.7, expressed in dorsal root ganglia neurons, is involved in pain, whereas Nav1.7 in chondrocytes regulates OA progression. This study explored the effect of blocking Na1.7 on the symptoms associated with OA.

To identify differentially expressed genes in OA, the researchers performed RNA sequence analysis on the cartilage of 22 non-OA and 165 OA patients scheduled for surgery. Electrophysiological studies were completed on human chondrocytes isolated from patients with OA, to identify the presence of Nav1.7 currents. The effect of blocking these channels was assessed with different concentrations of PF-04856264. Serial genetic ablation was completed in mouse models to assess the role of Nav1.7 in the progression of OA and pain.

The results indicate that Nav1.7 mRNA was upregulated among those with OA, as compared to controls (a 2.69-fold increase, $p<0.05$). In the animal model, Nav1.7 deletion in both dorsal root ganglia neurons and chondrocytes substantially attenuated cartilage loss and reduced the Osteoarthritis Research Society International (OARSI) scores ($p<0.001$), as well as osteophyte development ($p=0.007$) and subchondral bone plate thickness ($p<0.001$).

Conclusion: This study found that the sodium channel Nav1.7 affects the development of osteoarthritis related pain, synovitis and osteophyte development, and therefore presents as a potential therapeutic target.

Fu, W., et al. Nav1.7 as a Chondrocyte Regulator and Therapeutic Target for Osteoarthritis. **Nature**. 625: 557-565 (2024).

COMPRESSIVE VERSUS STANDARD CRYOTHERAPY AFTER TOTAL KNEE ARTHROPLASTY

For patients with end stage knee osteoarthritis (OA), total knee arthroplasty (TKA) is accepted as the preferred treatment. As both cryotherapy and compressive therapy have been shown to improve post-operative outcomes, this study compared knee range of motion between patients who underwent rehabilitation with compressive cryotherapy (CC) and those who received standard cryotherapy (SC).

Data were collected between March of 2019 and March of 2022 from the charts of 44 patients who underwent a TKA. The subjects were randomized to either a CC group or an SC group using ice packs, twenty minutes twice per day from the immediate postoperative period. Range of motion (ROM) was the primary outcome variable. Secondary outcome measures included knee circumference, pain at rest and during activity, the six-Minute Walk Test (6-MWT), and the Knee Injury Outcome Score (KOOS) questionnaire.

The changes in ROM did not differ between groups. Improvement at day 21 was superior in the CC group for pain during activity (p= 0.005) walking distance. (p=0.018) and KOOS scores (p=0.004).

Conclusion: This study of patients undergoing total knee arthroplasty found that, compared to standard cryotherapy, compressive cryotherapy resulted in better control of pain, swelling, and walking distance, but was not superior in improving range of motion.

Quesnot, A., et al. Randomized, Controlled Trial of Compressive Cryotherapy versus Standard Cryotherapy after Total Knee Arthroplasty: Pain, Swelling, Range of Motion, and Functional Recovery. **BMC Musculoskelet Dis**. 2024, Feb 28;25(1):182.

OSTEOARTHRITIS AMONG 30- to 44-YEAR-OLD ADULTS

Osteoarthritis (OA) is a common joint disease in the elderly population. This study used data from the Global Burden of Disease (GBD) study, 2019, to determine the burden of OA among individuals 30 to 44 years of age.

Data were reviewed from the GBD 2019 by gender, year, age, and location, including incidence, prevalence, years lost due to disability (YLD), as well as disability-adjusted life years (DALYS). The geographic regions were reviewed with regard to the socio-demographic index (SDI), an index used to assess the level of social development.

Globally, in 2019, the estimated number of new OA cases among individuals 30 to 44 years of age was 32,971,701, an increase from 7,794,008 new cases in 1990. The incidence of OA in this age group increased from 471.86 in 1990 to 478.97 in 2019. The prevalence of OA in this population increased from 1989.90 in 1990 to 2027.07 in 2019. The YLDs due to OA increased from 67.29 in 1990 to 68.62 in 2019. The highest incidence rates were found in high-income countries, with the U.S. at the top of this group. The lowest were found in Central Asia, Central Europe, and Southeast Asia.

Conclusion: This study, using data from the Global Burden of Disease, 2019, found that, among individuals 30 to 44 years of age, there has been a significant increase in incidence and prevalence of OA in the past decade.

He, Y., et al. Global Burden of Osteoarthritis in Adults Aged 30 to 44 Years, 1990 to 2019: Results from the Global Burden of Disease Study, 2019. **BMC Musculoskelet Disord** 25, 303 (2024). doi.org/10.1186/s12891-024-07442-w.

PHYSICAL ACTIVITY AFTER KNEE OR HIP ARTHROPLASTY

Historically, physical activity in orthopedic populations has been assessed primarily through self-recorded questionnaires. This study was designed to quantify differences in physical activity between controls, those with end stage osteoarthritis (OA), and those who had recently undergone knee or hip arthroplasty.

Between 2013 and 2016, over 100,000 U.K. Biobank participants agreed to wear an accelerometer on the dominant wrist for 24 hours per day for seven days. From a cohort of 94,707 participants with valid accelerometer wear time and complete self-reported data, the electronic health records were used to identify 3,506 having undergone a total hip arthroplasty (THA) or total knee arthroplasty (TKA) and 68,389 nonarthritic controls. Those who had undergone a primary TKA or THA less than 12 months after wearing the accelerometer were placed in an end stage arthritis (ESA) group. Those who wore the accelerometer at least 12 months after their TKA or THA were placed in an arthroplasty (AR) group. Accelerometer data were compared between groups.

Patient data were complete for 149 with ESA in the hip and 177 with ESA in the knee, with 556 in the hip AR group and 843 in the knee AR group. In the adjusted analysis, compared to the non-arthritic controls, those in the knee ESA group took 1,298 fewer daily steps ($p<0.001$), and those in the hip ESA group took 1,108 fewer daily steps ($p<0.001$). Compared to controls, the peak cadence was slower in the knee ESA group ($p<0.001$), but not in the hip ESA group. Compared to the ESA groups, the knee AR group took 877 more steps (p=0.004), and the hip AR group took 893 (p=0.008) more steps per day. Compared to controls, the knee AR group took 405 (p=0.009) fewer daily steps.

Conclusion: This study of patients with end stage arthritis of the hip or knee found that arthroplasty resulted in an average of 900 more steps per day.

Small, S., et al. Device Measured Physical Activity In 3,506 Individuals with Knee or Hip Arthroplasty. **Med Sci Sports Exerc**. 2024, May; 56(5): 805-812.

FEMOROACETABULAR IMPINGEMENT SYNDROME SURGERY AND OSTEOARTHRITIS

Femoroacetabular impingement syndrome (FAIS) is increasingly recognized as a cause of non-arthritic hip pain. Several prospective, randomized, controlled trials have demonstrated the efficacy of surgery over physical therapy, although the long-term durability is not well known. This study was designed to better understand the natural history of FAIS and the effect of arthroscopic surgery on this trajectory.

This retrospective analysis included all patients undergoing arthroscopic surgery after failed non-operative management. The patients' charts were reviewed for pre- and post-operative findings, including ten-year post-operative radiographic comparisons. Both operative and nonoperative hips were assessed using Tonnis grading, or by documenting the occurrence of hip arthroplasty at the latest follow-up.

Data were collected for 100 patients who underwent primary, unilateral hip arthroscopy, with no contralateral procedure for a minimum of 10 years. The progression of OA was compared between hips. At long-term follow up, the nonoperative hip advanced to a worse Tonnis grade in 48% (48/100) of the cases, as compared with 28% (28/100) among operative hips. These data demonstrate that hip surgery was associated with a relative risk reduction of 42% in osteoarthritis progression.

Conclusion: This study of patients with femoroacetabular impingement syndrome found that surgical repair was associated with a 42% relative risk reduction in OA progression.

Ramkumar, P., et al. Modern Hip Arthroscopy for FAIS May Delay the Natural History of Osteoarthritis in 25% of Patients. A 12-year Follow-Up

Analysis. **Am J Sport Med**. 2024, April; 52(5): 1137-1143.

TOPICAL CAPSAICIN FOR PERIPHERAL NEUROPATHIC PAIN

The transient receptor potential vanilloid 1 (TRPV1) has been shown to be a key molecule in peripheral neuropathic pain (PNP). As capsaicin is a highly selective agonist for TRPV1, this study explored the effect of topical treatment with capsaicin on the health-related quality of life of patients with PNP.

This retrospective study included 100 hospitalized patients with localized PNP, resistant to treatment, who received treatment at least once with an eight percent capsaicin patch. Pain was assessed using the Neuropathic Pain Questionnaire (DN4), with the response to treatment measured with the Patient Global Improvement Change Scale (PGIC). Pain-related interference in quality of life was assessed with the Portuguese version of the Brief Pain Inventory (BPI). Finally, quality of life was evaluated with EuroQol Questionnaire, Five Dimensions, Three Levels (EQ-5D-3L).

Data were analyzed for 68 patients with an average age of 61.4 years. The etiology of the PNP was post-surgery or traumatic in 67.6%, with the most frequent location being the lower limb. After placement of the capsaicin patch, 30.9% (N = 21) felt minimally improved, 22.1% (N = 15) felt much improved, and 13.2% (N = 9) felt very much improved. The majority of the patients continue to complain of limitations in mobility and daily activities, as well as moderate pain.

Conclusion: This study of patients with peripheral neuropathic pain found that treatment with capsaicin, eight percent, may result in a moderate reduction of pain.

Santos, M., et al. Topical Capsaicin Eight Percent Patch in Peripheral Neuropathic Pain: Efficacy and Quality of Life. **Br J Pain**. 2024, Feb; 18(1): 42-56.

TOPICAL DICLOFENAC AND ORAL IBUPROFEN FOR LOW BACK PAIN

Prior studies have supported the use of non-steroidal anti-inflammatory drugs (NSAIDS) as a first line treatment in patients with acute low back pain (LBP) without sciatica. This study assessed the efficacy of a topical NSAID for patients with acute LBP.

The subjects were 18 to 69 years of age, presenting to the emergency department with a chief complaint of LBP. The patients were randomized to one of three interventions, 400 mg oral ibuprofen plus placebo gel every six hours as needed, one percent diclofenac gel, four grams topically plus placebo capsules (every six hours as needed), or a combination of the two treatments. The primary outcome variable was the change in Roland Morris Disability Questionnaire (RMDQ) score between baseline and two days' follow-up.

Data were completed for 198 eligible patients. At follow-up, the mean changes in RMDQ scores were 10.1 in the ibuprofen group, 6.4 in the diclofenac gel group, and 8.7 in the combination group. Multivariate analysis revealed that the oral ibuprofen group had significantly better improvement in RMDQ scores than the topical diclofenac alone group, with no benefit noted with adding topical diclofenac.

Conclusion: This study of patients presenting to the emergency department with low back pain found that oral ibuprofen was superior to topical diclofenac for improving symptoms, with no additional benefit found with the addition of topical diclofenac.

Khankhel, N., et al. Topical Diclofenac versus Oral Ibuprofen versus Diclofenac Plus Ibuprofen for Emergency Department Patients with Acute Low Back Pain: A Randomized Study. **Ann Emerg Med**. 2024, March. https://doi.org/10.1016/j.annemergmed.2024.01.037.

VALPROATE WITHDRAWAL AMONG YOUNG ADULTS WITH EPILEPSY

Valproate (VPA) is one of the more effective drugs for treating epilepsy. In the United Kingdom, new guidelines will prohibit prescribing VPA for adults < 55 years of age, unless other treatments have been shown to be ineffective or poorly tolerated. This study examined the morbidity and mortality risks associated with VPA withdrawal.

This retrospective cohort study involved the search of internationally derived electronic health data within the TriNetX Global Collaborative Network involving >120 healthcare organizations. The database was queried for the records of men and women ages 16 to 54 years with a diagnostic code indicating epilepsy or seizure. Eligible patients had at least two VPA prescriptions over the preceding two years. Two cohorts were generated: those withdrawn from VPA (W) and those remaining on valproate (R) through January 2018. The primary outcome was the five-year risk of mortality or morbidity.

Data were analyzed from a study population of 14,412 individuals, including 4,436 (31%) in the W group and 9,976 in the R group. Compared to the R group the W group experienced increased risks of emergency department attendance (Hazard Ratio (HR): 1.236), hospital admission (HR 1.160), falls (HR 1.179), injuries (HR 1.095), burns (HR 1.592), and new-onset depression (HR 1.323).

Conclusion: This large study of patients receiving valproate found that patients withdrawn from valproate are at increased risk of experiencing one or more emergency department visits, hospital admissions, falls, injuries, burns, and new-onset depression.

Mbizvo, G., et al. Morbidity and Mortality Risks Associated with Valproate Withdrawal in Young Men and Women with Epilepsy. **Brain.** 2024. awae128, https://doi-org.proxy.library.emory.edu/10.1093/brain/awae128.

LAVENDER EXTRACT FOR MAJOR DEPRESSIVE DISORDER

Silexan is an essential oil, produced from the Lavandula angustifolia flower, which is registered as a medicinal product for the treatment of anxiety disorder. This trial was designed to assess the efficacy of silexan for the treatment of mild-to-moderate major depressive disorder.

The subjects were 498 subjects with mild or moderate major depressive disorder (MDD) randomized to receive 80 mg/day of silexan, 50 mg/day of sertraline (an SSRI), or a placebo for 56 days. The primary outcome was the change from baseline in the Montgomery Åsberg Depression Rating Scale (MADRS) total score.

Those treated with silexan, and sertraline demonstrated significantly

(Continued from page 2)

better improvements from baseline in their average MADRS scores than did those who received placebo (p=0.008 and p=0.001 respectively). Compared to baseline, much or very much improvement was noted in 47.7% of the silexan group, 50.3% of the sertraline group, and 40.1% of the placebo group. Also, significant differences were noted between silexan and placebo for each of the domains assessed by the Sheehan Disability Scale (work, social life/ leisure activities, family life/home responsibilities; p≤0.01 for all comparisons). Both treatments were well tolerated, with eructation being the most frequent adverse effect of silexan.

Conclusion: This study of patients found that silexan, derived from lavender oil is effective in treating mild-to-moderate major depressive disorder, and improves functional capacity, confirming its antidepressant efficacy.

Kasper, S., et al. Lavender Oil Preparation Silexan Is Effective in Mild-To-Moderate Major Depression: A Randomized, Placebo- And Reference-Controlled Trial. **Europ Arch Psych Clin Neurosci**. 2024, Https://Doi.Org/10.1007/S00406-024-01783-2.

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