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COLCHICINE FOR STROKE PREVENTION

Studies of patients with stable coronary artery disease (CAD) have suggested that colchicine may decrease the risk of myocardial infarction and other cardiac outcomes, with this effect related to a medication induced reduction in inflammation. This literature review and meta-analysis was designed to better understand the effect of colchicine treatment on the risk of stroke in patients with CAD.

A literature review was completed for studies of patients with a history of cardiovascular disease randomized to colchicine treatment or a control. Search terms for outcomes included 'stroke', 'cerebrovascular event', 'transient ischemic attack', and 'cerebral ischemia'. From the literature review, four, randomized, controlled trials were chosen, with data for 5,553 patients.

In the overall analysis, colchicine treatment was associated with a lower risk of incident stroke as compared with controls, with a risk ratio of 0.31 (p=0.006).

Conclusion: This literature review and meta-analysis suggests that, for patients with a history of cardiovascular disease, treatment with colchicine is associated with a reduced risk of stroke.

Katsanos, A., et al. Colchicine for Stroke Prevention in Patients with Coronary Artery Disease: A Systematic Review and Meta-Analysis. **Eur J Neurol**. 2020, June; 27(6): 1035-1038.

SUICIDE IN ELDERLY PATIENTS WITH HIP FRACTURE

The World Health Organization predicted that, by 2020, the number of deaths by suicide will reach 1.5 million worldwide. Hip fracture among the elderly affects the person's physical mobility and increases psychological stress and strain in family dynamics. This study evaluated the risk of suicide in elderly patients with hip fractures.

Patients with hip fractures and matched controls were identified from the National Health Insurance Service -Senior (NHIS-Senior) cohort of South Korea. This cohort consists of 558,047 individuals selected by random sampling of 5.5 million adults with an age of at least 60 years. Patients with incident hip fracture were matched to similar individuals without a fracture in a 1:2 ratio.

Data were analyzed for 11,477 patients with hip fracture and 22,954 matched controls. The median duration of follow-up was 4.6 years, during which a total of 172 suicides were identified. During the first year, comparisons at 180 days and 365 days showed that those with hip fractures were at higher risk of suicide than matched controls (p=0.009 and p=0.004, respectively).

Conclusion: This study found that patients with hip fracture were more likely to kill themselves in the first year after fracture than were matched controls.

Jang, S., et al. Suicide in Elderly Patients with Hip Fracture. A South Korean Nationwide Cohort Study. **Bone Joint Surg**. 2020, June 17; 102 (12): 1059.

AMINO ACID SUPPLEMENTATION AFTER KNEE ARTHROPLASTY

Following total knee arthroplasty (TKA), lower limb muscle atrophy is often slow to recover. Essential amino acid supplementation has been shown to contribute to the prevention of muscle atrophy in the elderly. Therefore, this study assessed the effectiveness of perioperative amino acid supplementation to help mitigate muscle atrophy after a (TKA).

Subjects were patients undergoing unilateral TKA secondary to primary osteoarthritis. Baseline assessments included the area of the rectus femoris muscle, serum albumin levels and a visual analogue scale (VAS) for pain during mobility. The participants were randomized to receive either a placebo or a daily nine-gram essential amino acid supplementation. All received the same diet, and post-surgery rehabilitation. The primary outcome measure was the change in the area of the rectus femoris.

The changes in the area of the rectus femoris muscles were significantly higher in the amino acid group than in the placebo group ($p<0.05$). In addition, the changes in VAS pain scores at four weeks post-surgery were superior in the amino acid group ($p<0.05$). Finally, the time of recovery of activities of daily living was significantly earlier in the amino acid group than in the placebo group ($p<0.05$). Multivariable analysis revealed that the addition of amino acid was independently related to the preservation of the area of the rectus femoris, with an odds ratio of 3.96 as compared to the placebo group.

Conclusion: This study of patients undergoing total knee arthroplasty found that the use of perioperative essential amino acid was effective in preventing postoperative atrophy and accelerating recovery.

Ueyama, H., et al. 2020 Chitranjan S. Ranawat Award: Perioperative Essential Amino Acid Supplementation Suppresses Rectus Femoris Muscle Atrophy and Accelerates Early Functional Recovery following Total Knee Arthroplasty. **Bone Joint J.** 2020, June; 102-B: 10-18.

PAIN PATTERNS AMONG NURSING HOME RESIDENTS WITH MILD COGNITIVE IMPAIRMENT

Previous studies have demonstrated that up to 80% of nursing home residents experience substantial pain, and that this pain is undertreated. This study was designed to better understand pain and treatment for pain among nursing

home residents with moderate to severe cognitive impairment.

Subjects were residents of 16, long-term care facilities, each diagnosed with dementia with moderately severe to severe impairment, as indicated on the Brief Instrument of Mental Status. Pain was evaluated using the Expert Clinician Pain Intensity Rating, with data obtained from medical records, physical examination and interviews with staff, family and primary care providers. Pain intensity reports were obtained from certified nursing assistants and nurses who had cared for the resident at least three times during the previous week.

Data were completed for 205 residents with an average age of 84 years. Of the total sample, 45% experienced moderate to severe "worst" pain, with usual pain rated as mild (1.6/10). The most common painful condition was arthritis, found in 47%.

Conclusion: This study of nursing home residents with moderate to severe cognitive impairment found that usual pain was mild, while 45% experienced moderate to severe "worst" pain during the week.

Ersek, M., et al. Pain Patterns and Treatment among Nursing Home Residents with Moderate to Severe Cognitive Impairment. **J Am Geriatr Soc**. 2020, April. 68(4): 794-802.

OMEGA THREE FATTY ACIDS AND VENOUS THROMBOEMBOLISM AFTER SURGERY IN THE ELDERLY

In patients undergoing hip fracture repair, pulmonary embolism and thromboses are among the major causes of morbidity and mortality. As previous studies have demonstrated that oral intake of omega-3 fatty acids exert strong antithrombotic effects in animal models, this study assessed the effect of dietary intake of omega-3 fatty acids on the incidence of venous thromboembolism.

Subjects were patients with hip fractures, admitted for surgical stabilization between February of 2015 and January of 2018. The participants were randomized to receive either 1,000 mg of omega-3 fatty acids or a placebo once daily for 30 days following surgery. The primary endpoints were complications, including incidence of pulmonary embolism and/or deep vein thrombosis, with secondary endpoints including hematoma, postoperative wound bleeding and postoperative infection.

Data were completed for 226 patients in the intervention group and 226 in the placebo group. Total deep vein thrombosis events were significantly lower in the intervention group than in the placebo group (p=0.03). The incidence of pulmonary embolism was also reduced in the treatment group as compared with the control group (p=0.04). No elevation in bleeding events was found in the treatment group as compared to the control group.

Conclusion: This study found that daily supplementation with omega-3 fatty acids decreases the risk of pulmonary embolism and symptomatic deep vein thrombosis after proximal femoral fracture surgery among elderly patients.

Zheng, X., et al. Omega-3 Fatty Acids Reduce Postoperative Risk of Deep Vein Thrombosis and Pulmonary Embolism after Surgery for Elderly Patients with Proximal Femoral Fractures: A Randomized, Placebo-Controlled, Double-Blind, Clinical Trial. **Int Orthop**. 2020. oi.org/10.1007/s00264-020-04610-0.

RECALCITRANT ACHILLES TENDINOPATHY

Chronic Achilles tendinopathy is common among adults between 30 and 60 years of age. This study compared the treatment efficacy of two nonsurgical treatment interventions, extracorporeal shockwave therapy (ESWT) and high -volume image guided injections (HVIGI).

Eligible subjects were patients with non-insertional Achilles tendinopathy recalcitrant to structured rehabilitation. All participants received either HVIGI, using a single injection of 10 ml of one percent lidocaine, followed by 40 mL of sterile saline, under ultrasound guidance, or ESWT, delivered in three weekly sessions at a frequency of 10 Hz and 2000 shocks per treatment. Following either procedure, the subjects were asked to rest for 24 hours, stretch for 48 hours and begin eccentric strengthening after 72 hours. The patients were followed up at six weeks, three months and six months with a numerical 0 to 10 pain scale to record their "average pain" and their "average stiffness." In addition, all participants completed both the Victoria Institute of Sport-Achilles Questionnaire (VISA-A) and the

Manchester-Oxford Foot Questionnaire (MOXFQ).

Follow-up data were available at three months for 29 in the HVIGI group and 17 in the ESWT group. At three months, VAS pain scores improved from 6.74 to 3.57 ($p < 0.001$) following HVIGI and from 6.57 to 4.35 ($p = 0.002$) following ESWT. At three months, VISA-A improved from 35% to 51% ($p< 0.001$) following HVIGI and from 34% to 49% ($p< 0.001$) following ESWT. There were no significant differences between the treatment groups.

Conclusion: This study of patients with chronic, non-insertional Achilles tendinopathy found significant improvements in pain and stiffness following extracorporeal shockwave therapy or high-volume image guided injections, with no significant difference between the two groups.

Wheeler, P., et al. Novel Interventions for Recalcitrant Achilles Tendinopathy: Benefits Seen following High Volume Image Guided Injection or Extracorporeal Shockwave Therapy-A Prospective, Cohort Study. **Clin J Sport Med.** 2020; 30: 14-19.

FREQUENT PHYSICAL THERAPY FOR PATIENTS WITH LUMBAR SPINAL STENOSIS

The Spine Patient Outcomes Research Trial (SPORT), the largest randomized controlled trial comparing surgical and nonsurgical treatment of patients with lumbar spine stenosis (LSS) reported that the nonsurgical treatment group had higher self-ratings of improvement and were less likely to cross over to surgery than those who did not undergo physical therapy (PT). This study assessed the relationship between the number of PT sessions and therapeutic effects in patients with LSS.

This study retrospectively reviewed data collected in a prospective study of patients with LSS receiving PT. In study one, 30, consecutive patients were enrolled between April of 2011 and April of 2012. In study two, 86 patients were randomly allocated to PT or home exercise between September of 2014 and May of 2018. All participants were enrolled in a six-week regimen of PT. The subjects were then stratified into groups receiving PT either twice a week (PT-2) or once a week (PT-1), or solely performing a home exercise program. Outcomes were recorded using the Zurich Claudication Questionnaire (ZCQ), a numerical rating scale (NRS) of back pain and leg pain and the Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOABPEQ).

At six weeks, as compared to those in the PT-1 group, those in the PT-2 group demonstrated significantly better improvements on all three scales ($p <0.05$). Relative to the home exercise group, the twice weekly group demonstrated significantly better improvement on all three scales ($p <0.05$). The home exercise and PT-1 groups did not demonstrate statistically significant differences in outcomes.

Conclusion: This study found that twice weekly physical therapy led to better patient outcomes after six weeks when compared to once weekly or home exercise programs.

Minetama, M., et al. Therapeutic Advantages of Frequent Physical Therapy Sessions for Patients with Lumbar Spinal Stenosis. **Spine.** 2020, May. 45(11): 639-646.

SPHENOPALATINE GANGLION PULSED RADIOFREQUENCY FOR CHRONIC CLUSTER HEADACHE

Cluster headaches (CH) are one of the most disabling pain disorders, with limited treatment options. Previous studies have found that low-frequency electrical stimulation of the sphenopalatine ganglion (SPG) may initiate CH pain, while increased stimulation frequency may reduce CH attacks. This study further evaluated the effect of pulsed radiofrequency (PRF) applied to the SPG in patients with chronic CH (CCH).

This study included 14 patients seen between January of 2016 and April of 2019, diagnosed with refractory CCH. The subjects were anesthetized and received PRF, applied for 10 minutes at a maximum of 42°C, with a maximum voltage of 100 V, a pulsed width of 20 ms and a pulse frequency of 2 Hz.

At a median follow-up of 6.5 years, eight of the 14 patients had at least a 30% reduction in weekly CH attacks for at least three months. Of the non-responders, two patients had a reduction in frequency and severity of headaches lasting less than three months, two patients had no improvement and one had a temporary worsening of symptoms.

Conclusion: This case series of patients with CCH found that pulsed radiofrequency targeted at the sphenopalatine ganglion may be effective in reducing the severity and frequency of symptoms.

Lazzari, Z., et al. A Prospective Case Series of Sphenopalatine Ganglion Pulsed Radiofrequency Therapy for Refractory Chronic Cluster Headache. **Euro J Neurol.** 2020, July; 27: 1190-1196.

FECAL TRANSPLANTATION AND OBESITY

Gut microbiota is a collection of microorganisms able to interact with the host via direct or indirect mechanisms that influence the host metabolism. Fecal microbiota transplantation (FMT) has been found to be effective in the treatment of recurrent *Clostridium difficile* infections. This animal study investigated the effect of autologous transplantation for the treatment of obesity.

Forty-two male mice were randomly assigned to one of three groups: controls (C) fed with a normal diet for 18 weeks, mice fed with a high-fat diet (HFD), caloric restriction (CR) mice fed for 12 weeks with a HFD and six weeks with a diet of 25% calorie restriction, FT-H mice provided the diets of CR with the addition of two rounds of fecal microbiota transplantation with feces from controls, and FT-A, the same as FT-H but with autologous fecal transplantation. For the FT-A group the feces were obtained before developing obesity. Body weight was measured at baseline and at the study completion.

Compared to the controls, body weight gain was greater in all other groups, with the highest weight gain in the HFD ($p < 0.0001$). Weight gain was mitigated in the CR group, as well as by fecal transplantation with the result greater in the FT-A group. The energy absorbed from the food (food efficiency) in the groups was greatest in the HFD, then in descending order, the CR, FH-H and FT-A groups.

Conclusion: This animal study found that two episodes of an autologous fecal transplantation from the same animal collected during a lean state could enhance the weight loss effects of a calorie restriction diet.

Perez-Matute, P., et al. Autologous Fecal Transplantation from a Lean State Potentiates Caloric Restriction Effects on Body Weight and Adiposity in Obese Mice. **Sci Rep.** 10, 9388

(2020). doi.org/10.1038/s41598-020-64961.

CHRONIC MUSCULOSKELETAL PAIN AND OBESITY

Researchers have estimated the prevalence of chronic musculoskeletal pain (CMP) to be quite high, with yearly costs of care estimated at over 60 billion dollars. This study investigated the association of multiple clinical markers of obesity and trajectories of excess weight with CMP among adults living in Brazil.

This cross-sectional study used ancillary data from the Brazilian Longitudinal Study of Adult Health. Complaints of CMP with evaluations at nine body sites with CMP defined as pain lasting longer than six months during the past year. General and abdominal obesity levels were classified according to accepted cut-offs for body mass index (BMI), waist circumference (WC) and waist–-height ratio (WHR). Binomial and multinomial logistic regressions were used to determine the associations between BMI and CMP at different sites.

Data were completed for 2,899 participants with a mean age of 56 years. Of these, 55% reported CMP, with sites including the knee (22.5%), lower back (18.6%) and shoulders (17.8%). In addition, 19.1% had multi-site involvement, and 10.3% reported generalized CMP. An adjusted model revealed that local, as well as multi-site, CMP was elevated among those with a BMI 30 kg/m² or greater. Associations of greater magnitude were found at higher obesity levels and among those with longer exposure to this excess weight.

Conclusion: This study demonstrates an association between a high body mass index and chronic musculoskeletal pain.

Costa, A., et al. Dose–Response Associations of Clinical Markers of Obesity and Duration of Exposure to Excess Weight with Chronic Musculoskeletal Pain: Cross-Sectional Analysis at Baseline of ELSA-Brasil Musculoskeletal Cohort. **Rheumatol Int.** 2020.40: 881–891.

ORAL PREVENTATIVE TREATMENTS AND BOTULINUM TOXIN IN CHRONIC MIGRAINE

For patients with chronic migraine (CM), the PREEMPT clinical trial demonstrated that onabotulinumtoxinA is an effective preventative treatment. However, the PREEMPT clinical trials compared onabotulinumtoxinA with placebo, and did not allow concurrent treatments. As real-life clinical practices usually use onabotulinumtoxinA concurrently with other interventions, this study explored the utility of onabotulinumtoxinA as an add on therapy.

This retrospective, multicentered, cross-sectional study was conducted in headache units across Spain. From these units, adult patients with CM who had taken or were currently taking oral preventive treatments who had already initiated onabotulinumtoxinA treatment were enrolled consecutively. Data included frequency and intensity with improvement of headaches measured as under 25%, 26% to 49% or 50% or greater. The primary outcome of the study was withdrawal of any oral preventative treatments.

Data were obtained for 542 patients with a mean age of 47.6 years. The mean time between the diagnosis of chronic migraines and the start of onabotulinumtoxinA therapy was 44.5 months. At the time when onabotulinumtoxinA was initiated, 91.1% were receiving concurrent oral preventative treatment. After the initiation of onabotulinumtoxinA injections, headache frequency and intensity were significantly reduced. In addition, 47.8% withdrew at least one oral preventative treatment and 41.5% completely stopped all oral preventative treatments.

Conclusion: This study of patients with chronic migraine headaches found that after the initiation of onabotulinumtoxinA injections, almost 50% of patients were able to stop using at least one preventive treatment and 41.6% successfully withdrew from all oral preventive treatments.

Alpuente, A., et al. Evaluation of the Concomitant Use of Oral Preventative Treatments and OnabotulinumtoxinA in Chronic Migraine: The PREVENBOX Study. **Euro J Neurol.** 2020 0: 1-7: doi:10.1111/ene.14331.

DAYTIME NAPPING AND INCIDENT STROKE

Several studies have investigated the relationship between napping habits and stroke, with inconsistent results. This study was designed to better understand the relationship between napping and the risk of stroke in a community population.

The Sleep Heart Health Study (SHHS) is a community-based, multicenter, prospective, cohort study enrolling 6,441 participants between 1995 and 1998. Baseline interviews included a self-report sleep habits questionnaire and a sleep study. Questions concerning the frequency and duration of naps were posed. Responses were divided by length into less than 30 minutes, 31 to 60 minutes and over 60 minutes.

At an average follow-up duration of 10.6 years, 220 participants had experienced an incident stroke. Compared to those taking no naps, those taking regular long naps or regular short naps had a higher incidence of stroke. A multivariate analysis revealed that the risk of stroke was higher among those taking regular long naps (>30 minutes), with a hazard ratio of 1.9, and regular short naps, with a hazard ratio of 1.45.

Conclusion: This large community-based study found an increased risk of stroke among those who take naps of 30 minutes or longer or those who nap five or more times per week.

Yan, B., et al. Association of Daytime Napping with Incident Stroke in Middle-Aged and Older Adults: A Large Community-Based Study. **Euro J Neurol.**2020, June;27(6): 1028-1034.

TEN-YEAR RISK OF RECURRENT STROKE BASED UPON SITE OF INTRACEREBRAL HEMORRHAGE

Spontaneous intracerebral hemorrhage (ICH) accounts for 10-15% of all strokes. Patients with ICH are at increased risk of recurrent stroke and other comorbidities. This study, the Oxford Vascular Study (OXVASC), with 10-year follow-up, assessed whether hematoma location influences the long-term risk of recurrent stroke.

This ongoing, population-based study included all vascular events in a sample of 92,720 individuals in nine general practices in the United Kingdom. Data included reports of transient ischemic attack (TIA) or minor stroke, stroke and death. The subjects were followed with face-to-face assessments at one, six, 12, 60 and 120 months for function, assessed using the modified Rankin scale (mRS) and the Health-Related Quality of Life measure.

During the study, 255 patients with primary ICH were included in the main analysis. Of those, 42.7% had lobar ICH and 56.5% non-lobar ICH. The risk of ICH was higher after lobar than non-lobar stroke (p=0.02), but the risk did not differ by location. The risk of disability or death did not differ between ICH locations. Patients with lobar ICH had significantly higher risk of any recurrent stroke than those with non-lobar stroke (Hazard Ratio (HR) 2.77). Among the 54 patients who were alive at five-year follow-up, 44% were disabled, with a higher proportion of disability after lobar than non-lobar stroke (60% versus 31%). Finally, the cumulative risk of dementia was higher after lobar than non-lobar stroke (p=0.047).

Conclusion: This population-based study of patients with primary intracerebral hemorrhage found a higher 10-year risk of recurrent stroke, and dementia after lobar ICH as compared to a non-lobar stroke.

Li, L., et al. Ten-Year Risks of Recurrent Stroke, Disability, Dementia and Cost in Relation to Site of Primary Intracerebral Haemorrhage: Population-Based Study. **J Neurol Neurosurg Psychiat.** 2020, June; 91(6): 580-585.

ASPIRIN AND COGNITIVE DECLINE IN THE ELDERLY

Low dose aspirin is one of the most widely used treatments for the secondary prevention of cardiovascular disease. Early observational data suggest that nonsteroidal anti-inflammatory drugs (NSAIDs), including aspirin, may be neuroprotective. This study, the Aspirin Reducing Events in the Elderly (ASPREE) trial examined the neurologic effects of low dose aspirin in healthy, older adults.

Subjects were 19,014 healthy, community dwelling adults, 65 to 98 years of age, randomized to receive 100 mg of aspirin or a placebo, once per day. Cognitive assessment tests were administered at baseline and year one, and then at years three, five and seven, or until study end in 2017. Outcome measures included Alzheimer's disease, mild cognitive impairment (MCI) and cognitive decline.

At a median follow up of 4.7 years, the diagnosis of dementia or MCI occurred in 488 of the aspirin group and 476 of the placebo group. Cognitive decline occurred in 838 of the aspirin group and 816 of the placebo group. Neither comparison was statistically significant. There were small changes in cognitive function over time but there was no evidence that the average trajectory differed between the aspirin and the placebo groups. The study was discontinued six months early for futility.

Conclusion: This large study of elderly adults found that a daily dose of aspirin did not reduce all cause dementia over five years but did increase the risk of hemorrhage.

Ryan, J., et al. Randomized, Placebo-Controlled Trial of The Effects of Aspirin on Dementia and Cognitive Decline. **Neurol.** 2020, (published ahead of print) DOI: 10.1212/WNL.0000000000009277.

SERUM PENTRAXIN 3 IN BRANCH ATHEROMATOUS DISEASE

Branch atheromatous disease (BAD) is an intracerebral lesion caused by an occlusion at the origin of a deep penetrating artery of the brain and is associated with a microatheroma or a junctional plaque.

As pentraxin 3 (PTX3) is directly produced by various cell types, such as endothelial cells and inflammatory macrophages, this study investigated whether PTX3 might be used as a potential diagnostic biomarker for branch atheromatous disease (BAD).

This retrospective analysis included data that were extracted from the medical records of consecutive stroke patients admitted over ten years. Clinical manifestations, laboratory findings and neuroradiological findings extracted from the medical records. The patients' modified Rankin Scale (mRS) scores were recorded at the time of discharge. From the MRI, stroke subtypes were identified, including BAD and LI, large-artery atherosclerosis (LAA) and cardioaortic embolic stroke (CES).

The median PTX3 values were higher in patients with BAD than in those with LI (p=0.0039), LAA (p<0.001), CES (p<0.001) or the control group (p<0.001). By maximizing the sum of sensitivity plus specificity, the PTX3 optimal cut-off value was found to be >2778 pg/mL.

Conclusion: This retrospective analysis of consecutively admitted stroke patients found that serum Pentraxin 3 levels were more elevated in branch atheromatous lesions than in any other stroke subtype.

Ninomiya, I., et al. Elevated Serum Pentraxin 3 Levels May Predict the Diagnosis of Branch Atheromatous Disease at a Very Early Stage. **Euro J Neurol.** 2020, June; 27: 1279-1284.

MOVEMENT DISORDERS FOLLOWING HYPOXIC BRAIN INJURY

Among patients with sudden cardiac arrest, a subpopulation of survivors develops movement disorders, which have been labeled post-hypoxic movement disorder (PMD), and/or chronic post-hypoxic myoclonus (CPM). This study investigated the clinical features, neuroimaging results, therapy and prognosis of these movement disorders.

This retrospective study included patients diagnosed with hypoxic ischemic encephalopathy following a cardiac arrest, each of whom had been treated in a neurological intensive care unit between January of 2007 and September of 2018. From these patients, those classified with PMD and/or CPM were chosen for analysis. Data were collected concerning neuroimaging studies, neuroprognostic testing (neuron-specific enolase, EEG, somatosensory-evoked potentials, neuroimaging), therapy and treatment response, as well as outcome assessment of movement disorders and neurological function. Long-term follow-up to assess final neurological outcome was performed by an interview of patients and/or their legal guardians, review of hospital records and inquiries of the date of death.

Subjects included 72 patients identified with hypoxic–ischemic encephalopathy, with an average age of 55 years and an overall survival of 36% during a median of 27 months of observation. Of these, 26.4% developed PMD and/or CPM. The survival rate of those with PMD/CPM was 63%, compared to 26% of those with hypoxic-ischemic encephalopathy without PMD/CPM (p=0.005). Of the 19 PMD/CPM patients 16 were assessed with MRI. Of these, post-hypoxic T1 hyperintensity of the lenticular nucleus was observed in 15. Successful early treatments included levomepromazine and intrathecal baclofen, while chronic myoclonus responded best to concurrent treatment with clonazepam, levetiracetam and primidone.

Conclusion: This study of patients with hypoxic-ischemic

encephalopathy after cardiac arrest found that those with movement disorders respond well to levomepromazine, clonazepam, levetracetam, primidone, or intrathecal baclofen.

Scheibe, F., et al. Movement Disorders after Hypoxic Brain Injury following Cardiac Arrest in Adults. **Euro J Neurol**. 2020, 0: 1-11. https://doi:10.1111/ene.14326.

ASYMPTOMATIC INTRACRANIAL STENOSIS AFTER TRANSIENT ISCHEMIC ATTACK AND MINOR STROKE

The management of recently symptomatic intracranial stenosis (ICS) has been established by randomized trials. However, data concerning the prognosis of asymptomatic ICS are scarce. This study was designed to determine the age-specific prevalence, predictors and prognosis of asymptomatic ICS.

Subjects were patients with transient ischemic attack (TIA) or mild ischemic stroke who were enrolled between 2011 and 2018. Participants were identified in a defined population of 92,728 covered by 100 primary care physicians. All underwent MRI evaluation. All 50% or greater stenoses were classified as symptomatic or asymptomatic in association with the most recent clinical presentation. All subjects received intensive medical management, including antiplatelet therapy for the first month and anticoagulation for patients with atrial fibrillation, hydrostatic therapy, and treatment of hypertension to guideline targets of less than 130/80. The patients were followed with face-to-face interviews at 1- 120 months, to determine any recurrent stroke and to ensure that medications and blood pressure were within compliance limits. All subjects were assessed with magnetic resonance angiography of the intracranial and cervical cranial arteries.

Of the 1,579 participants, 63.3% had a history of TIA and 36.7% had a history of minor stroke. Within the entire cohort, the prevalence of any asymptomatic intracranial stenosis was 14.8%. The prevalence of any asymptomatic intracranial stenosis was 4.8% for patients younger than 70 years to 34.6% for patients 90 years of age or older. There was no increase in the risk of recurrent ischemic stroke, major ischemic vascular events, or death in those with asymptomatic ICS compared with patients with no ICS.

Conclusion: This study of patients with an ischemic stroke or transient ischemic attack found a prevalence of 14.8% for any asymptomatic ICS, with the highest rates occurring at older ages.

Hurford, R., et al. Prognosis of Asymptomatic Intracranial Stenosis in Patients with Transient Ischemic Attack and Minor Stroke. **JAMA Neurol**. 2020. doi:10.1001/jamaneurol.2020.1326.

ENDOVASCULAR TREATMENT, WITH OR WITHOUT INTRAVENOUS ALTEPLASE, IN ACUTE STROKE

Endovascular thrombectomy has become a standard of treatment for patients with acute ischemic stroke. This study, the Direct Intraarterial Throbectomy in Order to Revascularize Acute Ischemic Stroke with Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: A Multicenter, Randomized, Clinical Trial (DIRECT-MT), compared thrombectomy alone with thrombectomy plus alteplase.

Eligible patients were seen in 41 academic tertiary centers in China. Eligible patients had an occlusion of the intracranial segment of the internal carotid artery or the first or proximal second segment of the middle cerebral artery or both. Patients were randomized to receive thrombectomy or intravenous alteplase, followed by thrombectomy. Subjects were assessed at 24 hours after randomization, at five to seven days or at the time of hospital discharge (whichever came first), and at 90 days (within a window of ±14 days). The primary outcome variable was the modified Rankin scale (mRS) score at 90 days.

Data were completed for 656 patients with a mean age of 69 years. At 90 days, the mRS scores of those in the thrombectomy alone group were noninferior to the scores in the combination group. Mortality at 90 days was 17.7% in the thrombectomy group and 18.80% in the combination group. Successful reperfusion on final angiography was 79.4% in the thrombectomy group and 84.5% in the combination group.

Conclusion: This study of patients with acute ischemic stroke found that thrombectomy alone was not inferior to a combination of thrombectomy and IV alteplase in functional outcome at 90 days.

Yang, P., et al. Endovascular Thrombectomy, with or without Intravenous Alteplase, in Acute Stroke. **N Engl J Med.** 2020, May 21; 382(21): 1981-1993.

ASSOCIATION OF BLOOD PRESSURE AND COGNITION AFTER STROKE

No clear association has been established between blood pressure and cognition following stroke. This study examined the association of cognition with blood pressure variables, including systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP) and mean arterial pressure (MAP), up to 90 days post-stroke.

This prospective, cross-sectional study obtained data of 432 dementia free stroke patients, with a median age of 66 years, from the population-based Brain Attack Surveillance in Corpus Christi (BASIC) project. The primary outcome measure was cognition, as assessed with the Modified Mini-Mental Status Exam (MMSE). Secondary outcome measures included the Animal Fluency Test (AFT) and Trail Making Tests A and B.

Higher SBP, lower DBP, higher PP and lower MAP were associated with poorer cognitive performance across all tests ($p < 0.001$ for all comparisons). Patient factors associated with lower cognitive performance included older age, lower education level, Mexican-American ethnicity, diabetes, higher stroke severity, more depressive symptoms and lower body mass index. However, an adjusted analysis revealed that no blood pressure measures were associated with significant changes in cognition across all tests.

Conclusion: This study of dementia-free elderly adults found that, within 90 days of a first stroke, blood pressure was not associated with changes in cognition.

Levine, D., et al. Association of Blood Pressure and Cognition after Stroke. **J Stroke Cerebrovasc Dis**. 2020, Jul:29 (7): 104754.

BIOMARKERS OF TAUOPATHY AND NEURONAL INJURIES

Symptoms of posttraumatic neurodegeneration may include memory loss, alterations in mood and personality and/or poor impulse control. Studies of patients with chronic traumatic encephalopathy (CTE) have described an increase in plasma tau concentrations which correlate with the severity of

symptoms. This study identified biomarker signatures in rats exposed to experimentally induced, repetitive, low-level blasts that developed chronic anxiety related traits, and in humans exposed to improvised explosive device (IED) blasts with behavior cognitive and/or memory complaints.

In the animal portion of the study, rats underwent one blast exposure per day for three consecutive days, with sham animals receiving identical care without receiving a blast exposure. Between six weeks and 12 months, the brains of these animals were extracted for analysis. The human portion of the study included 10 veterans with repetitive blast exposure and mild traumatic brain injury who reported behavioral and cognitive complaints.

All human subjects underwent magnetic resonance imaging for structural analysis as well as for the determination of regions of interest on PET images. For PET imaging, the subjects were injected with 370 MBq (10 mCi) of [^{18}F]AV45, with imaging performed 60 minutes post-injection. Blood samples were collected and processed to isolate plasma (human) or serum (rats).

In the animal study, total tau was increased in the right anterior cortex and left hippocampus. At 10 months after blast exposure, p-tau was increased in the left and right anterior cortex and in the hippocampus on the right, but not the left. In the veterans, [^{18}F]AV1451 retention was highest among those with the most severe clinical symptoms, and was located at the white/gray matter junction in frontal, parietal and temporal brain regions. Elevated levels of neurofilament light (NFL) chain protein was found in the plasma of veterans displaying excess [^{18}F] AV1451 retention, and among those with the most severe symptoms.

Conclusion: This study found that repeated mild traumatic brain injury induced by blast injuries increases levels of p-tau in study animals and in veterans with the most severe symptoms. The excessive retention of [^{18}F]AV1451 occurred at the white/gray matter junction in frontal, parietal and temporal brain regions, areas associated with elevated neurofilament light protein.

Dickstein, D., et al. Brain and Blood Biomarkers of Tauopathy and Neuronal Injury in Humans and Rats with Neurobehavioural Syndromes following Blast Exposure. **Mol Psychiat.** (2020). https://doi.org/10.1038/s41380-020-0674-z.

TESTOSTERONE REPLACEMENT AFTER MODERATE-TO-SEVERE TRAUMATIC BRAIN INJURY

Hypogonadism is common after traumatic brain injury (TBI). This study evaluated the effect of testosterone replacement on functional recovery during inpatient rehabilitation for men with TBI. This randomized, double-blind, placebo-controlled pilot trial included men hospitalized with moderate to severe TBI. Hospital lab values were used to assign patients to a normal testosterone group (N group) or, if testosterone was low, a low-testosterone treatment (T group) or placebo group (P group). The T group received transdermal testosterone patches. Outcome measures included changes in Functional Independence Measures (FIM) scores, grip strength and adverse events.

The T group demonstrated the largest absolute change in Total FIM score (30 points), compared to 17.5 for the N group and 19.5 for the P group. However, no significant differences were found in the rate of FIM improvement per day among the study groups. The T group demonstrated the greatest absolute improvement in grip strength (19.5 lbs.), followed by the P group (14.8 lbs.) and the N group (5.5 lbs.). The T group did not experience agitation or other adverse events at a greater rate than the other groups.

Conclusion: This study of men hospitalized with traumatic brain injury with low testosterone levels found that supplementation resulted in better Functional Independence Measures scores and strength, although the rate of change did not reach statistical significance.

Ripley D., et al. Testosterone Replacement in Hypogonadal Men During Inpatient Rehabilitation following Traumatic Brain Injury: Results from a Double-Blind, Placebo -Controlled, Clinical Pilot Study. **Neurorehab.** 2020; 46(3): 355-368.

TIMING OF THROMBOLYSIS AND ONE YEAR OUTCOME FOLLOWING ISCHEMIC STROKE

For patients with acute ischemic stroke, earlier treatment is associated with improved neurologic outcome. However, the effect of early treatment on long-term outcome is not clear. This study assessed all-cause mortality and hospital readmission at one year following neurolysis for suspected stroke.

Data for this study were obtained from Medicare beneficiaries age 65 years or older who were treated with intravenous tPA for acute ischemic stroke. Collected data included demographics, medical history, stroke onset time, hospital arrival time, in-hospital diagnostic studies, tPA treatment initiation time and in-hospital outcomes of consecutive patients treated for acute ischemic stroke or transient ischemic attack.

Primary outcome variables were one-year, all-cause mortality, one-year, all-cause readmission and the composite of all-cause mortality or readmission at one year. Data were completed for 61,426 patients with a mean age of 80 years. The median door to needle (DTN) time was 65 minutes. Of those treated with tPA, 79.2% had DTN times of longer than 45 minutes. Those in the delayed group had significantly higher one-year, all-cause mortality, and/or hospital readmission.

Those with DTN of longer than 60 minutes, compared to DTN of under 60 minutes, had significantly higher one-year, all-cause mortality, all cause readmission and all-cause mortality or readmission. Every 15 minutes increase in DTN time was associated with higher all-cause mortality within 90 minutes of hospitalization, but not after 90 minutes.

Conclusion: This study of patients with acute ischemic stroke found that those who underwent rapid thrombolytic administration had better one-year outcomes.

Man, S., et al. Association between Thrombolytic Door-to-Needle Time and One-Year Mortality and Readmission in Patients with Acute Ischemic Stroke. **JAMA.** 2020; 323 (21): 2170.

ATTITUDES ABOUT STATINS

Statins are one of the more frequently prescribed agents to decrease cholesterol levels, and reduce the risk of cardiovascular events. As negative beliefs about a medication are a deterrent to adherence, this study reviewed social media posts concerning beliefs about statins.

This study identified posts on Twitter that mentioned a statin. The tweets were collected from May 2013 to August 2018. The tweets were reviewed for eight statin medications including atorvastatin, rosuvastatin calcium, pitavastatin calcium, simvastatin, pravastatin sodium, lovastatin, fluvastatin sodium, and cerivastatin sodium. The tweets were

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reviewed with a content analysis performed.

Of the 1,097 posts which mentioned personal beliefs or attitudes, 71.7% referred to risk compensation behaviors, in which patients engage in behaviors such as poor diet and reduced physical activity or perceived themselves to be protected or at a lower risk by taking such preventative medications. Harm or medical mistrust accounted for 20% of the beliefs tweeted about statins. This was communicated through general reference terms such as "danger" or "poisonous" with named adverse events including dementia, liver failure and mortality. Others discussed alternatives to statins. Of the statin users, 6.8% described a personal experience of adverse events. Finally, 3.5% discussed costs.

Conclusion: This study of Twitter comments about statins found that 20% declared a concern about harm or mistrust of the medication.

Golder, S., et al. Assessment of Beliefs and Attitudes about Statins Posted on Twitter. A Qualitative Study. **JAMA Network Open**. 2020;3 (6):E208953. Doi:10.1001/ Jamanetworkopen.2020.8953.

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