Patients with a CT scan of the chest or abdomen done for other clinical indications within 6 months of this admission were reviewed for the presence or absence of CAC. Medical records were individually reviewed for mortality and type 1 acute myocardial infarctions at 1 year. RESULTS/ANTICIPATED RESULTS: In total, 144 patients (mean age 57 ± 14.8 years, 48% female) were included in the analysis. CAC was seen in 59% of these scans. Compared to those without detectable CAC, the CAC group had similar APACHE score (18 vs. 16.6, $p = 0.259$), peak TnI (3.64 vs. 2.11 mg/dL, $p = 0.363$), aspirin (63% vs. 51%, $p = 0.144$), and β blocker use (90% vs. 85%, $p = 0.357$) and had higher statin use (48% vs. 27%, $p = 0.013$). CAC was associated with increased all-cause mortality (59.5% vs. 38.9%, $p = 0.016$) and type 1 myocardial infarctions (10.6% vs. 1.7%, $p = 0.039$) compared with those without CAC. DISCUSSION/SIGNIFICANCE OF IMPACT: Coronary artery calcification is often seen when patients present with a noncardiac acute illness, such as sepsis, often making a new diagnosis for these patients. Mortality and acute MI after sepsis can be predicted by coronary calcification, and identify patients who should be targeted for therapy and close follow-up.

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HPA axis predictors of cue-induced intravenous alcohol self-administration in non-dependent drinkers

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OBJECTIVES/SPECIFIC AIMS: Alcohol craving, particularly in response to stress and alcohol cues, can lead to relapse in alcohol-dependent individuals. Hypothalamus-pituitary-adrenal (HPA) axis markers such as the cortisol to corticotrophin (CORT:ACTH) ratio have been shown to be a significant predictor of alcohol relapse. Our objective was to evaluate the influence of HPA-axis measures on intravenous alcohol self-administration (IV-ASA) in binge and nonbinge drinkers. METHODS/STUDY POPULATION: Healthy, non-dependent binge drinkers (n = 14) and nonbinge drinkers (n = 11) participated in this study. They underwent 3 personalized imagery sessions, where they heard 5-minute personalized audio scripts designed to trigger stress, alcohol craving, and neutral-relaxation states. Immediately following these cues, participants were given access to alcohol using a novel IV-ASA paradigm for 120 minutes. Serial blood samples were collected for cortisol and ACTH levels. Subjective measures were collected serially using the Subjective Units of Distress Scale (SUDS), Drug Effects Questionnaire (DEQ), and Alcohol Urge Questionnaire (AUQ). Analyses were conducted using linear regression. RESULTS/ANTICIPATED RESULTS: Results showed that peak and average ACTH levels as well as the CORT:ACTH ratio during the early phase of the IV-ASA session following the stress and alcohol cues were significantly higher than the neutral script; this effect was seen primarily in binge drinkers. After script administration, a greater change from baseline for ACTH predicted time to peak BrAC during IV-ASA. Gender and binge group predicted AUQ MAX (peak alcohol craving over the entire study session) and WANT MAX (peak "want more alcohol" scores over the session). There was a significant correlation between IV-ASA and increased ACTH peak and average values in binge drinkers. The DEQ and AUQ measures were positively correlated with ACTH peak and ACTH change from baseline. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings, to our knowledge, are the first demonstration that exposure to both stress and alcohol cues lead to an increase in ACTH during cue-induced IV-ASA, particularly in binge drinkers. These results suggest that changes in HPA-axis reactivity following stress and alcohol may be important determinants of alcohol consumption in non-dependent binge drinkers.

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The effects of fecal microbiota transplantation on the gut microbiota in subjects with *Clostridium difficile* infection

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OBJECTIVES/SPECIFIC AIMS: *Clostridium difficile* is the most common cause of infectious antibiotic associated diarrhea. It is often refractory to antimicrobial therapy and fecal microbiota transplantation (FMT) is emerging as a therapeutic

option. The objective is to characterize the direct effects of FMT on the gut microbiota. METHODS/STUDY POPULATION: Fecal specimens were obtained from a cohort of 29 subjects with recurrent *C. difficile* infection who received FMTs from 1 of 4 healthy donors as part of a phase 2 trial (Rebiotix). Fecal specimens were collected from the subject before FMT and up to 6 months post FMT. 16S rRNA sequencing and whole-genome shotgun sequencing were used to assess microbial community composition as compared by weighted Unifrac. RESULTS/ANTICIPATED RESULTS: Before treatment, the microbial community of subjects with *C. difficile* infection was highly distinct from the composition of the healthy donors in terms of metabolic profile. Quantification of phylogenetic community distance from donor by weighted Unifrac distance showed a significant decrease within the 1st week (Wilcoxon rank sum, $p < 0.01$). This metric was predictive of both treatment failures and antibiotic resistance gene count (LR = 22.45, $p < 0.0001$). DISCUSSION/SIGNIFICANCE OF IMPACT: We conclude that distance from donor is a useful metric to quantify FMT success and that FMTs are a promising treatment for otherwise untreatable carriage of antibiotic resistance genes and organisms.

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Delayed rewarming for neuroprotection in infants following congenital heart surgery: A safety study

Alexa Kanwit Craig

OBJECTIVES/SPECIFIC AIMS: Congenital heart disease (CHD) is the most frequently occurring birth defect in the United States affecting about 40,000 infants born every year. Despite significant advances in postsurgical survival, developmental outcomes remain disproportionately poor. Therapeutic hypothermia has been used for neuroprotection during cardiac surgery since the 1950s. Infants undergoing cardiac surgery are typically cooled to 28–33°C during the operation and then rapidly rewarmed to normothermia following surgery at a rate of 1°C every 3–5 minutes to minimize concerns surrounding the risks associated with prolonged bypass exposure. However, emerging evidence from animal models has shown rapid temperature changes following surgery may diminish or even negate the neuroprotective effect of intraoperative hypothermia. No prospective studies have assessed the safety or impact of alternative approaches to postoperative temperature management on the outcome of infants with CHD undergoing cardiac surgery. Therefore, we conducted a pilot study to examine the safety of a novel application of a temperature-regulating device to slowly rewarm infants with congenital heart disease over the 12 hours following cardiac surgery. METHODS/STUDY POPULATION: From November 2014 to July 2016, infants with CHD requiring surgery with cardiopulmonary bypass before the age of 12 months were prospectively recruited. Infants were randomized in blocks of 3 with 1 allocated to standard of care and 2 to the experimental protocol. Infants assigned to the standard of care were rewarmed in the operating room while on bypass at a rate of 1°C every 3–5 minutes back to a temperature of 37°C. Infants assigned to the experimental intervention, were rewarmed on bypass to 35°C and then over the subsequent 12 hours following surgery, gradually rewarmed using an FDA approved "cooling blanket" to increase temperature by 0.3°C every 2 hours for 6 hours and then by 0.2°C every 2 hours for 6 hours until the goal temperature of 36.5°C was achieved. Frequency of serious, moderate and other adverse events were tracked. Detailed vital sign data was collected hourly for the first 12 hours after surgery and then every 6 hours for the next 36 hours and included temperature, highest and lowest heart rate, highest and lowest systolic blood pressure, and highest and lowest diastolic blood pressure. Presence or absence of abnormal cardiac rhythms was recorded per 24-hour interval. Chest tube output was recorded in cc/kg/ 8 hours for as long as the chest tube was in place. Laboratory data points included serum creatinine level, serum glucose level, liver function tests (AST and ALT), platelet count, hematocrit level, PTT, INR, fibrinogen, white blood cell count and lactate. Blood samples for biomarkers of brain injury (s100b and NSE) were obtained on all infants at the following 4 intervals; the preoperative setting for baseline, postoperatively after bypass, on postoperative day 1, and on postoperative day 2. For this safety study, the primary outcome measure was a composite outcome of the frequency of serious adverse events as well as the frequency of any adverse events and was compared among treatment groups. Data were analyzed using an intent to treat analysis. The study was approved by the Maine Medical Center Institutional Review Board. RESULTS/ANTICIPATED RESULTS: Seven infants were randomized to the standard of care group and 9 were randomized to the experimental group. There were 2 exclusions after randomization in the standard of care group with 1 death in the operating room and 1 unsuccessful attempt to wean from bypass. The mean temperature upon arrival to the PICU for the experimental infants was 35.2°C (range 34–36°C) and for the standard of care infants was 37.5°C (range 36.9–38.9°C). For the first 8 hours after surgery, infants in the standard of care group had mean temperatures over 37.0°C. There were no significant differences in the

frequency of serious, moderate, or other adverse events between the standard of care group and experimental group. No infant in either group had need for cardiopulmonary resuscitation or exploratory surgery within 48 hours following surgery nor did any infant experience any clinically appreciated adverse neurological events such as stroke or seizure. No infant in either group experienced clinically significant bradycardia of less than 100 beats per minute or sustained tachycardia of greater than 160 beats per minute. There was a trend toward lower heart rates in the experimental group. Junctional Ectopic tachycardia (JET) occurred in 2 patients in the experimental group and 1 in the standard of care group. The mean highest INR in both groups was 1.4 (range 1.2–1.6). The mean lowest recorded platelet level in the first 48 hours was 128.8 (range 87–160) in the standard of care group and 123.8 (range 49–229) in the experimental group. Infants in the experimental group had lower chest tube output overall than the standard of care infants. The mean days of intubation for standard of care infants was 5 days (range 1–15 days) and for experimental infants the mean was 3.7 days (range 0–16 d). The PICU length of stay was shorter for the experimental infants (6.9 vs. 12 d for standard of care). The total length of stay was also shorter for experimental infants (12.4 vs. 16.4 d for standard of care). Serum biomarkers of brain injury (s100b and Neuron specific enolase) were elevated in the immediate postoperative period for infants in the standard of care group compared with the experimental group but normalized more quickly for standard of care. DISCUSSION/SIGNIFICANCE OF IMPACT: This small pilot study suggests that mild hypothermia following congenital heart surgery in infants under the age of 12 months is safe as there was no increase in the rate of severe, moderate, or other adverse outcomes in infants who received the experimental treatment of delayed rewarming. This study provides evidence for the efficacy of the cooling blanket in regulating the temperature of infants after surgery. Trends toward lower chest tube output, shorter intubation and decreased length of stay are possibly the result of improved hemodynamic stability in the absence of postoperative fever. Future studies will need to assess the effect of mild hypothermia compared with a normothemic control group.

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Association of chronic stress with alcohol seeking and health behaviors

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OBJECTIVES/SPECIFIC AIMS: The objective of this analysis was to characterize the impact of stress, both early life and chronic, on intravenous alcohol self-administration (IV-ASA) in healthy non-dependent drinkers using the Computer-Assisted Infusion System (CAIS). Personality measures also have shown to impact drinking behavior, particularly impulsivity. Few studies have assessed the impact of stress and impulsivity on drinking behaviors in a non-dependent population. METHODS/STUDY POPULATION: Healthy non-dependent drinkers (n = 28) completed a CAIS session, where they push a button adlib to self-administer standardized IV alcohol infusions. Participants completed the Cumulative Chronic Stress interview and the Early Life Stress Questionnaire (ELSQ) for stress measures. The Cumulative Chronic Stress interview was broken up into 4 sections: major life events, life traumas, recent life events, and chronic stressors. The number of endorsed events was added up to create 4 separate scores. Subjective response and craving measures were collected serially using the Drug Effects Questionnaire (DEQ) and Alcohol Urge Questionnaire (AUQ). The Impaired Control Scale (ICS) assessed failed control over recent drinking in the past 6 months. Impulsivity was assessed using the NEO personality inventory, which included the N-impulsive sub-facet, as well as the UPPS-P Impulsive Behavior Scale. RESULTS/ANTICIPATED RESULTS: Results showed early life stress events (ELSQ) are related to more chronic stressors in the cumulative chronic stress interview ($p = 0.005$). Participants with higher chronic stress scores showed lower subjective effects, as measured by the DEQ, following the priming exposure ($p = 0.036$) but had more craving for alcohol as measured by the AUQ ($p = 0.009$). A regression analysis showed the number of chronic stressful events predicted ICS failed attempts to control drinking ($p = 0.034$), after covarying for sex. Participants with more chronic stressful events showed more impulsivity on the N-impulsivity measure ($p = 0.034$) and the UPPS-P positive urgency measure ($p = 0.005$). DISCUSSION/SIGNIFICANCE OF IMPACT: Non-dependent drinkers with more early life stress tend to have a higher number of chronic stressful events. More chronically stressful events were associated with feeling less effects of alcohol and higher craving for alcohol. Participants with more chronically stressful events also appear to have more failed attempts at controlling their drinking. Future analysis will assess for mediation and moderation of these factors. Chronically stressful events and impulsive behaviors could serve as important areas for intervention for better treatment outcomes for alcohol use disorders.

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Ventriculo-arterial coupling and left ventricular mechanical work in systolic and diastolic heart failure

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OBJECTIVES/SPECIFIC AIMS: Our goal was to compare the ventriculo-arterial coupling and left ventricular mechanical work of patients with systolic and diastolic heart failure (SHF and DHF). METHODS/STUDY POPULATION: Patients with New York Heart Association Functional Class II-III HF symptoms were included. SHF was defined as left ventricular (LV) ejection fraction < 50% and DHF as > 50%. Analysis of the fingertip arterial blood pressure tracing captured with a finger plethysmography cuff according to device-specific algorithms provided brachial artery blood pressure and stroke volume. LV end-systolic volume was measured separately via transthoracic echocardiography. Arterial elastance (Ea), a measure of pulsatile and nonpulsatile LV afterload, was calculated as LV end-systolic pressure (ESP)/end-diastolic volume. End-systolic elastance (Ees), a measure of load-independent LV contractility, was calculated as LV ESP/end-systolic volume. Ventriculo-arterial coupling (VAC) ratio was defined as Ea/Ees. Stroke work (SWI) was calculated as stroke volume index × LV end-systolic pressure × 0.0136 and potential energy index (PEI) as $1/2 \times$ (LV end-systolic volume × LV end-systolic pressure × 0.0136). Total work index (TWI) was the sum of SWI + PEI. RESULTS/ANTICIPATED RESULTS: Patients with SHF (n = 52) and DHF (n = 29) were evaluated. Median (IQR) age was 57 (51–64) years. There were 48 (58%) and 59 (71%) patients were male and African American, respectively. Cardiac index was 2.8 (2.2–3.2) L/minute and 3.0 (2.8–3.3) L/minute in SHF and DHF, respectively ($p = 0.12$). Self-reported activity levels (Duke Activity Status Index, $p = 0.48$) and heart failure symptoms (Minnesota Living with Heart Failure Questionnaire, $p = 0.55$) were not different between SHF and DHF. Ea was significantly lower in DHF compared with SHF patients [1.3 (1.2–1.6) vs. 1.7 (1.4–2.0) mmHg; $p < 0.001$] whereas Ees was higher in DHF vs. SHF [2.8 (2.1–3.1) vs. 0.9 (0.7-1.3) mmHg; $p < 0.001$]. VAC was 1.8 (1.3–2.8) in SHF Versus 0.5 (0.4–0.7) in DHF ($p < 0.001$). Compared with SHF, DHF patients had higher SWI [71 (57–83) vs. 48 (39–68) gm × m; $p < 0.001$] and lower PEI [19 (12–26) vs. 44 (36–57) gm × m; $p < 0.001$]. TWI did not differ between SHF and DHF ($p = 0.14$). Work efficiency was higher in DHF than SHF [0.80 (0.74–0.84) vs. 0.53 (0.46–0.64); $p < 0.001$]. DISCUSSION/SIGNIFICANCE OF IMPACT: The results underscore the differences in pathophysiology between SHF and DHF patients with similar symptom burden and exercise capacity. These results highlight the difference in myocardial energy utilization between SHF and DHF.

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Cardiac abnormalities drive exercise intolerance in patients with nonslcoholic fatty liver disease

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OBJECTIVES/SPECIFIC AIMS: Nonalcoholic fatty liver disease (NAFLD) affects 1 in 3 Americans and can exist in 2 histological subtypes: simple hepatic steatosis (SHS) and nonalcoholic steatohepatitis (NASH), a clinically aggressive variant. Fatigue is the most common complaint in patients with NAFLD but the etiology of fatigue is unknown. Thus, the goal of this study was to objectively evaluate fatigue via maximal cardiopulmonary exercise testing and identify determinants of exercise intolerance in NAFLD. METHODS/STUDY POPULATION: In total, 14 subjects with histologically confirmed NAFLD were prospectively enrolled. Subjects with cirrhosis or those with known history of heart failure (systolic or diastolic) were excluded. Fatigue was quantified via the Duke Activity Status Index (DASI) questionnaire. A symptom-limited treadmill cardiopulmonary exercise test was performed in all subjects to measure exercise time (ET) and peak oxygen consumption (peak VO$_2$). Doppler-echocardiography was performed to measure systolic and diastolic function. RESULTS/ANTICIPATED RESULTS: The DASI score and ET was significantly reduced in patients with NASH (n = 10) when compared to those with SHS [40.2 (IQR = 24.2–50.7) vs. 58.2 (IQR = 50.7–58.2), $p = 0.04$]; [9.1 (IQR = 6.4–12.2) vs. 13.1 (IQR = 12.5–13.1) min, $p = 0.02$, respectively] reflecting moderate fatigue and impaired overall exercise capacity. The ET was directly linked to peak VO$_2$ (R = + 0.79, $p < 0.001$), VO$_2$ at anaerobic threshold (R = + 0.73, $p = 0.003$), and inversely to ventilatory efficiency index (R = − 0.785, $p = 0.001$) suggesting impaired cardiorespiratory fitness in those with reduced ET. ET was also linked to several parameters of diastolic dysfunction