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 × (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

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including left atrial volume index ($R = -0.798$, $p < 0.001$), and the ratio of early transmitral pulse-wave Doppler flow velocity (E) to early mitral annulus tissue Doppler velocity E' (E/E') ($R = -0.608$, $p = 0.036$), suggesting a role of diastolic dysfunction in patients with NAFLD with exercise intolerance. DISCUSSION/SIGNIFICANCE OF IMPACT: Cardiac abnormalities drive cardiorespiratory fitness and exercise intolerance in patients with NAFLD. These findings are exaggerated in patients with NASH suggesting a link between disease severity in NAFLD, exercise intolerance and diastolic dysfunction.

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Utility of the Modified Barium Swallow Impairment Profile as an outcome measure in oculopharyngeal muscular dystrophy

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OBJECTIVES/SPECIFIC AIMS: Oculopharyngeal muscular dystrophy (OPMD) is a rare, late-onset muscular dystrophy that causes severe swallowing impairment (dysphagia). Although promising therapies are in the pipeline, validated dysphagia outcome measures for use in OPMD trials have not been established. Videofluoroscopic swallow studies (VFSS) are considered the clinical gold standard for dysphagia assessment, yet the optimal objective measure of VFSS in OPMD is not known. Our aim was to investigate the utility of the Modified Barium Swallow Impairment Profile (MBSImP) as an objective measure of VFSS in OPMD patients. METHODS/STUDY POPULATION: This was a single-center, prospective, cross-sectional study. In total, 26 individuals with OPMD underwent VFSS and other measures of dysphagia including 50-mL water swallow time (ST). Validity was assessed by examining correlations with an OPMD Global Severity Score (GSS) and with dysphagia duration. RESULTS/ANTICIPATED RESULTS: The MBSImP demonstrated moderate correlations with GSS (Pearson $r = 0.52$, $p = 0.006$) and ST ($r = 0.39$, $p = 0.049$). The relationship between MBSImP and dysphagia duration appeared nonlinear, and levelled off with long dysphagia duration. In contrast, ST did not correlate significantly with GSS ($r = 0.27$, $p = 0.18$), nor with disease duration ($r = 0.05$, $p = 0.83$). DISCUSSION/SIGNIFICANCE OF IMPACT: Objective measurement of VFSS is a promising outcome measure in OPMD. With long disease duration, the MBSImP may not be sufficiently sensitive to detect disease progression. More sensitive measures for scoring dysphagia severity on VFSS should be explored for application to future s of OPMD.

2431

Characterization of immune cell differences with anti-thymocyte globulin (ATG) and granulocyte colony stimulating factor (GCSF) in both preclinical and clinical models of type 1 diabetes

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OBJECTIVES/SPECIFIC AIMS: Understand the immunomodulatory effects of anti-thymocyte globulin (ATG) and granulocyte colony stimulating factor (G-CSF) on type 1 diabetes patients using samples and in the preclinical model, the nonobese diabetic mouse. METHODS/STUDY POPULATION: Flow cytometry analysis of phase 1 peripheral blood samples treatment of nonobese diabetic mouse with ATG and GCSF and flow cytometry analysis of immune organs (spleen, lymph nodes, blood, bone marrow). RESULTS/ANTICIPATED RESULTS: Changes in both innate and adaptive immune cell subsets including plasmacytoid dendritic cells, naive, memory, effector CD4+ and CD8+ T-cells, and CD4+ T-regulatory cells and CD8+ T-regulatory cells DISCUSSION/SIGNIFICANCE OF IMPACT: Understanding of immune cell targets for immunotherapy in new-onset type 1 diabetes patients.

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A close examination of anti-retroviral drug selection and management in the optima study

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OBJECTIVES/SPECIFIC AIMS: Effective HIV therapeutic options for persons with advanced HIV disease whose regimens have failed multiple times are limited. Current clinical practice utilizes regimens comprised of combinations of anti-retroviral (ARV) drugs. Despite the widespread use of ARV medications, optimization of initial treatment composition and subsequent management remains challenging. The goals of this study are (a) to better understand the ARV treatment structuring using prior clinical and patient information including virtual phenotype data and measures of viral load and CD4 cell count. We evaluated the potential impact of ARV strategies on AIDS-defining events and mortality; (b) to assess and understand differences of treatment composition and management when comparing standard ARV strategy (<5 ARVs) with an intensive ARV strategy (at least 5 ARVs). METHODS/STUDY POPULATION: OPTIMA was a tri-national (United States, Canada, and United Kingdom) randomized open label of alternative ARV treatment strategies for patients with advanced HIV disease (CD4 ≤ 300 cells/mm^3) and evidence of resistance to 3 classes of ARV medications. OPTIMA used a 2 × 2 factorial design where the 2 factors were an ARV-free period Versus not; and standard Versus intensive ARV regimen. In this study, we focus on participants enrolled in OPTIMA at US participating sites and utilize demographic and clinical data including baseline virtual phenotype, ARV-related data (initial assignments and changes with drugs and dosages), follow-up lab data, AIDS-defining events, and vital status. RESULTS/ANTICIPATED RESULTS: Among 278 US-OPTIMA participants, 146 were randomly assigned to the standard ARV strategy and the rest were assigned to the intensive ARV strategy. Although not the sole factor, baseline virtual phenotype was used in selecting ARV medications within each assigned strategy. Participants in the standard arm exhibited better agreement between virtual phenotype results and the individual drugs selected for their regimen compared with participants in the intensive arm. This agreement had an almost statistically significant impact on survival time. No significant difference was detected in the frequency of ARV changes between standard and intensive ARV groups. DISCUSSION/SIGNIFICANCE OF IMPACT: Even though per design, OPTIMA assigned participants to an ARV strategy using a binary factor (standard vs. intensive ARV) and assessed its effect on HIV-related disease at a coarse level, the trial's design and rich database allowed for a closer examination of the ARV drug initial selection and subsequent management. Our findings summarize the patterns and discuss the effects of ARV and their management, on AIDS-defining events and survival. Such findings could provide preliminary, yet important insight, in understanding ARV use practice and could inform the conduct of future HIV treatment trials. Since the trial's randomization was at the ARV strategy level and not the individual ARV drugs, findings cannot be described in terms of causal pathways for specific ARVs.

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Dose-dependent nature of cocaine infusions on cardiovascular hemodynamics

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OBJECTIVES/SPECIFIC AIMS: Cocaine use is a significant health problem in the United States and associated with increased risk of adverse cardiovascular outcomes. Our goal was to evaluate the effects of rapid cocaine infusions on cardiovascular hemodynamics among patients with cocaine abuse disorder. METHODS/STUDY POPULATION: Patients with a history of cocaine abuse but no overt cardiovascular disease received 4 consecutive intravenous infusions of cocaine (0, 10, 20, 40 mg) given in randomized, double-blinded order. The infusion procedure was repeated on 2 consecutive days (4 infusions each day). Following each dose, patients underwent continuous monitoring via fingertip plethysmography for 30 minutes, followed by an additional 30 minutes washout procedure. Patients were surveyed throughout this timeline to record symptoms of cocaine response. Finger tracings were then used to calculate arterial pressure curves and parameters of heart rate, blood pressure, cardiac output, stroke volume, and systemic vascular resistance according to device-specific algorithms. Mean values were calculated over the entire 30 minutes follow-up and peak values were defined as the maximum value sustained over any 60-second interval during the follow-up period. RESULTS/ANTICIPATED RESULTS: Seven patients were enrolled and received cocaine infusions of 2 consecutive days. Cocaine dose was positively associated with mean cardiac output ($R = 0.489$, $p < 0.001$), peak diastolic blood pressure ($R = 0.435$, $p = 0.001$), mean heart rate ($R = 0.401$, $p = 0.003$), peak systolic blood pressure ($R = 0.399$, $p = 0.003$), peak mean arterial pressure ($R = 0.362$, $p = 0.008$), mean systolic blood pressure ($R = 0.399$, $p = 0.003$), + dP/dt ($R = 0.346$, $p = 0.012$), and peak heart rate ($R = 0.334$, $p = 0.015$). Hemodynamic parameters were also predictive of patient-reported symptoms of cocaine response. DISCUSSION/SIGNIFICANCE OF IMPACT: These data confirm the known pharmacologic effect of cocaine to prevent reuptake of neurotransmitters and demonstrate the feasibility of conducting a noninvasive assessment of cardiovascular

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