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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