RESULTS: The mean (SD) age was 53.9 (14.5) years; 50.7% were female and 36.7% were African-American. Compared to controls, CKD patients had significantly lower mean (SD) ISI [5.4 (3.2) vs. 3.1 (1.6), p < 0.0001]. Log ISI was positively correlated (r = 0.39, p < 0.0001) with eGFR and inversely correlated (−0.30, p < 0.0001) with BMI and log leptin (−0.42, p < 0.0001). In multivariable models adjusted for age, sex and race, a 10 ml/min/1.73m2 lower eGFR was associated with a greater decrease in ISI among non-obese (0.48; 95% CI: −0.25, −0.70) compared to obese participants (−0.18; 95% CI: −0.02, −0.35) (p-interaction = 0.04). Patients with low eGFR (in particular, the lower margin of the CKD stage 3 range, 30ml/min) had lower ISI even with BMI within normal range (Figure 1a). At higher eGFR, BMI had a greater impact on ISI. P-interaction = 0.046, for differential BMI effects at lower vs. higher eGFR. Log HOMA-IR was inversely correlated with eGFR (r = -0.49, p < 0.0001) and positively correlated with BMI (r = 0.52, p < 0.0001) and log leptin (0.46, p < 0.0001). HOMA-IR was lower for persons with higher GFR compared to lower GFR, at any BMI value. For example, at a BMI of 30 and a GFR of 120, HOMA-IR was 1.2 compared to 4.8 at a GFR of 30 (Figure 1b). Also, persons with high GFR had low HOMA-IR even with BMI in the obese range. BMI had a greater effect on HOMA-IR at lower eGFR. P-interaction = 0.005, for differential BMI effects at lower vs. higher eGFR. Similar findings were obtained when using log leptin in lieu of BMI in models for ISI and HOMA-IR.

DISCUSSION/SIGNIFICANCE OF IMPACT: Measures of adiposity (BMI and leptin) and GFR were independently predictive of insulin sensitivity (IS) but the magnitude of the effect of BMI (or leptin) on ISI varied significantly across GFR levels and type of IS (peripheral versus central). The effect of BMI on central IS (HOMA-IR) was more pronounced at lower GFR with small changes in BMI translating into greater variations in IS. Conversely, at low GFR, peripheral IS (ISI) is less affected by BMI. Persons with GFR at the lower margin of the CKD stage 3 range were significantly insulin resistant (low ISI) regardless of their BMI. More studies are required to further elucidate these interaction patterns for central and peripheral IS.

Effect of Long-Term NSAID Use on Opioid Abuse and Health Outcomes among Breast Cancer Patients

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OBJECTIVES/SPECIFIC AIMS: Cancer related pain presents a significant risk for opioid abuse among cancer survivors and contributes to the current opioid crisis. Nearly 90% of breast cancer patients have been reported to have cancer-related pain requiring treatment. Opioids, in combination with NSAIDs, have been widely used for pain management in this population despite the risk of abuse. Long-term NSAID use due to their antineoplastic and neuroprotective effects may offer additional protective effects against opioid abuse. Here, we assess the relationship between NSAID use and opioid abuse among breast cancer patients.

METHODS/STUDY POPULATION: Using ICD-9-CM codes, we identified and selected women aged >18 years with breast cancer from the National Inpatient Sample (NIS). Our primary predictor was a history of long-term NSAID use. Opioid abuse was the primary outcome of interest. Secondary outcomes were inpatient mortality and length of stay. Multivariable regression models were employed in assessing the association between predictors and outcomes while adjusting for relevant covariates.

RESULTS/ANTICIPATED RESULTS: Among 170,644 women with breast cancer, 7,838 (4.6%) reported a history of long-term NSAID use. Patients with a history of long-term NSAID use had lower odds of opioid abuse (aOR 0.53; 95% CI [0.32-0.88]) and in-hospital mortality (aOR 0.52; 95% CI [0.45-0.60]) and were likely to have shorter hospital stay (7.12 vs. 8.11 days) compared to women with no history of long-term NSAID use. DISCUSSION/SIGNIFICANCE OF IMPACT: Long-term NSAID use may offer a protective effect against opioid abuse and improve in-hospital outcomes translating to better quality of life and healthcare utilization indices among breast cancer patients.
Effects of exercise and a very low fat diet in metabolically abnormal obese adults

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OBJECTIVES/SPECIFIC AIMS: People with metabolically abnormal obesity (MAO), defined as those with insulin resistance and high intrahepatic triglyceride, are at high risk for developing type 2 diabetes and cardiovascular disease. Weight loss through reduced energy intake and increased physical activity has profound impacts on improving cardiometabolic function. However, the specific additional effects of exercise training with diet-induced weight loss on metabolic function are equivocal.

METHODS/STUDY POPULATION: A comparative trial is ongoing in MAO adults undergoing 8-10% weight loss induced by a very-low fat plant-based (PB) diet with structured exercise training (n=8) compared to the same weight loss induced by the PB diet alone (n=3).

RESULTS/ANTICIPATED RESULTS: Preliminary results indicate improvements in muscular strength and cardiorespiratory fitness, reduced intrahepatic triglyceride, reduced 24-hour postprandial glucose response, reduced fat mass, and reduced diastolic blood pressure. Those undergoing PB diet with exercise training had greater improvements in muscular strength and cardiorespiratory fitness than those undergoing PB diet alone. Differences between intervention groups for other cardiometabolic measures are not yet known.

DISCUSSION/SIGNIFICANCE OF IMPACT: Each of the interventions resulted in improved cardiometabolic measures; however the extent of the differences between the interventions is not yet clear. It is hypothesized that compared with weight loss induced by a PB diet, the same weight loss induced by a PB diet and structured exercise training will i) cause greater improvement in skeletal muscle insulin sensitivity, ii) will attenuate the usual decline in muscle mass while increasing strength, and iii) result in greater increases in left ventricular diastolic function. The long-term objective of this proposal is to provide a foundation for future studies evaluating mechanisms for the effects of exercise in cardiometabolic disease prevention and therapy.

Effects of intranasal ketamine on uncontrolled cancer related pain

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OBJECTIVES/SPECIFIC AIMS: If intranasal ketamine can be utilized for pain control in cancer patients, this could provide them with superior analgesia and better quality of life, without the risk of significant respiratory depression associated with opioid medications. We seek to obtain preliminary data via a clinical trial addressing safety, feasibility, and utility of this novel technique for the treatment of persistent uncontrolled cancer pain. These findings would be an important initial step towards testing the effectiveness of intranasal ketamine as a non-opioid medication for cancer pain used as potential maintenance outpatient therapy. These initial findings would be applied to a subsequent trial to determine the effectiveness and associated toxicities of ketamine in a larger sample of cancer patients, and address the compelling need to identify new, successful management therapies for cancer pain. Specific Aims: 1. To evaluate (pharmacodynamic) effects of NAS ketamine on Patient Reported Outcomes (PROs), such as pain scores, side effects, depression, quality of life, and functional status. A clinical trial will be conducted where NAS ketamine will be given to a sample of patients with cancer related pain. Patient Reported Outcomes (PROs), such as pain scores, depression, quality of life, and functional status will be noted on Numerical Pain Rating Scale (NPRS), Montgomery Asberg Depression Rating Scale (MADRS), and Edmonton Symptom Assessment (ESAS), Eastern Cooperative Oncology Group (ECOG) and Patient Reported Outcome Measurement Information System (PROMIS) scales respectively. 1. To measure pharmacokinetics of NAS ketamine through analysis of ketamine and its metabolite norketamine to determine pharmacokinetic properties. During this clinical trial blood samples will be drawn at specified intervals and sent for analysis. 3. To determine opioid sparing effect of NAS ketamine. Opioid use will be measured by documenting use of rescue medications prior to and during the study and by evaluating total opioid consumption prior to and during the study. METHODS/STUDY POPULATION: Study sample: In the search for improved therapies for chronic cancer pain, medications with novel mechanisms of action have been sought. One such promising pharmacologic approach is ketamine. We specifically intend to measure utility of ketamine in patients with pain related to cancer or cancer treatment. Ketamine has shown to reverse central sensitization and opioid tolerance in rat models. Since ketamine is Scheduled III in United States and has abuse potential, we do not intend for ketamine to replace opioids, but use in patients who have failed opioid therapy. Since the investigators of the study practice at Emory, subjects will be from oncology and pain clinics (the supportive oncology clinic, oncology clinics, the pain clinic and Acute Pain Service) at Emory. The trial will be conducted at the Phase 1 Unit of the Winship Cancer Institute (WCI) at

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