that mice that received 22 Gy developed cardiomyopathy at day 35 based on increased global longitudinal strain (GLS). Radiation decreased T cells, macrophages, and mast cells in the heart of irradiated mice by RT-qPCR at day 10 indicating damage to immune cells by radiation at all doses. Thus, we successfully created a clinically relevant model of RIHD in male BALB/c mice. DISCUSSION/SIGNIFICANCE: Patients undergoing radiation therapy for thoracic malignancies can develop cardiomyopathy (DCM) due to radiation damage. Previously published animal models utilized mouse strains resistant to developing DCM (female mice, C57BL/6 strain) and used high doses of radiation. Establishing a translational model is crucial for prevention of RIHD.

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Association between self-monitoring and ketogenic diet adherence in a technology-assisted lifestyle intervention

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OBJECTIVES/GOALS: Self-monitoring (SM) improves adherence to low-fat low-calorie (LFLC) diet for weight management. Ketogenic diet (KD) is a promising alternative to LFLC, however, it is unclear whether SM improves KD adherence. We examined the association between SM and KD adherence during the first 12 weeks of a 6-month technology-assisted lifestyle intervention. METHODS/STUDY POPULATION: We included 30 (50.8 ± 12.4 years, 70% female) overweight/obese (body mass index: 37.1 ± 7.2 kg/m2) participants in the analysis. They received personalized KD goals with very low-carbohydrate (22–62 g/d), moderate protein (52 -87 g/d), and high-fat (115 - 219g/d) and calorie intake goals (1338–2554 kcal/d). Additionally, participants performed daily diet, exercise, and weight SM. Adherence to KD was measured by (1) self-monitored dietary intake, and (2) percent of days in ketosis state (blood ketone≥0.5 mmol/L) captured by a fingerstick blood ketone meter. SM frequency was defined as percent of days participant logged food intake, wore fitness tracker, and weighed body weight. Pearson correlation coefficients were computed to examine the correlation between SM in diet, exercise, and weight with KD adherence. RESULTS/ANTICIPATED RESULTS: Percentage of days participants SM for diet, exercise, and weight was 58.4 ± 32.2%, 66.4 ± 30.9%, and 59.0 ± 32.6%, respectively. Correlational analysis more frequent diet SM was positively correlated with more days in ketosis ($r = 0.58$, $p = 0.003$), higher fat intake ($r = 0.68$, $p = 0.0001$), and higher calorie intake ($r = 0.67$, $p = 0.002$) within the fat and calorie goals set; more frequent weight SM was positively correlated with more days in ketosis ($r = 0.48$, $p = 0.02$), higher fat intake ($r = 0.45$, $p = 0.023$), and higher calorie intake ($r = 0.44$, $p = 0.027$). DISCUSSION/SIGNIFICANCE: We found that diet and weight SM were positively associated with fat and calorie intake, as well as days in ketosis. Given the reported promising effect of KD on weight loss and the challenges of adhering to KD, our findings suggested that promoting SM on diet and weight might be a promising avenue for improving KD adherence leading to successful weight loss.

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Beneficial Actions of SGLT2 Inhibition and H2S Therapy in Heart Failure with Preserved Ejection Fraction

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OBJECTIVES/GOALS: SGLT2i therapy is currently a cornerstone in heart failure with preserved ejection fraction (HFpEF) therapy. Similarly, H2S has been shown to be beneficial in preclinical models of heart failure. With this in mind, we sought to investigate the effects of the SGLT2i and H2S donor therapy alone or in combination in a rodent model of cardiometabolic HFpEF. METHODS/STUDY POPULATION: Male C57BL/6N mice (9 weeks of age) were fed a high fat, Western diet (HFD) and received L-NG-Nitro arginine methyl ester (L-NAME) in the drinking water (0.5 g/L) to induce HFpEF. At 5 weeks, animals were randomized to either control, H2S donor (SG-1002, 90 mg/kg/d, P.O), Empagliflozin (155 mg/L, P.O), or the combination of SG-1002 and Empagliflozin for an additional 5 weeks while being maintained on HFD and L-NAME. Echocardiography, left ventricular invasive LV and systemic hemodynamics, and exercise capacity testing were performed to assess cardiovascular disease severity. Fasted glucose, circulating triglyceride and cholesterol content were similarly measured to quantify key clinical metabolic parameters. H2S and its metabolite, sulfane sulfur, were quantified to assure adequate H2S donation. RESULTS/ANTICIPATED RESULTS: Administration of SG-1002 restored H2S and sulfane sulfur to normal circulating levels. All treatment groups exhibited similar improvements in LV diastolic dysfunction as measured by E/E'and LVEDP. Combination therapy significantly improved exercise capacity whereas the monotherapy groups did not. Treatment with SG-1002 decreased fasting glucose and circulating cholesterol while all treatment groups displayed decreased circulating triglycerides and body weight compared to HFpEF control. DISCUSSION/SIGNIFICANCE: These data indicate that restoring H2S or treatment with an SGLT2i in this preclinical HFpEF model attenuates pathology. Combination of both drugs exhibited greater benefit than either monotherapy in important HFpEF parameters such as exercise capacity. Further studies are underway to characterize the benefits observed from combination therapy.

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