Cardiovascular disease (CVD) and frailty have been linked at the mechanistic and epidemiological levels. Our goal is to identify if subclinical markers such as atherosclerosis, body composition, and fibrofatty infiltration measured from non-contrast whole-body magnetic resonance imaging (MRI) are markers of physical frailty. Community dwelling older adults with frailty status ascertained by Fried measurement are being recruited from an aging studies registry. MRI is performed using a Canon Galan3T with dedicated coils. Preliminary analysis from 4 frail individuals (86±15 years, 3 female, BMI=22±3kg/m2) and 2 age-matched robust controls (86±1 years, 1 female, BMI=28±0.2kg/m2) is presented. Of 4 frail one had a prior heart attack; one was previously diagnosed with heart failure. Mean atheroma score from 28 vessel segments (0.42±0.26 vs 0.18±0.10) and aortic tortuosity (2.3±0.4 vs 2.1±0.1) were higher in frail compared to robust indicative of higher atherosclerotic burden and vascular stiffness. Mean subcutaneous and visceral adipose tissue volumes were lower in frail compared to robust. However, mean myocardial (1113±27 vs 1089±2), liver (729±92 vs 683±104) and skeletal muscle (1106±25 vs 1072±64) T1 times (milliseconds) were each higher indicative of greater diffuse interstitial fibrosis. Averaged intramuscular fat percent measured across the pelvis, forearm, pectus, thigh, and calf was higher in frail compared to robust (14.8±4.1% vs 8.5±2.3%) indicative of higher fatty infiltration. Although these early results do not reach statistical significance, they support further study to determine cardiovascular and tissue related differences between physically frail and robust older adults, which in turn may inform intervention developments for frailty and CVD.

β-GPA: AN AMPK ACTIVATOR WITH POTENTIAL EFFECTS ON HEALTHSPAN AND FUNCTION

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β-Guanidinopropionic acid (β-GPA) is a naturally occurring compound reported to activate AMP Activated Protein Kinase (AMPK) signaling in vivo. Acute administration of β-GPA in young animals has been reported to improve multiple functional measures including a switch to oxidative fatigue-resistant muscle fibers, improved glucose uptake, and increased mitochondrial biogenesis. However, it is unknown if β-GPA may promote healthy aging or prevent late-life functional decline. To address this knowledge gap, we tested the effects of β-GPA on mitochondrial energetics and cellular function in young and old genetically heterogenous mice (HET3). Both age groups were fed either 1% β-GPA or control chow for ~5 months and basic functional parameters including metabolism were assessed. β-GPA treatment decreased lean and fat mass in young males, but prevented late-life losses in these parameters in old animals. Notably, glycated hemoglobin (HbA1c) levels were lower in treated young and old males suggesting improved glucose homeostasis. Citrate synthase activity was also higher in old males fed β-GPA suggesting increased mitochondrial biogenesis. At the molecular level, mitochondrial Complex I expression decreased with β-GPA treatment in old males versus controls. High resolution respirometry revealed generally decreased respiration in old animals compared to young and decreased Complex 1 coupled respiration in soleus of β-GPA treated young but not old males. These findings indicate that the mitochondrial effects attributed to β-GPA may be mediated by its action on Complex I. While treatment outcomes varied in young and old males these results suggest β-GPA may prove beneficial in combating age-related declines in function.

AGE, SEX, AND FRAILTY INFLUENCE AGE-DEPENDENT CHANGES IN VENTRICULAR STRUCTURE AND FUNCTION IN C57BL/6 MICE

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The heart undergoes maladaptive changes during aging that set the stage for cardiovascular diseases, but frail older individuals are most likely to develop such diseases. We investigated the impact of frailty on left ventricular (LV) remodeling in male and female mice (aged 9-23 mos). Ventricular function/structure and frailty were assessed with echocardiography (Vevo 2100) and a frailty index (FI) tool. Fractional shortening (systolic function) increased with age (9 vs 23 mos) in males (27.7±2.6 vs 38.4±1.6%; $p<0.05$) and females (26.9±1.4 vs 32.5±1.8%; $p<0.05$); similar results were seen with ejection fraction. Conversely, E/A ratios (diastolic function) declined with age in males (1.9±0.1 vs 1.3±0.1; $p<0.05$) and females (2.1±0.3 vs 1.6±0.1; $p<0.05$). LV mass and LV internal diameter (diastole) increased with age in females but not in males, while intraventricular septum (diastole) increased in males only. As age-dependent changes were heterogeneous, we stratified the data by FI scores. Interestingly, fractional shortening ($r=0.52$; $p=0.006$) and ejection fraction ($r=0.52$; $p<0.0001$) were graded by FI score, but only in males. By contrast, LV mass was graded by frailty, but only in females ($r=0.55$; $p<0.0001$). Thus, diastolic function declines with age in both sexes while systolic function actually increases. Aging females display increased LV mass and LV dilation whereas older males exhibit septal thickening. These maladaptive changes are graded by frailty, suggesting that cardiac aging is prominent in those with poor overall health. Age, sex and frailty influence cardiac aging, which may predispose frail older men and women to develop different cardiovascular diseases as they age.

CASE STUDY EXEMPLAR OF DETECTING SEVERE DIASTOLIC DYSFUNCTION USING BALLISTOCARDIOGRAM

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The specific aim of this case study was to describe how monitoring ballistocardiogram (BCG) waveforms can detect early heart failure (HF) changes. HF significantly impairs quality of life and is the principal cause for hospital readmissions in older adults. HF prevalence in American adults aged