

Over the past 25+ years, a focus of the Wake Forest Claude D. Pepper Older Americans Independence Center (OAIC) has been to study the consequences of and treatments for geriatric obesity. The Wake Forest OAIC has provided support for 18 clinical trials of caloric restriction (CR), with and without various exercise regimens, in 2,545 adults (71% women, 21% African American) with a mean±SD age of 67.5±5.9 years and BMI ≥27 kg/m². A priority of the Wake Forest OAIC is to collate and store common data (e.g., demographics, physical performance, cognitive function), biospecimens (blood, muscle, adipose), and images (DXA, CT) from these trials in the Integrated Aging Studies Databank and Repository (IASDR; <https://www.peppercenter.org/public/dspIASDR.cfm>). This IASDR serves as a resource for the scientific community to foster new scientific questions and analyses. This symposium will provide an overview of CR trials and participants included in the IASDR and how the IASDR supports secondary analyses of CR by highlighting several secondary analyses using data and/or samples from the IASDR. Justice and colleagues examined the effect of CR on a geroscience-guided biomarker index using blood samples from the biorepository. Weaver and colleagues examined the effect of different exercise regimens on CT-derived muscle and bone measures during CR. Miller and colleagues pooled data from 11 trials to determine if CR-induced appendicular lean mass loss is associated with changes in physical performance. Finally, Hsieh and colleagues pooled data from eight trials to examine whether the effect of CR on gait speed differed by baseline BMI and inflammation.

THE FIRST EVALUATION OF A GEROSCIENCE BIOMARKER INDEX (TAME-BI) IN A TRIAL OF CALORIC RESTRICTION AND EXERCISE

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We leveraged the WF OAIC biorepository to measure a consensus-derived panel of blood-based biomarkers of aging and constructed a geroscience-guided biomarker index (TAME-BI), testing it for the first time in a clinical trial. We measured IL-6, TNF- α -receptor-I, growth differentiating factor-15, cystatin C, and N-terminal pro-B-type natriuretic peptide in a 20-week randomized trial of caloric restriction (CR), aerobic exercise (EX), CR+EX, or attention-control in 88 patients (67±5 years) with heart failure with preserved ejection fraction (HFpEF). We calculated TAME-BI (analyte levels ranked, binned by quintile, and summed) and found a time×treatment interaction for improved TAME-BI with intervention ($p \leq 0.05$) and detected associations between change in TAME-BI and change in six-minute walk distance ($r = -0.24$), usual walk speed ($r = -0.23$), and left ventricular relative wall thickness ($r = 0.31$). In sum, CR+EX intervention improved TAME-BI and changes in TAME-BI were associated with changes in key functional measures in older HFpEF patients.

EXERCISE MODALITY AFFECTS OLDER ADULT CT-DERIVED MUSCLE AND BONE LOSS DURING CALORIC RESTRICTION

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Caloric restriction (CR) can exacerbate muscle and bone loss. We examined 18-month changes in computed tomography (CT)-derived trunk muscle, and volumetric bone mineral density (vBMD) and finite element-estimated bone strength of the spine and hip in 55 older adults randomized to CR alone or CR plus aerobic (CR+AT) or resistance (CR+RT) training. Trunk muscle area loss trended higher with CR+AT [-16.8 cm^2 (95% CI: $-26.4, -7.1$) vs CR: -6.7 ($-12.8, -0.5$), CR+RT: -9.0 ($-14.5, -3.4$)]. Spine vBMD loss trended higher with CR+AT [-0.014 g/cm^3 ($-0.027, -0.001$) vs. CR: -0.005 ($-0.022, 0.012$), CR+RT: -0.004 ($-0.019, 0.011$)], and similarly for vertebral bone strength. Hip vBMD losses trended lower with CR+RT [-0.015 g/cm^3 ($-0.024, -0.006$) vs. CR: -0.027 ($-0.036, -0.019$), CR+AT: -0.029 ($-0.037, -0.020$)]. Hip vBMD and trunk muscle losses were positively correlated ($r=0.53$), and spine vBMD loss tended to increase with trunk muscle loss ($r=0.21$) and fat infiltration ($r=0.17$). Collectively, aerobic training was less effective at preserving muscle-bone health during CR.

APPENDICULAR LEAN MASS LOSS DOES NOT IMPACT PHYSICAL PERFORMANCE CHANGE DURING CALORIC RESTRICTION IN OLDER ADULTS

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Data from 11 six-month randomized controlled trials were pooled, with 902 participants randomized to caloric restriction (CR; $n=762$) or Non-CR ($n=140$) to determine if CR-induced appendicular lean mass (ALM) loss was associated with change in physical performance among older adults. After adjusting for age, sex, race, body mass index, exercise assignment and baseline value of the outcome, CR had significant ALM loss [-0.77 kg (95% CI: $-0.89, -0.65$)], while Non-CR had ALM gain [$+0.28 \text{ kg}$ (0.08, 0.49)]; $p < 0.001$. Both groups experienced similar improvements in the Short Physical Performance Battery (SPPB) score [CR: $+0.45$ (0.35, 0.55) vs Non-CR: $+0.50$ (0.30, 0.69)]; $p=0.63$] and sit-to-stand time [CR: -1.42 s ($-1.81, -1.03$) vs Non-CR: -1.85 s ($-2.49, -1.21$)]; $p=0.19$]. Change in SPPB score and sit-to-stand time was not associated with change in ALM (both $p > 0.15$). In spite of significant ALM loss, CR resulted in overall improvements in physical performance in older adults.