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Frailty is a progressive physical decline leading to higher morbidity and mortality in older adults. Previous studies have demonstrated shared mechanisms between insulin resistance, inflammation, and frailty. The purpose of this trial is to determine whether metformin prevents frailty in non-frail, community-dwelling older adults (≥65 years) with pre-diabetes, determined by 2-hour oral glucose tolerance test (OGTT). Frail individuals (Fried criteria) and those with renal impairment (glomerular filtration rate <45 mL/min) are excluded. Eligible participants are randomized to metformin or placebo and followed for two years. The primary outcome is frailty; secondary outcomes include physical function (short physical performance battery), systemic and skeletal muscle inflammation (plasma and muscle inflammatory markers), muscle insulin signaling (muscle biopsy), insulin sensitivity (insulin clamp), glucose tolerance (OGTT), and body composition (dual-energy x-ray absorptiometry) measurements. Participants are followed every 3 months for safety assessments, every 6 months for frailty assessment and OGTT, and every 12 months for muscle biopsy. Currently, 99 participants, including 53 (53.5%) male and 91 (91.9%) white, are active (54) or have completed the study (35). At baseline, mean age was 72.3 ± 5.5 years, body mass index was 30.7 ± 5.9 kg/m2, and Hemoglobin A1c was 5.73 ± 0.37%. Mean frailty score was 0.5 ± 0.6 and the proportion of non-frail and pre-frail participants were 58.6% (n = 58) and 41.5% (n = 41), respectively. Findings of this clinical trial may have future implications for the use of metformin in older adults with pre-diabetes in order to prevent the onset of frailty.

ASSOCIATION OF FRAILTY INDEX WITH CLINICAL BPH PROGRESSION AND SERIOUS ADVERSE EVENTS: THE MTOPS TRIAL

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Lower urinary tract symptoms due to suspected benign prostatic hyperplasia (BPH) are increasingly treated with medications targeting obstruction among older men, but frailty may represent a novel risk factor for this condition. Our objective was to assess the associations between frailty and clinical BPH progression or serious adverse events (SAE) among 3047 men, age 50-89 years, enrolled in the Medical Therapy of Prostatic Symptoms Study, a placebo-controlled RCT of doxazosin, finasteride, or combination therapy on clinical BPH progression. We created a frailty index using 69 items collected at baseline and categorized men as fit (0-0.1), less fit (0.1-<0.25), or frail (0.25-1.0). The primary outcomes were time to 1) first composite event of clinical BPH progression, and 2) SAE requiring hospitalization. Cox proportional hazards models were adjusted for demographics, intervention, BPH surrogates, and comorbidities. At baseline, 28% men were fit, 58% were less fit, and 14% were frail. During follow-up (mean 4.5 years), the incidence rate of clinical BPH progression was 2.2/100p-y among fit, 3.0/100p-y among less fit (HR =1.28, 95% CI 0.98, 1.67), and 4.1/100p-y among frail men (HR=1.60, 95% CI 1.13, 2.26). Among men randomized to combination therapy, the SAE incidence rate was 3.4/100p-y for fit men versus 12.7/100p-y for frail men (HR=5.98, 95% CI 3.76, 9.52). In conclusion, frailty is independently associated with greater risk of both clinical BPH progression and SAE. The decision to initiate medical therapy for BPH among frail men should therefore include a discussion of both benefits and risks via shared decision making.

BODY MASS INDEX AND FRAILTY AMONG OLDER MEXICAN AMERICANS: FINDINGS FROM AN 18-YEAR OF FOLLOW-UP

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The objective of this study was to examine body mass index (BMI) as predictor of frailty among non-frail Mexican American older adults at baseline. Data are from an 18-year prospective cohort of 1,647 non-institutionalized Mexican American aged ≥ 67 years from the Hispanic Established Population for the Epidemiologic Study of the Elderly (1995/1996-2012/13). BMI (Kg/m2) was grouped according to the National Institutes of Health obesity standards (<18.5=underweight, 18.5–24.9=normal weight, 25.0–29.9=overweight, 30.0–34.9=obesity category I and ≥ 35=obesity category II and extreme obesity). Frailty was defined as meeting three or more of the following: unintentional weight loss of >10 pounds, weakness, self-reported exhaustion, low physical activity, and slow walking speed. Covariates included socio-demographics, comorbidities, cognitive function, depressive symptoms, and limitations in activities of daily living (ADL). General Estimating Equations were performed to estimate the odds ratio (OR) and 95% confidence interval (CI) of frailty as a function of BMI categories. All variables were analyzed as time varying except for gender and education. Participants in the underweight or obesity type II / morbidity obesity category had increased OR of frailty over time than those in the normal weight category (2.68, 95% CI=1.46-4.9 vs.1.55, 95% CI=1.02-2.35, respectively) after controlling for all covariates. Those who reported arthritis, hip fracture, depressive symptoms, or ADL disability had increased odds of frailty over time. This study showed a U-shaped relationship between BMI and frailty over an 18-year period of follow-up which has implications for maintaining a healthy weight to prevent frailty in this population.

COGNITIVE FRAILTY AND RISK OF FUNCTIONAL DISABILITY IN OLDER JAPANESE ADULTS: A 4-YEAR PROSPECTIVE STUDY

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