An increase in life expectancy and an aging population has resulted in increased risks and prevalence of age-related diseases. Previous studies have shown that factors, such as chronic stress, are associated with shorter telomere length. When telomeres become critically short, cells enter a state of senescence, which is a hallmark of aging. Several prior studies examining the relationship between caregiving and telomere length have reported mixed results. The present study utilized data from the Caregiving Transitions Study, an ancillary study to the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. The difference in telomere length across an average ~8.6 years was compared between 235 incident caregivers and 229 controls. Telomere length was determined using the qPCR telomere-to-single copy gene (IFNB1) ratio (T/S) for each participant at both baseline and follow-up timepoints. Regression models controlling for age, sex, race, and baseline telomere length examined the association between caregiving status (exposure) and the telomere length change (□T/S). Sensitivity models adjusted for potential lifestyle and socioeconomic factors, including income, education, BMI, cigarette smoking, and alcohol use. We did not observe a significant association between □T/S and caregiving (beta=0.041, p=0.615). Adding lifestyle and socioeconomic factors did not change the null relationship (beta=0.062, p=0.455). In conclusion, this study provides evidence against an association between caregiving and the change in telomere length. Ultimately, more research to address the complex relationship between caregiving and telomere attrition is needed in order to prevent or reduce adverse outcomes and improve the well-being of caregivers and care recipients.

Session 9295 (Poster)

Frailty

A NOVEL ALGORITHM FOR ANALYSIS OF MULTIPLE ENDPOINTS USING RISK–BENEFIT PROFILES

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Often it is necessary to evaluate effectiveness of an intervention on the basis of multiple event outcomes of variable benefit and harm, which may develop over time. An attractive approach is to order combinations of these events based on desirability of the overall outcome (e.g. from cure without any adverse events to death), and then determine whether the intervention shifts the distribution of these ordered outcomes towards more desirable (Evans, Follmann 2016). The win ratio introduced in Pocock et al 2012 was an earlier implementation of this approach. More recently Claggett et al 2015 proposed a more comprehensive method allowing nonparametric and regression-based inference in presence of competing risks. Key to the method is weighting observations by inverse probability of censoring (IPC) processes specific to participants and event types. The method has seemingly great practical utility, but computation of weights is a non-trivial challenge with real-life data when each event can have its own censoring time. We present a novel recursive algorithm solving this problem for an arbitrary number of events ordered by clinical importance or desirability. The algorithm can be implemented in SAS or R software, and computes IPC weights, as well as nonparametric or parametric estimates and resampling-based measures of uncertainty. We illustrate the approach using data from the SPRINT trial of antihypertensive intervention, comparing risk-benefit profiles for robust, pre-frail, and frail subpopulations, and in analysis of fall as a function of progressive risk factors. More general use of the software tools deploying the method is described.

A NOVEL ELECTRONIC FRAILTY INDEX AS A PREDICTOR OF CLINICAL OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

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Transcatheter aortic valve implantation (TAVI) is becoming the preferred therapeutic approach for older adults with severe aortic valve disease. Frailty portends increase mortality and adverse outcomes after TAVI. We sought to evaluate an electronic Frailty Index (eFI) as a predictor for increased healthcare utilization, adverse clinical and functional outcomes. We retrospective studied 302 adults older than 65 years that underwent TAVI at our institution between October 2017 and September 2020. The mean age of the cohort was 79 ±6.94 years old; 43% were female. Frail individuals (eFI >0.20), as compared to Fit (eFI <0.10) and Prefrail (0.10>eFI<0.20), were more likely to have a higher society of thoracic surgeons score and a greater burden of comorbidities. Subjects classified as Prefrail/Frail had longer intensive care unit stay post-TAVI than fit individuals (>24 hours: 17% vs 4%, respectively, p 0.02); and trended toward longer hospitalization time and discharge to a setting different than home. The Prefrail/Frail group also had a higher proportion of subjects with persistent New York Heart Association Class III heart failure symptoms 30 days post-TAVI as compared to Fit (14% vs 2%, p 0.04), however both groups demonstrated significant symptomatic improvement post-procedure. No significant differences in 30 day mortality, major adverse cardiovascular events or readmissions were found. TAVI is an effective treatment with a low incidence of early adverse clinical outcomes in older adults regardless of frailty status; eFI could help in identifying and targeting susceptible adults that may require additional resources to recover post-TAVI.

A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF METFORMIN FOR FRAILTY PREVENTION IN OLDER ADULTS

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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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