**Higher Quercetin Intake Is Associated with Reduced Odds of Frailty Onset in Middle-Aged and Older Adults**

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**Objectives:** The age-related accumulation of senescent cells and their secretory products are associated with a number of hallmarks of aging that predispose older adults to frailty. Senolytic compounds can eliminate senescent cells, and may be a viable strategy to prevent frailty. Quercetin is a dietary flavonoid and a powerful antioxidant that has senolytic properties, and supplementation of quercetin with other senolytic compounds has reduced the number of senescent cells in animal and human studies. Thus, our objective was to determine the association between quercetin intake and frailty. We hypothesize that higher quercetin intake is associated with reduced odds of frailty onset.

**Methods:** This prospective study included 716 non-frail individuals older than 60 years from the Framingham Heart Study Offspring Cohort with baseline diet assessment from a food frequency questionnaire (FFQ) in 1998-2001 and a follow-up frailty assessment in 2011-2014. Total quercetin intake (dietary and supplemental sources, mg/d) was taken from the FFQ. Frailty was defined as fulfillment of 3 or more Fried frailty phenotype criteria of unintentional weight loss, exhaustion, low physical activity, slow gait speed, and weak grip strength. Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for frailty onset per 10 mg/day higher intake of quercetin, adjusting for baseline age, sex, energy intake, current smoking, diabetes, cardiovascular disease, and non-skin cancers.

**Results:** Baseline mean (SD) age was 65(5) years (range: 60-81 years; 46% male) and 172 individuals developed frailty over ∼12 years. Mean(SD) quercetin intake was 10(6) mg/d (all participants), 10(6) mg/d (individuals without frailty), and 9(5) mg/d (individuals classified as frail). In this cohort, 10 mg/d higher intake of quercetin was associated with 30% reduced odds of frailty (95%CI:0.50, 0.99) after adjusting for relevant confounders.

**Conclusions:** Based on our cohorts mean intake, our results suggest that usual intake of ∼10 mg/day of quercetin, which is easily achievable a diet rich in fruits and vegetables, has potential to reduce odds of frailty up to 30%. Corroboration of our results in other cohorts is needed.

**Funding Sources:** National Institute of Health
National Institute of Aging