OR18-2: Higher Plasma Estradiol Concentration Is Independently Associated with Lower Biological Age, Assessed as Leucocyte Telomere Length, in Older Men

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Background: Telomeres are essential DNA-protein complexes comprising TTAGGG repeats binding specific proteins, which protect the physical ends of chromosomes from fusion and degradation. Attrition of telomeres results in cellular senescence. Leucocyte telomere length (LTL) reflects lengths of telomeres in various tissues, and shorter LTL is a marker of advancing biological age. Previous work has associated bioactive metabolites of T, dihydrotestosterone (DHT) and estradiol (E2) with LTL in a population of predominantly middle-aged men[1]. However, the relationship of these hormones to biological age in older men was unclear.

Methods: We aimed to clarify associations of sex hormones with LTL in a cohort of 2,913 community-dwelling men aged 70-89 years. Early morning blood samples were assayed for T, DHT and E2 using mass spectrometry, and for sex hormone-binding globulin (SHBG) using immunoassay. LTL was measured using a multiplex quantitative PCR method and expressed as the amount of telomeric DNA relative to beta-globin, a single copy control gene (T/S ratio). Cross-sectional analyses utilised multivariable linear regression. Mean (±SD) age was 76.7±3.2 years. The average difference per decade of age was T -0.46 nmol/L, DHT -0.11 nmol/L, E2 -7.5 pmol/L, SHBG +10.2 nmol/L, and LTL (T/S ratio) -0.065. E2 correlated with T/S ratio (r=0.038, p=0.039).

Results: After excluding highest and lowest 1% of values, the correlation between E2 and T/S ratio was largely unchanged (r=0.039, p=0.037). SHBG was inversely correlated with T/S ratio (r=-0.053, p=0.004), also unchanged in the trimmed analysis (r=-0.055, p=0.004.) After adjusting for age, BMI, cardiovascular disease, diabetes, alcohol, smoking, physical activity, lipids and hypertension, E2 remained associated with T/S ratio (per 1 SD increase E2: coefficient 0.011, p=0.043). When E2 and SHBG were simultaneously included in the multivariate model, E2 remained positively associated with T/S ratio (coefficient 0.014, p=0.014) and SHBG inversely associated (coefficient -0.013, p=0.037). The magnitude of increase in T/S ratio associated with a 1 SD higher plasma E2 concentration was comparable with having a BMI 3.6 kg/m2 lower, and two thirds that associated with being 3.6 years younger. T, DHT and LH were not associated with LTL in multivariate analyses.

Conclusion: To conclude, in older men, neither T nor DHT are associated with LTL while E2 is independently associated with LTL and SHBG is inversely associated. These findings associate activity of the gonadal axis with lower biological age in older men. However, causality cannot be inferred from an observational, cross-sectional study, thus additional research is necessary to determine whether sex hormone exposure modulates male biological aging.

Reference: [1]Yeap BB, et al. J Clin Endocrinol Metab 2016; 101: 1299-1306.

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