OR18-05: Thyroid Hormone Use and Relative Survival Among the BLSA Cohort

Jennifer Mammen. *Johns Hopkins University School of Medicine*

Enoch Joseph Abbey, MD, MPH[1], Eleanor M. Simonsick, PhD[2], John McGready, PhD[3], Jennifer Sophie Mammen, MD,PHD[4].
[1]Johns Hopkins Med Insts, Baltimore, MD, [2]National Institute of Aging, NIH, Baltimore, MD, [3]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, [4]Johns Hopkins University, Baltimore, MD.

Background: Thyrotropin (TSH) levels are higher on average and vary more widely among older adults even in the absence of frankly abnormal thyroid hormone levels.[1-3] Although typically called "subclinical hypothyroidism," both large meta-analyses and treatment trials for isolated elevated TSH do not demonstrate harm associated with TSH<10 mIU/L or, benefit from treatment in this population.[4,5] We have shown that isolated elevated TSH often reflects adaptations to aging rather than primary thyroid disease, implying that LT4 treatment could actually cause harm.[6] This study aims to determine the effects of LT4 on survival among older adults.

Design: Thyroid status was defined at each visit for 1,054 participants of the Baltimore Longitudinal Study of Aging aged 65 years or older with at least one TSH and FT4 level since 2003. Visits were excluded for use of interfering medications other than LT4 (e.g. oral steroids) or a history of thyroid cancer. Differential survival across thyroid function and with treatment was analyzed using multivariable Cox regression to estimate crude and adjusted hazard ratios. Overall survival was evaluated using Kaplan-Meier methods and summarized using log-rank tests. Covariates analyzed included age, sex, race, serum albumin, walking index, body mass index (BMI), smoking, self-reported health, and level of education.

Results: The mean age of the participants was 78.7 years and 43.3% were women. Sixty-eight percent of visits occurred in untreated, euthyroid individuals, with an untreated isolated elevated TSH found in 7.8%. Treatment with LT4 was present in 13.7% of visits. There was no clinical difference in markers of health status between treated and un-treated visits. Cumulative follow-up time was 8,483.3 years. A total of 245 deaths occurred during the study period. Visits on LT4 regardless of TSH contributed a 55% higher hazard of death compared to those who are euthyroid and not on thyroid hormone [HR=1.55, 95% CI 1.00 - 2.38] and an estimated doubling of risk compared to those with untreated isolated elevated TSH [HR=2.23, 95% CI 1.05 - 4.73] after adjusting for other covariates. The results remained true when limited to those who were never over-treated [HR=2.50, 95% CI 1.18- 5.30].

Conclusion: LT4 use in older adults is associated with a significantly increased mortality risk. This supports our hypothesis that isolated elevated TSH does not always represent subclinical hypothyroidism in older adults, and that treating TSH changes associated with aging adaptation could adversely alter key homeostatic compensations.

1. Vadiveloo et al *J Clin Endo. Met.* 2013;98(3):1147-1153. 2. Surks et al., *J Clin Endo. Met.* 2007;92(12):4575-4582. 3. Stott et al., *NEJM*. 2017;376(26):2534-2544. 4. Villar et al., *Cochrane Database of Syst. Reviews*. CD003419.pub2 5. Stott et al., *NEJM*. 2017;376(26):2534-2544 6. Mammen et al., *Thyroid*. 2017;27(11):1370-1377.