Subclinical thyroid dysfunction and the risk of heart failure events: an individual participant data analysis from five prospective cohorts

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Background/Introduction
Subclinical thyroid dysfunction has been associated with systolic and diastolic dysfunction. However, few prospective data exist regarding the association between subclinical thyroid dysfunction and heart failure (HF) events, as well as subgroups at increased risk.

Methods
We conducted a systematic review in MEDLINE and EMBASE databases without language restrictions, and included prospective observational cohorts with a baseline thyroid function measurement and subsequent follow-up of HF events. Individual data of 19728 person-years of follow-up were supplied from 5 prospective cohorts in the United States and Europe. Thyroid dysfunction was defined as a TSH 0.4-4.4 mIU/L, subclinical hypothyroidism as a TSH between 4.5-19.9 mIU/L, and subclinical hyperthyroidism as a TSH <0.45 mIU/L, both with normal free thyroxine levels.

Results
Among 19728 participants, 1618 had subclinical hypothyroidism (8.2%), 515 subclinical hyperthyroidism (2.6%) and 17553 were euthyroid. During follow-up, 1398 participants had HF events. In age- and gender-adjusted analyses, the risk of HF increased with higher TSH levels: hazard ratio (HR) was 1.04 (95% confidence interval [CI] 0.79-1.36) for a TSH level of 4.5-6.9 mIU/L, 1.81 (CI 0.88-3.71) for a TSH level of 7.0 to 9.5 mIU/L, and 1.93 (CI 1.07-3.48) for a TSH level of 10.0 to 19.9 mIU/L (p for trend <0.01). After further adjustment for cardiovascular risk factors, risk of HF was lower but remained significant among those with TSH ≥10 mIU/L (HR 1.55, CI 1.06-2.21). HR among those with TSH >10 mIU/L, was higher (HR 2.14, CI 1.15-3.97) in sensitivity analyses excluding thyroid medication users.

Conclusion
Subclinical hypothyroidism, but not subclinical hyperthyroidism, is associated with an increased risk of HF events in those with higher TSH levels, particularly in those with TSH levels ≥10 mIU/L. Given the high prevalence of subclinical hypothyroidism and of HF events among elderly, this question needs to be addressed in an appropriately powered randomized controlled trial.

Correlates of physical fitness in patients with type 2 diabetes

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Background/Introduction
Several fitness outcomes such as muscular strength, aerobic fitness or walking speed are important predictors of mortality and morbidity. We tested the following fitness outcomes: functional lower limb muscle strength (required time for chair stand; sec), balance (maximal time of standing; sec) and vibration sensibility (vibration score; ongoing).

Results
In this population of mostly treated patients with type 2 diabetes, classical morbidity and mortality risk factors, metabolic control, diabetic complications and socioeconomic status in patients with type 2 diabetes were inversely correlated with aerobic fitness and balance (r= -0.3, p=0.02 and -0.4, p=0.01). After further adjustment for cardiovascular risk factors, factors of HF were lower but remained significant among those with TSH ≥10 mIU/L (HR 1.55, CI 1.06-2.21). HR among those with TSH >10 mIU/L, was higher (HR 2.14, CI 1.15-3.97) in sensitivity analyses excluding thyroid medication users.

Conclusion
Subclinical hypothyroidism, but not subclinical hyperthyroidism, is associated with an increased risk of HF events in those with higher TSH levels, particularly in those with TSH levels ≥10 mIU/L. Given the high prevalence of subclinical hypothyroidism and of HF events among elderly, this question needs to be addressed in an appropriately powered randomized controlled trial.
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