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The impact of levothyroxine on cardiac function in older adults with subclinical hypothyroidism: a randomized clinical trial

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Importance: Subclinical hypothyroidism has been associated with heart failure, but no conclusive clinical trial assessed whether treating subclinical hypothyroidism with levothyroxine has an impact on cardiac function.
Objective: To assess the impact of levothyroxine treatment on cardiac function in subclinical hypothyroidism.
Design: This is a randomized, double-blind placebo-controlled, multicenter Swiss substudy within the TRUST trial.
Participants: Participants aged ≥65 years with subclinical hypothyroidism.
Intervention: Levothyroxine to achieve TSH normalization, or placebo including mock titrations.
Main outcome measures: Primary outcomes, assessed by echocardiography at the end of the trial were the left ventricular ejection fraction (LVEF, normal defined as >50%) for systolic function and the ratio between mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (e' (E/e' ratio) for diastolic function. Secondary outcomes included transmitral E and A waves, e' lateral/septal, left atrial (LA) volume index and systolic pulmonary artery pressure.
Results: Of 217 randomized Swiss participants of the TRUST trial, 185 (mean age 74.1 years, 47% women, mean TSH at baseline 6.35 ± SD 1.95 mIU/L) underwent echocardiography. After a median treatment duration of 18.4 months, the mean TSH among participants randomized to levothyroxine (n=95) decreased to 3.55 mIU/L, whereas it remained elevated in the placebo group (n=89; 5.29 mIU/L). The mean LVEF was similar in both arms (adjusted between-group difference 0.4%, 95% CI –1.8% to 2.5%, P=0.72) and no significant differences were found for the E/e' ratio (adjusted between-group difference 0.4, 95% CI –0.7 to 1.4, P=0.47). In intention-to-treat and per-protocol analyses, no clinically significant differences were found for secondary diastolic function parameters: e' lateral 8 vs. 8 cm/s, P=0.54; e' septal 6 vs. 6 cm/s, P=0.75; LA volume index 34 vs. 33 ml/m^2, P=0.57; E/A ratio 0.8 vs. 0.8, P=0.94; E deceleration time 225 vs. 216 ms, P=0.27, except for systolic pulmonary artery pressure (37 mm Hg in the levothyoxine group vs. 33 mm Hg in the placebo group, P=0.02 intention-to-treat and P=0.06 per protocol)
Conclusion: Treatment of subclinical hypothyroidism with levothyroxine was not associated with benefits regarding systolic and diastolic heart function in older adults with subclinical hypothyroidism.