

How to interpret subclinical thyroid dysfunction on the prevention and management of heart failure events ?

Individual participant data analysis from six prospective cohorts

Baris Gencer, Tinh-Hai Collet, Vanessa Virgini, Douglas C. Bauer, Jacobijn Gussekloo, Anne R. Cappola, David Nanchen, Wendy P. J. den Elzen, Philippe Balmer, Robert N. Luben, Massimo Iacoviello, Vincenzo Triggiani, Jacques Cornuz, Anne B. Newman, Kay-Teo Khaw, J. Wouter Jukema, Rudi G. J. Westendorp, Eric Vittinghoff, Drahomir Aujesky, Nicolas Rodondi for the Thyroid Studies Collaboration.

University of Lausanne, Switzerland; University of California, San Francisco, CA; Leiden University Medical Center, the Netherlands; University of Pennsylvania, Philadelphia, PA; University of Cambridge, UK; University of Bari, Italy; University of Pittsburgh, PA; University of Bern, Switzerland

Introduction

- Guidelines on the diagnosis and management of heart failure (HF) recommend measurement of thyroid function, but do not specify the impact of different Thyroid Stimulating Hormone (TSH) levels
- Few prospective data are available regarding the association of subclinical thyroid dysfunction and the risk of HF events
- To clarify the association between subclinical thyroid dysfunction and HF events, we performed a pooled analysis of individual participant data using all available prospective cohorts

Methods

Systematic review of articles in MEDLINE and EMBASE until June 2011

- Criteria: prospective cohort studies with baseline thyroid measurement and follow-up of HF events

- Pooled individual participant data from 6 cohorts from United States and Europe (Table)

Definitions:

- Euthyroid TSH 0.45-4.49 mIU/L
- Subclinical hypothyroidism TSH 4.5-19.9 mIU/L + normal free thyroxine (FT4)
- Subclinical hyperthyroidism TSH < 0.45 mIU/L + normal FT4 and T3 levels (if available)
- HF events Any diagnosis from a physician, hospitalization and deaths related to HF based on all available documents within each cohort

Results

- In age/sex-adjusted analyses, risk of HF events increased with higher and lower TSH levels, particularly among those with TSH ≥ 10.0 mIU/L and those with TSH < 0.10 mIU/L (Figure)
- Multivariate adjustment for other cardiovascular risk factors yielded similar results
- Sensitivity analyses yielded similar results after excluding participants with preexisting HF, or preexisting atrial fibrillation, or thyroid medication users at baseline and follow-up, or missing FT4 values

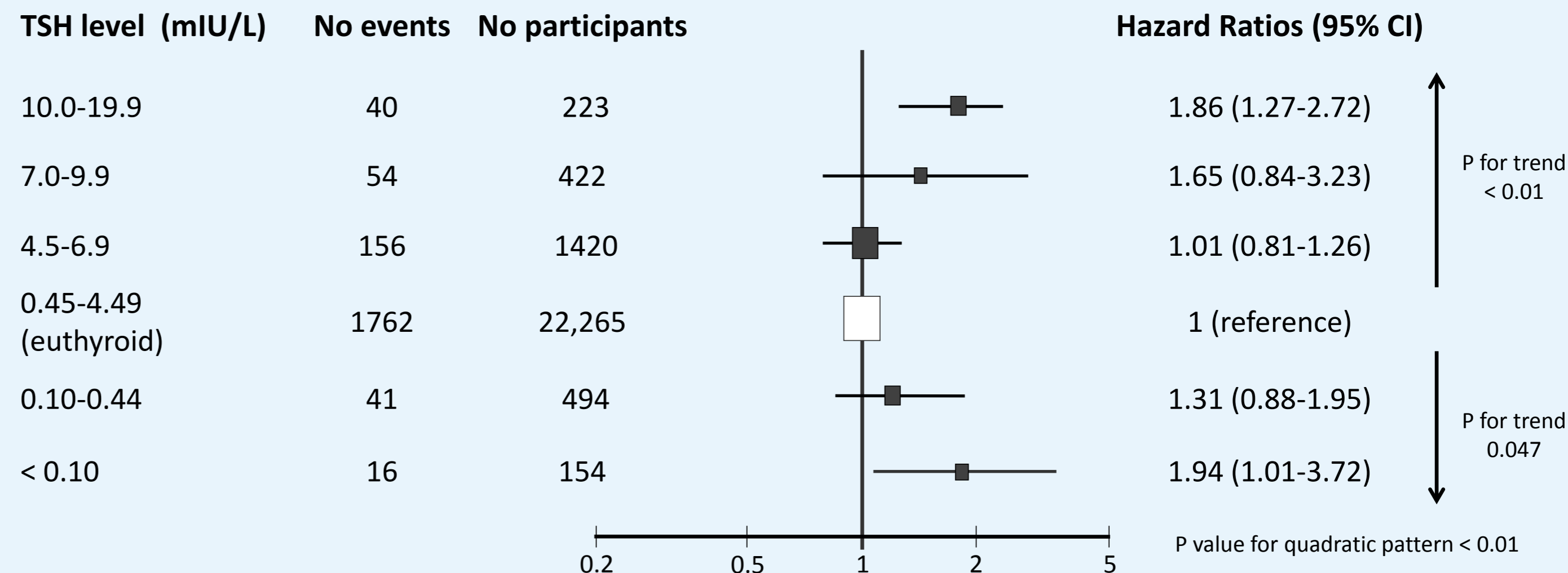
Conclusion/ Implications

- Our findings may contribute to a better interpretation of TSH in the management of HF
- Use of thyroxine replacement will be investigated with an appropriately powered randomized controlled trial (TRUST Trial, see right) with clinical HF and other cardiovascular outcomes

Contact Baris Gencer, MD, University of Lausanne, Switzerland
Baris.Gencer@chuv.ch
 Nicolas Rodondi, MD, MAS, University of Bern, Switzerland
Nicolas.Rodondi@insel.ch

	No events	No participants	Median age	Women	Sub Hypo	Sub Hyper	Person-years
Coordinating center							
Cardiovascular Health study	831	3064	71	60%	16.2%	1.4%	34,531
Health, Aging and Body Composition study	366	2762	74	51%	12.1%	3.0%	17,869
EPIC-Norfolk study	474	13,066	58	54%	5.5%	2.8%	143,694
Leiden 85-plus study	92	514	85	65%	6.8%	4.5%	1861
Bari study	77	335	66	23%	11.6%	2.1%	370
PROSPER	229	5649	75	51%	7.9%	2.3%	17,923
Overall	2069	25,390	70	53.8%	8.1%	2.6%	216,248

Hazard Ratios for Heart Failure (HF) Events according to Thyroid-Stimulating Hormone (TSH) levels



TRUST Trial (Thyroid hormone Replacement for Untreated older adults with Subclinical hypothyroidism : a randomized placebo-controlled Trial)

Design of TRUST trial

Participants: 3000 older adults (>65y) with persistent subclinical hypothyroidism
Intervention: levothyroxine replacement
Control: placebo
Outcomes:
 • Cardiovascular outcomes: cardiovascular mortality, coronary heart disease, heart failure
 • Disease specific outcomes: cognitive function, quality of life, muscle function
Design: randomized placebo-controlled trial

