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ORIGINAL PAPER

# Community-based study of the association of subclinical thyroid dysfunction with blood pressure

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**Abstract** The relationship between subclinical thyroid dysfunction and blood pressure has been controversial and received unsufficient attention. Thus, we performed a cross-sectional study conducted among 6,992 inhabitants from six districts of Jiangsu Province to investigate the association of subclinical thyroid dysfunction with blood pressure in China. The data from 6,583 subjects (4,115 women and 2,468 men) were included and divided into three groups: euthyroidism ($n = 5669$, 86.11%), subclinical hyperthyroidism ($n = 108$, 1.65%), and subclinical hypothyroidism ($n = 806$, 12.24%). In the groups with subclinical hypothyroidism and hyperthyroidism, systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse pressure were not significantly different from those in the groups with euthyroidism after being adjusted for age, sex, BMI, and smoking status ($P > 0.05$). More extensively, the SBP and DBP in the group of subclinical hypothyroidism with lower level of TSH (TSH 4.51–10.00 mIU/l, $SCH_1$) were significantly higher than those of participants with euthyroidism ($P < 0.05$). Multivariable logistic analysis revealed that subclinical hypothyroidism with lower TSH (TSH 4.51–10.00 mIU/l) was an independent risk factor for increased SBP (OR = 1.28, 95% CI 1.03–1.59, $P = 0.028$). Similar results could not be found between groups of euthyroid and subclinical hypothyroid with higher level of TSH (TSH > 10 mIU/l, $SCH_2$). Further subdivision of the euthyroid group on the basis of a TSH cut-off of 2.5 mIU/l, revealed still no significant difference in blood pressure after adjustment regardless of whether the TSH levels were in the lower reference (TSH 0.40–2.50 mIU/l, $n = 4093$) or in the upper reference ranges (TSH 2.51–4.50 mIU/l, $n = 1576$) ($P > 0.05$). We concluded that subclinical thyroid dysfunction was not associated with blood pressure. Neither subclinical hyperthyroidism nor subclinical hypothyroidism independently predicted increased blood pressure.

**Keywords** Subclinical hypothyroidism · Subclinical hyperthyroidism · Euthyroidism · Blood pressure · Hypertension

## Introduction

About 200 years ago, C. Parry noticed that thyroid goiter was possibly associated with heart failure [1]. Since then, researchers have found that thyroid function has profound effects on the cardiovascular system, and both hyperthyroidism and hypothyroidism were related to cardiovascular diseases, including hypertension. It has been convincingly shown that overt hyperthyroidism could generally induce increased systolic pressure and pulse pressure as a result of the interaction of augmented cardiac output and reduction of systemic vascular resistance [2, 3]. On the other hand, increased diastolic blood pressure was always viewed as a concomitant factor for hypothyroidism, which could be reversed by thyroxin replacement [4, 5].

Subclinical thyroid dysfunction (STD), including subclinical hyperthyroidism and subclinical hypothyroidism, is diagnosed biochemically and defined as an asymptomatic condition with normal levels of free thyroxin (FT4) in the presence of primary abnormalities of serum thyroid stimulating hormone (TSH) [6]. Until now, the relationship between STD and blood pressure has been controversial

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and has not received sufficient attention. Several recent studies showed that subclinical hyperthyroidism had no correlation with hypertension, while some community-based investigations stated that the relationship between subclinical hypothyroidism and hypertension was very similar to the relationship of overt hypothyroidism and blood pressure. The present study is a cross-sectional, community-based investigation of the possible association between subclinical thyroid dysfunction and blood pressure.

## Results

### General characteristics of participants

The 6,583 participants comprised 4,115 women and 2,468 men, with a mean of 49.02 ± 13.68 years of age (range 20–88 years). These individuals were divided into three groups according to their thyroid status: the group with euthyroidism ($n = 5{,}669$, 86.11%, 3,485 women and 2,184 men), the group with subclinical hyperthyroidism ($n = 108$, 1.65%, 74 women and 34 men), and the group with subclinical hypothyroidism ($n = 806$, 12.24%, 555 women and 250 men), respectively.

### Linear correlation between serum TSH and blood pressure

In the subjects who were not receiving treatment with antihypertensives ($n = 6044$), there was a weak correlation between levels of TSH and blood pressure; and the correlation coefficients for SBP, DBP, and pulse pressure were 0.0451, 0.0259, and 0.0433, respectively ($P < 0.05$). After adjustment for age, sex, BMI, and smoking habit, the positive relationships between levels of TSH, DBP, and pulse pressure were no longer significant.

### Association between blood pressure and different states of thyroid dysfunction

The analysis of baseline characteristics by thyroid function revealed that the fraction of participants who were women, the mean age, and the percentage who smoked were significantly higher in the group with subclinical hypothyroidism than those in the group with euthyroidism ($P < 0.01$); while the characteristics were very similar between the groups with subclinical hyperthyroidism and euthyroidism ($P > 0.05$) except the proportion of women ($P < 0.05$), (Table 1).

Concerning about the differences in blood pressure among the groups with subclinical hyperthyroidism, euthyroidism, and subclinical hypothyroidism, we found that the SBP in the subclinical hypothyroid group was almost 3 mmHg higher than that in the group with euthyroid, but this difference was not statistically significant after adjustment for age, sex, BMI, and smoking status ($P = 0.50$). Similarly, no statistical difference was seen in SBP, DBP, and pulse pressure between the subclinical hyperthyroid and euthyroid groups ($P > 0.05$) (Table 1). Multivariable logistic regression revealed that neither

**Table 1** Baseline characteristics of study population and correlation analyses of subclinical thyroid dysfunction with blood pressure

| | Subclinical hyperthyroid ($n = 108$) | $P_1$ | OR | 95%CI | $P_3$ | Euthyroid ($n = 5669$) | Subclinical hypothyroid ($n = 806$) | $P_2$ | OR | 95%CI | $P_4$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Women (*N* %) | 74 (68.52)* | 0.000 | – | – | – | 3485 (61.47) | 556 (68.98)* | 0.000 | – | – | – |
| Age (years) | 47.46 ± 15.06 | 0.32 | – | – | – | 48.74 ± 13.60 | 51.14 ± 13.89* | 0.000 | – | – | – |
| BMI (kg/m$^2$) | 23.65 ± 3.53 | 0.14 | – | – | – | 24.44 ± 6.68 | 24.65 ± 3.78 | 0.29 | – | – | – |
| Smokers (*N* %) | 27 (25.00) | 0.052 | – | – | – | 1359 (23.97) | 137 (17.00)* | 0.000 | – | – | – |
| SBP (mmHg) | 126.11 ± 16.89 | 0.60[a] | 0.91 | 0.55–1.52 | 0.73 | 126.72 ± 19.20 | 129.28 ± 20.09 | 0.50[a] | 1.14 | 0.95–1.36 | 0.16 |
| DBP (mmHg) | 80.33 ± 10.15 | 0.42[a] | 0.99 | 0.62–1.57 | 0.97 | 81.91 ± 11.15 | 82.70 ± 11.50 | 0.12[a] | 1.09 | 0.92–1.29 | 0.32 |
| Pulse pressure (mmHg) | 45.78 ± 13.33 | 0.14[a] | 1.23 | 0.73–2.06 | 0.44 | 44.81 ± 13.27 | 46.58 ± 14.80 | 0.16[a] | 1.18 | 0.98–1.42 | 0.08 |

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval; smoking status was defined as current smoker or non-current smoker

Continuous data are expressed as mean ± SD; Categorical data are presented as numbers and percentages; Mann–Whitney's U-tests, chi square test, and *t* test were used for the comparison of qualitative data; logistic regression test were used for correlation analyses and adjusted for age, sex, BMI, and smoking status; significance was set at $P < 0.05$ and 95% confidence intervals were calculated

$P_1$, comparisons of significance between groups of subclinical hyperthyroid and euthyroid; $P_2$, comparisons of significance between groups of subclinical hypothyroid and euthyroid; * represents $P < 0.01$ compared with euthyroid group; [a] data derived from adjustment for age, sex, BMI, and smoking status; $P_3$, correlation between subclinical hyperthyroid and increased blood pressure adjusted for age, sex, BMI, and smoking status; $P_4$, correlation between subclinical hypothyroid and increased blood pressure adjusted for age, sex, BMI, and smoking status; increased SBP defined as ≥140 mmHg, increased DBP defined as ≥90 mmHg, increased pulse pressure defined as >50 mmHg, evaluated above the 75th percentile

subclinical hyperthyroidism nor subclinical hypothyroidism could independently predict increased blood pressure (including SBP, DBP, and pulse pressure) (Table 1).

### Correlation analyses between blood pressure and different serum levels of TSH

To explore the association of blood pressure and serum levels of TSH, subjects in subclinical hypothyroid were classified into two groups, which were $SCH_1$ (TSH 4.51–10.00 mIU/l) and $SCH_2$ (TSH > 10.00 mIU/l). Compared $SCH_1$ with the group of euthyroid, the SBP and DBP were significantly higher in $SCH_1$ even after being adjusted for age, sex, BMI, and smoking status ($P < 0.05$), while the pulse pressure was slightly higher and no statistic difference was observed between the two groups ($P = 0.23$). With regard to the group of $SCH_2$, the SBP and pulse pressure were mildly increased, but the DBP was slightly lower than that in the group with euthyroid. However, there was no significant difference in blood pressure between these two groups when adjusted for age, sex, BMI, and smoking status. There was still no difference of SBP, DBP, and pulse pressure between $SCH_1$ and $SCH_2$ after adjustment ($P > 0.05$) (Table 2).

Further multivariable logistic analysis revealed that subclinical hypothyroid with lower level of TSH (TSH 4.51–10.00 mIU/l) was an independent risk factor for increased SBP (OR = 1.28, 95% CI 1.03–1.59, $P = 0.028$), but it could not independently predict either increased DBP or pulse pressure. Regarding subclinical hypothyroidism with a higher level of TSH (TSH > 10.00 mIU/l), it was not independently associated with increased blood pressure (Table 2).

More profound analyses had been done when the participants undergoing antihypertensive treatment were excluded. Among the 6,044 subjects, the results were very similar to those in all subjects (including participants who were on antihypertensive treatment). No factors predicting increased blood pressure (systolic, diastolic, or pulse pressure) could be found in the groups of either $SCH_1$ or $SCH_2$, and neither type of subclinical thyroid dysfunction was independently associated with increased blood pressure (Table 3).

### Comparison of blood pressures in participants with euthyroidism and different levels of TSH

Considering the relationship of TSH and blood pressure in the participants with euthyroidism, it was divided into two sub-groups depending on a cut-off of 2.5 mIU/l for the level of TSH. No significant difference was seen in SBP, DBP, and pulse pressure between those with levels of TSH in the lower reference (0.40–2.50 mIU/l) or in the upper reference ranges (2.51–4.50 mIU/l) after adjustment for age, sex, BMI, and smoking status ($P > 0.05$) (Table 4).

## Discussion

In this cross-sectional, community-based study, we found that neither subclinical hyperthyroidism nor subclinical hypothyroidism was associated with increased SBP, DBP, or pulse pressure. This result is consistent with those of other previous studies [6, 7]. Recently, Völzke et al. conducted a community-based cross-sectional study among 4,087 subjects in West Pomerania, the northeast area of Germany, to analyze the possible association between subclinical hyperthyroidism and blood pressure, but failed to show that either decreased or suppressed serum levels of TSH (<0.25 mIU/l and <0.1 mIU/l, respectively) were correlated with increased hypertension; nor was there an association between serum levels of free thyroxin in the

**Table 2** Correlation analyses between increased blood pressure and subclinical hypothyroidism with different levels of TSH

| (mmHg) | Euthyroid ($n = 5669$) | Subclinical hypothyroid (SCH) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | $SCH_1$ ($n = 477$) | $P_1$ | OR | 95%CI | $P_3$ | $SCH_2$ ($n = 329$) | $P_2$ | OR | 95%CI | $P_4$ |
| SBP | 126.72 ± 19.20 | 130.16 ± 20.84 | 0.02* | 1.28 | 1.03–1.59 | 0.03** | 127.99 ± 18.90 | 0.70 | 0.94 | 0.71–1.24 | 0.65 |
| DBP | 81.91 ± 11.15 | 83.37 ± 12.15 | 0.02* | 1.20 | 0.98–1.48 | 0.08 | 81.72 ± 10.42 | 0.74 | 0.93 | 0.72–1.21 | 0.60 |
| Pulse pressure | 44.81 ± 13.27 | 46.79 ± 14.99 | 0.23 | 1.21 | 0.96–1.52 | 0.10 | 46.27 ± 14.5 | 0.40 | 1.13 | 0.85–1.50 | 0.41 |

SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval; SCH, subclinical hypothyroid; TSH, thyroid stimulating hormone; $SCH_1$ is defined as TSH in the range of 4.50–10.00 mIU/l; $SCH_2$ is defined as TSH > 10.00 mIU/l; Continuous data are expressed as mean ± SD; Categorical data are presented as numbers; SBP, DBP, and pulse pressure are shown as unadjusted value

$P_1$, $P_2$ were derived from linear regression models and were adjusted for sex, age, BMI, and smoking status; $P_1$, comparisons of SBP, DBP, and pulse pressure between $SCH_1$ and Euthyroid; * represents significance as $P < 0.05$; $P_2$, comparisons of SBP, DBP, or pulse pressure between $SCH_2$ and Euthyroid; $P_3$, $P_4$ were derived from logistic regression analyses adjusted for age, sex, BMI, and smoking status; $P_3$, correlation analyses of increased SBP, DBP, and pulse pressure with $SCH_1$; $P_4$, correlation analyses of increased SBP, DBP, and pulse pressure with $SCH_2$; ** represents as independent correlation between SBP and $SCH_1$; increased SBP defined as ≥140 mmHg, increased DBP defined as ≥90 mmHg, increased pulse pressure defined as >50 mmHg, which pronounced above the 75th percentile

**Table 3** Relationships between blood pressure and thyroid function in participants with no antihypertensive treatment

| | Subclinical hyperthyroid | Euthyroid | Subclinical hypothyroid | | |
|---|---|---|---|---|---|
| | | | Total | $SCH_1$ | $SCH_2$ |
| Number | 104 | 5204 | 736 | 433 | 303 |
| Women (*N* %) | 70 (67.31) | 3196 (61.41) | 511 (69.43) | 307 (70.90) | 204 (67.33) |
| Age (years) | 47.4 ± 15.35 | 48.71 ± 14.19 | 51.34 ± 14.52 | 51.80 ± 13.86 | 50.67 ± 15.40 |
| BMI (kg/m$^2$) | 23.71 ± 3.59 | 24.41 ± 6.89 | 24.66 ± 3.86 | 24.76 ± 4.09 | 24.50 ± 3.49 |
| Smokers (*N* %) | 25 (25.25) | 1200 (23.95) | 118 (16.14) | 71 (16.51) | 47 (15.61) |
| SBP (mmHg) | 125.91 ± 16.95 | 126.72 ± 19.34 | 129.19 ± 20.28 | 130.00 ± 21.00 | 128.03 ± 19.18 |
| DBP(mmHg) | 80.20 ± 10.29 | 81.81 ± 11.17 | 82.47 ± 11.43 | 83.07 ± 12.03 | 81.62 ± 10.47 |
| Pulse pressure (mmHg) | 45.71 ± 13.43 | 44.91 ± 13.40 | 46.72 ± 15.08 | 46.93 ± 15.26 | 46.42 ± 14.82 |
| *SBP (≥140 mmHg)* | | | | | |
| OR | 0.91 | 1 (reference) | 1.11 | 1.23 | 0.95 |
| 95%CI | 0.54–1.53 | – | 0.92–1.34 | 0.98–1.55 | 0.71–1.27 |
| *P* (adjusted) | 0.72 | – | 0.26 | 0.079 | 0.72 |
| *DBP (≥90 mmHg)* | | | | | |
| OR | 0.99 | 1 (reference) | 1.07 | 1.17 | 0.93 |
| 95%CI | 0.62–1.60 | – | 0.90–1.28 | 0.94–1.46 | 0.70–1.22 |
| *P* (adjusted) | 0.99 | – | 0.46 | 0.16 | 0.58 |
| *Pulse pressure (≥50 mmHg)* | | | | | |
| OR | 1.20 | 1 (reference) | 1.15 | 1.16 | 1.13 |
| 95%CI | 0.71–2.02 | – | 0.95–1.40 | 0.91–1.48 | 0.83–1.52 |
| *P* (adjusted) | 0.51 | – | 0.16 | 0.22 | 0.44 |

SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval; BMI, body mass index; $SCH_1$ is defined as TSH in the range of 4.50–10.00 mIU/l; $SCH_2$ is defined as TSH > 10.00 mIU/l

Continuous data are expressed as mean ± SD, and categorical data are presented as numbers and percentages; SBP, DBP, and pulse pressure are shown as unadjusted values; OR and 95% CI were calculated from logistic regression analyses, adjusted for age, sex, BMI, and smoking status; increased SBP defined as ≥140 mmHg, increased DBP defined as ≥90 mmHg, increased pulse pressure defined as >50 mmHg, evaluated above the 75th percentile

**Table 4** Blood pressure in participants with euthyroidism and different serum levels of TSH

| | Euthyroid | | *P* |
|---|---|---|---|
| | TSH (0.40–2.50 mIU/l) $n = 4093$ | TSH (2.51–4.50 mIU/l) $n = 1576$ | |
| Women (*N* %) | 2413 (58.95) | 1072 (68.02) | 0.000 |
| Age (years) | 48.47 ± 13.54 | 49.45 ± 13.73 | 0.016 |
| BMI (kg/m$^2$) | 24.36 ± 6.92 | 24.64 ± 6.02 | 0.1413 |
| Smokers (*N* %) | 1078 (26.34) | 283 (17.96) | 0.000 |
| SBP (mmHg) | 126.49 ± 18.88 | 127.32 ± 20.01 | 0.72 |
| DBP (mmHg) | 81.88 ± 11.04 | 81.99 ± 11.41 | 0.61 |
| Pulse pressure (mmHg) | 44.61 ± 13.08 | 45.33 ± 13.74 | 0.96 |

TSH, thyroid stimulating hormone; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure. Continuous data are expressed as mean ± SD. Categorical data are presented as numbers and percentages. SBP, DBP, and pulse pressure are shown as unadjusted values. *P* values were derived from linear regression models and were adjusted for sex, age, BMI, and smoking status (defined as current smoker or non-current smoker)

reference range and blood pressure [6]. In contrast, Walsh et al. in a community-based study in Australia found that the prevalence of hypertension was higher in patients with subclinical hyperthyroidism than that in the group with euthyroidism [8]. However, the difference may have been caused by the small sample number of participants in the group with subclinical hyperthyroidism (35 subjects, compared to 1,591 individuals in the group with euthyroidism). Indeed, another study conducted by the same team disclosed that subclinical hyperthyroidism was not

significantly related to adverse cardiovascular diseases [9], which suggest that the significant difference in hypertension rates between groups with subclinical hyperthyroidism and euthyroidism was probably a chance finding.

The study of Biondi et al. examining the possible association between subclinical hyperthyroidism and morphological cardiac parameters found that patients with subclinical hyperthyroidism had similar SBP and DBP to those with euthyroidism [10], as has been observed by other researches [11]. Our findings that in a Chinese population, subclinical hyperthyroidism had no significant association with hypertension are in good agreement.

However, there remained some controversy as to the relationship of subclinical hypothyroidism and hypertension. In some cross-sectional studies, no difference has been reported in the hypertension rate and the average arterial pressure between individuals with subclinical hypothyroidism and those with euthyroidism [7, 12–15]. However, other researchers have found that DBP in the group with subclinical hypothyroidism was significantly higher than that in the group with euthyroidism [16, 17]. Possible reasons for this discrepancy may include differences in race, lifestyle, and genetic background of the sampled population, but no compelling explanation has yet been widely accepted.

In our study, we have found that SBP, DBP, and pulse pressure in the group with subclinical hypothyroidism were higher than in the group with euthyroidism, but these differences were not significant after adjustment for age, sex, BMI, and smoking status. Thus, we found that the presence of subclinical hypothyroidism could not predict the prevalence of hypertension, which is consistent with the previous epidemiologic studies [7, 8, 12–15].

An unexpected result from our research was that when the subjects with subclinical hypothyroidism were further divided into two sub-groups depending on the level of TSH, which were $SCH_1$ (TSH 4.50–10.00 mIU/l) and $SCH_2$ (TSH > 10.00 mIU/l), the SBP and DBP in the group of $SCH_1$ were both significantly higher than those of subjects with euthyroidism, even after adjustment for confounding factors. More importantly, it seemed that subclinical hypothyroidism with lower level of TSH (4.50–10.00 mIU/l) was an independent predictor of increased SBP. In contrast, the blood pressure data did not show this difference between the groups of $SCH_2$ and euthyroidism, suggested that subclinical hypothyroidism with higher level of TSH was not independently associated with increased blood pressure. When data from subjects undergoing antihypertensive treatment were omitted, the association of $SCH_1$ with increased blood pressure was not shown. A possible explanation for this result is that both age and BMI may act as stronger risk factors for hypertension than the level of TSH. On the other hand, we should not ignore the possibility that treatment with antihypertensive drugs might affect our results. This further suggests to us that other potential confounding factors should be explored in future studies.

Considering the possible association between serum levels of TSH and blood pressure in the group with euthyroidism, we found that SBP, DBP, and pulse pressure did not differ significantly between subjects whose levels of TSH fell in the lower reference range (0.40–2.50 mIU/l, $n = 4093$) and those in the upper reference range (2.51–4.50 mIU/l, $n = 1576$) after adjustment, which is very consistent with the results of Walsh [8]. Nevertheless, Gumieniak has found that the influence of thyroid function on blood pressure homeostasis extends into the euthyroid range, and even slight changes in thyroid function would probably induce alterations in the sensitivity of blood pressure to salt [18].

We conclude that in this community-based study, parameters of blood pressure, such as SBP, DBP, and pulse pressure, did not differ significantly among subjects with euthyroidism, subclinical hyperthyroidism or subclinical hypothyroidism. Furthermore, neither subclinical hyperthyroidism nor subclinical hypothyroidism plays a key role in increasing the prevalence of hypertension.

## Materials and methods

A cross-sectional study was carried out in six regions of Jiangsu Province from April 2005 to May 2006. Regions involved in our study were sampled from the southern, mid, and northern parts of Jiangsu Province, including Xuzhou, Huai'an, Zhenjiang, Wuxi, Gaochun, and Nanjing city. Local residents aged ≥20 years who had lived in the vicinity at least 5 years were enrolled into our study. A total of 6,992 residents finished the questionnaire, physical examination, and thyroid function test. Pregnant women and individuals with known severe renal, liver or heart failure, or abdominal ascites were not enrolled. Individuals who were taking medicines influencing thyroidal function were also excluded. Subjects who were accepting antihypertensive treatment ($n = 539$) were also registered but should be announced.

Among the 6,583 participants without overt thyroid dysfunction who were enrolled, 2,468 were men and 4,115 were women. Relevant histories were obtained by the research staff as reported by the participants themselves. The local ethics committees and other relevant regulatory bodies in Jiangsu province approved the study. Written informed consent was obtained from all participants before data collection.

Sociodemographic characteristics, hypertension and thyroid disease-related history, history of metabolic

disorders (e.g., diabetes mellitus, coronary disease, and dyslipidemia), smoking status, consumption of alcohol, and other background information were collected by a face-to-face interview. Physical examination was performed by the professional medical staff in a standard way. Blood pressure was measured in a seated position with a standard mercury sphygmomanometer after at least 5 min of rest with three measurements taken at a minimum interval of 1 min. Subjects were asked to avoid smoking, alcohol, caffeinated beverages, and heavy exercise at least 30 min before measurement. Systolic and diastolic blood pressure of $\geq$140 mmHg and $\geq$90 mmHg, respectively, were considered increased. Pulse pressure was calculated as the difference between the systolic and diastolic blood pressures, and increased pulse pressure was defined as the value above the 75th percentile of the pulse pressure distribution (50 mmHg). Body mass index (BMI) was calculated as weight (kg)/height$^2$ (m$^2$).

Blood samples were tested in a central laboratory, and thyroid function was measured by a chemiluminescence immunoassay (Diagnostic Products Company, US). Serum levels of thyrotropin were measured in all subjects, and then serum levels of free triiodothyronine and free thyroxin were analyzed in those individuals with abnormal serum thyrotropin.

The reference range for serum thyrotropin was derived from the 2.5th to 97.5th percentile of the values from 120 healthy men with no overt thyroid dysfunction, family history of thyroid disease, thyroid autoantibody (thyroid peroxidase autoantibody and thyroid globulin antibody), goiter, or nodules on B-mode ultrasonography. The reference for serum thyrotropin (TSH) in our laboratory was 0.40–4.50 mIU/l, while free triiodothyronine (FT3) and free thyroxin (FT4) were 2.3–6.3 pmol/l and 10.3–24.5 pmol/l, respectively. The analytical sensitivities for TSH, FT3, and FT4 were 0.004 mIU/ml, 1.536 pmol/l, and 3.861 pmol/l, respectively.

Subclinical hypothyroidism was defined as levels of TSH higher than 4.50 mIU/l in individuals whose FT3 and FT4 were in the normal range, while subclinical hyperthyroidism was defined as levels of TSH lower than 0.40 mIU/l in individuals with normal FT3 and FT4.

### Statistical methods

The data were entered in a double-track system by the EpiData 3.0 software. Statistical analyses were made using the SPSS 13.0 software package. Continuous data were presented as $\bar{x} \pm s$ or 25th, 50th, and 75th percentile; and categorical data were expressed as numbers and percentages. Comparisons between groups were analyzed by the *t*-test (*t*-test), chi squared, and Mann–Whitney tests.

Spearman correlation coefficients and linear regression models were applied to examine the relationship between blood pressure and serum levels of TSH, and multivariable analyses were performed using binary logistic regression to identify risk factors for hypertension. From the literature, it was disclosed that age, sex, BMI, and smoking habit might influence the rate of occurrence of hypertension [6, 8]; therefore, the multivariable linear and logistic regressions were both adjusted by these factors. Significance was set at $P < 0.05$.

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## References

1. G.J. Kahaly, W.H. Dillmann, Thyroid hormone action in the heart. Endocr. Rev. **26**, 704–728 (2005)
2. S. Danzi, I. Klein, Thyroid hormone and blood pressure regulation. Curr. Hypertens. Rep. **5**, 513–520 (2003)
3. G.W. Ching, J.A. Franklyn, T.J. Stallard, J. Daykin, M.C. Sheppard, M.D. Gammage, Cardiac hypertrophy as a result of long-term thyroxin therapy and thyrotoxicosis. Heart **75**, 363–368 (1996)
4. I. Saito, K. Ito, T. Saruta, Hypothyroidism as a cause of hypertension. Hypertension **5**, 112–115 (1983)
5. D.H. Streeten, G.H. Anderson Jr, T. Howland, R. Chiang, H. Smulyan, Effects of thyroid function on blood pressure. Recognition of hypothyroid hypertension. Hypertension **11**, 78–83 (1988)
6. H. Völzke, D. Alte, M. Dörr, H. Wallaschofski, U. John, S.B. Felix, R. Rettig, The association between subclinical hyperthyroidism and blood pressure in a population-based study. J. Hypertens. **24**, 1947–1953 (2006)
7. M. Dörr, B. Wolff, D.M. Robinson, U. John, J. Lüdemann, W. Meng, S.B. Felix, H. Völzke, The association of thyroid function with cardiac mass and left ventricular hypertrophy. J. Clin. Endocrinol. Metab. **90**, 673–677 (2005)
8. J.P. Walsh, A.P. Bremner, M.K. Bulsara, P. O'Leary, P.J. Leedman, P. Feddema, V. Michelangeli, Subclinical thyroid dysfunction and blood pressure: a community-based study. Clin. Endocrinol. **65**, 486–491 (2006)
9. J.P. Walsh, A.P. Bremner, M.K. Bulsara, P. O'Leary, P.J. Leedman, P. Feddema, V. Michelangeli, Subclinical thyroid dysfunction as a risk factor for cardiovascular disease. Arch. Intern. Med. **165**, 2467–2472 (2005)
10. B. Biondi, E.A. Palmieri, S. Fazio, C. Cosco, M. Nocera, L. Sacca, S. Filetti, G. Lombardi, F. Perticone, Endogenous subclinical hyperthyroidism affects quality of life and cardiac morphology and function in young and middle-aged patients. J. Clin. Endocrinol. Metab. **85**, 4701–4705 (2000)
11. M. Petretta, D. Bonaduce, L. Spinelli, M.S. Vicario, V. Nuzzo, F. Marciano, P. Camuso, V. De Sanctis, G. Lupoli, Cardiovascular haemodynamics and cardiac autonomic control in patients with subclinical and overt hyperthyroidism. Eur. J. Endocrinol. **145**, 691–696 (2001)
12. A.R. Cappola, L.P. Fried, A.M. Arnold, M.D. Danese, L.G. Kuller, G.L. Burke, R.P. Tracy, P.W. Ladenson, Thyroid status,

cardiovascular risk, and mortality in older adults. JAMA **295**, 1033–1041 (2006)
13. R.D. Lindeman, D.S. Schade, A. LaRue, L.J. Romero, H.C. Liang, R.N. Baumgartner, K.M. Koehler, P.J. Gary, Subclinical hypothyroidism in a biethnic, urban community. J. Am. Geriatr. Soc. **47**, 703–709 (1999)
14. J. Kvetny, P.E. Heldgaard, E.M. Bladbjerg, J. Gram, Subclinical hypothyroidism is associated with a low-grade inflammation, increased triglyceride levels and predicts cardiovascular disease in males below 50 years. Clin. Endocrinol. **61**, 232–238 (2004)
15. A.E. Hak, H.A. Pols, T.J. Visser, H.A. Drexhage, A. Hofman, J.C. Witteman, Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the rotterdam study. Ann. Intern. Med. **132**, 270–278 (2000)
16. R. Luboshitzky, A. Aviv, P. Herer, L. Lavie, Risk factors for cardiovascular disease in women with subclinical hypothyroidism. Thyroid **12**, 421–425 (2002)
17. T. Nagasaki, M. Inaba, Y. Kumeda, Y. Hiura, K. Shirakawa, S. Yamada, Y. Henmi, E. Ishimura, Y. Nishizawa, Increased pulse wave velocity in subclinical hypothyroidism. J. Clin. Endocrinol. Metab. **91**, 154–158 (2006)
18. O. Gumieniak, T.S. Perlstein, P.N. Hopkins, N.G. Brown, L.J. Murphey, X. Jeunemaitre, N.K. Hollenberg, G.H. Williams, Thyroid function and blood pressure homeostasis in euthyroid subjects. J. Clin. Endocrinol. Metab. **89**, 3455–3461 (2004)