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Association Between Peripheral Thyroid Hormone Sensitivity and Hypertriglyceridemia in Euthyroid Population

Yu Gong
The First People's Hospital of Hefei
Qianqian Zhang
The First People's Hospital of Hefei
Guojuan Wang
The First People's Hospital of Hefei
Ying Li
474731880@qq.com

The First People's Hospital of Hefei

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Abstract

Objective We aimed to investigate the correlation between peripheral thyroid hormone sensitivity and hypertriglyceridemia in euthyroid population.

Methods A total of 833 individuals who underwent physical examinations were randomly selected. Biochemical parameters including thyroid hormones, liver and kidney functions, blood glucose, and blood lipids were measured. Peripheral thyroid hormone sensitivity was assessed by the ratio of free triiodothyronine to free thyroxine (FT3/FT4). The data were analyzed for the relationship between peripheral thyroid hormone sensitivity and triglyceride (TG).

Results smooth curve fitting and threshold effect analysis showed that FT3/FT4 ratio was a positive correlation with TG before the inflection point at 0.426 (β=1.752, *P*<0.001). Tests for trend in multiple regression equations showed that with the increase of the quartiles of FT3/FT4 ratio, the gradually increasing trend of TG was statistically significant. For per SD increase in FT3/FT4 ratio, TG increased by 0.0587mmol/L (β=0.0587, *P*=0.001). Subgroup analysis revealed that

in female group (β=1.9040, *P*<0.001), age <65 years group (before the inflection point 0.4272, β=1.7773, *P*<0.001), and BMI<28 kg/m^2 group (β=1.4660, *P*<0.001), the FT3/FT4 ratio was positively correlated with TG.

Conclusion Increased peripheral thyroid hormone sensitivity, as reflected by an elevated FT4 to FT3 conversion rate, is associated with increased TG level in euthyroid population. This association is particularly pronounced in females, individuals with aged<65 years, and non-obese (BMI<28 kg/m^2) individuals.

Introduction

Hyperlipidemia is a chronic disease that seriously endangers human health [1]. Most clinical guidelines for dyslipidemia management focus predominantly on low-density lipoprotein cholesterol[2], while triglyceride (TG) receives comparatively less attention. Hypertriglyceridemia (HTG) often occurs secondary to metabolic disorders such as diabetes, alcohol consumption, and/or overweight, with a prevalence of 10% in the adult population[3]. Epidemiological and genetic studies have confirmed that TG-rich lipoproteins and their remnants are critical risk factors for atherosclerotic cardiovascular disease (ASCVD), and severe HTG also increases the risk of pancreatitis[4]. Despite the well-established clinical hazards of HTG, gaps remain in the identification of its specific risk factors and the formulation of screening strategies for high-risk populations. Additionally, existing risk assessment systems fail to fully incorporate the unique molecular pathophysiological mechanisms underlying HTG.

Multiple hormones participate in lipid metabolism within the body, among which thyroid hormone (TH) serves as a critical regulator of lipid homeostasis[5]. TH can achieve systematic regulation of lipid metabolism by regulating the processes of lipid synthesis, mobilization, and degradation, and coordinating the functional interaction between the liver and adipose tissue[6].

Recent studies have shown[7] that even fluctuations in thyroid hormone levels within the reference range can affect the metabolic prognosis of blood lipids in healthy adults. These changes may be related to impaired peripheral deiodination and down - regulation of deiodinase activity[8]. The ratio of free triiodothyronine to free thyroxine (FT3/FT4) is an important indicator reflecting deiodinase activity and the peripheral bioavailability of thyroid hormones[9]. An increasing number of studies have confirmed that an elevated FT3/FT4 ratio in the euthyroid population is associated with obesity, metabolic syndrome, diabetes, and hypertension[10][11][12]-13], and is even closely related to diseases such as heart failure and non - alcoholic fatty liver disease[14],[15]. These findings provide new research directions for in-depth analysis of the relationship between thyroid function and lipid metabolism.

Previous studies have preliminarily explored the association between peripheral thyroid hormone sensitivity and TG in patients with coronary heart disease[16], but no relevant studies have been reported for the general population with normal thyroid function. This study aims to investigate the association between the FT3/FT4 ratio and TG levels in euthyroid individuals, potentially offering insights for identifying subgroups at higher risk of HTG.

Methods and Materials

Study population and design

This cross-sectional analysis initially enrolled 1334 adults aged 18 to 90 years who underwent routine health examinations at the Physical Examination Center of the First People's Hospital of Hefei between January 2024 and June 2024. The study protocol was approved by the Research Ethics Committee of the Third Affiliated Hospital of Anhui Medical University (Approval No. 2024-167-01).

Participants were excluded based on the following criteria: (1) Individuals with histories of tumors, acute infections, severe liver and kidney dysfunction. (2) Individuals with abnormal thyroid functions, histories of thyroid diseases, including hyperthyroidism, hypothyroidism and hashimoto's thyroiditis. (3) Individuals who have recently used iodine-containing contrast agents, iodine-free salt, thyroid hormones, or anti-thyroid drugs. (4) Individuals who have recently used medications that affect lipid metabolism (such as statins and fibrates). (5) Pregnant or lactating women. (6) Individuals with missing data.

After applying these exclusion criteria, a total of 833 euthyroid individuals were included in the final analysis. A detailed flow diagram of participant selection is presented in **Fig. 1**. Based on their triglyceride levels, participants were categorized into a hypertriglyceridemia group (TG ³ 2.3 mmol/L, n = 166) and a normal TG group (TG < 2.3 mmol/L, n = 667). The diagnostic criteria and data collection methods followed standardized protocols similar to those described in our previous work [*Frontiers in Endocrinology*.2025;16:1616907.DOI: 10.3389/fendo.2025.1616907].

Clinical and laboratory assessments

The basic clinical information of all the individuals was collected, including name, gender, age, chronic medical histories including diabetes mellitus (DM), hypertension, hyperlipidemia, medical history and surgical history. Height, weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured in the state of fasting in the morning.

Venous blood samples were drawn from each participant after an overnight fast of at least 8 hours. Biochemical parameters, including fasting blood-glucose (FBG), TG, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), alanine transaminase (ALT), aspartic transaminase (AST), gamma-glutamyl transferase (GGT), total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), albumin (ALB), serum creatinine (SCr), serum uric acid (SUA) were measured by well-trained technicians (Roche automatic biochemical analyzer. Combas 8000). Thyrotropic hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) were determined using a standardized Chemiluminescence method (Abbott 12000SR), and all measurements were performed using the same assays. The reference ranges of thyroid function indicators are as follows: TSH ranges from 0.350 to 4.949 μIU/mL, FT4 ranges from 9.03 to 19.04 pmol/L, and FT3 ranges from 2.43 to 6.01 pmol/L.

Standard of diagnosis

Hypertension was defined as systolic blood pressure³140 mmHg or diastolic blood pressure ³90 mmHg or self-reported history of hypertension or use of any antihypertensive medication[17]. DM was defined as having a FBG level≥7.0 mmol/L, or a 2-hour postprandial blood glucose level≥11.1 mmol/L, or a HbA1c level≥6.5%, or a documented history of diabetes, or current use of any glucose-lowering medication[18]. HTG was defined as having a TG level of≥2.3 mmol/L without the use of oral lipid-lowering medications[19].

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics Software Version 27, GraphPad Prism 10.0.3, Empower(R) (www.empowerstats.com, X&Y Solutions, Inc.) (Boston, MA), and R (http://www.r-project.org) to complete the statistical analyses. Data normality was assessed using the Shapiro-Wilk test and Q-Q plots. Continuous variables with normal distribution are presented as mean±standard deviation (SD) and were compared between groups using the independent samples t-test. Non-normally distributed variables are expressed as median with interquartile range (IQR) and were compared using the Mann–Whitney U test. Categorical variables are presented as frequencies (percentages) and were compared using the chi-square test.

To examine the relationship between the FT3/FT4 ratio and TG levels, we performed multivariate linear regression analyses with progressive adjustment for confounders. Model I was unadjusted; Model II was adjusted for age, sex, BMI, blood pressure (SBP and DBP), FBG, lipid parameters (TC, HDL-C, LDL-C), and liver and kidney function indicators (ALB, ALT, AST, GGT, TBIL, SCr, SUA). Given the potential nonlinear relationship suggested by preliminary analyses, we employed smooth curve fitting (generalized additive models) and conducted a two-piecewise linear regression model to identify threshold effects. The inflection point was determined using a trial-and-error method, and the log-likelihood ratio test was used to compare the one-line linear model with the two-piecewise model.

To assess the robustness of the association, we performed trend tests by categorizing the FT3/FT4 ratio into quartiles and treating the quartiles as ordinal variables in regression models. Subgroup analyses were conducted stratified by sex (male vs. female), age (<65 vs. ≥65 years), and BMI (<28 vs. ≥28 kg/m²). All statistical tests were two-sided, and a *P*-value < 0.05 was considered statistically significant.

Results

The baseline clinical characteristics of all the individuals in this study

The research subjects were divided into two groups based on TG level: TG³2.3 mmol/L group (N=166) and TG<2.3 mmol/L group (N=667). Independent sample T-test analysis was conducted between the two groups. Compared with TG<2.3mmol/L group, TG³2.3mmol/L group showed a higher proportion of women, a lower age, and a significantly higher BMI. Biochemical indicators including FBG, ALB, ALT, AST, GGT, SUA, SCr and TC levels were significantly elevated. In terms of thyroid function, compared with TG<2.3mmol/L group, TG³2.3mmol/L group showed higher levels of TSH, FT3, and the FT3/FT4 ratio, while there was no significant difference in FT4 level between two groups(*P*>0.05) (**Table 1**,**Fig. 2**).

Table 1 Baseline characteristics of participants according to TG level

Characteristics	Total N=833	TG level(mmol/L)		*P* value
		<2.3	≥2.3	
		N=667	N=166	
Age (year)	47.40±11.95	47.66±12.29	46.36±10.45	0.165
Male	446（53.5）	331（49.60）	115（69.3）	<0.001
Female	387（46.5）	336（50.40）	51（31.7）	<0.001
BMI (kg/m^2)	24.83±3.27	24.41±3.20	26.55±2.97	<0.001
SBP (mmHg)	122.98±16.65	121.67±16.68	128.22±15.51	<0.001
DBP (mmHg)	75.35±10.92	74.23±10.81	79.86±10.19	<0.001
FBG (mmol/L)	5.17（4.84，5.57）	5.14（4.82，5.50）	5.19（4.94，5.86）	0.004
ALB (g/L)	47.17±2.82	47.06±2.91	47.61±2.38	0.024
ALT (U/L)	19（14，29）	17（13，26）	26（17，40）	<0.001
AST (U/L)	22（19，26）	22（19，26）	24（21，31）	<0.001
GGT (U/L)	34.94±35.81	29.61±29.96	56.36±47.62	<0.001
TBIL (umol/L)	19.25±7.58	19.63±7.63	17.71±7.21	0.003
IBIL (umol/L)	15.97±6.40	16.21±6.46	15.01±6.11	0.031
DBIL (umol/L)	3（2.30，4.00）	3.1（2.40，4.10）	2.55（1.80，3.20）	<0.001
SCr (umol/L)	71.92±16.14	70.87±16.06	76.14±15.81	<0.001
SUA （umol/L）	329.42±92.32	317.36±86.85	377.89±97.87	<0.001
TG （mmol/L）	1.72±1.21	1.27±0.49	3.54±1.49	<0.001
TC (mmol/L)	4.85±0.90	4.78±0.88	5.14±0.92	<0.001
LDL-C (mmol/L)	3.06±0.81	3.07±0.80	3.03±0.84	0.573
HDL (mmol/L)	1.33±0.35	1.40±0.34	1.04±0.19	<0.001
TSH (μIU/mL)	1.84±1.09	1.78±0.88	2.09±1.67	0.022
FT3 (pmol/L)	4.43±0.51	4.40±0.50	4.55±0.51	<0.001
FT4(pmol/L)	13.01±1.45	13.02±1.46	12.98±1.44	0.789
FT3/FT4	0.34±0.04	0.34±0.04	0.35±0.04	0.001

Data are expressed as means ± standard deviations, medians (interquartile ranges), or percentages. Independent samples T-test or Mann-Whitney U-test are used to compare the differences of continuous variables between two groups. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; FBG, fasting blood glucose; ALB, albumin; ALT, alanine transaminase; AST, aspartic transaminase; GGT, γ-glutamyl transferase; TBIL, total bilirubin; IBIL, indirect bilirubin; DBIL, direct bilirubin; TG, triglyceride ; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TSH, Thyrotropic hormone; FT3, free triiodothyronine; FT4, free thyroxine; FT3/FT4, The ratio of free triiodothyronine to free thyroxine.

Smooth curve fitting and threshold effect analysis of the relationship between peripheral thyroid hormone sensitivity and TG

After adjusting the confounding factors of gender, age, BMI, blood pressure, blood glucose, blood lipids, and liver and kidney function, the FT3/FT4 ratio was curvilinearly correlated with TG. The FT3/FT4 ratio was positively correlated with TG before the inflection point at 0.426, with a corresponding increase of 1.752 in TG for every 1-unit increase in the FT3/FT4 ratio (β=1.752, *P*<0.001). However, after the inflection point there was no significant difference observed in the correlation between the FT3/FT4 ratio and TG (*P*=0.053) (**Table 2**,**Fig. 3**).

Table 2 Threshold effect analysis of the relationship between the FT3/FT4 ratio and TG in the overall population

Outcome: TG	For exposure□FT3/FT4
Model □	
One-line effect	1.305 (0.508, 2.103) 0.001
Model □	
Inflection point (k)	0.426
< K segment effect1	1.752 (0.874, 2.629) <0.001
> K segment effect2	-6.271 (-12.624, 0.082) 0.053
Difference in effect of 2 and 1	-8.023 (-14.698, -1.349) 0.018
Log-likelihood ratio test	0.017

Trend tests of multiple regression equations for the relationship between the FT3/FT4 ratio and TG

The smooth curve fitting and threshold effect analysis of the overall data showed the FT3/FT4 ratio was positively correlated with TG before the inflection point. Further trend tests of multiple regression equations were performed to verify whether the correlation trend was statistically significant. P values for trend were calculated with quartiles as continuous variables.

The results showed that with the increase of quartiles of the FT3/FT4 ratio, the gradually increasing trend of TG was statistically significant. For each one-grade increase in the FT3/FT4 ratio, the level of TG increased by 0.0624 accordingly (β=0.0624, *P*<0.001). For each SD increase in the FT3/FT4 ratio, the level of TG increased by 0.0587 mmol/L (β=0.0587, *P*=0.001) (**Table 3**,**Fig. 4**).

Table 3 Logistic regression analysis of the correlation between the FT3/FT4 ratio and TG

Outcome	Adjust Model I		Adjust Model II	
	β (95%CI)	*P* value	β (95%CI)	*P* value
FT3/FT4 per SD	0.1750 (0.0939, 0.2560)	<0.001	0.0587 (0.0229, 0.0946)	0.001
Q1	0 (reference)		0 (reference)	
Q2	0.3164 (0.0866, 0.5463)	0.007	0.1069 (0.0096, 0.2041)	0.031
Q3	0.2563 (0.0265, 0.4861)	0.029	0.1522 (0.0549, 0.2494)	0.002
Q4	0.4572 (0.2276, 0.6868)	<0.001	0.1938 (0.0935, 0.2941)	<0.001
FT3/FT4 quartile continuous	0.1311 (0.0585, 0.2038)	<0.001	0.0624 (0.0309, 0.0940)	<0.001
P for trend		<0.001		<0.001

Model 1 did not correct for confounding factors

Model 2 Adjusted for gender, age, BMI, blood pressure, blood glucose, blood lipids, and liver and kidney function; β, regression coefficient; CI, confidence interval; *P* for trend was calculated using the quartiles as continuous variables.

Subgroup analysis of the correlation between the FT3/FT4 ratio and TG

After adjusting for confounders including age, BMI, SBP, DBP, ALB, ALT, AST, GGT, TBIL, CR, FBG, TC, HDL, and LDL, the FT3/FT4 ratio was positively correlated with TG in female group. For every unit increase in the FT3/FT4 ratio, TG increased by 1.9040 (β=1.9040, *P*<0.001). In male group, the FT3/FT4 ratio was no significant correlation with TG.

After adjusting for confounders including gender, BMI, SBP, DBP, ALB, ALT, AST, GGT, TBIL, CR, FBG, TC, HDL, and LDL, the FT3/FT4 ratio was curvilinearly correlated with TG in age <65 years group. The FT3/FT4 ratio was positively correlated with TG before the inflection point at 0.4272, with a corresponding increase of 1.7773 in TG for every 1-unit increase in the FT3/FT4 ratio (β=1.7773, *P*<0.001). However, after the inflection point there was no significant difference observed in the correlation between the FT3/FT4 ratio and TG. In age³65 years group, the FT3/FT4 ratio was no significant correlation with TG.

After adjusting for confounders including age, gender, SBP, DBP, ALB, ALT, AST, GGT, TBIL, CR, FBG, TC, HDL, and LDL, the FT3/FT4 ratio was positively correlated with TG in BMI<28 kg/m^2 group. For every unit increase in the FT3/FT4 ratio, TG increased by 1.4660 (β=1.4660, *P*<0.001). In BMI³28 kg/m^2 group, the FT3/FT4 ratio was no significant correlation with TG.

We concluded that the FT3/FT4 ratio was positively correlated with TG levels in the female population, in individuals aged <65 years, and in those with BMI <28 kg/m² (**Table 4**,**Fig. 5**).

Table 4 Subgroup analysis of the correlation between the FT3/FT4 ratio and TG

	gender		age（year）	
	female	male	³65	<65
Model □				
One-line effect	1.9040 (0.8208, 2.9872) <0.001	0.7922 (-0.2739, 1.8582) 0.146	1.0829 (-0.7187, 2.8845) 0.244	1.3245 (0.4722,
Model II				
Inflection point (k)	0.3680	0.4360	0.2971	0.4272
< K segment effect1	2.6989 (1.2115, 4.1863) <0.001	1.2753 (0.0798, 2.4708) 0.037	-2.8014 (-8.5552, 2.9523) 0.344	1.7773 (0.8366,
> K segment effect2	-0.4695 (-3.7053, 2.7664) 0.776	-8.2217 (-17.5129, 1.0694) 0.083	2.9270 (-0.2241, 6.0782) 0.074	-6.2261 (-12.996
Difference in effect of 2 and 1	-3.1684 (-7.2396, 0.9029) 0.128	5.1749 (-0.9653, 11.3152) 0.099	5.7285 (-2.3382, 13.7952) 0.170	-8.0033 (-15.123
Log-likelihood ratio test	0.119	0.078	0.110	0.026

Discussion

In this cross-sectional study of euthyroid adults, we observed that individuals with HTG had higher TSH, FT3, and the FT3/FT4 ratio compared to those with normal TG. After comprehensive adjustment for confounders, greater peripheral thyroid hormone sensitivity, which is reflected by a higher FT3/FT4 ratio, was independently associated with elevated TG levels. This association was particularly prominent in females, in individuals aged <65 years, and in those with BMI<28 kg/m².

Our findings align partially with those of Gu et al. [7] from the TCLSIH cohort, which also reported that higher FT3 levels within the euthyroid range were linked to an unfavorable lipid profile. Conversely, Gu et al. [16] observed in patients with coronary heart disease that a higher FT3/FT4 ratio was associated with a lower risk of dyslipidemia. This discrepancy might stem from differences in study populations: individuals with coronary heart disease often exhibit atherosclerosis and systemic inflammation, in which peripheral thyroid hormone metabolism could be altered as a compensatory response. In that context, an elevated FT3/FT4 ratio might represent an adaptive mechanism to preserve metabolic homeostasis [20],[21]. By contrast, our study focused on generally healthy adults, which may better capture associations under physiological conditions.

The elevation of plasma TG results from both the overproduction and impaired clearance of TG-rich lipoproteins—very-low-density lipoproteins and chylomicrons[22]. Experimental evidence indicates that HTG, accompanied by increased serum fatty acid concentrations, suppresses mitochondrial complex formation in pancreatic acinar cells, induces abnormal elevation of intracellular calcium, promotes cytokine release and tissue injury, and impairs pancreatic ductal function, thereby leading to acute pancreatitis[23]. In the context of HTG, elevated levels of triglyceride-rich lipoproteins and their remnants can penetrate the endothelial barrier and interact with macrophages, promoting foam cell formation and inflammatory responses within the arterial wall. These processes contribute to the development of atherosclerosis and increase the risk of coronary heart disease[24]. In summary, HTG is closely linked to the pathogenesis of multiple diseases, underscoring the importance of its management and control.

TH is key regulators of TG metabolism. TH concentrations correlate with hepatic TG content and influence HDL metabolism by enhancing the activity of cholesteryl ester transfer protein, which transfers cholesteryl esters from HDL to very-low-density lipoproteins and TG-rich lipoproteins[25]. T3 stimulates lipoprotein lipase, promoting the catabolism of TG-rich lipoproteins and thereby lowering TG levels[26]. Furthermore, studies in TSH receptor knockout mouse models demonstrate that TSH dose-dependently suppresses adipose TG lipase expression in mature adipocytes via the cAMP-protein kinase pathway, consequently promoting TG accumulation within fat cells[27]. Substantial evidence confirmed that both elevated and reduced TH levels altered the blood lipid profile. Patients with hypothyroidism exhibit increased levels of TC, LDL-C, and TG, along with decreased HDL-C, with the most pronounced changes observed in TC and LDL-C levels. In contrast, patients with hyperthyroidism showed significantly reduced levels of TC, TG, and LDL-C[28][29]-30]. Even within the normal range, thyroid function correlated with systemic metabolism: when TSH remained within normal limits, a rising TSH level was associated with significant increases in TC, TG, and LDL-C, and a significant decrease in HDL-C[31]. Additionally, elevated FT3 level was frequently observed in euthyroid individuals with obesity and non-alcoholic fatty liver disease[32].

Physiologically, TSH, FT4 and FT3 regulate and influence each other in HPA axis. Compared with a single indicator, the calculation of a composite indicator could systematically reflect the regulation of TH homeostasis. Since FT4 is peripherally converted to FT3 by deiodinases, the FT3/FT4 ratio serves as an indicator of peripheral deiodinase activity[33]. A study by Bilgin and Pirgon suggested that enhanced conversion of FT4 to FT3 via increased deiodinase activity might represent a compensatory mechanism in the context of fat accumulation, aimed at elevating energy expenditure and reflecting heightened TH sensitivity[34]. Our findings demonstrated a positive correlation between the FT3/FT4 ratio and level, suggesting that increased peripheral TH sensitivity was associated with elevated TG. Given the influence of sex hormones[35]and age[36]on thyroid function, we performed subgroup analyses by gender and age. The observed gender-based differences may be attributed to the distinct regulatory effects of sex hormones on thyroid function. For instance, estrogen and androgen exerted differential influences on serum thyroxine-binding globulin concentrations, thereby modulating thyroid activity[37]. The age-related variations in lipid metabolism may be explained by the impact of aging and menopausal hormonal changes. With advancing age, a reduction in thyroid hormone receptor expression occurred, leading to diminished tissue responsiveness to TH[38],[39]. The BMI subgroup differences may involve interactions between TH and leptin. Leptin, an adipokine secreted by adipose tissue, acted directly on the hypothalamic paraventricular nucleus to stimulate transcription

of the thyrotropin-releasing hormone (TRH) precursor, thereby promoting TRH secretion[40]. It may also indirectly stimulate TRH secretion in the arcuate nucleus by promoting production of downstream pro-opiomelanocortin derivatives[41].

From a clinical perspective, the FT3/FT4 ratio might serve as a useful adjunctive marker for identifying euthyroid individuals who could be at heightened risk of hypertriglyceridemia. This could be particularly relevant in subgroups such as women, middle-aged adults, and non-obese persons, in whom routine lipid screening might benefit from additional risk stratification. Although further prospective studies are needed to establish causality, incorporating thyroid function parameters into regular health check-ups may help highlight individuals who could benefit from closer metabolic monitoring or early lifestyle counseling. Given the well-documented burden of hypertriglyceridemia in relation to atherosclerotic cardiovascular disease and pancreatitis [42], even modest improvements in risk prediction could have public health implications. The potential utility of such an approach resonates with current recommendations that emphasize targeted screening and primary prevention strategies for high-risk populations [43].

Several limitations of this study should be acknowledged: 1. The cross-sectional design precludes any causal inference regarding the relationship between peripheral thyroid hormone sensitivity and hypertriglyceridemia. Therefore, the observed associations warrant confirmation in prospective cohort studies. 2. As a single-center study with a relatively modest sample size recruited from a specific geographic region, the generalizability of our findings to other populations may be limited and requires validation in larger, multicenter cohorts. 3. Although we adjusted for a wide range of potential confounders—including demographic characteristics, metabolic parameters, and liver and kidney function—the possibility of residual confounding due to unmeasured variables (e.g., insulin resistance, inflammatory markers such as high-sensitivity C-reactive protein, or detailed medication adherence) cannot be entirely excluded. 4. The absence of data on thyroid autoantibodies and urinary iodine levels precluded assessment of potential underlying thyroid autoimmunity or iodine nutritional status, which may influence thyroid hormone metabolism and confound the observed associations. 5. Because the study population consisted of individuals undergoing routine health check-ups, the medication histories relied on self-report and may be subject to recall bias, despite our efforts to exclude those taking lipid-lowering or thyroid-affecting medications. 6. While the FT3/FT4 ratio is a widely used surrogate marker of peripheral deiodinase activity, it remains an indirect measure of thyroid hormone sensitivity; direct assessment of deiodinase enzyme activity or tissue-level thyroid hormone action was not performed and should be addressed in future mechanistic studies.

Conclusion

In summary, increased peripheral thyroid hormone sensitivity was significantly associated with elevated TG level, with this correlation being more pronounced in female, young and middle-aged adults, and non-obese individuals. These findings highlight the need for longitudinal studies to clarify the directionality and potential mechanisms of this relationship. A better understanding of this association could contribute to more refined risk stratification and ultimately aid in the prevention of HTG and its complications.

Declarations

Data availability statement

All data generated and analysed during our study were included in the supplementary files in the article.

Ethics statement

This investigation was approved by the Research Ethics Committee of the Third Affiliated Hospital of Anhui Medical University (No.2024-167-01), adhereing to the tenets of the Declaration of Helsinki. Informed consents were obtained from all participants.

Author contributions

YG: Visualization, Validation, Investigation, Formal analysis, Conceptualization, Writing – original draft, Methodology and Data curation. QQZ: Visualization, Validation, Investigation, Formal analysis, Conceptualization, and Data curation. GJW: Visualization, Validation, Investigation, Formal analysis, Conceptualization, and Data curation. YL: Visualization, Validation, Investigation, Formal analysis, Conceptualization, Writing – review & editing, Methodology and Data curation.

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Conflict of interest

The authors declared that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Figures

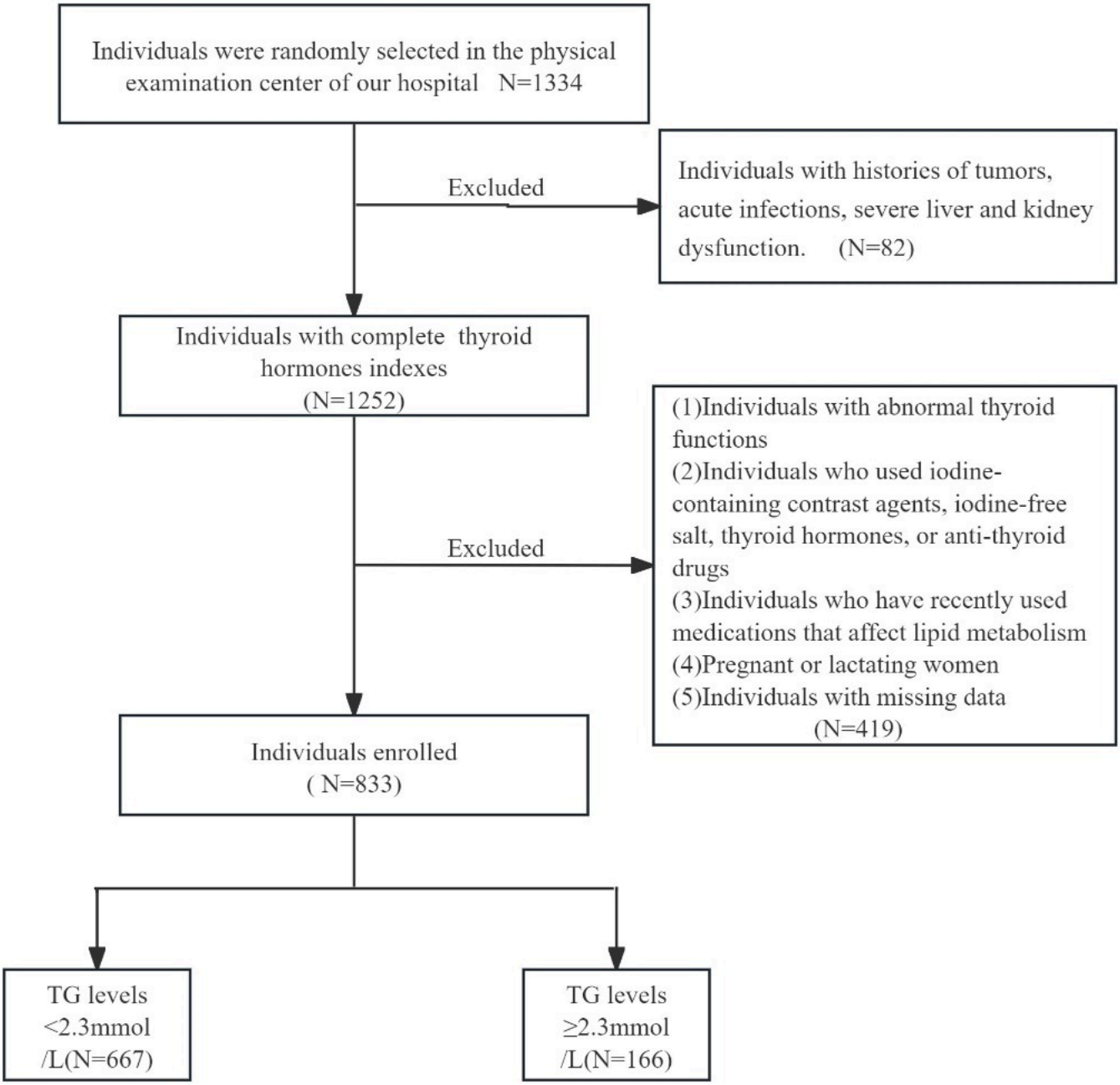


Figure 1

The flow chart of the study population

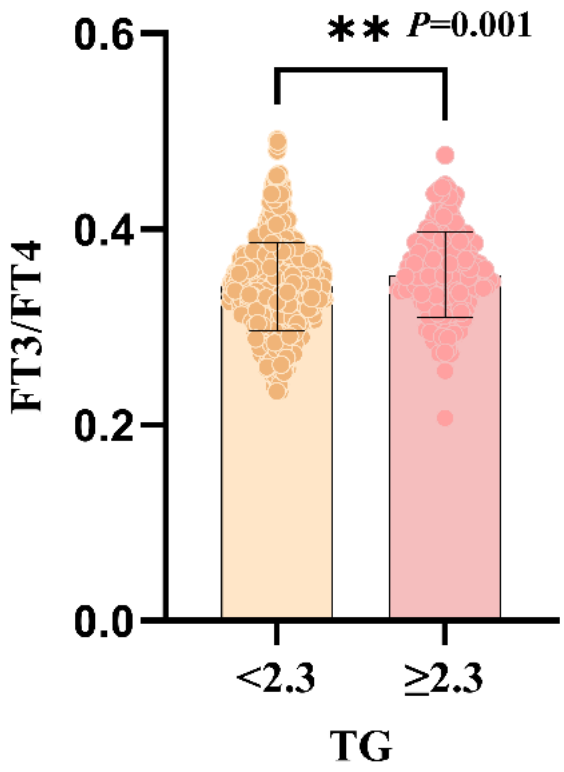


Figure 2

Graphical representation of independent samples T-test for comparison between two groups of TG subgroups

TG, total cholesterol; FT3/FT4, The ratio of free triiodothyronine to free thyroxine.

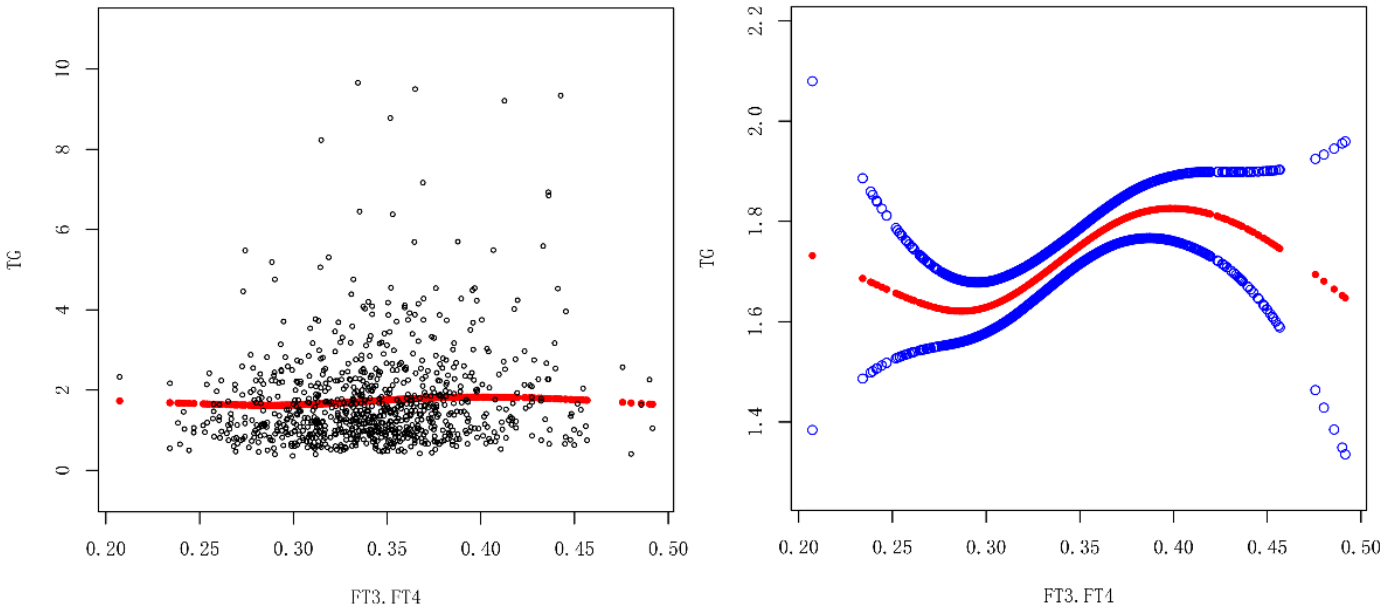


Figure 3

Smooth curve fitting diagram of the FT3/FT4 ratio and TG

TG, total cholesterol; FT3/FT4, The ratio of free triiodothyronine to free thyroxine.

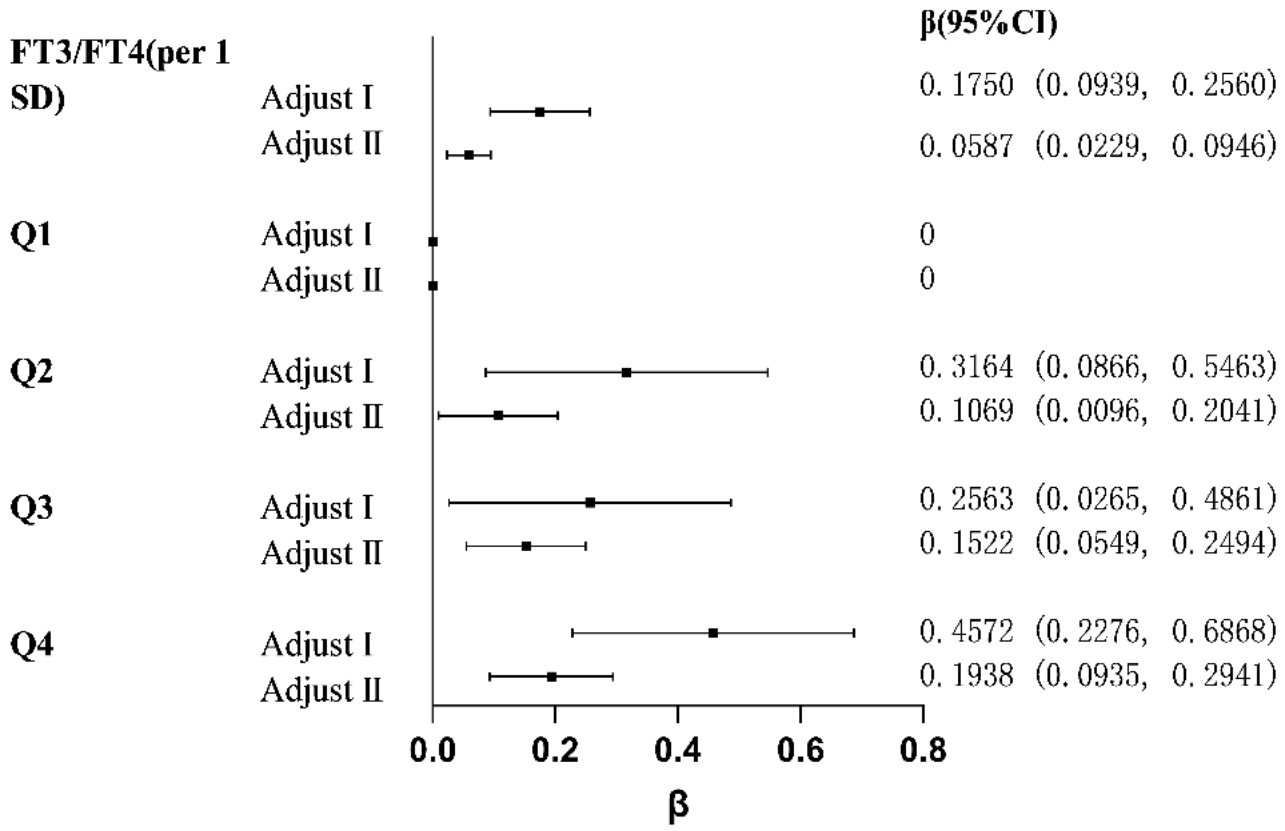


Figure 4

Forest plot of correlation between the FT3/FT4 ratio and TG

Model 1 did not correct for confounding factors

Model 2 Adjusted for gender, age, BMI, blood pressure, blood glucose, blood lipids, and liver and kidney function; β, regression coefficient; CI, confidence interval; *P* for trend was calculated using the quartiles as continuous variables.

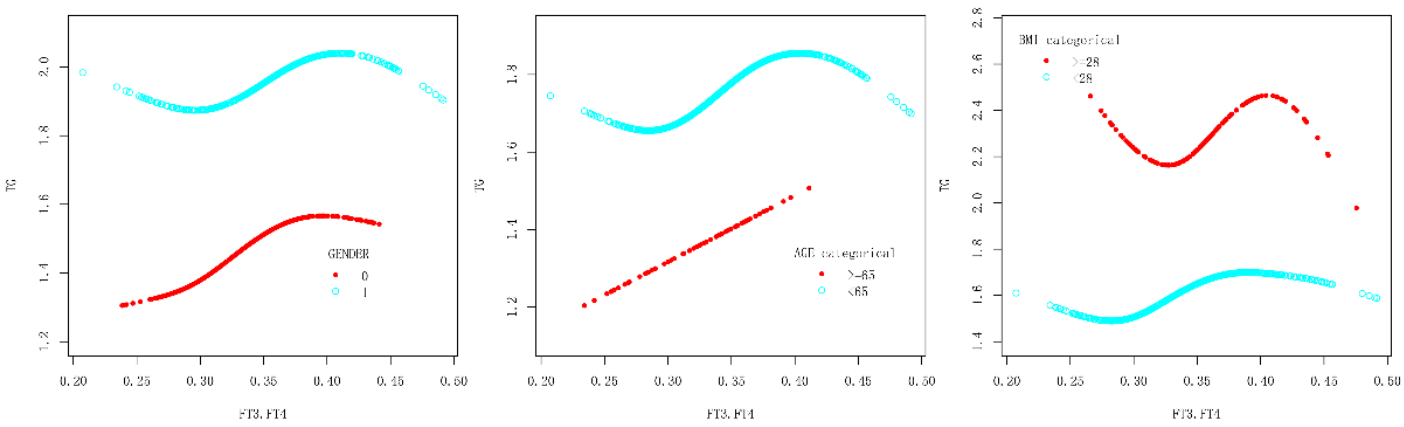


Figure 5

Smooth curve fitting of the association between the FT3/FT4 ratio and TG levels in subgroup analysis

Gender:0, female; 1, male; TG, total cholesterol; FT3/FT4, The ratio of free triiodothyronine to free thyroxine.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- data.xlsx