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Relationship of serum iron and thyroid hormone in obesity and after laparoscopic sleeve gastrectomy

Xingchun Wang[1†], Yaling Fang[1†], Xiu Huang[1†], Lei Du[1], Hui Ren[2], Chunjun Sheng[1], Peng Yang[1], Yueye Huang[1*] and Shen Qu[1*]

Abstract

Background Iron is an essential element for thyroid function. However, no study focuses on the association between iron and thyroid in individuals with obesity. Our research aimed to investigate the iron status in relation to baseline thyroid hormone levels and after laparoscopic sleeve gastrectomy (LSG).

Methods A total of 216 subjects with obesity were enrolled and divided into low and high iron groups depending on the median value. The association between iron and thyroid hormone was analyzed and compared before and after LSG at the 6-month follow-up in patients who underwent LSG.

Results 1) In all, Total Triiodothyronine (TT3) was significantly higher in high iron than low iron group ($P=0.008$). TT3 and thyroid stimulating hormone (TSH) were significantly higher in high iron than low iron group (1.92 ± 0.61 vs. 1.69 ± 0.28 nmol/l, $P=0.029$; 2.93 ± 1.66 vs. 1.88 ± 1.03 mU/l, $P=0.002$) in females while not in males (all $P>0.05$). 2) Iron was significantly positively associated with free triiodothyronine (FT3), free thyroxine (FT4), TT3 and TSH (all $P<0.05$). Adjusted for body mass index (BMI), total cholesterol (TCH), high-density lipoprotein cholesterol (HDL-C), fasting insulin (FINS) and homeostatic model assessment of insulin resistance (HOMA-IR), FT3, FT4 and TSH were still significantly associated with iron (all $P<0.05$). 3). Regression analysis showed that iron was significantly associated with FT4 ($\beta=0.338$, $P=0.038$). 3) LSG led to decreased FT3, FT3, TT3, total thyroxine (TT4) and TSH at 6 months follow-up (all $P<0.05$). Changed FT4 was significantly associated with changed iron ($r=0.520$, $P=0.009$). Subjects with iron decreased had more significant decreased TT4 than subjects without iron decreased ($P=0.021$).

Conclusion Serum iron overload is significantly associated with impaired thyroid function in subjects with obesity. LSG led to improved thyroid function which is associated with a change in iron.

Trial Registration NCT04548232 registration date is on October 9, 2022, registered in https://register.clinicaltrials.gov/.

Keywords Iron, Thyroid function, Obesity, Sleeve gastrectomy

[†]Xingchun Wang, Yaling Fang and Xiu Huang are co-first authors.

*Correspondence:
Yueye Huang
huangyueye19890603@163.com
Shen Qu
qushencn@hotmail.com
Full list of author information is available at the end of the article

Introduction

Obesity is an excessive accumulation of adipose tissue that may be related to the development of several comorbidities such as dyslipidemia, type 2 diabetes mellitus(T2DM), nonalcoholic fatty liver disease (NAFLD), and thyroid dysfunction [1, 2]. Obesity is significantly related to thyroid disorders such as hypothyroidism [3]. Complex and mutual relationships were found between the thyroid axis and adiposity as subclinical hypothyroidism may change basal metabolic rate with increasing body weight and obesity can also influence thyroid function [4]. It is reported that thyroid stimulating hormone (TSH) and free thyroxin (FT4) were increased in patients with obesity [5, 6], and elevated TSH was a kind of homeostatic compensation to thyroid hormone resistance(THR) [7, 8].

Obesity-related increased inflammatory signaling increases hepatic hepcidin expression which leads to disturbed iron homeostasis by increasing body iron stores while decreasing serum iron [9]. Increased iron stores are associated with T2DM [10], metabolic syndrome (MetS) [9] and central adiposity [11]. Iron metabolic process including absorption, storage, transport, and recycling is regulated in humans [12]. Iron accumulation in fatty liver is mainly due to inhibition of mobilization from hepatocytes and Kupffer cells [13]. Iron-induced oxidative stress has been reported to contribute to impaired glucose and lipid metabolism [14, 15]. Few articles investigate the association of serum iron levels with thyroid hormone in obesity.

Thyroid hormone (TH), active form, triiodothyronine (T3) which activation from thyroxine (T4), regulates metabolism and T3 exerts its actions through binding TH receptor(TR) [16]. Thyroid signaling defects in the syndromes of hormone resistance in obesity and related metabolic disorders [16]. Thyroid hormone action was altered in obesity as decreased TR A and B in adipose tissue and muscle in human subjects [17]. Normal thyroid function depends on many elements for both synthesis and action of thyroid hormone. Iodine is a critical element in thyroid hormone production while other elements such as iron are also involved in the regulation of thyroid hormone [18, 19]. Iron is essential for efficient iodine utilization and thyroid hormone synthesis [18, 20]. The first step in thyroid hormone synthesis is an iodine oxidation reaction catalyzed by the iron-containing enzyme, thyroid peroxidase (TPO), which is activated by TSH. Iron deficiency impairs TPO activity and thyroid metabolism, which may lead to decreased thyroid hormone synthesis [21]. Deficiency of iron effects over 30% of the population worldwide [18]. Iron-deficient women have lower levels of TSH, free triiodothyronine (FT3), and FT4 than the levels of controls [22, 23]. Autoimmune thyroid disease (AITD) patients are prone to iron deficiency [24]. However, no study has revealed the association between iron and thyroid hormones in obesity.

Laparoscopic sleeve gastrectomy (LSG) is the most effective method for the treatment of obesity. It not only led to improved glucose and lipid metabolism but also led to improved thyroid function [25, 26]. As to iron, LSG reduces iron levels while improving fat deposition in the liver [27]. However, the relationship between increased iron and subclinical hypothyroidism with slight thyroid hormone resistance in obesity and change after LSG is unclear.

Therefore, we inferred that the thyroid hormone regulates metabolic pathways which may interfere with iron status in subjects with obesity. We carried out a study to clarify the relationship between serum iron and thyroid hormones in obesity, and the changes in iron and thyroid function after LSG.

Material and methods

Subjects

Forty-nine normal-weight subjects and 216 subjects with obesity were enrolled from the Department of Endocrinology, Shanghai Tenth People's Hospital. Among patients with obesity, 24 subjects with obesity underwent LSG. The inclusion criteria were aged over 16 and less than 65 years old, BMI $\geq$ 37.5 kg/m^2, or BMI $\geq$ 32.5 kg/m^2 complicated with T2DM. The exclusion criteria were: 1) history of overt hypothyroidism or autoimmune thyroid disease; 2) taking medications that affect thyroid function and iron levels; 3) hypothalamus obesity and Cushing syndrome, etc., 4) Women who are pregnant or breastfeeding, 5) having contraindications of laparoscopic surgery, such as infection, adhesion and gastrointestinal diseases, 6) contraindications to surgery such as serious heart, liver, and kidney failure. Subjects were measured baseline and followed up 6 months after surgery for the measurement of body weight, thyroid function and iron levels. Subjects who underwent LSG did not take iron supplements or vitamain or any other intervention affecting iron status after surgery. Subjects enrolled were evaluated by an endocrinologist for thyroid function and iron levels and assessed for compliance with enrollment criteria.

The protocol for this study was approved by the Ethics Committee of the Shanghai Tenth People's Hospital. All the subjects provided and signed a written informed consent. The Clinical Trial Registration Number was NCT04548232.

Measurements

Age and gender were adopted and recorded. The height and body weight of subjects with light clothes and

without shoes was measured by the professional staff of the hospital. Body mass index (BMI) was calculated as formula: BMI = body weight(kg)/height(m)^2. Venous blood was collected after subjects fasting over for 8 h in the next morning. Laboratory indexes of glucose metabolism included fasting plasma glucose (FPG), fasting insulin (FINS) and glycated hemoglobin (HbA1c). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as FPG × FINS/22.5. Markers of lipid metabolism including triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were measured by Roche Cobas c701 fully automatic biochemical analyzer. Thyroid hormones including FT3, FT4, total thyroxine (TT3), total triiodothyronine (TT4), and TSH were tested by ADVIA Centaur XP Immunoassay System. Additionally, serum iron also tested among the included subjects by chemiluminescent immunoassay. All above anthropometric and laboratory markers were measured at baseline and follow-up 6 months after LSG. TSH were categorized as below normal levels(< 0.45uU/ml), normal levels(0.45 ~ 3uU/ml) and above normal(> 3uU/ml) [28].

Statistical analysis

Data was analyzed by SPSS (Version 22.0). Continuous data normally distributed was expressed as mean ± standard deviation(X ± SD). Continuous data non-normally distributed was expressed as medians (interquartile ranges, IQR). Categorical variables were presented as numbers or percentages. An independent sample t-test was adopted to compare normally distributed data and the Mann & Whitney U test was used to compare non-normally distributed data. Using Pearson's or Spearman's test investigate the correlations. Using paired two-tailed t-test to compare the data before and after surgery. A P-value less than 0.05 was considered statistically significant.

Results

Demographics and anthropometrics of subjects

In total, 49 normal-weight subjects (BMI 23.34 ± 1.17 kg/m^2) and 216 subjects with obesity (BMI 38.96 ± 6.09 kg/m^2) were enrolled in this study. The average age was 31.14 ± 11.37 years old in total. The average age of the subjects with obesity and the subjects with normal-weight had no difference(31.90 ± 11.50 vs. 30.20 ± 9.24 years old, $P = 0.675$). Serum iron was significantly higher in the obesity group than healthy control ($P < 0.01$) as in Fig. 1A. When patients with obesity were divided into groups based on the degree of obesity, it was observed that iron levels slightly increased with increasing BMI, but decreased when BMI exceeded 50 kg/m^2, as shown in Fig. 1B. Meanwhile, FT3, FT4, TT3, TT4, and TSH levels were significantly higher in the obesity group compared to the control group, as shown in Fig. 2A. Also, increased with BMI increasing when getting peak in group of BMI ranging from 45 ~ 50 kg/m^2 and decreased when BMI over 50 kg/m^2 as presented in Fig. 2B.

Comparison of thyroid hormone between different iron levels

To investigate the association between thyroid function and iron levels, thyroid function was compared across different degrees of iron levels in all subjects with

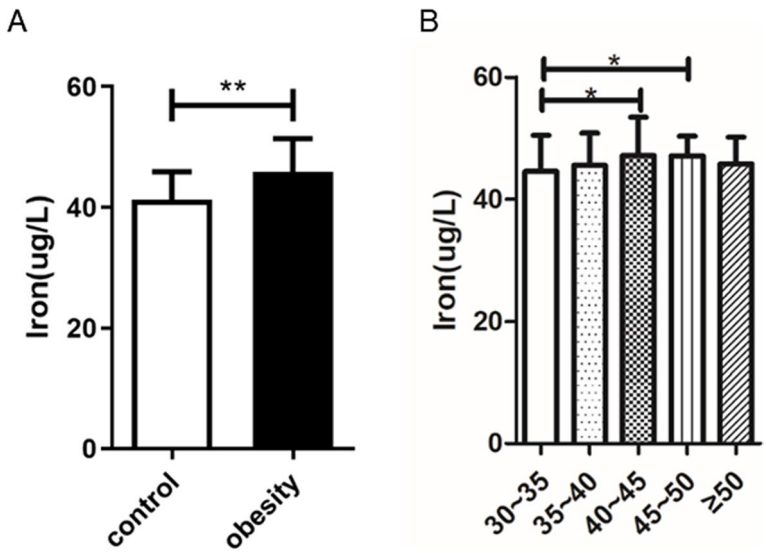

Fig. 1 Iron levels in different degree of body weight. *statistically significant ($P < 0.05$); **statistically significant ($P < 0.01$)

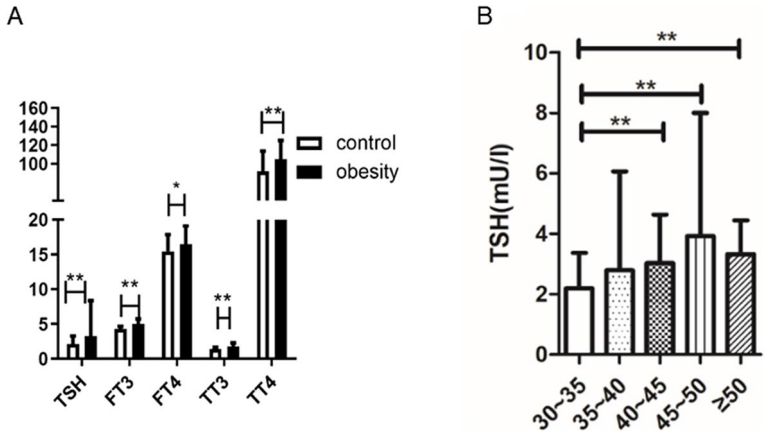

Fig. 2 Thyroid function in different degree of body weight. *statistically significant ($P<0.05$); **statistically significant ($P<0.01$). FT3, free triiodothyronine; FT4, free thyroxine; TT3, total thyroxine; TT4, total triiodothyronine; TSH, thyroid stimulating hormone

obesity. In all subjects with obesity, TT3 was significantly higher in high iron than low iron group (1.94 ± 0.62 vs. 1.74 ± 0.30 nmol/l, $P=0.008$) while there were no significant differences in FT3, FT4, TT4 and TSH (all $P>0.05$). As to females, the TT3 and TSH were significantly higher in high iron group than low iron group (1.92 ± 0.61 vs. 1.69 ± 0.28 nmol/l, $P=0.029$; 2.93 ± 1.66 vs. 1.88 ± 1.03 mU/l, $P=0.002$) while no significant differences were found in males (all $P>0.05$) as shown in Table 1.

To compare the difference between genders, males had higher iron and higher FT3 and FT4 levels than females as in Fig. 3 (all $P<0.05$). 27.4% of subjects with obesity had subclinical hypothyroidism. Additionally, subclinical hypothyroidism (SCH) group had higher iron levels than non-SCH group in females as in Fig. 4 ($P<0.05$). This may be due to females having lower BMI than males in our enrolled individuals with obesity (39.31 ± 5.5 vs. 42.41 ± 6.20 kg/m2, $P=0.001$). Therefore, it is inferred that the association existed in

Table 1 Demographics and anthropometrics of subjects

Variables	Female ($n=123$)		Male ($n=93$)	
	Low iron (< 45.54)	High iron (≥ 45.54)	Low iron (< 45.54)	High iron (≥ 45.54)
Age, years old	34.13 ± 16.03	30.95 ± 10.98	30.00 ± 10.25	31.46 ± 11.09
BMI, kg/m2	37.78 ± 5.42	39.61 ± 5.50	42.46 ± 6.71	42.35 ± 5.58
FPG, mmol/l	5.77 ± 0.99	5.80 ± 1.02	5.52 ± 0.88	5.50 ± 1.00
FINS, mU/L	23.72(15.38,34.53)	25.88(18.87,40.61)	25.28(19.15,40.31)	34.76(21.54,50.03)
HOMA-IR	6.74(4.82,8.01)	6.69(4.65,10.45)	6.40(4.39,9.83)	8.33(6.23,12.12)
HbA1C, %	6.15 ± 1.18	6.24 ± 1.08	6.62 ± 1.61	6.63 ± 1.72
TG, mmol/l	2.66 ± 0.97	2.71 ± 0.69	2.81 ± 0.57	2.77 ± 1.09
LDL-C, mmol/l	2.66 ± 0.97	2.71 ± 0.69	2.81 ± 0.57	2.77 ± 1.09
HDL-C, mmol/l	1.05 ± 0.16	1.05 ± 0.21	0.96 ± 1.19	1.08 ± 0.99
FT3, pmol/l	4.99 ± 0.61	5.02 ± 0.67	5.31 ± 0.74	5.42 ± 0.68
FT4, pmol/l	16.19 ± 3.44	16.07 ± 2.48	17.20 ± 2.31	17.57 ± 2.82
TT3, nmol/l	1.69 ± 0.28	1.92 ± 0.61*	1.76 ± 0.31	2.00 ± 0.67
TT4, nmol/l	104.46 ± 24.69	106.24 ± 23.01	102.64 ± 19.22	104.07 ± 14.96
TSH, mU/l	1.88 ± 1.03	2.93 ± 1.66**	3.31 ± 4.22	3.24 ± 3.73

Data are presented as means ± SD or medians (interquartile ranges, IQR)

* statistically significant (*$P<0.05$; ** $P<0.01$)

BMI Body mass index, *FPG* Fasting plasma glucose, *FINS* Fasting insulin, *HOMA-IR* Homeostasis model assessment of insulin resistance; TG, triglyceride, *LDL-C* Low-density lipoprotein, *HDL* High-density lipoprotein, *FT3* Free triiodothyronine, *FT4* Free thyroxin, *TT3* Total thyroxine, *TT4* Total triiodothyronine, *TSH* Thyroid stimulating hormone

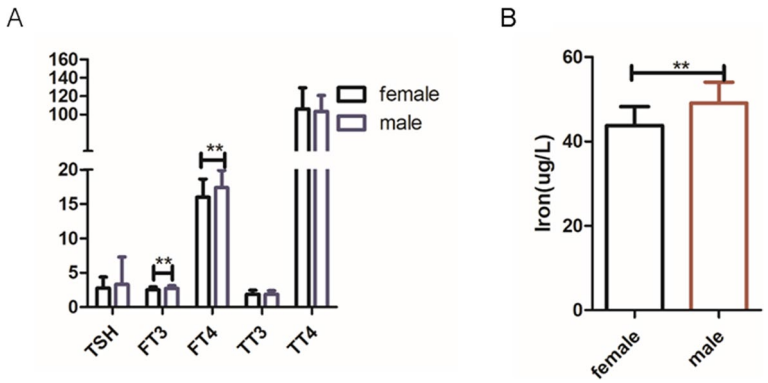

Fig. 3 Iron levels and thyroid function according to gender difference. **statistically significant ($P<0.01$). FT3, free triiodothyronine; FT4, free thyroxine; TT3, total thyroxine; TT4, total triiodothyronine; TSH, thyroid stimulating hormone

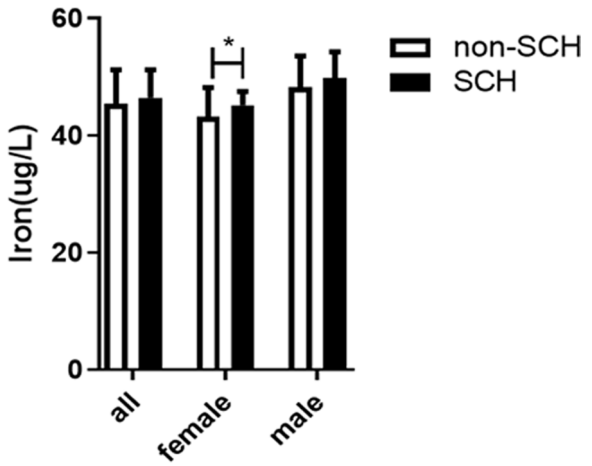

Fig. 4 Iron levels in subjects with or without SCH. *statistically significant ($P<0.05$). SCH, subclinical hypothyroidism

the compensatory phase while was not obvious in the decompensated period.

Association of iron and thyroid hormone

The relationship analysis showed that serum iron was significantly positively associated with BMI, FINS, HOMA-IR, TCH and negatively associated with HDL-C in enrolled subjects ($r=0.205$, $P=0.002$; $r=0.223$, $P=0.001$; $r=0.193$, $P=0.005$; $r=0.224$, $P=0.001$; $r=$-0.149, $P=0.029$) as in Table 2. As to the relationship between iron and thyroid hormone, it was found that iron was significantly positively associated with FT3, FT4, TT3, TSH, TSHI and GD ($r=0.232$, $P=0.001$; $r=0.201$, $P=0.003$; $r=0.190$, $P=0.006$; $r=0.140$, $P=0.044$; $r=0.293$, $P<0.001$; $r=0.244$, $P<0.001$). Serum iron was still significantly associated with FT3, FT4, TSH, TSHI and GD when adjusted for BMI, TCH, HDL-C, FINS and HOMA-IR ($r=0.178$, $P=0.013$; $r=0.199$, $P=0.006$; $r=0.142$, $P=0.043$; $r=0.258$, $P<0.001$; $r=0.188$, $P=0.009$). All the results were shown in Table 2.

Table 2 Relationship of iron and thyroid hormone

Variables	All subjects with obesity	Adjusted for BMI, TCH, HDL-C, FINS and HOMA-IR
	r(P)	r(P)
Age	NS	/
BMI	0.205(0.002)**	/
FPG	NS	/
FINS	0.223(0.001)**	/
HOMA-IR	0.193(0.005)**	/
HGB	NS	/
TG	NS	/
LDL-C	NS	/
HDL-C	-0.149(0.029)*	/
FT3	0.232(0.001)**	0.178(0.013)*
FT4	0.201(0.003)**	0.199(0.006)**
TT3	0.190(0.006)**	NS
TT4	NS	/
TSH	0.140(0.044)*	0.142(0.043)*

Statistically significant (*$P<0.05$; ** $P<0.01$)

NS No significant, *BMI* Body mass index, *FPG* Fasting plasma glucose, *FINS* Fasting insulin, *HOMA-IR* Homeostasis model assessment of insulin resistance, *TG* Triglyceride, *LDL-C* Low-density lipoprotein, *HDL* High-density lipoprotein, *FT3* Free triiodothyronine, *FT4* Free thyroxine, *TT3* Total thyroxine, *TT4* Total triiodothyronine, *TSH* Thyroid stimulating hormone

To better explore the association between iron and thyroid hormone, we further performed regression analysis and the results also showed that iron was also significantly associated with FT4 levels ($\beta=0.338$, $P=0.038$) as shown in Table 3.

Changed thyroid hormone after LSG associated with iron

LSG led to significantly decreased FT3, FT3, TT3, TT4 and TSH (all $P<0.05$) and unchanged iron levels($P>0.05$)

Table 3 Regression analysis of iron and metabolic indexes

Variables	β	95%CI	P value
FT3	0.041	-0.102–0.184	0.576
FT4	0.338	0.018–0.658	0.038*
TT3	0.961	-0.625–2.548	0.233
HDL-C	-0.135	-0.708–0.437	0.642

* statistically significant ($P<0.05$)

FT3 Free triiodothyronine, *FT4* Free thyroxine, *TT3* Total thyroxine, *HDL-C* High-density lipoprotein

Table 4 Change in thyroid hormone after LSG

Variables	Pre-surgery	6 M post-LSG	P value
Age, years old	28.71 ± 10.35	/	/
Male/female	13/10	/	/
Weight, kg	140.57 ± 20.57	104.97 ± 12.51	< 0.001**
BMI, kg/m2	46.15 ± 5.99	34.40 ± 3.73	< 0.001**
FT3, pmol/l	5.04 ± 0.97	4.65 ± 0.58	0.014*
FT4, pmol/l	17.00 ± 2.51	15.79 ± 2.70	0.020*
TT3, nmol/l	2.09 ± 0.71	1.64 ± 0.33	0.013*
TT4, nmol/l	111.43 ± 14.43	100.75 ± 17.15	0.003**
TSH, mU/l	3.91 ± 3.98	2.67 ± 1.79	0.047*
Iron, ug/l	47.22 ± 6.48	46.97 ± 6.50	0.850

Continuous data are presented as means ± SD

* statistically significant ($P<0.05$)

** statistically significant ($P<0.01$)

BMI Body mass index, *FPG* Fasting plasma glucose, *FINS* Fasting insulin, *FT3* Free triiodothyronine, *FT4* Free thyroxine, *TT3* Total thyroxine, *TT4* Total triiodothyronine, *TSH* Thyroid stimulating hormone

Table 5 Association of changed thyroid hormone and changed iron by LSG

		r	P
ΔFT3	-0.39 ± 0.73	0.111	0.607
ΔFT4	-1.21 ± 2.37	0.520	0.009**
ΔTT3	-0.44 ± 0.77	-0.054	0.808
ΔTT4	-11.04 ± 15.98	0.364	0.088
ΔTSH	-0.25 ± 6.43	0.125	0.479

** statistically significant ($P<0.01$)

FT3 Free triiodothyronine, *FT4* Free thyroxine, *TT3* Total thyroxine, *TT4* Total triiodothyronine, *TSH* Thyroid stimulating hormone

at a short time of 6 months follow up as in Table 4. Additionally, the changed FT4 was significantly associated with changed iron levels as in Table 5. The association of changed FT3, TT3, TT4, TSH and iron levels was not significant (all $P>0.05$). Additionally, when subjects were divided into iron decreased group and not decreased group, it was found TT4 was significantly more decreased in iron decreased group than not decreased group (-18.16 ± 15.05 vs. -3.27 ± 13.63 nmol/l, $P=0.021$) as in Fig. 5.

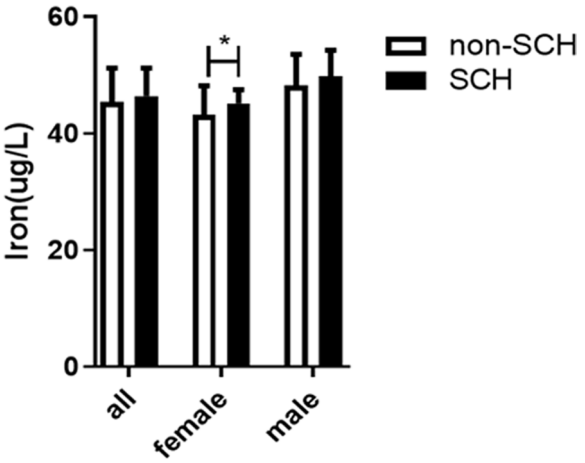

Fig. 5 Change in thyroid hormone in subjects with iron decreased or not. *statistically significant ($P<0.05$) FT3, free triiodothyronine; FT4, free thyroxine; TT3, total thyroxine; TT4, total triiodothyronine; TSH, thyroid stimulating hormone

Discussion

Obesity-related diseases such as MetS and body weight gain are positively associated with TSH [29]. It is reported that a moderate elevation of TSH concentrations, which is associated with T3 values in or slightly above the upper normal range, is frequently found in obesity [30]. The alterations of thyroid hormones in obesity may be an adaptation process with not fully understood underlying pathways. Weight loss is associated with a decrease in TSH and T3 [30]. Additionally, iron is involved in cell proliferation, differentiation and DNA synthesis [31]. As to its association with obesity, a previous study showed that obesity increases inflammatory signaling which is associated with increased hepatic hepcidin expression [32], leading to increased iron stores [9]. No study involves the association of iron and thyroid hormones in obesity. Our study investigated their association and found that iron is significantly associated with impaired thyroid function in subjects with obesity.

Thyroid hormone action may be influenced by tissue and cell-specific thyroid hormone transporters, corepressors, coactivators; TR isoform-specific action, etc. [16]. Several minerals including iron are essential for normal thyroid hormone metabolism [19]. Iron deficiency is associated with lower plasma thyroid hormone concentration which is a central regulatory defect while not peripheral alteration with lower levels of TSH, FT3 and FT4 [22]. The mean values of FT3 and FT4 were found to be lower in iron deficiency women than in the age-matched healthy control women and there was a positive

correlation between serum iron concentration and TSH ($r=0.85$, $p=0.01$), FT3 ($r=0.95$, $p=0.003$), and FT4 levels ($r=0.98$, $p=0.007$) [23]. The underlying mechanism of iron on thyroid hormone may involve thyroid hormone synthesis, storage and secretion [18]. A previous study showed that AITD (Hashimoto's thyroiditis (HT) and Graves' disease (GD)) patients are frequently iron-deficient due to autoimmune gastritis, which reduces iron absorption and coeliac disease which causes iron loss [24]. However, obesity is easily complicated by mild thyroid hormone resistance and relative thyroid insufficiency as our study found that 27.4% of the obese had subclinical hypothyroidism.

Additionally, iron overload is associated with metabolic disorders, including hypothyroidism characterized by increased TSH levels. Increased iron stores have been found to predict the development of T2DM while iron depletion was protective Iron-induced damage might also modulate the development of chronic diabetes complications [10]. As to the enrolled subjects with obesity in our study, iron levels slightly increased with BMI increasing within 50 kg/m2, and iron levels slightly decreased when BMI was over 50 kg/m2. Additionally, iron levels increased with BMI, peaking in the group with BMI levels ranging from 45 to 50 kg/m^2, and then decreased when BMI exceeded 50 kg/m^2. Few studies focus on the relationship between thyroid function and iron in subjects with obesity. We investigate whether iron levels in individuals with obesity affect thyroid function. The results of our study showed that TT3 was significantly higher in high iron group than low iron group. In females, the TT3 and TSH were significantly higher in high iron group than low iron group while no significant difference was found in males. This may be due to females having lower BMI than males in our enrolled individuals with obesity which leads to significantly higher iron and FT3 and FT4 in males than females. It is inferred that the association may exist in the compensatory phase while was not obvious in the decompensated period. Further association analysis found that iron was significantly positively associated with FT3, FT4, TT3 and TSH, and iron was still significantly associated with FT3, FT4 and TSH when adjusted for BMI, TCH, HDL-C, FINS and HOMA-IR. Also, the subjects with SCH had higher iron levels than subjects without SCH group. We inferred that the possible mechanism behind the observed associations between iron levels and thyroid function may be due to thyroid hormone alterations and hepatic iron accumulation are strongly related to metabolic factors, such as insulin resistance and hepatic fat accumulation in obesity [33, 34]. Overall, iron may play a role in thyroid function in subjects that need further study to explore the underlying mechanism.

LSG, a restrictive bariatric surgery technique, increased gastric emptying and intestinal transit, and activation of hormonal mechanisms such as increased GLP-1 hormone and decreased ghrelin [35], is one of the most effective methods for treating obesity by decreasing body weight, improving glucose-lipid metabolism as well as improving thyroid function [36]. One study included 64 adolescents (mean age = 11.2 ± 2.3 years) who underwent laparoscopic SG, and the results showed that thyroid hormones and nutritional biomarkers remained unchanged from baseline after 12 months follow-up [37]. However, other studies showed that TSH was significantly decreased at 3, 6, and 12 months after LSG(3 months: from 4.43 ± 2.70 to 2.63 ± 1.46 mU/l, $P<0.001$; 6 months: from 4.43 ± 2.70 to 3.84 ± 2.34 mU/l, $P=0.041$; 12 months: from 4.43 ± 2.70 to 2.85 ± 1.68 mU/l, $P=0.024$) [38]. LSG proved to improve thyroid function in hypothyroid obese patients with 11 ± 9 0.73 months follow-up [39]. Our study also identified that LSG may lead to improved thyroid function with decreased TSH, FT3, FT3, TT3 and TT4. This means the central thyroid hormone resistance may improve with LSG intervention. Additionally, as to the influence of LSG on iron, a previous study found that long-term proton pump inhibitors in LSG patients may increase the severity of iron deficiency after surgery [40]. The incidence of iron deficiency increased after LSG with 5 years of follow-up [41]. However, a one-year follow-up showed that the development of iron deficiency was insignificant after LSG [42]. Our study also found unchanged iron levels after LSG with a short time follow-up of 6 months. Moreover, we found that the changed FT4 was significantly associated with changed iron levels after LSG and the iron decreased group had more decreased TT4 than iron not decreased group. Therefore, it is inferred that the crosstalk between iron and thyroid function after LSG, and iron is closely related to thyroid function in patients with obesity and after LSG.

There were some limitations of our study. Firstly, the sample of this study is relatively small. The study groups are imbalanced, with a relatively small number of normal-weight subjects compared to the obese group, and a very small subset undergoing LSG, which is the prime focus group. This imbalance could skew the results, particularly in subgroup analyses. The relationships between thyroid hormone and iron are complex and sex-specific and need further mechanism studies. Secondly, thyroid-associated antibodies such as TPOAb and TgAb were not measured and analyzed in this study. Therefore, we may expand sample and mechanism research in vitro and animal studies are needed in the future.

In conclusion, iron levels affect thyroid function in subjects with obesity. Higher iron may impair thyroid

function. The decreased iron levels after LSG was associated with improvement of thyroid function.

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Authors' contribution
Conception or design: XCW、YYH and SQ. Acquisition, analysis, or interpretation of data: YLF、XH and HR Drafting the work or revising: CJS, PY and LD.

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Data availability
Our data cannot be shared publicly to protect the privacy of study participants.

Declarations

Ethics approval and consent to participate
The protocol for this study was approved by the Ethics Committee of the Shanghai Tenth People's Hospital. All the subjects provided and signed a written informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Endocrinology and Metabolism, Shanghai Tenth People's Hospital, School of Medicine, Tongji University, Shanghai 200072, China. [2]Central Laboratory, Shanghai Tenth People's Hospital, Tongji University, Shanghai 200072, China.

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