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ORIGINAL

Serum free thyroxine levels are associated with the efficacy of weight reduction therapy in obese female patients

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Abstract. Thyroid function is strongly associated with obesity. The aim of this study is to investigate whether serum free thyroxine (FT4) and/or thyrotropin (TSH) levels are associated with the efficacy of weight reduction therapy in obese patients. We enrolled a total of 283 obese patients and cross-sectionally investigated the association of serum FT4 and/or TSH levels with metabolic features. Furthermore, in 97 obese patients who received 6-month weight reduction therapy, we assessed the relationship of serum FT4 and/or TSH levels to the efficacy of weight reduction therapy. Neither baseline serum FT4 nor TSH levels showed any correlations with body weight (BW) and body mass index (BMI) in these obese patients. However, in 57 obese female patients who underwent weight reduction therapy for six months, serum FT4 levels prior to the therapy was negatively correlated with the degrees of reduction of BW ($r = -0.354$, $p = 0.007$) and BMI ($r = -0.373$, $p = 0.004$). The correlation between baseline serum FT4 levels with the efficacy of weight reduction therapy was not observed in obese male or postmenopausal female patients. This study demonstrates that baseline serum FT4 levels are associated with weight reduction in obese female premenopausal patients. Therefore, baseline FT4 levels can be used as a clinical, noninvasive, hormonal predictor of weight reduction efficacy in obese patients.

Key words: Thyroid function, Free thyroxine, TSH, Obesity, Weight reduction therapy

OBESITY leads to several metabolic diseases, such as type 2 diabetes, hypertension, and dyslipidemia. The incidence of obesity is increasing, especially in developed countries. Thus, obesity is currently a major global threat to health [1].

Weight reduction therapy is the first step in the management of obesity, followed by a decrease of obesity-related metabolic sequelae and cardiovascular disease (CVD) complications [2-4]. However, to date, no useful method of predicting outcomes of weight reduction therapy in obese patients has been established.

It is well known that thyroid hormone is related to systemic energy expenditure, thereby influencing body weight (BW) [5, 6]. Recently, there have been an increasing number of reports regarding the relationship between thyroid function and BW [7-9]. For instance, it was reported that serum thyrotropin (TSH) levels are positively correlated to body mass index (BMI), which is calculated as weight in kilograms divided by the square of the height in meters as an index of obesity, and that serum free thyroxine (FT4) levels are negatively correlated to BMI [6, 10]. Moreover, higher TSH levels are found in severely obese subjects compared with those in nonobese ones [11].

As mentioned above, although there have been sev-

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eral studies on cross-sectional and longitudinal associations among BW, BMI, and thyroid function, no prospective studies regarding the association between thyroid function and weight changes through lifestyle intervention in obese patients have been reported. Against this background, observation of the association of thyroid function with the efficacy of weight reduction therapy may provide important evidence influencing the treatment for obesity.

In this study, we focused on the clinical significance of baseline thyroid function in weight reduction therapy. Therefore, the present study was performed as a prospective observational study in order to examine the relationship of the baseline thyroid function with weight loss during weight reduction therapy in obese Japanese patients.

Methods

Subjects

A total of 283 obese Japanese patients (Table 1) were consecutively enrolled in the outpatient clinic at the National Hospital Organization Kyoto Medical Center during the period from 2010 to 2014. We defined and recruited obese subjects with a BMI of $\geq$ 25 kg/m^2 as previously reported in Japan [12].

The exclusion criteria were a previous history of thyroid disorders including overt hypothyroidism (TSH$\geq$10μIU/mL); renal disease; severe liver dysfunction; or secondary obesity due to endocrine disorders, such as Cushing syndrome, polycystic ovary syndrome, and acromegaly. None of the patients had received anti-obesity drugs or had recently been treated with glucocorticoids, estrogen, or L-thyroxine therapy. This study protocol was approved by the ethics committee for human research at Kyoto Medical Center (#15-014) and at Tokyo Medical and Dental University (#2079). All participants provided written informed consent.

Data collection and laboratory measurements

The systolic and diastolic blood pressure (SBP and DBP) levels were measured after a 15-minute rest in the sitting position twice with an automatic electronic sphygmomanometer (BP-103i II; Nippon Colin, Komaki, Japan). Blood was taken in the morning after an overnight fast and used to determine fasting plasma glucose (FPG), glycosylated hemoglobin A1c (HbA1c), immunoreactive insulin (IRI), low-density-lipoprotein cholesterol (LDL-C), high-density-lipoprotein cholesterol (HDL-C), triglycerides (TG), FT4 and TSH according to standard procedures [4]. The value for HbA1c is estimated as a National Glycohemoglobin Standardization Program (NGSP) equivalent value (%). Serum levels of high-sensitivity C-reactive protein (hs-CRP), adiponectin, and leptin were also determined, as previously described [4, 13].

Weight reduction therapy

Ninety-seven out of 283 obese patients (40 men and 57 women, Supplemental Table 1) underwent weight reduction therapy involving lifestyle modification for 6 months and they were instructed to maintain the same

Table 1 Baseline clinical and biochemical characteristics of the study cohort

	Total	Male	Female	*p*
n	283	103	180	
Age (years)	49.1 ± 0.9	49.4 ± 1.4	49.0 ± 1.1	0.807
BW (kg)	87.0 ± 1.2	95.8 ± 2.1	81.9 ± 1.4	<0.001
BMI (kg/m^2)	33 ± 0.4	33 ± 0.6	33 ± 0.5	0.892
Waist (cm)	105 ± 0.9	108 ± 1.4	103 ± 1.1	0.011
FBS (mg/dL)	110 ± 1.9	116 ± 3.5	107 ± 2.1	0.039
HbA1c (NGSP) (%)	6.1 ± 0.1	6.2 ± 0.1	6.1 ± 0.1	0.407
IRI (μU/mL)	28.1 ± 2.3	40.5 ± 5.4	21.0 ± 1.8	<0.001
HOMA-R	8.6 ± 0.9	13.0 ± 2.2	6.0 ± 0.6	0.002
FT4 (ng/dL)	1.16 ± 0.01	1.20 ± 0.02	1.15 ± 0.01	0.025
TSH (μIU/mL)	2.15 ± 0.09	2.02 ± 0.14	2.22 ± 0.11	0.275

Data are expressed as mean ± SE. *p*-value: *t*-testing: Male *vs* Female

levels of energy intake and physical activity for the entire period, as recommended by the Japan Atherosclerosis Society's Guidelines for the Diagnosis and Treatment of Atherosclerotic Cardiovascular Diseases, as previously reported [4, 14, 15]. Before and after the therapy, we measured anthropometric and metabolic parameters for each patient. For the assessment of weight reduction, we analyzed the change in weight (post-intervention BW – baseline BW) during the therapy [16]. We defined the patients who reduced their BW by more than 5% from their baseline BW as being successful at weight reduction for 6 months, as reported previously [17]. We measured baseline FT4 and TSH in the 97 obese patients who enrolled, in order to analyze the association of baseline FT4 and TSH with the change in weight during lifestyle intervention. We also measured serum FT4 and FT3 (triiodo-thyronine) before and after the reduction therapy in some patients.

Statistical analysis

Data are presented as the mean ± SE, and $p < 0.05$ was considered statistically significant. Data for all quantitative variables were normally distributed. A two-tailed, unpaired *t*-test was used to assess differences between the two groups before and after treatment for continuous and categorical variables. Pearson's correlation coefficients were used to investigate the correlations between the baseline thyroid function and baseline metabolic parameter values, and the correlations between the change in weight and the baseline thyroid function and baseline metabolic parameter values. All statistical analyses were performed using SPSS 12.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Baseline clinical characteristics of obese patients

Table 1 summarizes the characteristics of the study cohort of 283 obese patients. There was no significant difference in the baseline serum TSH levels between the male and the female patients. However, BW, Waist, FBS, IRI, HOMA-R and FT4 levels in the male patients were significantly higher than those in the female patients.

Baseline correlation among body weight, BMI, and thyroid function

Neither BW nor BMI showed significant correlations with serum baseline FT4 and TSH levels in the patients irrespective of sex (Table 2).

Effect of body weight reduction on metabolic parameters in obese patients

Ninety-seven out of 283 obese patients had received weight reduction therapy for 6 months, according to the protocol as previously reported [4, 14]. In those, BW, BMI, Waist, SBP, DBP, FBS, HbA1c (NGSP), IRI, HOMA-R, AST, ALT, and eGFR were significantly decreased after the 6-month weight reduction therapy (Supplemental Table 1). In addition, γ-GTP, TC, LDL-C, BUN, and hs-CRP in the male patients and TG, HDL-C, Cre, and serum leptin levels in the female patients were significantly decreased after the 6-month weight reduction therapy (Supplemental Table 1). However, serum adiponectin levels were not significantly different after the therapy both in the male and the female patients (Supplemental Table 1).

Table 2 Correlation of baseline clinical and metabolic parameters with baseline serum FT4 and TSH levels

	Male				Female			
	FT4		TSH		FT4		TSH	
	r	*p*	r	*p*	r	*p*	r	*p*
Age (years)	-0.212	0.032	-0.014	0.891	-0.119	0.111	-0.042	0.575
BW (kg)	0.041	0.683	0.146	0.140	0.109	0.147	0.043	0.563
BMI (kg/m^2)	0.072	0.473	0.161	0.104	0.087	0.248	0.097	0.199
Waist (cm)	0.005	0.961	0.149	0.135	0.107	0.158	-0.004	0.953
FBS (mg/dL)	-0.102	0.306	-0.115	0.247	0.094	0.207	0.000	1.000
HbA1c (NGSP) (%)	-0.122	0.219	-0.099	0.318	0.114	0.129	0.005	0.946
IRI (μU/mL)	-0.108	0.276	0.058	0.563	0.078	0.297	0.048	0.525
HOMA-R	-0.100	0.316	0.017	0.866	0.100	0.182	0.025	0.736

Serum FT4 and FT3 levels before and after the 6-month weight reduction therapy

We measured serum FT4 and FT3 levels in some patients who underwent the 6-month weight reduction therapy before and after the tharapy. Serum FT4 levels were not significantly different before and after the therapy both in the male and the female patients (Table 3A). On the other hand, serum FT3 levels were significantly different in the female but not in the male patients before and after the therapy (Table 3B).

Correlations of changes of body weight and BMI with baseline serum FT4 levels

The changes in BW, BMI and Waist after the 6-month weight reduction therapy showed significant negative correlations with baseline serum FT4 levels in the female, but not in the male patients (Table 4). We categorized the fifty-seven female patients into 6 groups according to the baseline serum FT4 levels with 0.1pg/mL increments and the trend test by analysis of variance (ANOVA) revealed that the changes in BW and BMI were significantly correlated with the baseline serum FT4 levels among the groups, which validated the correlation (Supplemental Table 2).

Furthermore, in the female patients who were successful at achieving weight reduction, baseline serum FT4 levels but not TSH levels were significantly correlated to the changes in BW, BMI, and Waist (Table 5).

On the other hand, the baseline FT3 levels were not correlated with the changes in BW, BMI and Waist after the 6-month weight reduction therapy both in the male and the female patients (Supplemental Table 3).

Since it is well known that menopause is associated the thyroid function in women [18], we categorized the fifty-seven female patients into two groups, one is premenopausal (n=29) and the other one is postmenopausal (n=28). Interestingly, significant negative correlations of the changes in BW, BMI and Waist after the 6-month weight reduction therapy with baseline serum FT4 levels were found in the premenopausal, but not in the postmenopausal patients, suggesting that female sex hormone might be related to the correlation (Table 6). In the female patients who were successful at achieving weight reduction, the changes in BW, BMI and Waist after the 6-month weight reduction therapy showed significant negative correlations with baseline serum FT4 levels only in the premenopausal patients (Supplemental Table 4).

Table 3 Serum FT4 (ng/dL) (A) and FT3 (pg/mL) (B) levels in some patients who underwent the 6-month weight reduction therapy

A	Baseline	After 6 months	*p*
Total (n=41)	1.30 ± 0.03	1.33 ± 0.04	0.503
Male (n=14)	1.29 ± 0.05	1.38 ± 0.08	0.334
Female (n=27)	1.31 ± 0.04	1.30 ± 0.04	0.638
B	**Baseline**	**After 6 months**	***p***
Total (n=43)	3.32 ± 0.07	3.25 ± 0.08	0.354
Male (n=14)	3.43 ± 0.14	3.54 ± 0.21	0.557
Female (n=29)	3.27 ± 0.08	3.10 ± 0.06	0.036

Data are expressed as mean ± SE. *p*-value: *t*-testing: Baseline *vs* After 6 months

Table 4 Correlations of changes of clinical and metabolic parameters with baseline serum FT4 and TSH levels after the 6-month weight reduction therapy

	Male (n=40)				Female (n=57)			
	FT4		TSH		FT4		TSH	
	r	*p*	r	*p*	r	*p*	r	*p*
ΔBW	0.104	0.524	-0.131	0.421	-0.354	0.007	0.139	0.304
ΔBMI	0.082	0.617	-0.141	0.386	-0.373	0.004	0.163	0.227
ΔWaist	0.143	0.379	-0.071	0.664	-0.265	0.046	0.100	0.459
ΔFBS	0.014	0.932	0.008	0.961	0.092	0.496	0.017	0.901
ΔHbA1c (NGSP)	0.129	0.427	0.042	0.797	-0.032	0.813	0.138	0.307
ΔIRI	-0.020	0.913	-0.165	0.350	-0.304	0.033	-0.230	0.112
ΔHOMA-R	-0.043	0.811	-0.165	0.352	-0.288	0.045	-0.158	0.280

Table 5 Correlations of changes of clinical and metabolic parameters with baseline serum FT4 and TSH levels In those who reduced their BW by more than 5% from their baseline BW after the 6-month weight reduction therapy

	Male (n=23)				Female (n=36)			
	FT4		TSH		FT4		TSH	
	r	*p*	r	*p*	r	*p*	r	*p*
ΔBW	0.210	0.337	0.176	0.422	-0.501	0.002	0.096	0.579
ΔBMI	0.177	0.419	0.186	0.396	-0.546	0.002	0.099	0.565
ΔWaist	0.013	0.954	0.013	0.954	-0.378	0.023	0.168	0.328
ΔFBS	0.211	0.335	0.118	0.590	0.138	0.421	-0.030	0.864
ΔHbA1c (NGSP)	0.124	0.572	0.131	0.550	-0.007	0.966	0.094	0.587
ΔIRI	0.105	0.670	-0.127	0.606	-0.365	0.037	-0.232	0.194
ΔHOMA-R	0.146	0.551	-0.125	0.610	-0.349	0.047	-0.154	0.392

Table 6 Correlations of changes of clinical and metabolic parameters with baseline serum FT4 and TSH levels in pre- and post-menopausal females after the 6-month weight reduction therapy

	Premenopausal (n=29)				Postmenopausal (n=28)			
	FT4		TSH		FT4		TSH	
	r	*p*	r	*p*	r	*p*	r	*p*
ΔBW	-0.434	0.019	0.141	0.467	-0.133	0.501	0.210	0.283
ΔBMI	-0.458	0.012	0.139	0.472	-0.160	0.415	0.261	0.179
ΔWt	-0.510	0.005	-0.105	0.588	-0.039	0.845	0.290	0.134
ΔFBS	0.355	0.059	0.126	0.516	-0.300	0.121	-0.140	0.476
ΔHbA1c	0.037	0.848	0.146	0.449	-0.219	0.264	0.111	0.575
ΔIRI	-0.223	0.307	-0.377	0.076	-0.354	0.076	0.034	0.868
ΔHOMA-R	-0.158	0.471	-0.228	0.295	-0.403	0.041	-0.018	0.932

Correlations of changes of metabolic parameters with thyroid function

The changes in IRI and HOMA-R during the therapy showed significant negative correlations to baseline serum FT4 levels in the female patients, but not in the male patients (Table 4). Furthermore, in those who were successful at weight reduction, baseline serum FT4 levels were significantly correlated to the changes in IRI and HOMA-R (Table 5).

In addition, the changes in metabolic parameters examined in the current study such as, HbA1c, IRI and HOMA-R showed no correlations to baseline serum FT3 levels both in the male and the female patients. FBS showed a significant positive correlation to baseline serum FT3 levels in the female but not in the male patients (Supplemental Table 3).

Discussion

We demonstrated for the first time that baseline serum FT4 levels are associated with the efficacy of weight reduction therapy in obese female patients. In the current study, we performed weight reduction therapy for 6 months for 97 obese patients, as previously reported [19]. Numerous anthropometric and metabolic parameters were improved after the 6-month weight reduction therapy, confirming that our intervention for weight reduction was successful (Supplemental Table 1). Moreover, when focusing on the obese patients who were successful at weight reduction, only in the female patients were serum FT4 levels in prior to the therapy significantly correlated to the changes in body weight and BMI.

It is of note that only in the female patients, baseline

serum FT4 levels were significantly correlated to the outcome of the weight reduction therapy. The trend test analysis for groups according to serum FT4 levels with 0.1 pg/mL increments (Supplemental Table 2) revealed that baseline serum FT4 levels within reference range were significantly correlated to the changes in BW and BMI.

Baseline serum leptin levels in female obese patients are higher than those in the male patients. Furthermore, serum leptin levels are significantly decreased only in female obese patients after the 6-month weight reduction therapy and serum adiponectin levels, which reflects the mass of visceral fat were not significantly different after the therapy both in the male and the female patients (Supplemental Table 1). Since serum leptin levels are correlated with the percentage of body fat, especially subcutaneous fat [20], these data suggest that more adiposity in the female patients compared to the male patients and that the body weight reduction after the therapy could be due to the reduction of subcutaneous fat in the female patients. On the other hand, since leptin leads to an increase in type 1 deiodinase (D1) activity, which results in the conversion of T4 to T3 [21], we speculate that in the female patients, D1 would be more activated to convert T4 to T3, thereby promoting the energy expenditure. In fact, since serum FT3 levels were significantly decreased only in the female patients, we speculated that during the 6-month weight reduction therapy, the reduction of adipose tissue leads a decrease in serum leptin levels followed by a decrease in D1 activity, which might result in a decrease of serum FT3 levels.

As it is known that in humans, subtle changes in deiodinase enzyme activity might affect energy metabolism and as such BMI or risk for obesity, D1 polymorphisms between the male and the female patients should be taken into the consideration. However, so far, no effect of D1 polymorphisms on BMI was found in a cohort of healthy elderly men [22, 23].

In addition, since baseline serum FT4 levels were significantly correlated to the outcome of the weight reduction therapy only in the premenopausal female patients, a female sex hormone could be another factor, which affects the difference between the male and female patients.

In our study, baseline serum FT4 and TSH levels in subjects prior to the weight reduction therapy were not correlated to baseline BW and BMI, which is somewhat inconsistent with previous studies [8, 24]. However, the reported findings on the influences of the biological variability of thyroid hormones on weight are still contradictory [6, 8, 11, 24, 25].

Additionally, in the present study, the changes in IRI and HOMA-R during the therapy showed significant negative correlations to baseline serum FT4 levels in obese female patients, suggesting that elevated serum FT4 levels prior to the therapy would predict the improvement of insulin resistance upon the successful weight reduction therapy.

Some limitations of this study merit consideration. Firstly, the follow-up used in the weight reduction program was relatively short, so it is necessary to conduct a long-term prospective cohort study with a larger sample size in order to clarify the long-term effectiveness of the baseline serum FT4 levels to predict the efficacy of the weight reduction therapy. Secondly, in the current study, the fat composition such as visceral and subcutaneous fat was not evaluated before and after the weight reduction therapy. To elucidate the sex difference in the correlation of the efficacy of the weight reduction therapy with baseline serum FT4 levels, the analysis of the fat composition should be performed in further study.

In conclusion, the present study suggested that baseline serum FT4 levels, even though they are within the reference range, would predict the outcome of the weight reduction therapy in obese female patients.

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Disclosure

The authors declare that there is no conflict of interest associated with this manuscript.

Supplemental Table1 Effect of body weight reduction on metabolic parameters in obese patients after the 6-month weight reduction therapy

	Male		Female	
	Baseline	After 6 months	Baseline	After 6 months
n	40		57	
Age (years)	50.3 ± 2.2		50.0 ± 1.7	
BW (kg)	101 ± 3.7	95 ± 3.4**	81 ± 2.3	76 ± 2.1**
BMI (kg/m^2)	35 ± 1.2	32 ± 1.1**	33 ± 0.9	31 ± 0.9**
Waist (cm)	110 ± 2.4	106 ± 2.3**	104 ± 2.1	98 ± 2.0**
SBP (mmHg)	147 ± 3.0	133 ± 2.3**	145 ± 2.8	136 ± 2.4**
DBP (mmHg)	90 ± 1.9	82 ± 1.7**	86 ± 1.7	80 ± 1.5**
FBS (mg/dL)	120 ± 6.3	103 ± 3.7**	113 ± 4.4	102 ± 2.8**
HbA1c (NGSP) (%)	6.3 ± 0.2	5.8 ± 0.1**	6.5 ± 0.2	5.9 ± 0.1**
IRI (μU/mL)	36.5 ± 8.5	16.2 ± 2.4*	21.7 ± 3.2	14.2 ± 1.8*
HOMA-R	12.0 ± 3.0	4.2 ± 0.7*	6.6 ± 1.1	3.8 ± 0.6**
AST (IU/L)	38.1 ± 3.6	30.2 ± 2.5**	30.1 ± 2.7	21.6 ± 1.0**
ALT (IU/L)	60.3 ± 7.6	41.8 ± 5.4**	36.2 ± 3.6	21.3 ± 1.2**
γ-GTP (IU/L)	75.7 ± 8.2	59.6 ± 6.8*	45.0 ± 8.8	30.7 ± 4.3
TC (mg/dL)	191 ± 5.7	178 ± 4.7*	202 ± 4.9	196 ± 3.7
TG (mg/dL)	173 ± 12.7	145 ± 17.2	152 ± 10.0	120 ± 8.0**
HDL-C (mg/dL)	49 ± 1.5	50 ± 1.5	57 ± 1.7	60 ± 1.6*
LDL-C (mg/dL)	119 ± 5.8	108 ± 3.9*	124 ± 3.5	119 ± 3.1
BUN (mg/dL)	14.2 ± 0.5	16.0 ± 0.9*	13.1 ± 0.5	13.2 ± 0.5
Cre (mg/dL)	0.83 ± 0.03	1.13 ± 0.24	0.59 ± 0.02	0.61 ± 0.01*
eGFR	83 ± 3.7	75 ± 3.5**	88 ± 3.1	83 ± 2.6*
Leptin (ng/mL)	11.7 ± 1.7	11.3 ± 2.2	22.7 ± 2.2	17.5 ± 1.7*
Adiponectin (μg/mL)	7.4 ± 1.0	6.0 ± 0.4	7.7 ± 0.7	7.7 ± 0.5
hs-CRP (μg/mL)	2.06 ± 0.41	1.91 ± 0.48*	2.36 ± 0.42	2.11 ± 0.55

** p<0.010, * p<0.05 by t-testing. eGFR, mL /min/1.73 m^2; Data are expressed as mean ± SE.

Supplemental Table 2 Changes in BW and BMI according to baseline serum FT4 levels with 0.1pg/mL increments in the female patients

FT4 (pg/mL)	n	ΔBW	ΔBMI
≤ 1.0	12	-3.2 ± 1.2	-1.2 ± 0.5
1.1	14	-5.5 ± 1.0	-2.1 ± 0.4
1.2	10	-5.7 ± 2.0	-2.2 ± 0.7
1.3	8	-5.0 ± 1.4	-2.0 ± 0.6
1.4	10	-5.9 ± 2.4	-2.3 ± 0.9
1.5 ≤	3	-13.2 ± 3.8	-5.3 ± 1.6
Total	57	p=0.043	p=0.030

Data are expressed as mean ± SE. (trend test by ANOVA)

Supplemental Table 3 Correlations of changes of clinical and metabolic parameters with baseline serum FT3 after the 6-month weight reduction therapy

	Male (n=14)		Female (n=29)	
	FT3		FT3	
	r	p	r	p
ΔBW	-0.067	0.819	0.107	0.579
ΔBMI	-0.075	0.799	0.082	0.673
ΔWaist	0.080	0.785	0.069	0.721
ΔFBS	0.187	0.523	0.480	0.008
ΔHbA1c	0.011	0.971	0.242	0.206
ΔIRI	-0.195	0.523	0.174	0.396
ΔHOMA-R	-0.187	0.542	0.363	0.068

Supplemental Table 4 Correlations of changes of clinical and metabolic parameters with baseline serum FT4 and TSH levels in pre- and post-menopausal females those who reduced their BW by more than 5% from their baseline BW after the 6-month weight reduction therapy

	Premenopausal (n=17)				Postmenopausal (n=19)			
	FT4		TSH		FT4		TSH	
	r	p	r	p	r	p	r	p
ΔBW	-0.537	0.026	0.105	0.688	-0.195	0.425	0.208	0.392
ΔBMI	-0.587	0.013	0.099	0.705	-0.243	0.317	0.225	0.355
ΔWt	-0.564	0.018	-0.079	0.762	-0.234	0.335	0.438	0.061
ΔFBS	0.517	0.034	0.117	0.656	-0.350	0.142	-0.189	0.440
ΔHbA1c	0.134	0.608	0.168	0.518	-0.280	0.245	-0.028	0.910
ΔIRI	-0.362	0.204	-0.429	0.126	-0.377	0.112	0.157	0.520
ΔHOMA-R	-0.272	0.347	-0.276	0.339	-0.438	0.061	0.061	0.805

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