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Changes in liver function, fluctuations in blood glucose, insulin secretion and gender differences in patients with hyperthyroidism after treatment with propranolol hydrochloride tablets coalition with methimazole tablets

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Abstract: To investigate liver function changes, blood glucose fluctuation, insulin secretion, and gender differences in hyperthyroidism patients before and after propranolol with methimazole. Clinical data 110 hyperthyroidism patients admitted to Zhangzhou Affiliated Hospital of Fujian Medical University from February 2023 to February 2024 were retrospectively analyzed. They were categorized into the methimazole group (methimazole, n = 55) and the coalition medication group (Methimazole with propranolol, n = 55). The therapeutic effects of both groups were observed. Pre- and post-treatment liver function dynamic blood glucose parameters, and insulin secretion characteristics were analyzed between the two groups. Gender differences prior to treatment were also examined. Overall efficacy was significantly higher in the oalition group (96.35%) than in the methimazole group (83.64%) ($P<0.05$); Post-treatment, the TBiL, AST, ALT, FT_3, FT_4, FBG, P1BG, HOMA-IR, HOMA-β, postprandial blood glucose peak value, LAGE, MAGE, MODD and SDBG levels in the coalition group were lower compared to the methimazole group, while TSH was higher ($P<0.05$). Female patients exhibited significantly lower LAGE, MAGE, MODD and SDBG levels compared to the male group ($P<0.05$). The combination of methimazole and propranolol enhances thyroid and liver functions for hyperthyroid patients while improving insulin resistance along with reducing postprandial blood glucose variability.

Keywords: Hyperthyroidism, propranolol, methimazole, liver function, blood sugar fluctuation, insulin secretion characteristics, sex difference.

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INTRODUCTION

Hyperthyroidism, referred to as "hyperthyroidism", is an autoimmune disease caused by Graves' disease (GD), thyroid tumors and other factors, among which GD accounts for more than 85% of all hyperthyroidism patients (Yoo *et al.*, 2021). The prevalence of hyperthyroidism in women exceeds that in men. Hyperthyroidism is mainly caused by endocrine disorders within the body and the continuous secretion of thyroid hormone, causing all body systems to be in a state of heightened excitation and hypermetabolism, leading to symptoms such as palpitations, insomnia, hyperactivity, and emaciation in patients (Wiersinga *et al.*, 2023; Lee *et al.*, 2023; Chaker *et al.*, 2024; Li *et al.*, 2023). If not treated promptly, it can result in hyperthyroid heart disease and hyperthyroidism crisis. Additionally, hyperthyroidism can cause damage to the liver, giving rise to hyperthyroid liver disease. Studies have pointed out that the incidence of abnormal liver function in people with hyperthyroidism will increase significantly (Li *et al.*, 2023).

Thyroid hormone plays a crucial role as a humoral factor in regulating glucose and protein levels within the human body (Chen *et al.*, 2023; Ma *et al.*, 2023). Glucose tolerance metabolism, including glucose, along with insulin resistance and impaired insulin secretion, have been observed in individuals with hyperthyroidism (Fasciolo *et al.*, 2022; Fasciolo *et al.*, 2023; Popoviciu *et al.*, 2023). Factors known to cause impaired glucose tolerance include abnormal metabolic rate, endogenous gluconeogenesis and glucose absorption, all of which are influenced by thyroid hormones. However, diabetes is a chronic metabolic disease that is harmful to human health, and can involve many important organs such as eyes, kidneys, nerves, cardiovascular and cerebrovascular vessels and lower limb vessels. Hyperthyroidism can accelerate the advancement of diabetes mellitus and facilitate the development and development of certain complications (Roa Dueñas *et al.*, 2022; Grigoriadis *et al.*, 2023). In recent years, people have paid attention to chronic diseases such as thyroid disease and diabetes, and diabetes mellitus coalition with thyroid disease has gradually attracted attention. It has been reported that 44%~65% of patients with hyperthyroidism have impaired glucose tolerance (Bukhari *et al.*, 2022). It has also been shown that when hyperthyroidism is controlled,

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glucose tolerance improves and gradually returns to normal blood glucose levels (Conrad *et al.*, 2023). For this disease, the clinical use of drugs, surgery, radiation therapy, but the adverse reaction of radiation therapy is more, surgical treatment is more traumatic, so clinical use of drug therapy.

Methimazole is a commonly used drug in clinical treatment of hyperthyroidism, which has an inhibitory effect on thyroid hormone synthesis, but can impact the liver function of patients and promote the increase of aminotransferase, resulting in certain adverse reactions (Li *et al.*, 2023; Mao *et al.*, 2023). At the same time, it is difficult to control clinical symptoms and the treatment cycle is long and the risk of relapse is high after stopping the drug. The coalition of β-blockers and antithyroid drugs is recommended for the treatment of hyperthyroidism (Lu *et al.*, 2023). Propranolol is a non-selective β-blocker, which is capable of lower blood pressure, dilate blood vessels, and reduce the damage of hyperthyroidism to the heart (Rezgani *et al.*, 2022; Kalam *et al.*, 2020). At present, there are few clinical reports on the changes of liver function, blood glucose fluctuation, insulin secretion characteristics and gender differences in patients with hyperthyroidism before and after propranolol coalition with methimazole. The purpose of this study was to explore the changes of liver function, blood glucose fluctuation, insulin secretion and gender differences in patients with hyperthyroidism before and after propranolol coalition with methimazole.

MATERIALS AND METHODS

Information of participants

he clinical data of 110 patients with hyperthyroidism, who were admitted to Zhangzhou Affiliated Hospital of Fujian Medical University from February 2023 to February 2024, were retrospectively analyzed. Inclusion criteria: (1) Meet the diagnostic criteria for hyperthyroidism (Morcel *et al.*, 2022); (2) No history of drug allergy; (3) can comply with medical drugs, good compliance; (4) Complete clinical data. Exclusion criteria: (1) Receiving other study treatments within 1 month prior to study participation; (2) a mental or conscious disorder that prevents normal communication; (3) accompanied by malignant tumor disease; (4) accompanied by immune dysfunction; (5) There are serious infectious diseases; (6) Pregnant or lactating women; (7) Withdrawal from the study due to personal reasons.

They were categorized into the methimazole group (n = 55) and the coalition group (n=55). The two groups showed homogeneity in age (t=-0.125, P=0.901), gender (χ^2=0.170, P=0.680), and duration of illness (t=0.157, P=0.875) comparisons (all P>0.05). As indicated in table 1.

Treatment method

The treatment methods of the two groups are shown in table 2.

Observation index

(1) Clinical efficacy: Clinical efficacy includes cure: clinical symptoms disappear completely, thyroid hormone indicators and indicators reach normal levels; Obvious effect: all indexes and symptoms were significantly improved, and thyroid hormone indexes decreased by more than 70%; Effective: all indexes and symptoms were improved, and the reduction of thyroid hormone indexes < 30% was less than 70%; Ineffective: symptoms did not improve or even worsen, all indexes did not change, and the reduction of thyroid hormone indexes was less than 30% (Sun *et al.*, 2022). Total effective rate =[(cure + obvious + effective) cases/total cases]×100%.

(2) Liver function: Pre and post-treatment, 10 mL fasting vein was collected from patients in 2 groups and divided into 2 parts on average. A blood sample was taken, promoted coagulation with heparin and centrifugally treated (rotation speed 2500r/min, radius 10 cm, time 8 min). The supernatant was separated and the levels of alanine transaminase (ALT), total bilirubin (TBIL), aspartate transaminase (AST) and were determined.

(3) Thyroid hormone levels: Another blood sample was taken, centrifugation was performed (rotational speed: 3 500 r/min, time: 10 min), supernatant was taken, and the levels of thyroid stimulating hormone (TSH), free thyroxine (FT_4), free triiodothyronine (FT_3) were determined by immunofluorescence method.

(4) Insulin secretion characteristics: Pre-treatment and post-treatment, an oral glucose tolerance test (OGTT) as well as insulin release test were carried out. The following indicators were measured in patients: fasting glucose (FBG), 2-hour postprandial blood glucose (P2BG), 1-hour postprandial blood glucose (P1BG), fasting insulin (FINS), 1-hour postprandial insulin (1hINS), and 2-hour postprandial insulin (2hINS). The insulin resistance index (HOMA-IR) was calculated as follows: HOMA-IR = (FINS × FPG)/22.5 (Chen *et al.*, 2017). The assessment of β-cell function in the steady-state model (HOMA-β) was computed by applying the formula: HOMA-β = 20 × FINS/(PFG - 3.5) (Haffner *et al.*, 1996).

(5) Dynamic blood glucose parameters: Pre-treatment and post-treatment, the continuous glucose monitoring system (cCGM) was used for dynamic blood glucose monitoring. Dynamic blood glucose parameters (using Abbott as the dynamic blood glucose processing software) : The blood glucose spectrum for a total of 7 days from 6 o 'clock on the next day to 6 o 'clock on the 8th day was uniformly intercepted. variable coefficient (CV): 24h variability of blood glucose. Standard Deviation of Blood Glucose

(SDBG): The standard deviation of blood glucose measurements during continuous glucose monitoring (CGM). Mean Amplitude of Glycemic Excursions (MAGE): For subjects with a 24-hour fluctuation amplitude greater than 1 SDBG, the first valid fluctuation direction is used to calculate the average value of all blood glucose fluctuation amplitudes as MAGE. Mean of daily differences (MODD) in blood glucose levels: The average absolute difference between matched blood glucose measurements during two 24-hour monitoring periods of dynamic blood glucose. Largest amplitude of glycemic excursions (LAGE): The difference in blood glucose values during dynamic monitoring.

(6) Gender differences: The group was divided into female group and male group according to gender, and the relevant clinical characteristics of the two groups before treatment were compared.

ETHICAL APPROVAL

This study was approved by Zhangzhou Affiliated Hospital of Fujian Medical University (No.2023KYB370).

STATISTICAL ANALYSIS

The project data was processed using the statistical software (SPSS version 29.0). The description form of measurement data that is confirmed by K-S test to be consistent with normal distribution is (mean±sd); The measurement data (non-normal distribution) is represented in the form of (Q_{25}, Q_{75}). Counting variables are described by [n(%)]; The above descriptions were described by t test, non-parametric test and $\chi 2$ test. The difference is statistically significant, described as $P<0.05$.

RESULTS

Clinical effect

In terms of overall efficacy, the oalition group showed a significantly higher rate (96.35%) compared to the methimazole group (83.64%) ($P<0.05$) (table 3).

Liver function

Pre-treatment, the TBiL, AST and ALT comparisons between the coalition group and methimazole group maintained homogeneity ($P>0.05$). Post-treatment, the coalition group's TBiL, AST, and ALT were all lower than those of the methimazole group ($P<0$ .05). As shown in table 4.

Thyroid hormone levels

Pre-treatment, the FT_3, FT_4 and TSH comparisons between the coalition group and methimazole group maintained homogeneity ($P>0.05$). Post-treatment, the coalition group's FT_3 and FT_4 both lower than the methimazole group, while the TSH levels in the coalition group was higher than that in the methimazole group ($P<0$ .05) (table 5).

Insulin secretion characteristics

Pre-treatment, there were no significant differences in FBG, P1BG, P2BG, FINS, 1hINS, 2hINS, HOMA-IR, HOMA-β between coalition group and methimazole group ($P>0.05$). Post-treatment, the P2BG, FINS, 1hINS, and 2hINS comparisons between the coalition group and the methimazole group maintained homogeneity ($P>0.05$); Post-treatment, FBG, P1BG, HOMA-IR and HOMA-β of the coalition group were all lower than those of the methimazole group ($P<0.05$). table 6.

Dynamic blood glucose

Pre-treatment, the postprandial peak blood glucose, LAGE, CV, MAGE, MODD and SDBG were compared between the two groups, showing homogeneity ($P>0.05$). Post-treatment, postprandial blood glucose peak, LAGE, CV, MAGE, MODD and SDBG of the coalition group were lower than those of the methimazole group ($P < 0.05$). As shown in table 7.

Blood glucose spectrum changes in male and female hyperthyroid patients pre-treatment

Pre-treatment, patients with hyperthyroidism were divided into female group and male group according to sex. The levels of LAGE, MAGE, MODD and SDBG in female group were significantly lower than the male group ($P < 0.05$). table 8.

DISCUSSION

The main cause of hyperthyroidism is diffuse thyroid enlargement accompanied by hyperthyroidism. The pathogenesis of the disease is not yet clear. At present, the academic community generally believes that it is closely related to factors such as heredity, mental state or external infection (Chaker *et al.*, 2024). Surgical treatment and 131I radiotherapy are both destructive treatments. After treatment, hyperthyroidism is not easy to relapse, but it will increase the risk of hypothyroidism and thyroid-associated ophthalmopathy (Wu *et al.*, 2017). Conservative treatment of drugs is one of the commonly used treatment methods in clinical practice.

Methimazole belongs to thiourea anti-thyroid drugs and is the first choice for most doctors in China to treat hyperthyroidism. Related studies have shown that methimazole can inhibit the activity of peroxidase in the thyroid gland and indirectly inhibit the synthesis of FT3, FT4 and thyroxine for the treatment of patients with hyperthyroidism (Wu *et al.*, 2022; Iwaki *et al.*, 2021). However, methimazole has no intervention effect on the pathogenesis of hyperthyroidism. Taking methimazole alone has limited control effect on a variety of clinical

symptoms associated with hyperthyroidism patients. The treatment cycle is long, the total dose of drugs is large and the recurrence is high after the end of the treatment cycle (Lu *et al.*, 2024).

Excessive thyroid hormones in patients with hyperthyroidism induce a dramatic increase in the number of β receptors on the membrane of myocardial cell membrane, as well as an increase in the affinity of catecholamines for β receptors. Consequently, clinical symptoms such as tachycardia, eyelid tremor and anxiety occur in patients (Zhang *et al.*, 2023). Propranolol, as an adjuvant medication for treating hyperthyroidism, can significantly improve symptoms of neuroexcitation such as tachycardia and hand tremors, thereby enhancing the treatment efficacy (Allam *et al.*, 2023).

The study found that post-treatment, In terms of overall efficacy, the oalition group showed a significantly higher rate (96.35%) compared to the methimazole group (83.64%). In addition, the levels of FT4 and FT3 in the combined group were reduced, and the levels of TSH were increased more conspicuously. The use of methimazole combined with propranolol in the treatment can effectively improve the clinical symptoms of patients and enhance their thyroid function. It is speculated that the main reason is that propranolol reduces the myocardium load by blocking the β receptor of cardiomyocytes in the body, eliminates the excessive β effect, controls the deiodinase activity and prevents the transformation of thyroxine, so that the hyperthyroidism can be controlled to a certain extent.

As an anti-thyroid drug, methimazole enters the body after oral administration, directly inhibits the local tissue peroxide activity, resulting in a significant decrease in FT3 and FT4 and effectively improving thyroid hormone levels and related symptoms in patients. In addition, propranolol can also directly act on thyroid tissue, inhibit the activity of 5 'deiodinase, block the transformation of thyroxine into triiodothyronine and then inhibit the synthesis and release of thyroid hormone, thereby reducing cardiac excitation, alleviating clinical symptoms, preventing FT3 synthesis, and improving thyroid function in patients (Kalam *et al.*, 2020; Ben *et al.*, 2015).

Hepatic dysfunction is commonly observed in patients with hyperthyroidism, possibly due to the toxic effects of excessive thyroid hormones, liver hypoxia caused by high metabolism, and malnutrition (Scappaticcio *et al.*, 2021). In addition, the use of antithyroid drugs is also an important cause of liver function injury. Lu et al. (Lu *et al.*, 2024) pointed out that liver function injury in hyperthyroidism patients was related to thyroid hormone levels, and ALT, AST and TBiL were all important indicators for detecting liver function. In this study, the improvement of FT3, FT4, TBiL in the coalition group post-treatment was better than the methimazole group. 1. It is proposed that combined propranolol may improve liver function by reducing thyroid hormone levels in patients. Hyperthyroid patients often have abnormal glucose metabolism to varying degrees due to excessive secretion of thyroid hormone, and even lead to type 2 diabetes (Mohammed *et al.*, 2021).

Research has shown that in hyperthyroidism, elevated levels of thyroid hormones lead to impaired pancreatic β-cell function and insulin resistance, causing a sugar metabolism disorder (Venditti *et al.*, 2019). Hyperthyroidism patients often suffer from glucose metabolism disorders, resulting in decreased insulin sensitivity and damage to the secretion function of islet beta cells (Laclaustra *et al.*, 2019). This study observed that the two groups of patients showed higher levels of fasting blood glucose and insulin before treatment, suggesting that patients with hyperthyroidism may have developed insulin resistance.

Post-treatment, the coalition group showed lower postprandial blood glucose peak, LAGE, MAGE, MODD and SDBG compared to the methimazole group ($P<0.05$). This suggests that the blood glucose fluctuation range of hyperthyroidism patients post-treatment is relatively large. Compared with methimazole alone, the improvement in blood glucose levels in patients after combined treatment with propranolol is more significant. In this study, after treatment, there were no significant differences in P2BG, FINS, 1hINS, and 2hINS between the coalition group and the methimazole group. However, the FBG, P1BG, HOMA-IR and HOMA-β in the coalition group were all lower than those in the methimazole group ($P<0.05$). This indicates that the combination of methimazole and propranolol has improved the insulin resistance in patients after treatment.

In this study, levels of LAGE, MAGE, MODD and SDBG were significantly lower in female patients compared to male patients. The analysis suggests a possible association with the inhibitory impact of estrogen on glucagon secretion (Aldhoon-Hainerová *et al.*, 2017). In the experimental model (Díaz *et al.*, 2019), it was also demonstrated that estrogen might exert a protective effect on maintaining insulin sensitivity in female rats. However, the study (Zaniqueli *et al.*, 2021) contend that the body fat content of females is higher than that of males, thereby making the body fat content of females more prone to increase FBG, FINS and HOMA-IR. In this study, FINS, FBG and HOMA-IR in the female group showed no statistical difference compared with that in the male group, but they were all significantly increased, which was basically consistent with the above conclusions.

Table 1: Patient baseline data

Group	Age (years)	Sex		Duration of disease (month)
		Male	Female	
Coalition group (=55)	38.95±6.25	18(32.73)	37(67.27)	7.75±1.89
Methimazole group (n=55)	39.09±5.96	16(29.09)	39(70.91)	7.69±1.75
t/χ^2	-0.125	0.170		0.157
P	0.901	0.680		0.875

Table 2: Treatment methods of the two groups

Group	Methods of treatment	Dosage	Treatment time
Methimazole group (n=55)	Oral treatment with methimazole tablets	10mg/ time, 3 times/day, adjusted to 1 time/day after 30 days of continuous use	1 month was a course of treatment, 3 courses of treatment
Coalition group (n=55)	Based on the methimazole group, propranolol hydrochloride tablets were given oral treatment	10mg/ time, 3 times/day	1 month was a course of treatment, 3 courses of treatment

Table 3: Comparison of clinical efficacy between the coalition group and the methimazole group

Group	Cure	Obvious	Effective	Invalid	Total effective rate (%)
Coalition group (n=55)	8(14.55)	38(69.09)	7(12.73)	2(3.64)	53(96.36)
Methimazole group (n=55)	4(7.27)	26(47.27)	16(29.09)	9(16.36)	46(83.64)
χ^2					11.560
P					0.009

Table 4: Comparison of liver function indexes between the two groups

Group	Coalition group (n=55)	Methimazole group (n=55)	t	P
TBiL (μmol/L)				
Pre	32.16±8.75	31.53±8.49	0.377	0.707
Post	16.40±3.22[f]	19.25±3.30[f]	-4.577	<0.001
AST (U/L)				
Pre	90.54±9.67	89.45±9.50	0.602	0.549
Post	42.20±10.25[f]	54.38±9.40[f]	-6.500	<0.001
ALT (U/L)				
Pre	84.87±15.05	83.73±14.69	0.399	0.691
Post	35.44±7.60[f]	42.60±9.15[f]	-4.462	<0.001

Note: AST, Aspartate aminotransferase; ALT, alanine aminotransferase; TBiL, total bilirubin; [f]P < 0.000001

Table 5: Comparison of thyroid hormone levels between the two groups

Group	Coalition group (n=55)	Methimazole group (n=55)	t	P
FT_3 (pmol/L)				
Pre	12.10±3.13	11.86±3.15	0.401	0.689
Post	5.86±1.52[f]	7.45±1.75[f]	-5.134	<0.001
FT_4 (pmol/L)				
Pre	30.66±8.19	29.84±8.40	0.512	0.610
Post	15.83±3.57[f]	18.58±4.80[f]	-3.422	<0.001
TSH (mU/L)				
Pre	0.45±0.10	0.44±0.09	0.251	0.802
Post	2.80±0.35[f]	2.10±0.24[f]	12.043	<0.001

Note: TSH, thyroid stimulating hormone; FT3, free triiodothyronine; FT4, free thyroxine; NsP > 0.05; FP < 0.000001

Table 6: Comparison of insulin secretion characteristics between the two groups pre-treatment and post-treatment

Group	Coalition group (n=55)	Methimazole group (n=55)	t	P
FBG(mmol/L)				
Pre	5.14±0.70	5.08±0.63	0.476	0.635
Post	4.46±0.51	4.94±0.63	-4.403	<0.001
P1BG(mmol/L)				
Pre	9.95±2.13	9.88±2.09	0.174	0.862
Post	8.59±1.83	9.65±2.06	-2.853	0.005
P2BG(mmol/L)				
Pre	6.75±1.75	6.72±1.68	0.092	0.927
Post	6.46±1.43	6.55±1.48	-0.290	0.772
FINS(mIU/mL)				
Pre	11.20±3.12	11.16±3.07	0.068	0.946
Post	9.77±3.04	10.36±3.29	-0.977	0.331
1hINS(mIU/mL)				
Pre	103.55±19.25	102.67±19.35	0.239	0.812
Post	98.68±18.33	99.68±18.31	-0.286	0.775
2hINS(mIU/mL)				
Pre	71.55±18.19	70.84±18.27	0.207	0.836
Post	56.37±15.80	62.34±16.12	-1.959	0.053
HOMA-IR				
Pre	2.57±0.85	2.52±0.73	0.316	0.753
Post	1.92±0.61	2.26±0.73	-2.625	0.010
HOMA-β				
Pre	138.27(108.24, 211.67)	220.71(138.04, 361.82)	-0.266	0.790
Post	134.69(104.74,185.63)	139.16(96.71,223.97)	-2.699	0.007

Table 7: Comparison of dynamic blood glucose parameters pre and post-treatment between the two groups

Group	Coalition group (n=55)	Methimazole group (n=55)	t	P
Postprandial blood glucose peak (mmol/L)				
Pre	7.99±0.95	8.08±1.10	-0.445	0.657
Post	7.02±1.06	7.69±1.11	-3.269	0.001
LAGE (mmol/L)				
Pre	5.38±0.74	5.15±0.88	1.500	0.137
Post	4.26±0.45	4.85±0.68	-5.445	<0.001
CV (%)				
Pre	23.78±4.24	22.33±4.30	1.779	0.078
Post	20.92±3.54	21.26±3.38	-0.520	0.604
MAGE (mmol/L)				
Pre	2.46±0.53	2.43±0.42	0.296	0.768
Post	2.18±0.32	2.36±0.39	-2.827	0.006
MODD (mmol/L)				
Pre	0.39±0.11	0.39±0.12	-0.048	0.962
Post	0.28±0.09	0.34±0.11	-2.996	0.003
SDBG (mmol/L)				
Pre	1.35±0.28	1.30±0.25	0.975	0.332
Post	1.17±0.20	1.32±0.22	-3.670	<0.001

CONCLUSION

In summary, the blood glucose levels in patients with hyperthyroidism generally exhibit gender differences. The combination of methimazole and propranolol has been shown to enhance thyroid and liver function in individuals with hyperthyroidism, as well as facilitate the recovery of insulin resistance, postprandial blood glucose levels, and overall blood glucose variability. However, this study is constrained by its limited sample size and brief observation period, necessitating further validation of the comprehensiveness of its conclusions. Future research will focus on increasing the sample size and extending the duration of observation to more thoroughly assess the actual effects of progressive rehabilitation exercises.

Table 8: Blood glucose spectrum changes in male and female hyperthyroid patients pre-treatment

Group	Female group (n=76)	Male group (n=34)	t	P
Age (years)	39.54±6.17	37.85±5.80	1.349	0.180
FT3 (pmol/L)	11.89±3.22	12.17±2.96	-0.429	0.669
FT4 (pmol/L)	30.14±7.59	30.50±9.74	-0.208	0.836
TSH (mU/L)	0.44±0.10	0.46±0.09	-1.178	0.242
FBG (mmol/L)	5.13±0.67	5.09±0.66	0.238	0.812
P1BG (mmol/L)	10.01±1.99	9.69±2.33	0.729	0.467
FINS (mIU/mL)	11.30±3.08	10.89±3.11	0.647	0.519
1hINS (mIU/mL)	102.85±19.36	103.72±19.19	-0.219	0.827
HOMA-IR	2.58±0.81	2.47±0.76	0.635	0.527
LAGE (mmol/L)	5.13±0.79	5.56±0.81	-2.558	0.012
CV (%)	22.62±4.33	23.55±4.84	0.999	0.320
MAGE (mmol/L)	2.38±0.43	2.60±0.55	-2.278	0.025
MODD (mmol/L)	0.37±0.11	0.42±0.14	-2.004	0.048
SDBG (mmol/L)	1.29±0.26	1.41±0.26	-2.327	0.022

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