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Relationship between Abdominal Obesity and Insulin Resistance, Growth Hormone, and Insulin-like Growth Factor-1 in Individuals with Type 2 Diabetes

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ABSTRACT

This experiment was designed to investigate the correlation between abdominal obesity and insulin resistance (IR), growth hormone (GH) and insulin-like growth factor-1 (IGF-1) in patients with type 2 diabetes mellitus (T2DM). To do this experiment, 200 patients with T2DM were enrolled in this cross-sectional study. They were divided into the control group (T2DM without abdominal obesity) and the observation group (T2DM combined with abdominal obesity) according to the diagnostic criteria of abdominal obesity. General data and biochemical indices were recorded from all patients. Results showed that 97 patients (48.50%, 97/200) with abdominal obesity were included in the observation group, and 103 patients (51.50%,103/200) without abdominal obesity were included in the control group. Meanwhile, the body weight, BMI, waist circumference and waist-to-hip ratio were higher in the observation group than in the control group (P<0.05). Meanwhile, the visceral fat in the observation group, TC, and TG were higher (P<0.05) compared with the control group (Visceral Fat, 92.55±3.07 vs 87.63±3.14. TC, 5.14±0.48 vs 4.97±0.51), and TG,1.89±0.13 vs 1.53±0.16). In addition, the levels of FBG, FINS and HOMA-IR were higher (P<0.05) in the observation group than those in the control group (FBG, 13.06± 2.17 vs 10.62±2.35. FINS, 16.25±2.14 vs 13.33±3.21. HOMA-IR, 9.43±1.90 vs 6.29±2.10). However, the levels of GH and IGF-1 were lower (P<0.05) in the observation group than those in the control group (GH, 1.16±0.08 vs 1.24±0.11. IGF-1, 125.14 11.46 vs 135.71±12.33). Spearman's correlation analysis showed that abdominal obesity was positively correlated with IR (R=0.372, P=0.000) in patients with T2DM, while negatively correlated with GH (R=-0.271, P=0.000) and IGF-1(R=-0.219, P=0.000) levels. In conclusion, abdominal obesity in patients with T2DM is positively associated with IR, and negatively correlated with GH and IGF-1 levels. Thus, improvement of IR as well as regulating the levels of growth hormone and IGF-1 might play crucial roles in the early prevention and efficient clinical treatment of T2DM with abdominal obesity patients.

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Introduction

In recent years, the socio-economic challenges have been enormous as the burden of diabetes has risen rapidly across the globe. It is estimated that the number of people with diabetes will further increase from 415 million in 2015 to 642 million by 2040, with type 2 diabetes mellitus (T2DM) being the most common type of diabetes, accounting for approximately 90% of diabetes cases (1). T2DM is a pathological condition caused by a combination of environmental, genetic and endocrine factors that can cause serious damage to several body systems, including the kidneys, eyes and heart, and more generally the vascular system (2). According to statistics, China is by far the world's leading country in terms of the number of T2DM cases, and the overall prevalence of T2DM in people over 20 years of age is nearly 10%(3). While obesity and T2DM are both chronic diseases that have reached pandemic proportions, which are closely related, to weight gain, especially in obese patients, and also have both significant metabolic disorders and insulin resistance. Studies have also reported that the prevalence of diabetes is three times higher in obese patients than in the normal population (4). Insulin and growth hormone are two important hormones in the regulation of glucose metabolism, and in obese patients, there is often an imbalance between these two hormones, which increases the body's insulin levels and reduces growth hormone levels (5). However, insulin mainly controls the uptake and utilization of glucose in peripheral tissues, and insulin resistance is one of the main causes of pathogenesis in T2DM patients. It has also been shown that insulin resistance is significantly higher in overweight T2DM patients compared to those with normal body mass (6). At the same time, growth hormone is also one of the important endocrine hormones in the body, which can play a growth promotion, metabolism and immune regulation function, and is a key regulator of adipose tissue lipolysis. The liver releases insulin-like growth factor-1 (Insulin-like growth factor-1, IGF-1), stimulated by growth hormone, and related studies have reported that IGF-1 is reduced in obese patients (7). Meanwhile, relevant studies found that the serum IGF-1 levels were normal in patients with acromegaly associated with diabetes, indicating that the diabetic status has a certain effect on IGF-1(8). Howe-

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ver, the changes in IGF-1 in obese T2DM patients have been more controversial as insulin resistance, obesity and inflammatory cytokines can all have an impact on IGF-1 levels. To date, the correlation between the disease associated with growth hormone and IGF-1 levels in T2DM patients has not been clearly reported in China. Based on this, this study investigated the correlation between insulin resistance, growth hormone and IGF-1 in abdominally obese patients with T2DM, and is reported below.

Materials and Methods

General information

Two hundred patients with T2DM admitted to our hospital between January 2019 and January 2020 were screened for the study according to the inclusion and exclusion criteria. The study was approved by the hospital ethics committee.

Inclusion criteria. Patients have reached the age of 18 years. Meet the diagnostic criteria for type 2 diabetes (9). Normal blood, liver and kidney function and thyroid function. Complete clinical profile.

Exclusion criteria. Patients with type I diabetes and other specific types of diabetes. With acute complications of diabetes mellitus. Combined with severe chronic complications. Patients during pregnancy or lactation.

Study grouping

According to the diagnostic criteria for abdominal obesity in China (10) (waist circumference ≥90cm for men and ≥85cm for women), the selected T2DM patients were divided into a control group (T2DM without abdominal obesity) and an observation group (T2DM combined with abdominal obesity).

Observation indicators and methods

(i) General information was collected from both groups, including gender, age, duration of diabetes, smoking history and physical indicators.

Body mass index (BMI), waist circumference, waist-hip ratio, etc. BMI = weight/(height^2). Light weight: <18.5kg/m^2; normal weight: (18.5~24.9) kg/m^2; overweight: (25~29.9) kg/m^2; obese: ≥30kg/m^2. Waist-to-hip ratio = waist circumference/hip circumference; waist-to-hip ratio <0.85 for women and <0.9 for men is defined as a healthy state.

(ii) Serum indicators: growth hormone levels, IGF-1 levels, fasting blood glucose (FBG), fasting insulin (FINS), visceral fat, total cholesterol (TC), triglyceride (TG), hepatic steatosis, liver stiffness, urine microalbumin (UMA), blood urea nitrogen (BUN), etc.

Patients are required to fast for at least 8 hours before a blood sample is drawn and a blood sample is collected by venipuncture. An 8mL blood sample is collected into an anticoagulation tube and the sample is sent to the laboratory. Growth hormone and IGF-1 levels were measured by chemiluminescence, FBG detection was performed using the oxidase assay, FINS by immunofluorescence, and visceral fat, TC, TG, hepatic steatosis quantification, liver stiffness, UMA and BUN by enzymatic methods using a fully automated blood biochemistry analyser.

(iii) Insulin resistance level: Insulin resistance index (HOMA-IR) was assessed using a homeostatic model assessment, HOMA-IR = FBG x FINS /22.5.

Statistical analysis

SPSS 22.0 was used for the statistical analysis of the data. The measures were tested for normality, and data conforming to a normal distribution were expressed using $\bar{x}\pm$ s. Comparisons between groups were made using the independent samples t-test. Data that did not conform to a normal distribution were expressed using the median (quartiles) and comparisons between groups were made using the Mann-Whitney U test. Categorical counts were expressed as percentages, and unordered categorical data were compared between groups using the χ^2 or Fisher exact test; ordered categorical data were compared between groups using the Mann-Whitney U test. Spearman's correlation analysis of abdominal obesity in T2DM with insulin resistance, growth hormone and IGF-1. $p<0.05$ was considered a statistically significant difference.

Results

Comparison of general information between the two groups of patients

Of the 200 patients, 97 (48.50%) were included in the observation group with abdominal obesity and 103 (51.50%) were included in the control group without abdominal obesity. There was no significant difference in gender, age, duration of diabetes, smoking history and height between the two groups (P>0.05). Meanwhile, the weight (73.68± 4.36) kg, BMI (27.19± 4.89) kg/m^2, waist circumference [male (94.57± 6.31) cm, female (90.11± 5.48) cm] and the waist-hip ratio [male (0.94± 0.18), female (0.89± 0.21)] were significantly higher in the observation group than in the control group, and the differences were statistically significant (P<0.05, Table 1).

Comparison of general laboratory indicators between the two groups of patients

There was no significant difference in the amount of hepatic steatosis, liver stiffness, UMA, and BUN between the two groups (P>0.05). Also compared to the control group, patients in the observation group had significantly higher visceral fat (92.55± 3.07) mm, TC (5.14± 0.48) mmol/L and TG (1.89± 0.13) mmol/L, with statistically significant differences (P<0.05, Table 2, Figure 1).

Comparison of blood glucose, insulin, growth hormone and IGF-1 levels between the two groups

FBG (13.06± 2.17) mmol/L, FINS (16.25± 2.14) IU/L and HOMA-IR (9.43± 1.90) were significantly higher in the observation group than in the control group, while growth hormone (1.16± 0.08) ng/mL and IGF-1 (125.14± 11.46) ng/mL were significantly lower in the observation group than in the control group. The differences were all statistically significant (P<0.05, Table 3, Figure 2).

Correlation analysis

Spearman's correlation analysis showed that abdominal obesity in T2DM was positively correlated with insulin resistance levels and negatively correlated with growth hormone and IGF-1 (P<0.05, Tables 4 and 5 and Figures 3 and 4.

Table 1. Comparison of general information between the two groups of patients.

General information		Control group (n=103)	Observation group (n=97)	χ^2 /t	*P*
Gender (cases, %)	Male	52 (50.49%)	47 (48.45%)	0.083	0.774
	Female	51 (49.51%)	50 (51.55%)		
Age (years,$\bar{x}$± s)		49.78± 11.38	51.63± 12.73	1.085	0.279
Duration of diabetes (years,$\bar{x}$± s)		5.73± 1.49	6.08± 1.52	1.644	0.102
Smoking (cases, %)		48 (46.60%)	43 (44.33%)	0.104	0.747
Height (cm,$\bar{x}$± s)		167.74± 15.38	166.39± 14.62	0.635	0.526
Body weight (kg,$\bar{x}$± s)		62.55± 8.27	73.68 4.36	11.799	0.000
BMI (kg/m^2,$\bar{x}$± s)		22.71± 5.14	27.19± 4.89	6.307	0.000
Waist circumference (cm,$\bar{x}$± s)	Male	83.67± 6.28	94.57± 6.31	12.239	0.000
	Female	77.14± 5.36	90.11± 5.48	16.918	0.000
Waist-to-hip ratio ($\bar{x}$± s)	Male	0.76± 0.15	0.94± 0.18	7.700	0.000
	Female	0.74± 0.13	0.89± 0.21	6.112	0.000

Table 2. Comparison of general laboratory indicators between the two groups ($\bar{x}$±s)

Indicators	Control group (n=103)	Observation group (n=97)	t	*P*
Visceral fat (mm)	87.63± 3.14	92.55± 3.07	11.195	0.000
TC (mmol/L)	4.97± 0.51	5.14± 0.48	2.424	0.016
TG (mmol/L)	1.53± 0.16	1.89± 0.13	17.401	0.000
Quantification of hepatic steatosis	204.25± 21.17	203.76± 20.89	0.165	0.869
Liver hardness (Kpa)	5.89± 1.43	6.12± 1.68	1.045	0.298
UMA (mg/L)	21.18± 0.79	20.96± 0.83	1.921	0.056
BUN (mmol/L)	5.89± 1.18	6.13± 1.36	1.335	0.183

Table 3. Comparison of blood glucose, insulin, growth hormone and IGF-1 levels between the two groups of patients ($\bar{x}$± s).

Indicators	Control group (n=103)	Observation group (n=97)	t	*P*
FBG (mmol/L)	10.62± 2.35	13.06± 2.17	7.616	0.000
FINS (IU/L)	13.33± 3.21	16.25± 2.14	7.522	0.000
HOMA-IR	6.29± 2.10	9.43± 1.90	11.066	0.000
Growth hormone (ng/mL)	1.24± 0.11	1.16± 0.08	5.852	0.000
IGF-1 (ng/mL)	135.71± 12.33	125.14± 11.46	6.270	0.000

Discussion

Obesity is a heterogeneous disease that poses certain health risks when abdominal fat begins to accumulate, which is an important factor in the development of T2DM (11). In recent years, the results of several studies have shown a positive association between obesity and the development of T2DM (12). It has also been shown that over 90% of patients with T2DM have varying degrees of obesity, which is also a major symptom and clinical manifestation of T2DM (13,14). However, the relationship between abdominal obesity and T2DM has been easily overlooked in clinical studies. In this study, the clinical data of patients with T2DM showed that there was no significant difference between the general basic information of patients with abdominal obesity and those without abdominal obesity, but there were significant differences in weight, BMI, waist circumference and the waist-hip ratio between the two groups (p<0.05). It was also found in the study that visceral fat, TC and TG were significantly higher in T2DM patients with abdominal obesity than in T2DM patients with normal body size (P<0.05).

After the onset of T2DM, patients will have obvious symptoms in performance, part of the patients with the disease is mainly insulin resistance, due to the high content of free fatty acids in the body of obese patients, a large number of free fatty acids will affect the transport of glucose in the blood, the function of cells, insulin sensitivity is reduced, thus reducing the role of insulin pro-glucose metabolism, blood insulin increased to compensate for their insulin resistance, but relative to the patient Insulin

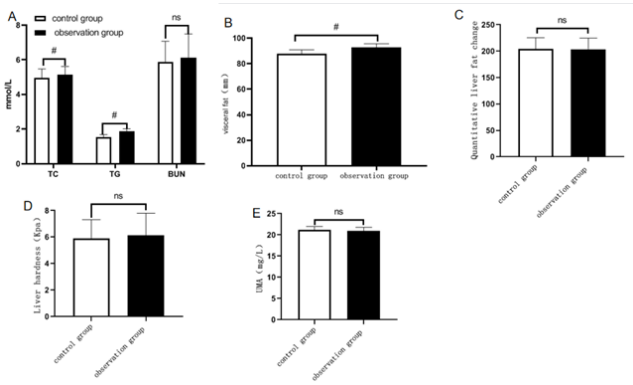

Figure 1. Comparison of general laboratory indicators (Note: #P<0.05, ns*P*>0.05.).

Table 4. Correlation of waist circumference with insulin resistance, growth hormone and IGF-1 in men with T2DM.

Related indicators	R	Deviation	SE	*P*	95% confidence interval
HOMA-IR	0.372**	0.001	0.061	0.000	0.249~ 0.487
Growth hormones	-0.271**	0.001	0.069	0.000	-0.402 ~ -0.134
IGF-1	-0.219**	0.003	0.067	0.000	-0.351 ~ -0.082

**. The correlation is significant at a confidence level (double test) of 0.01.

*. The correlation is significant at a confidence level (double test) of 0.05.

Table 5. Correlation of waist circumference with insulin resistance, growth hormone and IGF-1 in women with T2DM.

Related indicators	R	Deviation	SE	P	95% confidence interval
HOMA-IR	0.443**	-0.002	0.055	0.000	0.333~0.542
Growth hormones	-0.301**	0.003	0.068	0.000	-0.435~ -0.161
IGF-1	-0.340**	0.003	0.061	0.000	-0.455~ -0.213

**. The correlation is significant at a confidence level (double test) of 0.01.

*. The correlation is significant at a confidence level (double test) of 0.05.

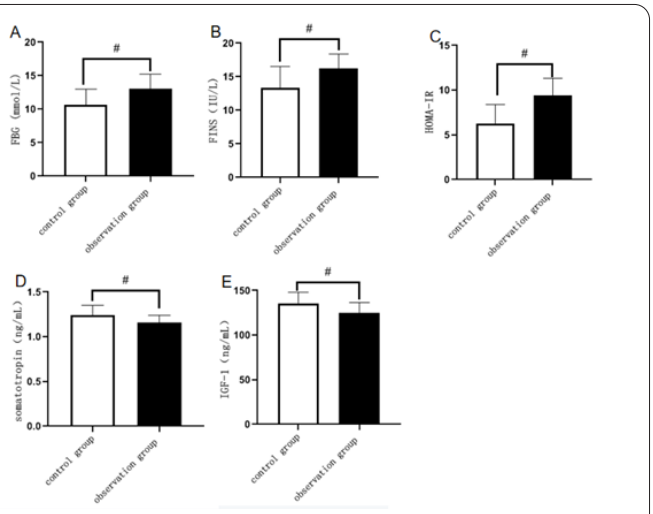

Figure 2. Comparison of patients' blood glucose, insulin, growth hormone and IGF-1 levels (Note: #*P*<0.05.).

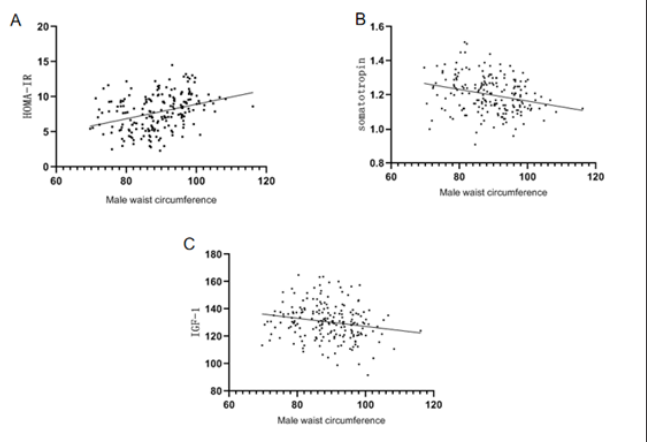

Figure 3. Correlation of waist circumference with insulin resistance, growth hormone and IGF-1 in men with T2DM.

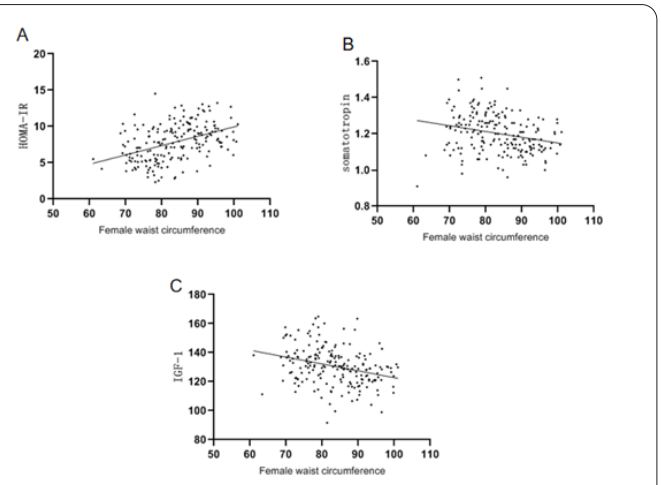

Figure 4. Correlation of waist circumference with insulin resistance, growth hormone and IGF-1 in women with T2DM.

secretion is still relatively low compared to the patient's hyperglycaemia (15,16). Insulin resistance is particularly severe in patients with abdominally obese T2DM. The results of relevant studies have shown that as adipose tissue and BMI rise, so does the incidence of diabetes, while excessive visceral fat content is highly likely to lead to insulin resistance (17). And in the current study, it could be found that the level of insulin resistance was significantly higher in T2DM patients with concomitant abdominal obesity (p<0.05). This is also consistent with the conclusion of the study by Tan-Chen S et al (18). This may be due to the fact that patients with abdominal obesity have a higher release of free fatty acids from intra-abdominal adipose tissue, and the accumulation of lipids from these fatty acids towards non-adipocytes such as hepatocytes and pancreatic islet cells, thus aggravating insulin resistance.

Previous studies have reported that growth hormone is mostly deficient in obese patients (19), while in the current study it was also confirmed that abdominally obese patients with T2DM had significantly lower growth hormone levels than normal-sized patients (p<0.05). IGF-1 is mainly synthesized in the liver in response to growth hormone stimulation, and several studies have confirmed that in the presence of growth hormone deficiency, patients with low IGF-1 serum concentrations are more likely to have T2DM (20,21). In the results of the present study, it was found that IGF-1 levels were significantly lower in abdominally obese patients with T2DM than in patients with normal body sizes (p<0.05). The reason for this may be that diabetic patients have reduced growth hormone receptor expression on the surface of hepatocytes and/or impaired intracellular IGF-1 synthesis after the receptor as a direct result of the absolute reduction in portal insulin levels, which also leads to reduced serum IGF-1 concentrations, Interestingly, the degree of absolute reduction in insulin levels is more pronounced in abdominally obese

T2MD patients compared to non-abdominally obese T2MD patients, and intracellular The more severe the impairment of IGF-1 synthesis, the lower the serum IGF-1 level. The study also looked at the relationship between abdominal obesity and insulin resistance, growth hormone and IGF-1 levels in patients with abdominal obesity (waist circumference ≥90cm in men and ≥85cm in women). This further confirms the close association between abdominal obesity and insulin resistance, growth hormone and IGF-1 in T2DM patients, which is also consistent with several reports (22-25).

In summary, insulin resistance levels were significantly higher in patients with T2DM with abdominal obesity, while growth hormone levels and IGF-1 levels were significantly lower, and abdominal obesity in T2DM patients was positively correlated with insulin resistance levels and negatively correlated with growth hormone and IGF-1 levels. Therefore, insulin resistance, growth hormone and IGF-1 levels could be used as predictors of abdominal obesity in clinical T2DM patients. However, this study has not yet been conducted to analyse the factors influencing the development of abdominal obesity in patients with T2DM and the relationship between these factors, so further investigation is needed.

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