Association of Triglyceride-Glucose Index with the Incidence of Ketoacidosis in Chinese Children with Type 1 Diabetes

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Research

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Abstract

Objective: The relationship between triglyceride-glucose index (TyG index) and the prevalence of type 2 diabetes mellitus (T2DM) has been confirmed by former studies. However, it remains uncertain whether TyG index has a predictive value in T1DM patients with diabetic ketoacidosis (DKA).

Methods: The study retrospectively enrolled 143 patients ((boys/girls = 60/83) with T1DM in the Endocrine inpatient wards of Tianjin Children's Hospital from June 2017 to May 2019.TyG index was calculated as follows: ln[fasting triglycerides (mg/dL)×fasting plasma glucose (mg/dL)/2]. These patients stratifed by the optimal cut-off point of TyG index were divided into the lower TyG index group (n=73) and higher TyG index group (n=70).

Results: TyG index and related lipid parameters were significantly higher in patients with DKA compared with those without. Compared with patients in lower TyG index group, those with higher TyG index seemed to be younger. Multiple linear regression analysis showed that increase of TC (95%CI: 0.018~0.568, p=0.037) level and decrease of T3(95%CI:-2.314~-0.668,p=0.001) level were associated with the risk of higher TyG index. A linear equation was obtained between TC, T3 and TyG index (TyG index=10.226+0.299*TC-1.384*T3, R2=0.481).

Conclusions: Increased TyG index is a significant predictor of DKA in children with T1DM. Higher TC and lower T3 levels were associated with higher TyG index. Further studies need to be conducted to determine whether interventions for TyG index have a positive impact on improving clinical prognosis.

1. Introduction

Type 1 diabetes mellitus (T1DM) is a chronic disease with genetic predisposition and environmental influences predominantly early in life, induces pancreatic β-cell autoimmunity eventually resulting in both loss of function and destruction [1]. Diabetic ketoacidosis (DKA) is a potentially life-threatening complication of T1DM, which is characterized by metabolic acidosis, hyperketonaemia, and hyperglycemia [2]. DKA is the presenting manifestation of diabetes in approximately 30% of people with T1DM, with higher numbers in children (up to 55%) than adults (up to 6%)[3]. Recurrent episodes of DKA in particular are associated with an increase in mortality of up to a 23.3% risk of death in people who have had more than five episodes of DKA compared with 5.2% in people with one episode[4]. The identification of rapidly available and reliable markers may have great clinical significance of occurrence DKA risk.

Insulin resistance (IR), characterized by decrease in cell sensitivity to insulin, is one of the leading causes of metabolic disorders[5].The homeostasis model assessment (HOMA), derived from the fasting levels of insulin and glucose, is a robust tool used as a surrogate measure for IR. An insulin-free equation for estimating IR was developed because of the measurement of fasting insulin is cumbersome with no standard assay available[6].The triglyceride-glucose index (TyG index) has been regarded as a useful

alternative marker for early identification of IR individuals[7].Research had showed that the value of the TyG index in reflecting metabolic health status and predicting the development of diabetes[8].A study firstly estimated the cut-off values of TyG index for metabolic syndrome in adolescents[6]. A Rural Chinese Cohort Study suggested higher TyG index can increase risk of incident T2DM [9].However, population-based studies of TyG index in T1DM children, especially in the occurrence of DKA, are lacking.

There was evidence suggested that traditional lipid ratios, such as TC/HDL-C, non-HDL-C/HDL-C, and TG/HDL-C, are more effective than single measures of lipids in detecting IR[10]. The prevalence of hypertriglyceridemia and low HDL-C are key metabolic abnormalities in patients with IR and represent diabetic dyslipidemia [11]. Other lipid metabolism markers, such as combined lipid ratio, may better reflect the overall interaction between lipid/lipoprotein fractions [12].But for now at least, it is unclear whether dyslipidemia contributes significantly to the excess risk of DKA events in patients with diabetes. The purpose of this study was to explore the predictive value of the TyG index and routine lipid profiles on the clinical outcomes of DKA in children with T1DM.

2 Materials And Methods

2.1 Subjects

The present study is a single-center, retrospective study among patients who were diagnosed with T1DM and treated with insulin being subcutaneous injections such as Novolin and Novorapid in the Endocrine inpatient wards of Tianjin Children's Hospital between June 2017 and May 2019. The inclusion criteria for T1DM include: (1)previously or newly diagnosed T1DM under treatment of antidiabetic medication (insulin); (2)the typical symptoms of diabetes with a random blood glucose≥11.1 mmol/L, and/or fasting plasma glucose(FPG) ≥7.0 mmol/L, and/or 2-h blood glucose after oral glucose tolerance test (OGTT)≥11.1 mmol/L; (3)HbA1c level≥6.5% on admission. Ultimately, a totalof 143 patients were included for the present study. They were aged from 10 months to 15 years.DKA was defined as blood glucose concentration > 13.9 mmol/l, Venous pH <7.3 or serum bicarbonate (HCO_3) <15 mmol/L, ketonemia or ketonuria, anion gap>12. Major medical abnormalities, including central nervous system diseases, angiocardiopathy, or life-threatening medical illnesses (infections or cancer) were excluded. 143 patients were divided into two groups: T1DM without DKA group (n=43) and T1DM with DKA group(n=100). All subjects were Han Chinese.

After the study procedure was explained in detail to the parents of patients included in the study, they signed the informed consent document. Before this study began, the research protocol was approved by the Institutional Review Board of Tianjin Children's Hospital.

2.2 Data collection and measures

Data of demographic and clinical characteristics, including age, sex, weight, height, medical history, family history, and medical treatment were extracted from the medical information recording system of

Tianjin Children's Hospital. BMI was calculated as follows: BMI=weight (kg)/ [height (m)]^2.

Blood samples were collected before an initial insulin therapy. The plasma was separated, aliquoted, and stored at -70 °C before use. The routine hematology and biochemical parameters, including lipid profiles [triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C)], FPG, HbA1c, C-peptide, and other lipid metabolism markers, were measured by standard laboratory methods at the diagnostic laboratory of Tianjin Children's hospital.

The level of vitamin D was measured by equipment [API 3200MD^{TM} LC/MS/MS System, AB Sciex]. It was defined as deficient, insufficient, and sufficient if vitamin D level was ≤15, ≤20 >15, and >20 ng/ml, respectively.

Non-HDL-C levels were calculated from the difference between serum TC and HDL-C. The TyG index was calculated using the formula: ln [fasting TGs (mg/dL) ×FPG (mg/dL)/2]

2.3 Autoantibody assays

To confirm autoimmune diabetes origin, three kinds of typical autoantibodies were tested. The level of GAD-ab was determined by the GAD-Ab ELISA Kit, GAD-ab assay (positivity: >5u/ml). IA2-ab and ZnT8-ab were measured by the enzyme-linked immunosorbent assay ([ElisaRSR^{TM} IA-2 Ab Version 2, UK]/[ElisaRSR^{TM} ZnT8 Ab™, UK]). Autoantibody for positivity were >7.5u/ml and >15u/ml for IA2-ab and ZnT8, respectively. The level of GAD-ab, IA2-ab, and ZnT8-ab were logarithmically transformed prior to analysis due to non-normal distributions.

2.4 Statistical analysis

Continuous variables were presented as Mean±SD or median in the case of normal or non-normal distribution, and differences between the two groups were examined by independent-sample t-test or Mann–Whitney U test correspondingly. Categorical variables were described as counts (percentages) and compared by Pearson chi-square test (Pearson $\chi 2$ test) or Fisher's exact test appropriately. Analysis of covariance (ANCOVA) was further conducted to control for the effects of sex, age, and BMI on metabolic disturbances. Pearson correlation test was used for evaluating the correlations between the TyG index and clinical variables. Bonferroni corrections were applied to each test to adjust for multiple testing. Receiver-operating characteristic (ROC) curve analysis was used to determine the optimal cut-off point value of TyG index for predicting DKA in T1DM children. A binary logistic regression analysis was performed to predict risky variables. Finally, a multiple linear regression analysis was used to identify significant predictive variables associated with TyG index. Statistical analyses were carried out using SPSS version 21, and Graphpad Prism version 9.0.2 was used to draw Forest plot and scatter plot. $P<0.05$ were considered indicative of statistical significance.

3 Results

3.1 Comparison of demographic and clinical variables between non-DKA and DKA patients

A total of 143 T1DM patients (60 boys, 83 girls) were enrolled in present study. The average age of patients without DKA was 8.53±3.54 years, and 7.23±3.50 years in patients with DKA. The mean age of onset was younger in patients with DKA than in another group (6.06±3.31 vs. 7.00±3.21 years, p=0.044). The mean BMI was 16.23±2.15 and 15.52±2.15 between non-DKA and DKA patients, respectively. Baseline characteristics of the total patients and groups stratifed by the occurrence of DKA were presented in **Table 1**.TyG index was significantly higher in patients with DKA compared with those without.

HbA1c in patients with DKA were higher than that of patients without DKA (p<0.001). There was no significant difference in C-peptide between the two groups (p=0.355). The DKA patients had significantly higher TG, TC, LDL-C, Non-HDL-C, ApoB, free fatty acid, TG/HDL-C, TC/HDL-C, LDL-C/HDL-C, Non-HDL-C/HDL-C, and ApoB/ApoA(all p<0.05). In contrast, HDL-C, ApoA, and Lipoprotein were lower in patients with DKA (all p<0.05). Analysis of covariance (ANCOVA) was further conducted to control for the effects of gender, age, and BMI on lipid parameters, significant differences still existed between the two groups.

3.2 Baseline clinical characteristics of patients stratifed by the optimal cut-off point of TyG index

ROC curve analysis showed that the area under the curve (AUC) of TyG index for predicting DKA was 0.912 (P<0.001). The TyG index of 10.13 was determined as the optimal cut-off point for predicting DKA with a sensitivity of 71.55% and a specificity of 100.00%. Baseline characteristics of groups according to the optimal cutoff point of TyG index were summarized in **Table 2**. Compared with patients in lower TyG index group, those with higher TyG index seemed to be younger. Laboratory indexes including TC, LDL-C, PCT, Cortisol, K, Mg and HbA1c were significantly higher in patients with higher TyG index, while HDL-C, T3, T4, and C3 were relatively lower. In higher TyG index group, higher concentration and positive rate of ZnT8A were prescribed compared to those with lower TyG index.

3.3 Incidence of adverse events according to the optimal cut-off point of TyG index

The incidence of adverse events was compared between groups stratifed by the optimal cut-off point of TyG index determined by ROC curve analysis. The incidence of DKA increased significantly in T1DM children with higher TyG index compared with those with lower TyG index (P<0.001). However, the prevalence of Vitamin D deficiency or Insufficiency, thyroid disease , family history of thyroid disease, family history of diabetes, and peripheral neuropathy was similar between the two groups (all P>0.05) (**Table 3**).

3.4 Correlation analysis of TyG index and clinical measures

Pearson or Spearman correlation analysis showed that TyG index were positive correlated with TC (r =0.572, P<0.001), LDL-C (r =0.200, p=P=0.018), PCT((r =0.425, P<0.001),Cortisol (r = 0.420, P<0.001),K(r =0.221, P=0.008),Mg(r =0.208, P=0.013), and ZnT8A levels (r = 0.221, P=0.049). TyG index level was inversely correlated with HDL-C (r =-0.657, P<0.001), T3(r =-0.647, P<0.001), T4(r =-0.547, P<0.001) and

C3(r =-0.350, P<0.001) in T1DM patients. Correlation analysis of TyG index and clinical measures were showed in **Table 4**.

Binary logistic regression analyses found that TC level in patients with higher TyG index was 1.035 times compared with lower TyG index(OR=2.454,P<0.001). Moreover, LDL-C, Cortisol and ZnT8A level were higher in patients with higher TyG index (all p<0.05).Decreasing HDL-C (OR=0.042, P<0.001), T3 (OR=0.021, P<0.001), T4(OR=0.958,P<0.001),and C3(OR=0.022, P<0.001) levels were also important predictors for patients with higher TyG index. The forest plot of binary logistic regression analyses with TyG index as dependent variable was showed in **Figure 1**.

3.5 Multiple linear regression to predict higher TyG index in T1DM patients

Furthermore, a multiple linear regression was performed to predict higher TyG index in T1DM patients. Five variables statistically predicted higher TyG index in T1DM children, including TC, C3, T3,Cortisol and lg(ZnT8A). The coefficients of these variables were showed in **Table 5**. Finally, TC (95%CI: 0.018~0.568, p=0.037) and T3(95%CI:-2.314~-0.668,p=0.001) were statistically significant in the multiple linear regression. Using the scatter plot, a linear equation was obtained between TC, T3 and TyG index (TyG index=10.226+0.299*TC-1.384*T3, R2=0.481).Scatter plot of TC and T3 was showed in **Figure 2**.

4 Discussion

In our present study, we retrospectively investigated the predictive significance of IR assessed by TyG index for DKA in patients with T1DM. The major findings are listed as follows:(1) Compared with patients in lower TyG index group, those with higher TyG index seemed to be younger and lower BMI;(2) compared to patients with lower TyG index, those with higher TyG index had an apparently higher incidence of DKA; (3) the TyG index was significantly correlated with TC and T3 levels for T1DM patients.

Insulin resistance (IR), characterized by a decrease in cell sensitivity to insulin, is one of the leading causes of metabolic abnormalities[6].Lipidomics studies of young and at-risk patients that progressed to clinical disease revealed that some classes of lipids shown dysregulation in the blood. A few lipid metabolites were found to be associated with T1DM [13]. Metabolomics techniques have shown that patients who progress to diabetes have different levels of certain lipids when compared with persons who remain non-diabetic [1]. Diabetic patients with dyslipidemia commonly suffer from a higher risk of adverse outcomes[14].

The TyG index is an advantageous surrogate marker of IR among adolescents, as it is a non-invasive method that uses common components to clinical practice, making it accessible and low cost[15]. Besides, the TyG index has the advantage of being based on FPG levels, which is directly related to the development of IR, β-cell dysfunction, pre-DM, and T2DM in young adults. Thus, the FPG of the TyG index may potentiate it for the prediction of diabetes concerning lipid ratio [9]. IR with higher TG and lower HDL-C concentrations is a clustered pathway of different metabolic disorders [5]. A population-based study

explored the associations of lipid parameters with prevalent IR and diabetes. The potential value of using the Non-HDL-C/HDL-C ratio and TG/HDL-C ratio as the dyslipidemia management tool among patients with diabetes should be given more consideration in the clinical approach [14]. Besides, TC/HDL-C ratio, and ApoB/ApoA ratio both predict adverse events independently of non-lipid risk factors, albuminuria and C-reactive protein [16].

IR and impaired β-cell function are the two key components in the pathogenesis of T2DM in youth [17]. However, the relationship between T1DM children with DKA and IR is unclear. Our study has shown that the TyG index is a predictor of an increased risk of DKA in T1DM children. A study confirmed that the index provided a good alternative to the gold standard test for recognizing IR in children aged 7-17[18].IR is an increasingly important issue for the early identification of children at risk, and the TyG index offers the advantage that it not requires insulin measurements and is based on routine laboratory assessments. One study reported that sex and puberty may influence associations between adiposity and IR in US Hispanic/Latino Youth[19].

Our study suggested that patients with higher TyG index were younger compared with patients in lower TyG index group. When it comes to the age of DKA onset, the risk begins to increase after early childhood (>5 years) and plateaus in the age group between 13 years and 25 years; thereafter, the DKA risk decreases with increasing age[20]. Our study suggested that T1DM children with DKA is younger, not only the age of onset (5.81±3.23 years vs. 7.16±3.12 years) but also current age (6.94±3.54 years vs. 8.62±3.42 years). Heterotopic lipid deposition leads to lipid toxicity and causes insulin resistance. Therefore, obesity is clearly a heterogeneous disease, with a part of obese people being insulin sensitive and another part of normal weight people being insulin resistant, which is the evidence[11]. In our study, there was no statistically significant difference in BMI between the two groups.

In our study, we found a lower level of T3 in higher TyG index group. As we all know that patients with diabetes have a high risk of AITD [21].27 of 70 patients in higher TyG index group suffered from thyroid disease, such as multiple cystic nodules of the thyroid, hypothyroidism, Autoimmune Polyendocrine Syndrome. The pathogenesis of AITD involves cellular and humoral autoimmune mechanisms against the thyroid gland. T lymphocytes infiltrate the glands, then subsequent development of various degrees of thyroid dysfunction [22]. Thyroid hormones T4 and T3 were produced by a glycosylated transmembrane protein named thyroid peroxidase, which is distributed in the apical part of follicular thyroid cells [23].Metabolomics techniques have shown that people who develop diabetes have different levels of certain lipids when compared with people who remain non-diabetic[24].In addition, thyroid dysfunction can lead to metabolic disorders. This in turn results in stimulation of glycogenolysis and gluconeogenesis, increased glucose absorption, and lipolysis, causing deterioration of metabolic control [25]. Anyway, recognition of these metabolic alterations may aid in studies of disease progression and may open a time window for DKA prevention strategies, it is reasonable to recommend TC and T3 as effective and convenient indicators of higher TyG index. The lipid metabolism abnormality may be the reaction of IR, which can predict the risk of DKA by calculating the TyG index.

The following limitations of our study should be addressed. Firstly, the findings were restricted to a selected group of Chinese patients from a single center. Hence, results should be interpreted with caution. Secondly, glucose and all lipid parameters measures were evaluated based on a single measurement, variability existed in experimental error, which may cause some bias and attribute to the discrepancies of results. Thirdly, although we did find a significant association between most lipid parameters and glucose metabolism, other potential factors were not evaluated in the present study, such as dietary characteristics and other concomitant therapies influencing lipid levels. Moreover, we had a comparatively small sample size of subjects, which had become smaller when dividing into two groups. Therefore, the results and conclusions in our study should be regarded as preliminary. Larger sample size and multicentre trials are necessary to confirm our findings.

5. Conclusions

In conclusion, increased TyG index is a significant predictor of DKA in children with T1DM. Higher TC and lower T3 levels were associated with higher TyG index. Further prospective, randomized studies need to be conducted to determine whether interventions for TyG index have a positive impact on improving clinical prognosis.

Abbreviations

T1DM
Type 1 diabetes mellitus
DKA
Diabetic ketoacidosis
TyG index
triglyceride-glucose index
IR
Insulin resistance
FPG
fasting plasma glucose
$HbA1_C$
Hemoglobin $A1_C$
TG
Triglyceride
TC
Total cholesterol
HDL-C
High density lipoprotein cholesterol
LDL-C
Low density lipoprotein cholesterol

Apo A
apolipoprotein A
ApoB
apolipoprotein B
GADA
Glutamic acid decarboxylase autoantibody
IA-2A
Protein tyrosine PhosPhatase-2 antibody
ZnT8A
Zinc transporter 8 autoantibody

Declarations

Ethics approval and consent to participate

The study was ethically approved by the Institute Ethics Committee of Tianjin Children's Hospital(Tianjin University Children's Hospital), Tianjin, China.Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

L.G., X.W., and J.S. are responsible for the work described in this paper. M.Z., and J.G. conceived, designed, and/or planned the study, and interpreted the results. X.Z., C.G., and L.P. conducted data analysis. J.S. and X.W. drafted the manuscript. C.C., W.Y., and L.L. critically reviewed and/or revised the

manuscript for important intellectual content. All authors approved the final version of the manuscript to be published and agreed to be accountable for all aspects of the work.

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Tables

Table 1

Baseline clinical characteristics of patients with and without DKA

Characteristics	T1DM without DKA (n = 43)	T1DM with DKA (n = 100)	t or χ2	P value
Age(years)	8.53 ± 3.54	7.23 ± 3.50	2.037	p = 0.044
Boys (%)	18/43(41.9)	42/100(42.0)		
Girls (%)	25/43(58.1)	58/100(58.9)	0.000	p = 0.988
BMI(kg/m2)	16.23 ± 2.15	15.52 ± 2.15	1.564	p = 0.121
Age of onset(years)	7.00 ± 3.21	6.06 ± 3.31	1.573	p = 0.118
HbA1c (%)	9.40 ± 2.58	12.80 ± 2.27	-7.763	p < 0.001
C-peptide(nmol/l)	0.16 ± 0.19	0.13 ± 0.10	0.934	p = 0.355
FPG (mmol/l)	11.43 ± 6.21	23.85 ± 9.41	-10.023	p < 0.001
FPG(mg/dl)	203.37 ± 110.75	423.72 ± 170.31	-9.187	p < 0.001
TG(mmol/L)	0.65	2.53	-8.200	p < 0.001
TG(mg/dl)	57.57	224.09	-8.200	p < 0.001
TC (mmol/L)	4.17 ± 0.89	5.24 ± 1.33	-5.510	p < 0.001
HDL-C(mmol/L)	1.88 ± 0.36	1.17 ± 0.41	9.134	p < 0.001
LDL-C(mmol/L)	2.29 ± 1.24	3.00 ± 1.84	-3.233	p = 0.002
Non-HDL-C (mmol/L)	2.37 ± 1.05	4.12 ± 1.66	-7.445	p < 0.001
ApoA(mmol/L)	147.92 ± 27.04	131.55 ± 30.41	2.892	p = 0.004
ApoB(mmol/L)	73.16 ± 29.25	111.49 ± 31.39	-6.491	p < 0.001

Characteristics	T1DM without DKA (n = 43)	T1DM with DKA (n = 100)	t or χ2	P value
Lipoprotein(mmol/L)	13.80	4.80	-3.782	p < 0.001
Free fatty acid(mmol/L)	0.59	1.16	-6.554	p < 0.001
TC/HDL-C	2.25	4.55	-7.110	p < 0.001
LDL-C/HDL-C	1.19	2.44	-6.382	p < 0.001
Non-HDL-C/HDL-C	1.46 ± 1.05	4.45 ± 4.04	-6.318	p < 0.001
ApoB/ApoA	0.46	0.84	-6.381	p < 0.001
TyG index	8.65 ± 0.71	10.74 ± 1.36	-11.942	p < 0.001

Table 2
Baseline clinical characteristics of patients stratifed by the optimal cut-off point of TyG index

	TyG index ≤ 10.13 (n = 73)	TyG index > 10.13 (n = 70)	t or χ2	P Value
Age(years)	8.62 ± 3.42	6.94 ± 3.54	2.833	p = 0.005
Boys (%)	27/73(37.0)	33/70(47.1)		
Girls (%)	46/73(63.0)	37/70(52.9)	1.514	p = 0.219
BMI(kg/m2)	15.90 ± 2.20	15.37 ± 1.98	1.467	p = 0.145
Age of onset(years)	7.16 ± 3.12	5.81 ± 3.23	2.494	p = 0.014
HbA1c (%)	9.84 ± 3.01	13.15 ± 1.90	-8.459	p < 0.001
C-peptide(nmol/l)	0.13 ± 0.16	0.14 ± 0.09	-0.513	p = 0.609
Vitamin D(ng/ml)	21.31 ± 8.67	19.19 ± 8.93	1.438	p = 0.153
TC(mmol/L)	1.67 ± 0.49	5.70 ± 1.56	-6.843	p < 0.001
HDL-C(mmol/L)	1.67 ± 0.49	1.07 ± 0.38	8.708	p < 0.001
LDL-C(mmol/L)	2.52 ± 0.96	3.03 ± 1.23	-2.939	p = 0.004
T3(nmol/L)	1.51 ± 0.48	0.83 ± 0.39	9.161	p < 0.001
T4(nmol/L)	107.37 ± 24.14	68.56 ± 35.68	7.517	p < 0.001
TSH(mIU/L)	2.11 ± 2.00	1.89 ± 1.59	0.712	p = 0.478
CRP(mg/L)	1.10	1.75	-0.764	p = 0.445
PCT(ng/ml)	0.05	0.10	-4.356	p < 0.001
C3(g/L)	1.02 ± 0.21	0.86 ± 0.20	4.426	p < 0.001
C4(g/L)	0.24 ± 0.08	0.23 ± 0.09	0.714	p = 0.477
Cortisol(nmol/L)	403.70	627.71	-3.743	p < 0.001
ACTH(pg/ml)	21.25	20.17	-0.662	p = 0.508
K(mmol/l)	4.34 ± 0.55	4.57 ± 0.83	-6.843	p < 0.001
Ca(mmol/l)	2.45 ± 0.11	2.42 ± 0.15	1.273	p = 0.206
P(mmol/l)	1.45 ± 0.28	1.45 ± 0.40	0.114	p = 0.909
Mg(mmol/l)	0.80 ± 0.07	0.85 ± 0.11	-2.924	p = 0.004
Autoantibodies				

	TyG index ≤ 10.13 (n = 73)	TyG index > 10.13 (n = 70)	t or χ2	P Value
GADA(%)	73.7	71.4	0.051	p = 0.821
lg(GADA)(u/ml)	1.41 ± 1.03	1.34 ± 0.95	0.310	p = 0.757
IA-2A (%)	50.0	61.9	1.149	p = 0.284
lg(IA-2A)(u/ml)	1.39 ± 1.04	1.68 ± 1.18	-1.169	p = 0.246
ZnT8A(%)	28.9	59.5	7.536	p = 0.006
lg(ZnT8A)(u/ml)	0.89 ± 0.84	1.44 ± 0.95	-2.716	p = 0.008

Table 3
Incidence of adverse events according to the optimal cut-off point of TyG index

	TyG index ≤ 10.13 (n = 73)	TyG index > 10.13 (n = 70)	t or χ2	P Value
With or without DKA				
T1DM (%)	43/73(58.9)	0/70(0.0)		
TIDM + DKA(%)	30/73(41.1)	70/70(100.0)	58.963	P < 0.001
25(OH)D level				
Deficiency(%)	18/73(24.7)	28/70(40.0)		
Insufficiency(%)	19/73(26.0)	16/70(22.9)	3.983	P = 0.137
Sufficient(%)	36/73(49.3)	26/70(37.1)		
Thyroid disease				
No (%)	51/73(69.9)	43/70(61.4)		
Yes (%)	22/73(30.1)	27/70(38.6)	1.129	p = 0.288
Family history of thyroid disease				
No (%)	68/73(93.2)	69/70(98.6)		
Yes (%)	5/73(6.8)	1/70(1.4)	2.612	p = 0.106
Family history of diabetes				
No (%)	53/73(72.6)	44/70(62.9)		
Yes (%)	20/73(27.4)	26/70(37.1)	1.555	p = 0.212
Peripheral neuropathy				
No (%)	53/73(72.6)	49/70(70.0)		
Yes (%)	20/73(27.4)	21/70(30.0)	0.118	p = 0.731

Table 4
Correlations between the TyG index and clinical characteristics

	Correlation coefficient	P Value
Age(years)	-0.116	P = 0.136
BMI(kg/m2)	-0.152	P = 0.083
Age of onset(years)	-0.041	p = 0.579
HbA1c (%)	0.663	P < 0.001
C-peptide(nmol/l)	-0.027	P = 0.733
Vitamin D(ng/ml)	-0.157	P = 0.061
TC(mmol/L)	0.572	P < 0.001
HDL-C(mmol/L)	-0.657	P < 0.001
LDL-C(mmol/L)	0.200	P = 0.018
T3(nmol/L)	-0.647	P < 0.001
T4(nmol/L)	-0.547	P < 0.001
TSH(mIU/L)	0.022	P = 0.797
CRP(mg/L)	0.088	P = 0.297
PCT(ng/ml)	0.425	P < 0.001
C3(g/L)	-0.350	P < 0.001
C4(g/L)	-0.026	P = 0.767
Cortisol(nmol/L)	0.420	P < 0.001
ACTH(pg/ml)	0.024	P = 0.811
K(mmol/l)	0.221	P = 0.008
Ca(mmol/l)	-0.123	P = 0.143
P(mmol/l)	-0.025	P = 0.768
Mg(mmol/l)	0.208	P = 0.013
Ig(GADA)(u/ml)	-0.016	p = 0.885
Ig(IA-2A)(u/ml)	0.080	P = 0.480
Ig(ZnT8A)(u/ml)	0.221	P = 0.049

Table 5

Predictors generated by multiple linear regression with TyG index as dependent variables

					Collinearity statistics	
	B	t	P value	95%CI for B	Tolerance	VIF
(constant)	9.507	7.690	P < 0.001	7.020 ~ 11.995		
TC(mmol/L)	0.293	2.144	P = 0.037	0.018 ~ 0.568	0.760	1.316
C3(g/L)	0.469	0.601	P = 0.551	-1.100 ~ 2.038	0.703	1.422
T3(nmol/L)	-1.491	-3.643	P = 0.001	-2.314~-0.668	0.565	1.770
Cortisol(nmol/L)	0.001	1.900	P = 0.064	0.000 ~ 0.002	0.869	1.151
Ig(ZnT8A)(u/ml)	0.108	0.557	P = 0.580	-0.283 ~ 0.499	0.794	1.259

Figures

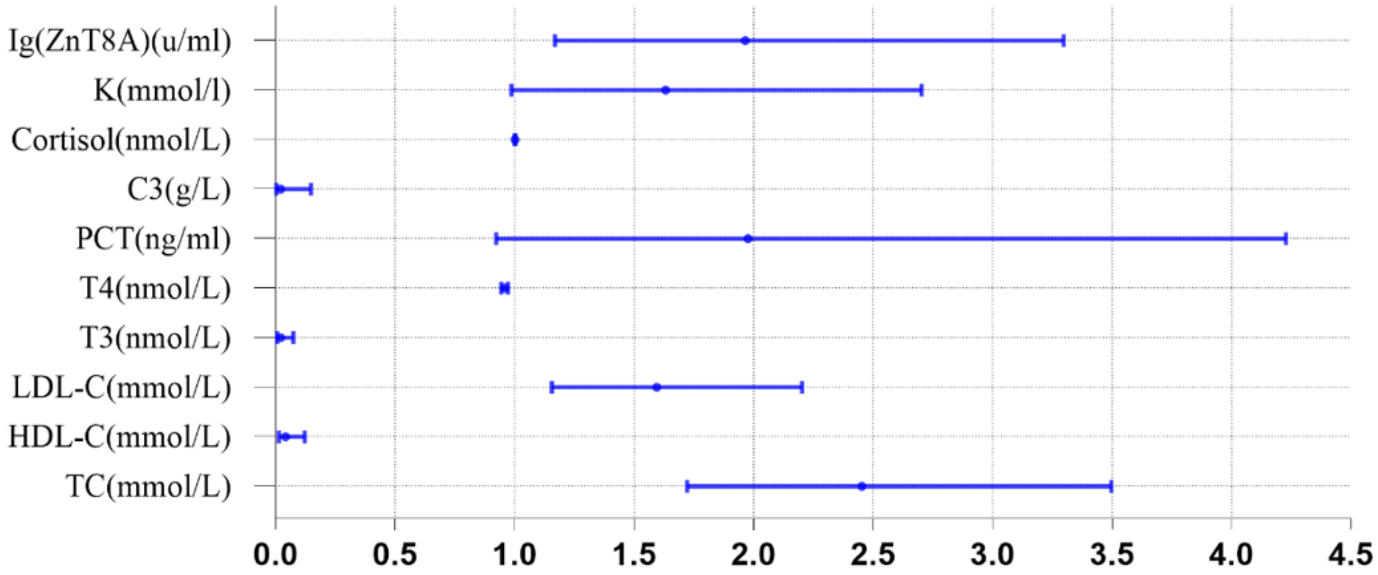

Figure 1

Binary logistic regression analyses with TyG index as dependent variable

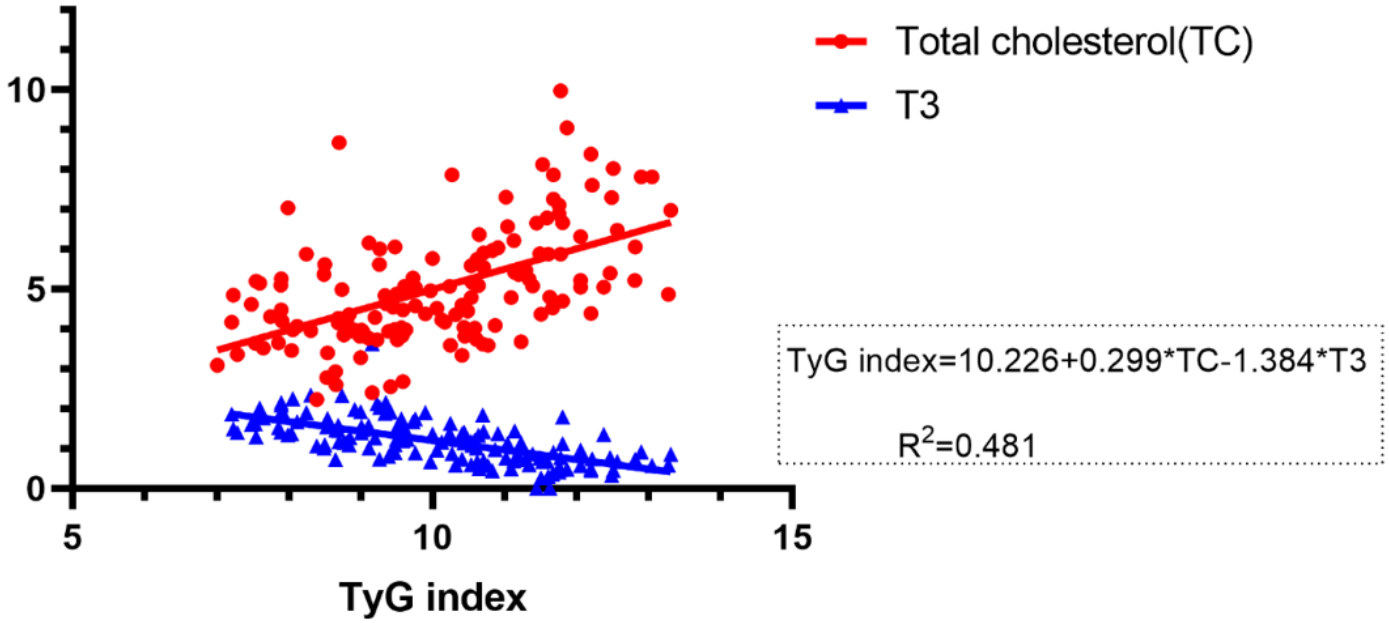

Figure 2

Scatter plot of total cholesterol and T3 generated in multiple linear regression