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Association Between a New Model of Insulin Sensitivity and Hypertension in Patients With Type 2 Diabetes: A Cross-Sectional Study

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ABSTRACT

Type 2 diabetes (T2D) and hypertension often coexist, and insulin resistance (IR) plays an important role in their pathological progression. An increasing number of studies have focused on the relationship between different IR indices and hypertension. A natural log transformation of the glucose disposal rate ($\log_e$ GDR) has been proposed as a new model for insulin sensitivity in patients with T2D. The study aimed to explore the relationship between $\log_e$ GDR and hypertension in T2D patients. This cross-sectional study included 1544 Chinese T2D patients. Clinical and biochemical characteristics were collected. The $\log_e$ GDR was calculated based on triglycerides, urinary albumin to creatinine ratio, gamma-glutamyl transferase, and body mass index. Patients were categorized into hypertension and nonhypertension groups stratified by gender. Among both females and males, compared with the nonhypertension group, the level of $\log_e$ GDR was significantly decreased in the hypertension group (both $p < 0.001$). As the $\log_e$ GDR increased, the levels of systolic and diastolic blood pressure, and the prevalence of hypertension were obviously increased (all $p < 0.001$). Univariate analysis displayed that $\log_e$ GDR was negatively related to hypertension (correlation coefficient: −0.243, $p < 0.001$ in females; correlation coefficient: −0.181, $p < 0.001$ in males). Furthermore, the logistic regression analysis showed that $\log_e$ GDR was independently associated with hypertension (OR: 0.456; 95% CI: 0.224–0.927 in females; OR: 0.544; 95% CI: 0.314–0.941 in males). This study revealed that $\log_e$ GDR was closely related to hypertension, which might help monitor and manage hypertension in T2D patients.

1 | Introduction

The prevalence of diabetes, especially type 2 diabetes (T2D), is increasing worldwide and remains a substantial public health issue due to various acute and chronic complications [1]. Evidence shows that T2D and hypertension often coexist, and more than half of the population suffers from hypertension among T2D patients [2]. Additionally, hypertension is one of the main risk factors for both microvascular and macrovascular complications of diabetes [3]. Therefore, screening precipitating factors for hypertension may be important to prevent the occurrence and progression of complications under the condition of diabetes.

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Insulin resistance (IR) plays a crucial role in the pathogenesis of hypertension, and the molecular mechanisms may be involved in inappropriate activation of the renin-angiotensin-aldosterone system, mitochondrial dysfunction, and inflammation [4]. It is widely known that the hyperinsulinemic clamp technique is the gold standard for evaluating IR [5], but its time-consuming and invasiveness limit its use in large-scale epidemiological studies. The homeostasis model assessment index (HOMA-IR) has been proposed as a simpler method for assessing IR [6]. Although this method facilitates large cohort studies, it relies on fasting plasma insulin (FINS), which are not commonly conducted and can fluctuate significantly. Additionally, fasting insulin levels are often unreliable in insulin-treated T2D patients. Fortunately, a series of noninsulin dependent IR replacement indices have been proposed. Recently, based on the routinely available clinical and biomarker data, including triglycerides (TG), gamma-glutamyl transferase (GGT), urinary albumin to creatinine ratio (UACR), and body mass index (BMI), Ciardullo et al. [7] proposed a new model of insulin sensitivity (IS) named the natural log transformation of the glucose disposal rate ($\log_e$ GDR) and found that the model was significantly associated with all-cause mortality and cardiovascular mortality in T2D patients.

At present, there was a lack of research to elucidate the correlation between $\log_e$ GDR and hypertension. Previous studies have demonstrated that the impact of various components of $\log_e$ GDR on cardiometabolic risk differs significantly between males and females [8, 9]. Therefore, our study aimed to explore the relationship between $\log_e$ GDR and hypertension in patients with T2D with stratification by gender. Meanwhile, we also included other commonly used effective IR indicators and related derivative parameters, including HOMA-IR, insulin resistance metabolic score (METS-IR) [10], triglyceride glucose index (TyG index) [11], TyG-BMI [12], TyG-GGT [13], combination of BMI and FPG (ByG) index [14], uric acid (UA)/high-density lipoprotein cholesterol (HDL-c) ratio (UHR) [15], and TG/HDL-c ratio [16], to analyze the relationships between them and hypertension.

2 | Methods

2.1 | Study Design and Study Population

This cross-sectional study analyzed the inpatients with T2D aged ≥ 18 years from the Department of Endocrinology of Linyi People's Hospital, from January 2020 to March 2023. The exclusion criteria were (1) patients with other types of diabetes; (2) patients with liver insufficiency (exceeding two times the upper limit of normal reference value) and renal insufficiency (eGFR < 90 mL/min/1.73m^2); (3) patients with other identifiable causes of secondary hypertension. In the end, a total of 1544 patients with T2D were included in this study.

2.2 | General Conditions and Physical Examinations

The patients' general conditions, including age, sex, duration of diabetes, height, weight, and smoking and drinking status, were recorded. The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the nondominant arm of seated participants with an automated electronic device. Hypertension was defined as SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, or a history of hypertension currently taking antihypertensive medications. Patients were categorized into hypertension and nonhypertension groups. The visceral fat area (VFA) and subcutaneous fat area (SFA) were tested by bioelectrical impedance analysis (HDS-2000, Omron, Kyoto, Japan).

2.3 | Laboratory Measurements

Following an overnight fast, blood samples were collected and analyzed in the morning for TG, total cholesterol (TC), HDL-c, low-density lipoprotein-cholesterol (LDL-c), aspartate aminotransferase (AST), alanine aminotransferase (ALT), GGT, fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c, high-performance liquid chromatography), UA, serum creatinine (Scr), cystatin C (Cys C), and hemoglobin (Hb) by a biochemical autoanalyzer (Cobas c 702, Roche, Germany). UACR was measured using an autoanalyzer (Beckman Coulter AU5821). FINS was measured using a direct chemiluminescence method with a fully automated sample processing system (Aptio Automation, SIEMENS, USA).

2.4 | Parameter Calculations

1. HOMI-IR = FPG (mmol/L) * FINS (μU/mL)/22.5 [6];
2. Log_e GDR = 5.3505 − 0.3697 * $\log_e$ (GGT, IU/L) − 0.2591 * $\log_e$ (TG, mg/dL) − 0.1169 * $\log_e$ (UACR, mg/g) − (0.0279 * BMI, kg/m^2) [7];
3. BMI = weight (kg)/height (m)^2 [2];
4. METS-IR = Ln [(2 * FPG (mg/dL)) + TG (mg/dL)] * BMI)/(Ln [HDL-c (mg/dL)]) [10];
5. TyG index = Ln [TG (mg/dL) * FPG (mg/dL)/2] [11];
6. TyG-BMI = TyG * BMI [12];
7. TyG-GGT = TyG * GGT [13];
8. ByG index = Ln [1/2 BMI (kg/m^2) * FPG (mg/dL)] [14];
9. UHR (%) = UA (mg/dL)/HDL (mg/dL) *100 [15];
10. TG/HDL-c ratio = TG (mmol/L) / HDL-c (mmol/L) [16];
11. eGFR = 175 * Scr (mg/dL) $^{-1.234}$ * age $^{-0.179}$ × (0.79, if female) [17].

2.5 | Statistical Analysis

Statistical analysis was performed using SPSS 26.0 (SPSS, Inc., Chicago, USA). Normally distributed variables were expressed as mean ± SD and were compared using an independent-samples *T* test between two groups. Abnormal distributions were expressed as median and interquartile ranges, and were compared using the Mann–Whitney *U* test between two groups. Among the $\log_e$ GDR categories groups, an analysis of variance test was performed for multiple comparisons of normally distributed data, and a Kruskal–Wallis test for abnormal distributions. Categorical variables were presented as percentages (%), and were compared

using the Chi-square test. Spearman correlation analysis was applied to estimate the corrections between hypertension and various variables. Logistic regression analysis was used to analyze the independent correlates of hypertension. Statistical differences were defined by a p value (two-tailed) less than 0.05.

3 | Results

3.1 | Baseline Clinical and Biochemical Characteristics

The baseline clinical and biochemical characteristics of the subjects are presented in Table 1. In females, compared with the nonhypertension group, age, duration of diabetes, BMI, VFA, SFA, SBP, DBP, TG, FINS, ALT, AST, GGT, Cys C, UA, Scr, UACR, Hb, TyG index, TyG-BMI, TyG-GGT, ByG index, TG/HDL-c ratio, HOMA-IR, and METS-IR were higher (all $p < 0.05$), while eGFR and $\log_e$ GDR were lower in the hypertension group (both $p < 0.001$). However, there were no obvious differences between the two groups in TC, LDL-c, HDL-c, FPG, HbA1c, and UHR, and the percentage of smoking and drinking (all $p > 0.05$). In males, age, BMI, VFA, SFA, SBP, DBP, ALT, AST, GGT, UA, UACR, TyG-BMI, TyG-GGT, UHR, and METS-IR were significantly increased (all $p < 0.05$), while FPG, HbA1c, and $\log_e$ GDR were obviously decreased in the hypertension group (all $p < 0.05$). However, there were no obvious differences between the two groups in duration of diabetes, TC, TG, LDL-c, HDL-c, FINS, Cys C, Scr, eGFR, Hb, TyG index, ByG index, TG/HDL-c ratio, and HOMA-IR, as well as the percentages of smoking and drinking (all $p > 0.05$).

According to the $\log_e$ GDR levels, the subjects were divided into three groups (Table 2). The tertiles of $\log_e$ GDR were defined as follows: for females, T1 ($0.38 \leq \log_e$ GDR < 1.85), T2 ($1.85 \leq \log_e$ GDR ≤ 2.17), and T3 ($2.17 < \log_e$ GDR ≤ 3.12); for males, T1 ($0.29 \leq \log_e$ GDR < 1.69), T2 ($1.69 \leq \log_e$ GDR ≤ 2.06), and T3 ($2.06 < \log_e$ GDR ≤ 2.88). In females, across the tertiles, age, duration of diabetes, and HDL-c were elevated (all $p < 0.05$), while BMI, VFA, SFA, SBP, DBP, TC, LDL-c, TG, FPG, FINS, HbA1c, ALT, AST, GGT, Cys C, UA, UACR, Hb, TyG index, TyG-BMI, TyG-GGT, ByG index, UHR, TG/HDL-c ratio, HOMA-IR, and METS-IR, and the percentage of hypertension were decreased (all $p < 0.05$). There were no significant differences among the three groups for Scr and eGFR, and the percentage of smoking and drinking (all $p > 0.05$). In males, across the tertiles, age, HDL-c and duration of diabetes were elevated (all $p < 0.05$), while BMI, VFA, SFA, SBP, DBP, TC, LDL-c, TG, FPG, FINS, ALT, AST, GGT, UA, UACR, Hb, TyG index, TyG-BMI, TyG-GGT, ByG index, UHR, TG/HDL-c ratio, HOMA-IR, and METS-IR, and the percentage of hypertension, smoking, and drinking were decreased (all $p < 0.05$). No significant differences were observed among the three groups in terms of HbA1c, Cys C, Scr, and eGFR (all $p > 0.05$).

3.2 | Univariate Analysis

Table 3 demonstrates the correlations between hypertension and each variable by a Spearman correlation analysis. In females, the results showed that age, duration of diabetes, BMI, VFA, SFA, TG, FINS, ALT, AST, GGT, Cys C, UA, UACR, Hb, TyG index, TyG-BMI, TyG-GGT, ByG index, TG/HDL-c ratio, HOMA-IR, and METS-IR were positively correlated with hypertension (all $p < 0.05$), while eGFR and $\log_e$ GDR were negatively correlated with hypertension (both $p < 0.001$). Smoking, drinking, TC, LDL-c, HDL-c, FPG, HbA1c, and UHR showed no significant correlation with hypertension (all $p > .05$). In males, the results showed that age, BMI, VFA, SFA, ALT, AST, GGT, UA, UACR, TyG-BMI, TyG-GGT, UHR, and METS-IR were positively correlated with hypertension (all $p < 0.05$). In contrast, TC, FPG, HbA1c, eGFR, and $\log_e$ GDR were negatively correlated with hypertension (all $p < 0.05$). Smoking, drinking, duration of diabetes, TG, LDL-c, HDL-c, FINS, Cys C, Hb, TyG index, ByG index, TG/HDL-c ratio, and HOMA-IR were not correlated with hypertension (all $p > 0.05$).

3.3 | Multivariate Analysis

For females, hypertension was served as the dependent variable, while age, duration of diabetes, BMI, VFA, SFA, TG, FINS, ALT, AST, GGT, Cys C, UA, eGFR, UACR, Hb, TyG index, TyG-BMI, TyG-GGT, ByG index, TG/HDL-c ratio, HOMA-IR, METS-IR, and $\log_e$ GDR were considered as the independent variables according to the results of univariate analysis (Table 3). A logistic regression analysis was performed to identify the independent correlates of hypertension (Table 4). After adjusting for other variables, the analysis revealed that $\log_e$ GDR (OR: 0.456; 95% CI: 0.224–0.927), VFA (OR: 1.012; 95% CI: 1.005–1.020), and age (OR: 1.039; 95% CI: 1.017–1.062) were independently associated with hypertension.

For males, adjusting for age, BMI, VFA, SFA, TC, FPG, HbA1c, ALT, AST, GGT, UA, eGFR, UACR, TyG-BMI, TyG-GGT, UHR, and METS-IR, the results showed that $\log_e$ GDR (OR: 0.544; 95% CI: 0.314–0.941), VFA (OR: 1.013; 95% CI: 1.008–1.019), age (OR: 1.027; 95% CI: 1.010–1.044) and HbA1c (OR: 0.866; 95% CI: 0.795–0.944) were independently associated with hypertension.

4 | Discussion

In this cross-sectional study, we observed a strong correlation between $\log_e$ GDR and hypertension, with the prevalence of hypertension decreasing progressively as the $\log_e$ GDR tertiles increased. Additionally, multivariate analysis indicated that the $\log_e$ GDR was independently associated with hypertension in patients with T2D.

IR is well known to play a key role in the development of hypertension and is an important target point for monitoring and managing hypertension. The $\log_e$ GDR was a new noninsulin-based IS indicator proposed in patients with T2D [7]. Our study found that it was closely related to other IR indicators, including HOMA-IR, TG/HDL-c ratio, TyG index, TyG-BMI, METS-IR, and UHR, and as the $\log_e$ GDR tertiles increased, these indicators all gradually decreased, which suggested that this model might have strong generalizability.

The $\log_e$ GDR was a composite index based on GGT, TG, UACR, and BMI, and any component of this model had been proven to be related to hypertension. Research showed that GGT activity could predict hypertension independent of multiple confounders, including BMI [8]. TG was another indicator

TABLE 1 | Clinical and biochemical characteristics by presence of hypertension.

Variables	All	Female			Male		
		Nonhypertension	Hypertension	*p* value	Nonhypertension	Hypertension	*p* value
Number (*n*, %)	1544	500	454		319	271	
Sex (male, *n*, %)	590 (38.2%)						
Smoking (*n*, %)	234 (15.2%)	3 (0.6%)	3 (0.7%)	0.908	118 (37.0%)	110 (40.6%)	0.371
Drinking (*n*, %)	212 (13.7%)	3 (0.6 %)	1 (0.2 %)	0.626	102 (32.9%)	106 (39.1%)	0.070
Age (years)	56.4 ± 12.1	54.9 ± 11.8	59.9 ± 11.4	< 0.001	53.9 ± 12.6	56.6 ± 12.0	0.007
Duration of diabetes (years)	7.00 (2.00–12.00)	6.0 (2.0–10.0)	7.0 (3.0–13.3)	0.002	7.0 (2.0–12.0)	8.0 (3.0–13.0)	0.139
BMI (kg/m^2)	25.43 ± 3.65	24.37 ± 3.57	26.08 ± 3.86	< 0.001	25.15 ± 3.11	26.63 ± 3.47	< 0.001
VFA (cm^2)	88.00 (63.00–118.00)	68.50 (49.25–92.00)	89.00 (69.00–112.00)	< 0.001	96.00 (70.00–122.00)	121.00 (94.00–145.00)	< 0.001
SFA (cm^2)	180.00 (138.50–226.00)	157.00(118.00–207.50)	190.00 (148.75–240.00)	<0.001	175.00 (138.00–212.00)	201.50 (167.00–243.75)	< 0.001
SBP (mmHg)	129.0 ± 17.8	118.6 ± 11.7	141.5 ± 16.8	< 0.001	119.0 ± 11.0	139.0 ± 16.1	< 0.001
DBP (mmHg)	80.7 ± 10.8	75.1 ± 7.6	84.7 ± 11.7	< 0.001	76.9 ± 7.4	88.6 ± 10.3	< 0.001
TC (mmol/L)	4.84 ± 1.22	4.94 ± 1.13	5.08 ± 1.32	0.060	4.66 ± 1.12	4.49 ± 1.23	0.080
LDL-c (mmol/L)	3.08 ± 1.02	3.15 ± 0.97	3.20 ± 1.08	0.444	2.99 ± 0.93	2.85 ± 1.05	0.103
TG (mmol/L)	1.37 (0.97–2.03)	1.32 (0.88–1.84)	1.42 (1.04–2.08)	0.001	1.35 (0.95–2.11)	1.47 (1.01–2.17)	0.183
HDL-c (mmol/L)	1.20 ± 0.35	1.26 ± 0.32	1.29 ± 0.43	0.267	1.09 ± 0.24	1.06 ± 0.26	0.191
FPG (mmol/L)	8.99 ± 3.42	8.96 ± 3.52	9.06 ± 3.40	0.665	9.25 ± 3.51	8.61 ± 3.11	0.021
FINS (μIU/mL)	16.40 (10.00–21.70)	15.79 (7.59–21.33)	17.80 (12.29–23.39)	< 0.001	14.89 (9.95–20.25)	16.86 (10.12–20.48)	0.428
HbA1c (%)	9.34 ± 2.20	9.43 ± 2.30	9.27 ± 2.03	0.284	9.71 ± 2.33	8.86 ± 2.07	< 0.001
ALT (U/L)	18.10 (13.48–26.20)	15.80 (12.10–23.80)	18.05 (13.00–25.50)	0.002	19.30 (14.63–28.35)	21.50 (16.20–34.50)	0.034
AST (U/L)	17.40 (14.20–22.30)	16.40 (13.30–22.00)	17.40 (14.50–22.40)	0.012	17.40 (14.70–21.80)	19.00 (15.50–23.30)	0.011
GGT (U/L)	21.00 (15.00–31.00)	17.25 (13.00–25.00)	19.00 (15.00–27.08)	< 0.001	24.00 (17.00–36.00)	28.00 (19.80–43.00)	0.001
Cys C(mg/L)	0.82 ± 0.18	0.80 ± 0.19	0.84 ± 0.17	0.006	0.82 ± 0.18	0.84 ± 0.16	0.267
UA (μmolL)	269.25 ± 81.35	242.96 ± 74.08	257.01 ± 80.05	0.005	293.90 ± 78.19	309.22 ± 76.64	0.017
Scr (μmol/L)	57.83 ± 11.05	51.27 ± 7.64	52.94 ± 8.06	0.001	66.61 ± 8.59	67.77 ± 9.14	0.112
eGFR (mL/min/1.73 m^2)	130.16 ± 27.47	137.47 ± 28.77	130.23 ± 28.44	< 0.001	125.45 ± 23.06	122.08 ± 24.65	0.087
UACR (mg/g)	9.60 (5.60 ~ 24.50)	8.60 (5.30 ~ 18.45)	12.60 (7.00 ~ 31.80)	<0.001	7.90 (4.30 ~ 21.60)	9.10 (5.60 ~ 30.30)	0.015
Hb (g/L)	141.89 ± 16.33	133.69 ± 13.44	136.42 ± 13.33	0.002	153.64 ± 13.30	152.20 ± 15.40	0.226
TyG index	9.18 ± 0.77	9.08 ± 0.73	9.22 ± 0.73	0.003	9.21 ± 0.81	9.23 ± 0.82	0.804

(Continues)

TABLE 1 | (Continued)

Variables	All	Female			Male		
		Nonhypertension	Hypertension	*p* value	Nonhypertension	Hypertension	*p* value
TyG-BMI	234.22 ± 43.73	222.00 ± 40.68	241.32 ± 44.93	0.001	232.42 ± 39.72	246.97 ± 45.78	< 0.001
TyG-GGT	191.12 (133.24–294.27)	157.56 (113.48–227.29)	178.57 (133.54–262.40)	< 0.001	220.05 (152.32–333.80)	256.40 (174.20–399.33)	0.002
ByG index	7.55 ± 0.40	7.50 ± 0.41	7.58 ± 0.41	0.002	7.57 ± 0.40	7.57 ± 0.37	0.916
UHR (%)	10.72 ± 5.22	9.11 ± 4.48	9.54 ± 4.64	0.146	12.52 ± 5.39	13.58 ± 5.40	0.018
TG/HDL-c ratio	1.20 (0.75–1.91)	1.07 (0.65–1.73)	1.17 (0.77–1.90)	0.009	1.34 (0.81–2.14)	1.45 (0.84–2.33)	0.113
HOMA-IR	6.00 (3.38–9.38)	5.71 (2.81–8.88)	6.68 (3.88–9.75)	0.001	6.03 (3.35–9.41)	5.66 (3.40–10.18)	0.884
METS-IR	41.27 ± 8.44	38.74 ± 7.73	41.60 ± 8.42	< 0.001	41.82 ± 7.84	44.75 ± 9.01	< 0.001
Log_e GDR	1.93 ± 0.40	2.08 ± 0.36	1.89 ± 0.37	< 0.001	1.92 ± 0.40	1.76 ± 0.42	< 0.001

Note: Data were presented as mean ± SD for normally distributed variables, and median (interquartile ranges) for abnormal distributions. Independent samples *T* test and Mann–Whitney *U* test were used for comparisons of normally and abnormally distributed continuous variables between nonhypertension and hypertension groups, respectively. Categorical variables were presented as percentage (%) and were compared by chi-square test. Statistical differences were defined by a *p* value (two-tailed) less than 0.05.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Cys C, cystatin C; DBP, diastolic blood pressure; FINS, fasting serum insulin; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyl transferase; GDR, glucose disposal rate; Hb, hemoglobin; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; LDL-c, low-density lipoprotein cholesterol; METS-IR, Insulin resistance metabolic score; SBP, systolic blood pressure; Scr, serum creatinine; SFA, subcutaneous fat area; TC, total cholesterol; TG, triglyceride; UA, uric acid; UACR, urinary albumin to creatinine ratio; UHR, serum uric acid-to-high-density lipoprotein cholesterol ratio; VFA, visceral fat area.

significantly associated with the development of hypertension [9, 18], and even normal fasting TG was also prospectively associated with incident hypertension [19]. Besides, evidence indicated significant relationships between UACR and hypertension, T2D, and hypertension with T2D within the normal range of UACR [20], and moreover, elevated UACR was associated with a higher risk of major adverse cardiovascular events in T2D patients [21, 22]. In our study, the levels of GGT, TG, UACR, as well as BMI, were all significantly increased in the hypertension group; however, they did not enter the regression equation. In accordance with the research from Ciardullo et al. [7], as the log_e GDR increased, the levels of SBP, DBP, and the prevalence of hypertension were significantly decreased across the tertiles in our study, and furthermore, only the log_e GDR was retained in the final regression model. These findings suggest that log_e GDR, as an integrative index, is more closely associated with hypertension. However, the underlying mechanism has not yet been fully elucidated, and may involve factors such as inflammation, oxidative stress, endothelial dysfunction, and renal injury based on the constituent components of log_e GDR [8, 9, 20, 23].

As a traditional insulin-based IR index, HOMA-IR had an independent association with an exacerbated risk of hypertension in the general population [24], and was a reliable predictor of all-cause mortality in patients with coronary heart disease and hypertension [25]. In the study of Esteghamati et al. [26], the data showed that HOMA-IR was associated with hypertension in both diabetic and nondiabetic subjects. However, in our study, although the Spearman's correlation analysis displayed a relationship between HOMA-IR and hypertension, it did not fit into our regression model in T2D patients. Additionally, a series of noninsulin-based IR indices were derived, including the TyG index, TyG-BMI, TG/HDL-c ratio, METS-IR, and UHR, and they were confirmed to be related to hypertension [27, 28]. Moreover, we included other new composite indicators reflecting metabolism that share some similarities with the components of log_e GDR, such as the ByG index and TyG-GGT, which had been shown to be associated with diabetes and nonalcoholic steatohepatitis [13, 14]. In our study, we only found that there existed a correlation by univariate analysis. However, similar to HOMA-IR, further regression analysis showed that these indicators were not independently correlated with hypertension.

Undoubtedly, age and obesity were the most important correlates for hypertension among patients with diabetes [29]. Our study also found that the age and VFA were obviously increased in the hypertension group, and after adjusting for other confounding factors, both of them were still closely related to hypertension. Additionally, in contrast to prior research that indicated that poor glycemic control was associated with a higher risk of hypertension in diabetic patients [30], our study revealed a negative association between HbA1c levels and the incidence of hypertension in males. The multifactorial nature of hypertension's influencing factors may contribute to this phenomenon. As previously discussed, the age in the hypertension group was significantly higher compared to that in the nonhypertension group, while older diabetic patients had better glycemic control [31].

However, a few limitations to our study should be considered. First, the cross-sectional nature of the study limits the ability to

TABLE 2 | Comparison of variables according to the tertiles of $\log_e$ GDR.

Variables	Female				Male			
	T1 (0.38–1.85)	T2 (1.85–2.17)	T3 (2.17–3.12)	*p* value	T1 (0.29–1.69)	T2 (1.69–2.06)	T3 (2.06–2.88)	*p* value
Number	312	321	321		195	196	199	
Smoking (*n*, %)	4 (1.3%)	2 (0.6%)	0 (0.0%)	0.091	88 (45.1%)	77 (39.3%)	63 (31.7%)	0.023
Drinking (*n*, %)	3 (1.0%)	1 (0.3%)	0 (0.0%)	0.131	82 (42.1%)	66 (33.7%)	60 (30.2%)	0.040
Age (years)	56.1 ± 13.1	58.7 ± 10.9	56.7 ± 11.3	.009	50.6 ± 11.8	55.8 ± 11.8	58.9 ± 12.3	< 0.001
Duration of diabetes (years)	6.0 (2.0–10.0)	6.0 (2.0–10.0)	7.0 (3.0–12.0)	0.007	6.0 (2.0–10.0)	7.0 (2.0–12.0)	10.0 (2.9–15.0)	0.012
BMI (kg/m^2)	27.50 ± 4.13	25.02 ± 3.01	23.10 ± 2.81	< 0.001	27.74 ± 3.34	26.00 ± 2.40	23.79 ± 3.03	< 0.001
VFA (cm^2)	99.00 (78.00–125.75)	79.00 (62.00–98.00)	61.00 (41.50–79.00)	< 0.001	131.00 (105.00–158.00)	107.00 (86.00–125.75)	80.00 (54.00–110.00)	< 0.001
SFA (cm^2)	216.00 (166.00–260.75)	176.00 (135.50–216.00)	145.00 (106.50–180.00)	< 0.001	217.00 (176.00–257.00)	190.00 (162.75–225.25)	159.50 (114.00–196.25)	< 0.001
SBP (mmHg)	134.2 ± 18.3	130.7 ± 17.4	123.8 ± 17.9	< 0.001	132.4 ± 17.3	127.9 ± 16.0	124.3 ± 16.2	< 0.001
DBP (mmHg)	83.2 ± 11.2	79.7 ± 10.6	76.2 ± 9.7	< 0.001	85.9 ± 10.9	81.8 ± 9.2	79.2 ± 10.6	< 0.001
TC (mmol/L)	5.41 ± 1.40	4.96 ± 1.11	4.66 ± 1.04	< 0.001	4.85 ± 1.31	4.67 ± 1.09	4.23 ± 1.01	< 0.001
LDL-c (mmol/L)	3.42 ± 1.14	3.20 ± 0.96	2.90 ± 0.89	< 0.001	2.97 ± 1.09	3.06 ± 0.95	2.75 ± 0.89	0.005
TG (mmol/l)	2.05 (1.45–2.90)	1.35 (1.11–1.75)	0.90 (0.71–1.25)	< 0.001	2.34 (1.59–3.72)	1.45 (1.15–2.03)	0.90 (0.69–1.18)	< 0.001
HDL-c (mmol/L)	1.17 ± 0.37	1.24 ± 0.32	1.41 ± 0.40	< 0.001	0.97 ± 0.23	1.06 ± 0.22	1.20 ± 0.24	< 0.001
FPG (mmol/L)	10.02 ± 3.81	9.10 ± 3.17	7.92 ± 3.06	< 0.001	9.60 ± 3.43	9.16 ± 3.19	8.12 ± 3.26	< 0.001
FINS (μU/mL)	19.04 (14.44–24.10)	17.32 (10.74–23.19)	13.64 (5.66–20.35)	< 0.001	16.68 (11.85–21.50)	16.72 (10.29–21.47)	13.10 (8.68–19.48)	< 0.001
HbA1c (%)	9.75 ± 2.07	9.53 ± 2.12	8.80 ± 2.22	< 0.001	9.39 ± 2.17	9.31 ± 2.11	9.25 ± 2.46	0.845
ALT (U/L)	21.30 (15.38–34.00)	16.25 (12.80–23.58)	14.30 (10.80–19.30)	< 0.001	26.10 (18.85–40.30)	20.00 (16.00–29.00)	16.90 (13.20–22.60)	< 0.001
AST (U/L)	19.15 (15.13–27.28)	16.30 (13.70–19.85)	15.80 (13.00–20.43)	< 0.001	19.50 (16.00–27.60)	18.10 (15.43–21.98)	17.00 (13.70–20.60)	< 0.001

(Continues)

TABLE 2 | (Continued)

Variables	Female				Male			
	T1 (0.38–1.85)	T2 (1.85–2.17)	T3 (2.17–3.12)	*p* value	T1 (0.29–1.69)	T2 (1.69–2.06)	T3 (2.06–2.88)	*p* value
GGT (U/L)	28.30 (22.00–42.00)	19.00 (16.00–23.00)	13.00 (11.00–16.00)	< 0.001	42.00 (31.00–63.00)	26.00 (21.00–34.75)	17.00 (13.40–22.00)	< 0.001
Cys C (mg/L)	0.84 ± 0.21	0.83 ± 0.18	0.78 ± 0.15	0.004	0.84 ± 0.19	0.81 ± 0.17	0.85 ± 0.14	0.214
UA (μmolL)	282.83 ± 86.87	243.70 ± 68.36	223.34 ± 62.97	< 0.001	329.79 ± 81.77	298.00 ± 72.58	275.55 ± 69.18	< 0.001
Scr (μmol/L)	52.65 ± 8.40	51.87 ± 7.83	51.68 ± 7.39	0.262	67.14 ± 9.27	67.80 ± 8.35	66.50 ± 8.94	0.347
eGFR (mL/min/1.73 m^2)	133.20 ± 29.01	134.17±31.40	134.68±25.88	0.805	126.28 ± 26.23	121.55 ± 21.25	123.90 ± 23.69	0.146
UACR (mg/g)	20.30 (9.03 ~ 72.00)	10.70 (6.80–22.10)	6.90 (4.50–11.15)	< 0.001	23.80 (7.90–105.20)	7.95 (4.60–17.23)	5.80 (3.50–10.80)	< 0.001
Hb (g/L)	136.65 ± 13.79	136.24 ± 13.02	132.14 ± 13.11	< 0.001	155.84 ± 14.31	153.67 ± 13.70	149.49 ± 14.25	< 0.001
TyG index	9.67 ± 0.70	9.18 ± 0.53	8.62 ± 0.55	< 0.001	9.81 ± 0.78	9.25 ± 0.59	8.62 ± 0.57	< 0.001
TyG-BMI	265.97 ± 44.11	229.48 ± 29.20	199.11 ± 27.53	< 0.001	272.34 ± 41.30	240.59 ± 26.86	205.08 ± 30.22	< 0.001
TyG-GGT	281.18 (207.62–421.97)	171.87 (145.04–209.22)	112.54 (92.61–138.38)	< 0.001	409.89 (309.45–625.08)	236.43 (196.04–316.90)	147.83 (115.03–193.79)	< 0.001
ByG index	7.74 ± 0.40	7.56 ± 0.36	7.33 ± 0.37	< 0.001	7.72 ± 0.37	7.61 ± 0.34	7.38 ± 0.38	< 0.001
UHR (%)	11.65 ± 5.89	8.99 ± 3.23	7.38 ± 2.97	< 0.001	15.81 ± 6.52	12.71 ± 4.15	10.53 ± 3.83	< 0.001
TG/HDL-c ratio	1.87 (1.25–2.81)	1.17 (0.86–1.54)	0.67 (0.47–0.98)	< 0.001	2.30 (1.63–4.63)	1.47 (1.01–2.03)	0.76 (0.57–1.07)	< 0.001
HOMA-IR	8.09 (5.33 ~ 11.87)	6.10 (3.77 ~ 9.46)	4.19 (1.80 ~ 7.03)	< 0.001	7.21 (4.12–10.26)	6.65 (3.36–10.25)	4.35 (2.74–7.36)	< 0.001
METS-IR	46.25 ± 8.50	39.84 ± 5.73	34.42 ± 5.24	< 0.001	49.35 ± 8.61	43.31 ± 5.60	36.91 ± 5.91	< 0.001
Hypertension (*n*, %)	192 (61.5%)	157 (48.9%)	105 (32.7%)	< 0.001	112 (57.4%)	87 (44.4%)	72 (36.2%)	< 0.001

Note: Data were presented as mean ± SD for normally distributed variables, and median (interquartile ranges) for abnormal distributions. Analysis of variance test was performed for multiple comparisons of normally distributed data, and Kruskal–Wallis test for abnormal distributions. Categorical variables were presented as percentage (%) and were compared by Chi-square test. Statistical differences were defined by *p* value (two-tailed) less than 0.05.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Cys C, cystatin C; DBP, diastolic blood pressure; FINS, fasting serum insulin; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyl transferase; GDR, glucose disposal rate; Hb, hemoglobin; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; LDL-c, low-density lipoprotein cholesterol; METS-IR, Insulin resistance metabolic score; SBP, systolic blood pressure; Scr, serum creatinine; SFA, subcutaneous fat area; TC, total cholesterol; TG, triglyceride; UA, uric acid; UACR, urinary albumin to creatinine ratio; UHR, serum uric acid-to-high-density lipoprotein cholesterol ratio; VFA, visceral fat area.

TABLE 3 | The correlation between hypertension and different variables by univariate analysis.

	Female		Male	
Variables	**Correlation coefficient**	***p* value**	**Correlation Coefficient**	***p* value**
Age	0.233	<0.001	0.122	0.003
Smoking	0.004	0.908	0.037	0.372
Drinking	−0.029	0.364	0.074	0.071
Duration of diabetes	0.106	0.002	0.066	0.139
BMI	0.224	< 0.001	0.210	< 0.001
VFA	0.280	< 0.001	0.289	< 0.001
SFA	0.241	< 0.001	0.245	< 0.001
TC	0.057	0.079	−0.082	0.047
LDL-c	0.015	0.644	−0.077	0.062
TG	0.110	0.001	0.055	0.183
HDL-c	0.002	0.963	−0.072	0.082
FPG	0.022	0.497	−0.099	0.016
FINS	0.149	< 0.001	0.046	0.429
HbA1c	−0.023	0.494	−0.177	< 0.001
ALT	0.099	0.002	0.088	0.034
AST	0.081	0.012	0.105	0.011
GGT	0.124	< 0.001	0.142	0.001
Cys C	0.147	< 0.001	0.089	0.100
UA	0.081	0.012	0.114	0.005
eGFR	−0.148	< 0.001	−0.105	0.010
UACR	0.199	< 0.001	0.100	0.015
Hb	0.090	0.006	−0.032	0.436
TyG index	0.088	0.006	0.001	0.979
TyG-BMI	0.214	< 0.001	0.152	< 0.001
TyG-GGT	0.130	< 0.001	0.129	0.002
ByG index	0.094	0.004	−0.029	0.490
UHR	0.043	0.182	0.102	0.014
TG/HDL-c ratio	0.085	0.009	0.065	0.113
HOMA-IR	0.132	0.001	−0.008	0.884
METS-IR	0.169	< 0.001	0.158	< 0.001
Log_e GDR	−0.243	< 0.001	−0.181	< 0.001

Note: Correlation coefficients between hypertension and different variables were determined by Spearman's correlation analysis.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Cys C, cystatin C; DBP, diastolic blood pressure; FINS, fasting serum insulin; FPG, fasting plasma glucose; eGFR, estimated glomerular filtration rate; GGT, gamma-glutamyl transferase; GDR, glucose disposal rate; Hb, hemoglobin; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; LDL-c, low-density lipoprotein cholesterol; METS-IR, Insulin resistance metabolic score; SBP, systolic blood pressure; Scr, serum creatinine; SFA, subcutaneous fat area; TC, total cholesterol; TG, triglyceride; UA, uric acid; UACR, urinary albumin to creatinine ratio; UHR, serum uric acid-to-high-density lipoprotein cholesterol ratio; VFA, visceral fat area.

establish causal relationships. Longitudinal studies are essential to confirm the temporal sequence of events and to explore the long-term implications and underlying mechanisms of changes in log_e GDR on hypertension development. Second, other causes of secondary hypertension were not routinely screened unless the patients had typical clinical manifestations. Additionally, most hypertensive patients had been previously diagnosed and were receiving antihypertensive medication. Further research is warranted to investigate the correlation between log_e GDR and newly diagnosed hypertension. Third, the study population was predominantly Chinese T2D patients. Moreover, other factors like genetic predisposition and lifestyle habits may also contribute to the development of hypertension. Future research should investigate the generalizability of these findings to diverse populations, and the complex interplay between these factors.

TABLE 4 | The independent variables for hypertension.

Variables	B	SE	Wald	*p* value	OR	95.0% CI for OR
In Females						
Log_e GDR	−0.786	0.362	4.712	0.030	0.456	0.224–0.927
VFA	0.012	0.004	10.330	0.001	1.012	1.005–1.020
Age	0.039	0.011	12.701	< 0.001	1.039	1.017–1.062
In Males						
Log_e GDR	−0.609	0.280	4.733	0.030	0.544	0.314–0.941
VFA	0.013	0.003	21.673	< 0.001	1.013	1.008–1.019
Age	0.027	0.008	10.186	0.001	1.027	1.010–1.044
HbA1c	−0.144	0.044	10.629	0.001	0.866	0.795–0.944

Note: The independent variables for hypertension were assessed by logistic regression analysis.
Abbreviations: CI, confidence interval; GDR, glucose disposal rate; OR, odd ratio; SE, standard error; VFA, visceral fat area.

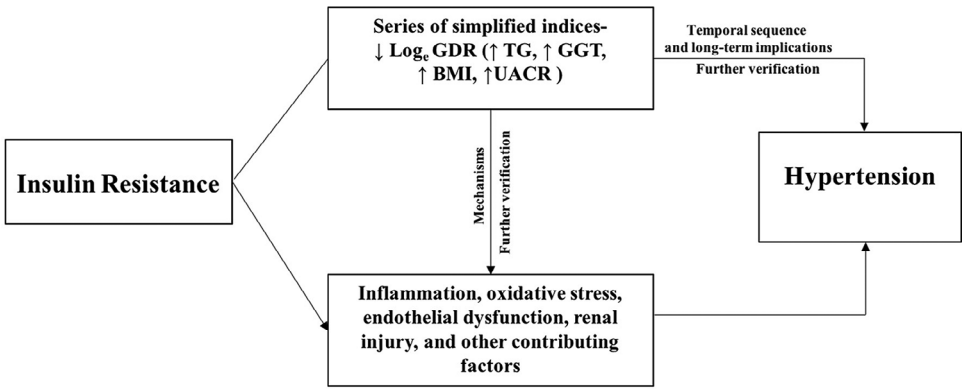

FIGURE 1 | A framework diagram illustrating the study of loge GDR in relation to hypertension. BMI, body mass index; GDR, glucose disposal rate; GGT, gamma-glutamyl transferase; TG, triglyceride; UACR, urinary albumin to creatinine ratio.

5 | Conclusion

Among numerous IR indices, log_e GDR exhibited a strong association with hypertension in patients with T2D. We acknowledge both the strengths and limitations of our study, as well as outline directions for future research. Future studies should encompass multicenter, large-scale, prospective designs to comprehensively validate the interrelationship between log_e GDR and hypertension, thereby providing deeper insights into the pathophysiological mechanisms linking log_e GDR and hypertension in T2D patients. A framework diagram is presented in Figure 1.

Ethics Statement

The study received approval from the Human Ethics Committee of Linyi People's Hospital. All procedures adhered to the ethical standards outlined in the Declaration of Helsinki.

Consent

Informed consent was obtained from all patients.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from Baolan Ji upon reasonable request.

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