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Original Paper

The Relationship between Hypertriglyceridemic Waist Phenotype and Early Diabetic Nephropathy in Type 2 Diabetes

Chun-Ming Ma Rui Wang Xiao-Li Liu Na Lu Qiang Lu Fu-Zai Yin

Department of Endocrinology, The First Hospital of Qinhuangdao, Qinhuangdao, China

Keywords
Hypertriglyceridemic waist phenotype · Early diabetic nephropathy · Type 2 diabetes

Abstract
Background/Aims: The aim of this study was to explore the relationship between hypertriglyceridemic waist (HW) phenotype and early diabetic nephropathy in type 2 diabetes. ***Methods:*** A cross-sectional study was conducted on 538 type 2 diabetes patients in Qinhuangdao. The HW phenotype was defined as serum triglyceride concentrations ≥1.7 mmol/L and waist circumference ≥90 cm (males) and ≥85 cm (females). ***Results:*** The prevalence of the HW phenotype was 34.9%. The prevalence of early diabetic nephropathy was 10.6% in type 2 diabetes patients with normal waist circumference and triglycerides and 24.5% in type 2 diabetes patients with HW phenotype. After adjustment for sex, age, body mass index, hypertension, history of diabetes, and glycosylated hemoglobin A1c, the prevalence of early diabetic nephropathy among type 2 diabetes patients with the HW phenotype was 2.81 (95% confidence interval 1.36–5.80, p = 0.005) times higher than that among type 2 diabetes patients with normal waist circumference and triglycerides. ***Conclusion:*** There was a significant correlation between HW phenotype and early diabetic nephropathy in type 2 diabetes.

Introduction

The hypertriglyceridemic waist (HW) phenotype is represented by the simultaneous presence of elevated serum triglyceride (TG) levels and increased waist circumference (WC). Lemieux et al. [1] suggested that the simultaneous measurement and interpretation of WC and fasting TG levels could be used as an inexpensive screening tool to identify men charac-

Fu-Zai Yin
Department of Endocrinology, The First Hospital of Qinhuangdao
No. 258 Wenhua Road
Qinhuangdao, Hebei 066000 (China)
E-Mail yinfuzai62@163.com

terized by the atherogenic metabolic triad (hyperinsulinemia, elevated apolipoprotein B, and small, dense low-density lipoprotein) and at high risk of coronary artery disease. In China, the cardiovascular mortality has significantly increased in recent years [2]. The HW phenotype has been associated with a substantially elevated risk of coronary heart disease and increased arterial stiffness in Chinese adults [3, 4].

Due to changes in lifestyle characterized by a lack of physical activity and an energy-dense diet, the prevalence of diabetes has increased significantly in the recent decades and is now reaching epidemic proportions in China. In 2010, the estimated prevalence of diabetes among a representative sample of Chinese adults was 11.6%, and the prevalence of prediabetes was 50.1% [5]. These findings indicate the importance of diabetes as a public health problem in China. Diabetes mellitus is a chronic metabolic disease. Long-term hyperglycemia is the factor that promotes vascular lesions and dysfunction, leading to a variety of complications of diabetes mellitus. Diabetic nephropathy is a frequent and severe complication of diabetes mellitus that frequently leads to end-stage renal disease. Its diagnosis in incipient stages may allow prompt interventions and an improved prognosis.

Among Chinese adults, the HW phenotype was also strongly associated with diabetes risk [6, 7]. A longitudinal study provides evidence that the HW phenotype can be used as a simple screening approach to predict diabetes [8, 9]. The predictive power of the HW phenotype was similar to metabolic syndrome. Due to simpler and fewer components, the HW phenotype might be more practical than metabolic syndrome, and it might be recommended in most clinical practices [10]. In type 2 diabetes, the presence of the HW phenotype translated into a deteriorated blood lipid profile and more extensive coronary artery disease on computed tomographic coronary angiography [11]. The HW phenotype is a significant marker of coronary artery disease manifestations occurring at an earlier age in those with type 2 diabetes [12]. A slight elevation of albuminuria is a significant determinant of intima-media thickness and pulse wave velocity independent of conventional cardiovascular risk factors in type 2 diabetic patients. This significant association might point to a link between the pathogenesis of atherosclerosis and that of diabetic nephropathy [13]. To our knowledge, no investigators have attempted to use the HW phenotype for the screening for early diabetic nephropathy. The aim of our study was to determine the relationship between the HW phenotype and early diabetic nephropathy.

Methods

Subjects

After obtaining informed consent from subjects with type 2 diabetes, a cross-sectional study was conducted. All subjects were recruited from the First Hospital of Qinhuangdao. All subjects were men and women over 18 years of age with a diagnosis of type 2 diabetes (based on American Diabetes Association diagnostic criteria) [14]. The exclusion criteria included the following: (1) subjects with type 1 diabetes; (2) subjects with clinical evidence of another endocrinopathy, such as Cushing syndrome, hyperthyroidism, etc.; (3) subjects who were taking medications known to affect lipid metabolism, such as glucocorticoids and fibrates; (4) subjects who were taking medications known to affect urinary microalbuminuria, such as renin-angiotensin-aldosterone system-blocking agents (angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers); (5) urine microalbumin (UMA) >200 μg/min; (6) diagnosis of nondiabetic chronic kidney disease (CKD) currently or in the past, and (7) subjects with acute or chronic inflammation. This study was approved by the ethics committee of the First Hospital of Qinhuangdao. All subjects provided written informed consent before study initiation.

Measurements

Anthropometric measurements, including height, weight, and WC, were obtained while the subjects were in light clothing and barefoot. Height and weight were measured to the nearest 0.1 cm and 0.1 kg, respectively. WC was accurately measured midway between the lowest rib and the top of the iliac crest. All measurements were taken twice, and the 2 measurements were averaged for analysis. Body mass index (BMI) was calculated by dividing weight (kg) by height squared (m^2). Blood pressure was measured 3 times with a mercury sphygmomanometer while the subjects were seated after 10 min of rest, and the 3 measurements were averaged for analysis.

After a 10-h overnight fast, blood samples were collected from an antecubital vein into heparinized tubes. Fasting plasma glucose concentration was measured using the glucose oxidase method, and serum lipid levels, as well as renal function, were measured using enzymatic assays with an autoanalyzer (Hitachi, Tokyo, Japan). Glycosylated hemoglobin A1c (HbA1c) was measured by high-performance liquid chromatography. Subjects were asked to collect consecutive 24-h urine once, and UMA was measured by radioimmunoassay.

Definition

The HW phenotype was defined as serum TG concentrations ≥1.7 mmol/L and WC ≥90 cm (males) and ≥85 cm (females) [15]. Subjects were categorized into 4 phenotype groups on the basis of the mentioned cutoffs: (A) normal WC (<90 cm for males and <85 cm for females) and normal serum TG concentrations (<1.7 mmol/L); (B) enlarged WC (≥90 cm for males and ≥85 cm for females) and normal serum TG concentrations (<1.7 mmol/L); (C) normal WC (<90 cm for males and <85 cm for females) and elevated serum TG concentrations (≥1.7 mmol/L), and (D) enlarged WC (≥90 cm for males and ≥85 cm for females) and elevated serum TG concentrations (≥1.7 mmol/L). The definition of early diabetic nephropathy was according to Mogensen stage III (UMA of 20–200 μg/min) [16].

Statistical Analyses

All analyses were performed using the SPSS 11.5 statistical software (SPSS 11.5 for Windows; SPSS, Inc., Chicago, IL, USA). Numerical variables were reported as means ± standard deviations. Comparisons were conducted between groups using ANOVA. The comparison of prevalence data was performed by χ^2 analysis. Multiple logistic regression models were used for modeling relationships between HW phenotype and early diabetic nephropathy. $p < 0.05$ was considered statistically significant.

Results

Among the study population, 34.9% of the patients were characterized by the HW phenotype. The prevalence of the HW phenotype was similar between males and females (males 34.5% vs. females 35.5%, $\chi^2 = 0.055$, $p = 0.815$). Among these subjects, 19.1% had early diabetic nephropathy. Characteristics of subgroups classified on the basis of WC and TG levels are presented in Table 1. Sex, history of diabetes, and creatinine were similar in the 4 groups ($p > 0.05$). Age was significantly higher in group B than in group A ($p < 0.05$). The levels of systolic blood pressure, diastolic blood pressure, HbA1c, fasting plasma glucose, and UMA were all significantly higher in group D than in group A ($p < 0.05$). The level of HDL-C was significantly lower in group D than in group A ($p < 0.05$).

Multivariate-adjusted odds ratios (and 95% confidence intervals [CI]) for early diabetic nephropathy across different phenotypes of serum TG concentrations and WC are shown in Table 2. The prevalence of early diabetic nephropathy was 10.6% in type 2 diabetes patients with normal WC and TG and 24.5% in type 2 diabetes patients with the HW phenotype. After control for age, sex, BMI, hypertension, history of diabetes, and HbA1c, subjects with the HW phenotype were 2.81 (95% CI 1.36–5.80, $p = 0.005$) times more likely to have early diabetic nephropathy.

Table 1. Characteristics of subjects with type 2 diabetes by phenotypes of serum TG concentrations and WC

Variables	Group A	Group B	Group C	Group D	F or χ^2	p
Subjects (males/females)	132 (75/57)	156 (74/82)	62 (39/23)	188 (99/89)	5.140	0.162
Age, years	52.6±15.4	58.5±11.9[a]	55.0±11.0	55.0±13.7	4.175	0.003
History of diabetes, years	6.9±6.1	8.3±7.0	6.9±5.9	7.7±6.9	1.200	0.309
BMI	22.3±2.9	27.0±2.9[a]	25.3±1.8[a]	26.9±3.1[a, c]	80.146	<0.001
WC, cm	80.0±6.6	95.7±7.4[a]	81.8±5.5	96.1±7.8[a, c]	187.818	<0.001
SBP, mm Hg	123.2±15.3	131.5±17.0[a]	126.6±15.3	131.0±17.6[a]	7.909	<0.001
DBP, mm Hg	79.7±10.8	80.4±10.3	81.8±9.4	83.5±10.4[a, b]	4.275	0.005
HbA1c, %	8.0±2.4	8.3±1.6	8.5±2.0	8.9±2.1[a, b]	4.528	0.004
FPG, mmol/L	8.9±4.4	8.6±3.1	10.5±3.7[a]	10.9±4.3[a, b]	11.357	<0.001
TG, mmol/L	1.01±0.38	1.22±0.32	3.92±3.70[a]	4.23±3.65[a, b]	65.537	<0.001
HDL-C, mmol/L	1.24±0.33	1.21±0.26	1.03±0.29[a]	1.00±0.27[a, b]	25.416	<0.001
Cr, μmol/L	57.1±14.3	59.4±15.0	60.1±11.7	59.3±17.1	0.750	0.523
UMA, μg/min	10.4±13.5	17.8±25.6	22.0±38.7[a]	27.5±45.0[a, b]	7.123	<0.001

Values are numbers or means ± standard deviations. Group A, normal TG levels and normal WC; group B, normal TG levels and elevated WC; group C, elevated TG levels and normal WC; group D, elevated TG levels and elevated WC. BMI, body mass index (in kg/m^2); WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycosylated hemoglobin A1c; FPG, fasting plasma glucose; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; CR, creatinine; UMA, urine microalbumin. [a] Compared with group A, $p < 0.05$; [b] compared with group B, $p < 0.05$; [c] compared with group C, $p < 0.05$.

Table 2. Prevalence of early diabetic nephropathy across phenotypes of serum TG concentrations and WC

Group	Early diabetic nephropathy, n (%)	Model 1		Model 2	
		OR (95% CI)	p	OR (95% CI)	p
A (n = 132)	14 (10.6)	1		1	
B (n = 156)	31 (19.9)	2.09 (1.06–4.12)	0.033	1.61 (0.74–3.52)	0.228
C (n = 62)	12 (19.4)	2.02 (0.87–4.68)	0.100	1.90 (0.72–5.00)	0.192
D (n = 188)	46 (24.5)	2.73 (1.43–5.21)	0.002	2.81 (1.36–5.80)	0.005

Group A, normal TG levels and normal WC; group B, normal TG levels and elevated WC; group C, elevated TG levels and normal WC; group D, elevated TG levels and elevated WC. Model 1, univariate logistic regression analysis; model 2, multiple logistic regression analysis, adjustment for sex, age, body mass index, hypertension, history of diabetes, and glycosylated hemoglobin A1c. WC, waist circumference; TG, triglyceride; OR, odds ratio; CI, confidence interval.

Discussion

Our study shows that the prevalence of the HW phenotype in type 2 diabetes patients was 34.9%, which is similar to a previous study [7]. The HW phenotype, the indicator used in this study, was associated with elevated UMA and early diabetic nephropathy in type 2 diabetes patients. In the present study, it was observed that almost a quarter of individuals with the HW phenotype had early diabetic nephropathy, thus highlighting the importance of the simultaneous analysis of WC and TG levels in the clinical screening of individuals at risk for early diabetic nephropathy.

The cutoffs of the HW phenotype have not always been consistent. In our study, the specific WC cutoffs of 90 cm for males and of 85 cm for females were chosen. These cutoffs were in agreement with an epidemiological data analysis of the metabolic syndrome of our country's population and were recommended by the Chinese Diabetes Society. The appropriate cutoffs of WC were 90 cm in males and 85 cm in females and were associated with a high risk in female Chinese [17].

Some studies have observed that the CKD prevalence varied materially in different TG waist phenotypes. Zeng et al. [18] found that participants with the HW phenotype were 1.95 times as likely to have CKD as those with normal WC and TG concentrations. Huang et al. [19] and Li et al. [20] also reported similar results. The HW phenotype was also associated with worse carotid atherosclerosis in CKD patients [21]. The present study provides evidence that type 2 diabetes patients with the HW phenotype were 2.81 times as likely to have early diabetic nephropathy as those with normal WC and TG concentrations, independent of age, sex, BMI, hypertension, and history of diabetes.

The biological mechanisms linking the HW phenotype and early diabetic nephropathy are still unclear, but visceral obesity plays a critical role according to currently acknowledged hypotheses. Visceral obesity is associated with an excessive depot of TGs and other lipid products in the kidneys, which further affects the renal hemodynamic pattern and related metabolic function [18].

The evaluation of visceral adipose tissue (VAT), for example by magnetic resonance imaging (MRI) and computed tomography (CT), is very expensive and may involve exposure to radiation; also, the availability of MRI and CT is limited. WC is the most accurate surrogate marker of visceral adiposity in adults and is a good indicator of insulin resistance and a powerful predictor of the presence of hepatic steatosis [22]. But individuals with a high WC do not always have excessive VAT because the accumulation of adipose tissue can be subcutaneous. A Japanese study showed that increased visceral but not subcutaneous fat is independently associated with microalbuminuria in adult patients with type 2 diabetes [23]. In the Framingham Heart Study, VAT was associated with microalbuminuria; albuminuria may be a manifestation of visceral adiposity [24]. The use of high serum TG levels in combination with a high WC strengthens the association with VAT. Several studies have shown that the HW phenotype was associated with VAT excess [25], especially in type 2 diabetes patients [26]. This is why the prevalence of early diabetic nephropathy was so high in subjects with the HW phenotype.

However, there are limitations to our study. First, because of the cross-sectional design of this study, we could not identify the causal relationship between early diabetic nephropathy and the HW phenotype. Second, UMA was obtained on the basis of single measurements without repeated tests. Third, although multiple variables were adjusted, other confounding factors, such as diet, medications (oral agents/insulin), and family history of CKD, may exist.

In summary, there was a significant correlation between the HW phenotype and early diabetic nephropathy in type 2 diabetes patients. Early diabetic nephropathy should be routinely examined in type 2 diabetes patients with the HW phenotype.

Statement of Ethics

All subjects have given their informed written consent, and the study protocol was approved by the ethics committee of the First Hospital of Qinhuangdao.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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References

1 Lemieux I, et al: Hypertriglyceridemic waist: a marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small, dense LDL) in men? Circulation 2000;102:179–184.
2 Liu MB, Wang W, Zhou MG: Trend analysis on the mortality of cardiovascular diseases from 2004 to 2010 in China (in Chinese). Zhonghua Liu Xing Bing Xue Za Zhi 2013;34:985–988.
3 Zhang X, et al: Visceral adiposity and risk of coronary heart disease in relatively lean Chinese adults. Int J Cardiol 2013;168:2141–2145.
4 Chen K, et al: Sex disparity in the association between hypertriglyceridemic waist phenotype and arterial stiffness in Chinese healthy subjects. Postgrad Med 2016;128:783–789.
5 Xu Y, et al: Prevalence and control of diabetes in Chinese adults. JAMA 2013;310:948–959.
6 Du T, et al: Visceral adiposity index, hypertriglyceridemic waist and risk of diabetes: the China Health and Nutrition Survey 2009. Int J Obes (Lond) 2014;38:840–847.
7 Ren Y, et al: Association of the hypertriglyceridemic waist phenotype and type 2 diabetes mellitus among adults in China. J Diabetes Investig 2016;7:689–694.
8 Zhang M, et al: Hypertriglyceridemic-waist phenotype predicts diabetes: a cohort study in Chinese urban adults. BMC Public Health 2012;12:1081.
9 Han KJ, et al: Increased risk of diabetes development in subjects with the hypertriglyceridemic waist phenotype: a 4-year longitudinal study. Endocrinol Metab (Seoul) 2014;29:514–521.
10 He S, et al: Hypertriglyceridemic waist might be an alternative to metabolic syndrome for predicting future diabetes mellitus. PLoS One 2013;8:e73292.
11 de Graaf FR, et al: Usefulness of hypertriglyceridemic waist phenotype in type 2 diabetes mellitus to predict the presence of coronary artery disease as assessed by computed tomographic coronary angiography. Am J Cardiol 2010;106:1747–1753.
12 St-Pierre J, et al: Relation of the "hypertriglyceridemic waist" phenotype to earlier manifestations of coronary artery disease in patients with glucose intolerance and type 2 diabetes mellitus. Am J Cardiol 2007;99:369–373.
13 Yokoyama H, et al: Subclinical atherosclerosis is increased in type 2 diabetic patients with microalbuminuria evaluated by intima-media thickness and pulse wave velocity. Kidney Int 2004;66:448–454.
14 American Diabetes Association: Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37(suppl 1):S81–S90.
15 Chinese Diabetes Society: Chinese guideline for type 2 diabetes. Chin J Endocrinol Metab 2014;30:893–942.
16 Mogensen CE, Christensen CK, Vittinghus E: The stages in diabetic renal disease. With emphasis on the stage of incipient diabetic nephropathy. Diabetes 1983;32(suppl 2):64–78.
17 Bao Y, et al: Optimal waist circumference cutoffs for abdominal obesity in Chinese. Atherosclerosis 2008;201:378–384.
18 Zeng J, et al: The association of hypertriglyceridemic waist phenotype with chronic kidney disease and its sex difference: a cross-sectional study in an urban Chinese elderly population. Int J Environ Res Public Health 2016;13:1233.
19 Huang J, et al: Visceral adiposity index, hypertriglyceridemic waist phenotype and chronic kidney disease in a southern Chinese population: a cross-sectional study. Int Urol Nephrol 2015;47:1387–1396.
20 Li Y, et al: Hypertriglyceridemic waist phenotype and chronic kidney disease in a Chinese population aged 40 years and older. PLoS One 2014;9:e92322.
21 Zhe X, et al: Hypertriglyceridemic waist is associated with increased carotid atherosclerosis in chronic kidney disease patients. Nephron Clin Pract 2012;122:146–152.
22 Borruel S, et al: Surrogate markers of visceral adiposity in young adults: waist circumference and body mass index are more accurate than waist hip ratio, model of adipose distribution and visceral adiposity index. PLoS One 2014;9:e114112.
23 Hanai K, et al: Involvement of visceral fat in the pathogenesis of albuminuria in patients with type 2 diabetes with early stage of nephropathy. Clin Exp Nephrol 2010;14:132–136.
24 Foster MC, et al: Association of subcutaneous and visceral adiposity with albuminuria: the Framingham Heart Study. Obesity (Silver Spring) 2011;19:1284–1289.
25 Cunha de Oliveira C, et al: Hypertriglyceridemic waist phenotype: association with metabolic disorders and visceral fat in adults. Nutr Hosp 2014;30:25–31.
26 Sam S, et al: Hypertriglyceridemic waist phenotype predicts increased visceral fat in subjects with type 2 diabetes. Diabetes Care 2009;32:1916–1920.