Diabetes, Metabolic Syndrome and Obesity

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Association of Hyper-Triglyceridemic Waist Phenotype and Diabetic Vascular Complication in the Chinese Population

Kun Li[1,2,*], Bin Cao[1,2,*], Jing Ke[1,2], Longyan Yang[1,2], Dong Zhao[1,2]

[1]Center for Endocrine Metabolism and Immune Diseases, Beijing Luhe Hospital, Capital Medical University, Beijing, 101149, People's Republic of China; [2]Beijing Key Laboratory of Diabetes Research and Care, Beijing, 101149, People's Republic of China

*These authors contributed equally to this work

Correspondence: Dong Zhao; Longyan Yang, Center for Endocrine Metabolism and Immune Diseases, Beijing Luhe Hospital, Capital Medical University, Beijing, 101149, People's Republic of China, Tel +86-10-69543901, Email zhaodong@ccmu.edu.cn; lingbeiyangstudent@163.com

Background: Diabetic vascular complications are the leading cause of crippling and death of diabetic patients and seriously affect patients' quality of life. It is essential to control the risk factors contributing to vascular complications in patients with Type 2 diabetes (T2DM). This study aimed to examine the association between hyper-triglyceridemic waist phenotype (HWP) and the risk of vascular complication index of diabetes in T2DM patients.

Methods: The participants with type 2 diabetes mellitus in this study registered at the National Metabolic Management Center (MMC) of Beijing Luhe Hospital from June 2017 to June 2021. Data were collected by trained personnel according to the protocol. The questionnaire containing information on demographic characteristics and lifestyle factors (including alcohol drinking and cigarette smoking et al) was administered by trained interviewers. Logistic regression analysis assessing the associations between the hyper-triglyceridemic waist phenotype and vascular complication index of diabetes. In addition, the subgroup analysis was performed by age, sex, HbA1c, hypertension or not, and education level.

Results: After data cleaning, a total of 3221 participants with T2DM were enrolled. The median (IQR) duration of diabetes was 47.00 (3.00, 125.00) months. Compared to the participants in the Normal triglycerides level and Normal waist circumference group (NTNW), those in the Elevated triglycerides level and Enlarged waist circumference group (HTGW) have a higher risk of CKD-related vascular complications; the OR of decreased estimated glomerular filtration rate (GFR) and elevated urinary albumin creatinine ratio (UACR) were 2.21 (95% CI:1.32–3.82) and 2.18 (95% CI:1.69–2.81), respectively. Moreover, compared to the participants in the NTNW group, the ORs of the decreased ankle-brachial index (ABI) and elevated Brachial-ankle pulse wave velocity (baPWV) were 2.24 (95% CI:1.38–3.80) and 1.63 (95% CI:1.28–2.06) in the HTGW group.

Conclusion: In summary, there was an association between hyper-triglyceridemic waist phenotype and diabetic vascular complications in the Chinese population.

Keywords: hyper-triglyceridemic waist phenotype, type 2 diabetes mellitus, vascular complication

Introduction

Type 2 diabetes mellitus (T2DM) is a significant health problem, especially in low and middle-income countries.[1] The new epidemiological investigation showed that 537 million people had diabetes in 2021.[2] Diabetic vascular complications are the leading cause of crippling and death of diabetic patients and seriously affect patients' quality of life, including diabetic nephropathy (DN), cardiovascular (CVD), and diabetic retinopathy (DR) et al[3–5] Therefore, it is essential to control the risk factors contributing to vascular complications in patients with T2DM.

In the new decade, several studies have concentrated on finding metabolism-related indexes to predict chronic disease complications. For example, Wu et al found a relationship between triglyceride glucose (TyG) index and arterial stiffness

Received: 1 June 2023
Accepted: 22 July 2023
Published: 26 July 2023

progression.[6] Moreover, there was an association between Visceral Adiposity Index (VAI) and artery disease in normal-weight adults with hypertension.[7]

The hyper-triglyceridemic waist phenotype (HWP) is a physical characterized classified by triglycerides (TG) and waist circumference, which is characterized by enlarged waist circumference and elevated TG levels.[8] As a composite index-related metabolism, HWP was used to predict hypertension.[9] In addition, several studies have shown that HWP was associated with coronary artery disease and metabolic syndrome.[10–12] Long-term obesity leads to abnormal lipid metabolism.[13] When TG level is present at a high level, heparin activates lipoprotein lipase, which increases intravascular lipolysis of circulating TG, thereby increasing tissue exposure to free fatty acids, ultimately leading to insulin resistance and impaired B-cell function.[14] As a result, there is an association between HWP and T2DM. However, the relationship between the risk of vascular complications and HWP in diabetic patients is unclear.

Therefore, this study aimed to investigate the association between HWP and the risk of vascular complication index of diabetes in T2DM patients.

Method

Study Participants

The participants with type 2 diabetes mellitus in this study registered at the National Metabolic Management Center (MMC) of Beijing Luhe Hospital from June 2017 to June 2021. The MMC is a national project to manage metabolic patients according to the same standard. All the patients accepted systematic physical examination, blood sample collection, and oral questionnaire interviews. The protocol of this project was published previously.[15] The MMC is a long-term follow-up program. Considering the life expectancy of patients, the present study only included participants under 80 years.

Participants were excluded according to the following criteria: (1) Pregnant or nursing women. (2) Malignant tumor or life expectancy <5 years, (3) Acute complications of diabetes, (4) Presence of severe heart, kidney, and liver disease.

The protocol was approved by the Medical Ethics Committee of Beijing Luhe Hospital, Capital Medical University. This study was performed by the Declaration of Helsinki. All participants provided written informed consent.

Data Collection

Data were collected by trained personnel according to the protocol. The questionnaire containing information on demographic characteristics, and lifestyle factors such as alcohol drinking and cigarette smoking, was administered by trained interviewers. For the participants who smoked daily or almost daily, smoking status was defined as "yes". And for the participants who drank weekly or nearly weekly, drinking status was described as "yes". Education level was categorized as less than high school and high school or more.

Weight and height were measured with a standard protocol at 8:00–10:00 AM, and body mass index (BMI) was calculated as weight divided by height squared. Peripheral venous blood was withdrawn from all subjects in the morning after fasting for 8 hours or more. Glycated hemoglobin (HbA1c) levels were assayed using the method of high-performance liquid chromatography (HPLC) with a D10 set (Bio-RAD, Hercules, CA, USA). An auto biochemical analyzer measured LDL, HDL, and triglyceride (AU5800, Beckman Coulter, USA).

Brachial-ankle pulse wave velocity (baPWV) and ankle-brachial index (ABI) were measured by an automated recording apparatus with participants in the supine position after at least 5 minutes of rest (BP-203RPE III, form PWV/ABI, Omron Healthcare Co.). In this study, baPWV was calculated as $La-Lb/\Delta T$ (La and Lb are the distance from the heart to the ankle and the distance from the heart to the brachium, respectively, ΔT is the time between the wavefront of the brachial waveform and that of the ankle waveform).

Diabetic retinopathy (DR) severity was classified according to the International Clinical Diabetic Retinopathy and Diabetic Macular Oedema Disease Severity Scales.[16] DR of the present study was defined as severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy, also called vision-threatening DR (VTDR).

Definitions

The 1999 World Organization criteria were used to diagnose T2DM. Patients who had fasting plasma glucose ≥ 7.0 mmol/L or 2-h plasma glucose ≥ 11.1 mmol/L or a self-reported physician diagnosis were diagnosed with T2DM.

Triglyceride waist circumference phenotypes were divided into four groups. (1) Normal TG level and Normal waist circumference, NTNW (TG≤1.7 mmol/L and males' waist <90cm or females' waist <85cm). (2) Normal TG level and Enlarged waist circumference, NTEW (TG≤1.7 mmol/L and males' waist ≥90 cm or females' waist ≥ 85cm). (3) Elevated TG level and Normal waist circumference, ETNW (TG>1.7 mmol/L and males' waist < 90 cm or females' waist < 85cm). (4) Elevated TG level and Enlarged waist circumference, HTGW (TG> 1.7 mmol/L and males' waist ≥90 cm or females' waist ≥ 85cm).

ABI and baPWV were the arterial stiffness-related index; decreased ABI and elevated baPWV were defined as <0.9 and >1400 m/s, respectively.[17–19] Decreased estimated glomerular filtration rate (GFR) and elevated urinary albumin creatinine ratio (UACR) were defined as <60mL/min/1.73 m^2 and ≥ 30mg/g.[20] GFR was calculated by the aCKD-EPI formula.[21]

Statistical Analysis

Continuous variables were described as mean ± standard deviation (SD) or median [interquartile range (IQR)], and categorical variables were described as frequency (%). Data should be evaluated for normal distribution and, if necessary, the logarithmic transformation would be performed for statistical analysis. The differences between groups were assessed using Pearson's χ^2 test for categorical variables and the *t*-test or Mann–Whitney *U*-test for continuous variables.

The associations between the hyper-triglyceridemic waist phenotype and vascular complication index of diabetes were assessed by the Logistic regression model. Two models were constructed with different covariables: model 1 inputs major variables of diabetes, including sex, duration, and HbA1c. History of hypertension, smoking, drinking, education, LDL, and HDL were primary factors in the vascular research and associated with the vascular complication index of diabetes.[9,22–24] To avoid these confounding effects, model 2 adjusted for a history of hypertension, smoking, drinking, education, LDL, HDL, plus the covariable of model 1.

In addition, the subgroups analysis was performed by age (<60, ≥60 years), sex (male, female), HbA1c (<7.0%, ≥7.0%), hypertension or not, an education level (less than high school, high school education or higher level).

R statistical software (version 4.1.2) was used for statistical analysis. Two-tailed P <0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics

The data cleaning procedure can be seen in Figure 1. After excluding participants aged not 20–80 years, missing value, and using antilipemic agents, there were 3221 participants including the current analysis.

Table 1 shows the demographic and clinical characteristics of this study. A total of 1914 (59.4%) participants were males. The median (IQR) duration of diabetes was 47.00 (3.00, 125.00) months. Compared to the participants in the NTNW group, those in the HTGW group were younger with a shorter duration of diabetes, higher fasting blood glucose, HbA1c, baPWV, UACR, and ABI (all $P < 0.01$). Moreover, the participants in the HTGW tend to be obese, which has a larger value of physical measurement index including waist circumference, body weight, and BMI.

The Associations Between the HWP and Vascular Complication Index of Diabetes

The HWP was associated with the vascular complication index of diabetes in T2DM patients. Table 2 gives the model information on the vascular complication index of T2DM, which includes decreased ABI, decreased GFR, elevated

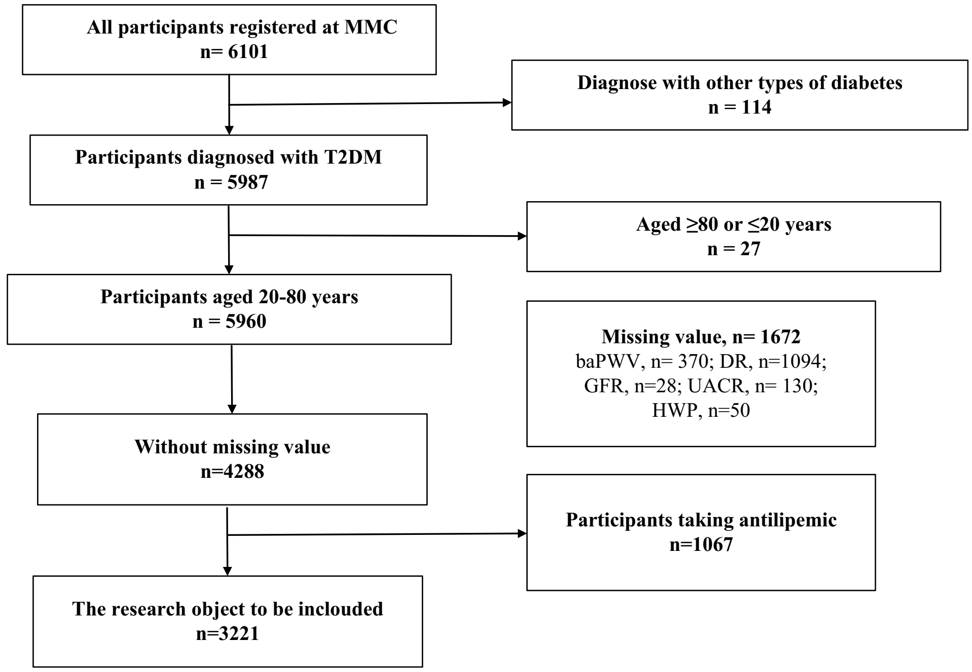

Figure 1 Date cleaning procedure. After excluding participants aged not 20–80 years, missing value, and using antilipemic agents, there were 3221 participants including the current analysis.

UACR, elevated baPWV, and DR. The effect of HWP on the vascular complication index was described as odds ratios (ORs) and 95% confidence interval (CI).

Compared to the participants of NTNW, those in the HTGW group have a higher risk of CKD-related vascular complications; the OR of decreased GFR and elevated UACR were 2.21 (95% CI:1.32–3.82) and 2.18 (95% CI:1.69–2.81), respectively. Moreover, compared to the participants in the NTNW group, the ORs of decreased ABI and elevated baPWV were 2.24 (95% CI:1.38–3.80) and 1.63 (95% CI:1.28–2.06) in the HTGW group. However, there was no association between DR and HWP.

Stratified Analysis

We further examined the association between vascular complication index in subgroups of age (<60 years, ≥60 years), sex, HbA1c (<7.0%, ≥7.0%), history of hypertension, and education (less than high school, high school education or higher level), the results were shown in forest plots (Figure 2).

In groups of HbA1c<7.0%, both the 95% CI of OR of deceased ABI and GFR crossed the invalid line (P>0.05), and the OR was 0.95 (95% CI:0.37–2.48) and 2.38 (95% CI:0.95–6.45), respectively. The stratified analysis results for each vascular complication index show differences in patients with a history of hypertension or not, except for UACR.

Discussion

In this study, we found that HWP was associated with vascular complications of diabetes: Compared with the participants of NTNW, those patients of HTGW have a higher risk of CKD-related vascular complications (elevated UACR and decreased GFR) and diabetic macrovascular complications (elevated baPWV and decreased ABI). This implies that HWP could be a screening tool for diabetic vascular complications and may help to reduce the incidence of serious diabetic vascular complications.

Several studies suggested that HWP was associated with coronary artery disease and metabolic syndrome in community crowds. Compared with Isabelle's study, our results adjusted for HbA1c in diabetes patients, demonstrating the consistency of the conclusions in the insulin-resistant states. In addition, the present study focuses on

Table 1 Demographic Information and Clinical Character of the Present Study

	Total	NTNW	ETNW	NTEW	HTGW	P*
n	3221	660	275	1209	1077	–
Males, n (%)	1914 (59.4)	374 (56.7)	174 (63.3)	673 (55.7)	693 (64.3)	<0.001
Age, years, mean (SD)	50.00 (12.27)	51.53 (11.92)	47.19 (10.90)	52.52 (12.00)	46.94 (12.32)	<0.001
Course, months, median (IQR)	47.00 (3.00, 125.00)	61.00 (10.00,135.25)	50.00 (3.00,115.00)	61.00 (5.00,136.00)	34.00 (1.00, 98.00)	<0.001
Height, cm, mean (SD)	166.53 (8.62)	164.68 (8.34)	165.64 (8.05)	166.12 (8.61)	168.36 (8.61)	<0.001
Weight, kg, mean (SD)	74.57 (14.52)	62.22 (8.74)	65.97 (8.73)	76.66 (13.12)	82.00 (14.10)	<0.001
BMI, kg/m2, mean (SD)	26.76 (4.03)	22.90 (2.38)	23.98 (2.15)	27.68 (3.60)	28.81 (3.64)	<0.001
Waist, cm, mean (SD)	94.28 (10.54)	82.04 (5.64)	84.35 (4.53)	97.95 (7.68)	100.21 (8.61)	<0.001
High school education, n (%)	1947 (60.6)	388 (59.1)	185 (67.3)	650 (53.9)	724 (67.3)	<0.001
Hypertension, n (%)	1104 (34.3)	145 (22.0)	75 (27.3)	477 (39.5)	407 (37.8)	<0.001
Drinking, n (%)	1327 (41.2)	233 (35.4)	125 (45.5)	461 (38.2)	508 (47.2)	<0.001
Smoking, n (%)	1093 (33.9)	192 (29.1)	107 (38.9)	377 (31.2)	417 (38.7)	<0.001
LDL-c mmol/l, mean (SD)	3.24 (0.91)	3.02 (0.83)	3.55 (0.93)	3.05 (0.84)	3.50 (0.94)	<0.001
HDL-c, mmol/l, mean (SD)	1.20 (0.29)	1.31 (0.32)	1.15 (0.26)	1.22 (0.28)	1.11 (0.27)	<0.001
Fasting glucose, mmol/L, mean (SD)	9.50 (4.05)	8.93 (4.20)	10.15 (4.19)	9.06 (3.79)	10.18 (4.07)	<0.001
Triglyceride, mmol/L, median (IQR)	1.51 (1.05, 2.32)	0.96 (0.75, 1.28)	2.51 (2.00, 3.71)	1.19 (0.94, 1.43)	2.57 (2.05, 3.68)	<0.001
HbA1c,%, mean (SD)	8.48 (2.30)	8.24 (2.53)	8.97 (2.40)	8.32 (2.16)	8.68 (2.25)	<0.001
Decreased GFR, n (%)	177 (5.5)	23 (3.5)	16 (5.8)	66 (5.5)	72 (6.7)	0.006*
Decreased ABI, n (%)	188 (5.8)	21 (3.2)	12 (4.4)	61 (5.0)	94 (8.7)	<0.001*
Elevated baPWV, n (%)	2065 (64.1)	381 (57.7)	162 (58.9)	840 (69.5)	682 (63.3)	0.003*
Elevated UACR, n (%)	914 (28.4)	119 (18.0)	100 (36.4)	312 (25.8)	383 (35.6)	<0.001*
DR, n (%)	125 (3.9)	22 (3.3)	17 (6.2)	50 (4.1)	36 (3.3)	0.685*

Note: *P for trend was calculated by Cochran Armitage Test.
Abbreviations: BMI, Body mass index; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TG, Triglyceride; HbA1c, Glycated hemoglobin; NTNW, Normal Triglyceride and Waist; ETNW, Elevated Triglyceride and normal Waist; NTEW, Normal Triglyceride and enlarged Waist; HTGW, Hypertriglyceridemic-waist; DR, Diabetic retinopathy; UACR, Urinary Albumin Creatinine Ratio; GFR, Glomerular filtration rate; ABI, ankle brachial index; baPWV, Brachial-ankle pulse wave velocity.

analyzing the association between arterial stiffness index (ABI and baPWV) and HWP.[10] The result of CKD-related vascular complications was consistent with Yan's study.[25] However, we did not find an association between HWP and DR.

Although the underlying mechanism of HWP with the vascular complication of diabetes has not been fully understood, there are several possible explanations. HWP is a particular biomarker that comprises both enlarged waist circumference and elevated TG.[8] First, Elevated triglyceride levels cause heparin to activate lipoprotein lipase and increase intravascular lipolysis of circulating triglycerides, thereby increasing tissue exposure to free fatty acids, ultimately leading to insulin resistance.[13] Second, the sedentary lifestyle contributes to the formation of the HTGW state, and the sedentary life was associated with atherosis in diabetes. The mechanism between HWP and vascular complication may be similar to the association between VAI and CVD, while both VAI and HWP are metabolic indicators.[26,27] Visceral fat cells stimulate the secretion of inflammatory factors such as interleukin-6 (IL-6), tumor necrosis factor α (TNF-α), and adipokines, which lead to the production of reactive oxygen in arterioles.[25] Therefore, pro-inflammatory cytokines and reactive oxygen species produced by obesity can directly affect endothelial cells, leading to endothelial dysfunction.[28]

In our study, there was an age difference in the result between HWP and vascular complications of diabetes. This phenomenon may be contributing to the prevalence of HWP in different age groups.[29] A similar result was also seen in Huelgas's study.[11] Elderly population has a lower prevalence of HTGW, and the survival bias should be considered. Moreover, the association between HWP and vascular complications of diabetes was more significant in the population

Table 2 Logistic Regression Analysis Assessing the Associations Between the Hypertriglyceridemic-Waist Phenotype and Vascular Complication Index of Diabetes

	Model 1		Model 2	
	OR	P	OR	P
Decreased ABI				
NTNW	Reference	–	Reference	–
ETNW	1.32[0.62, 2.69]	0.460	1.13 [0.53, 2.33]	0.740
NTEW	1.57 [0.96, 2.66]	0.082	1.49 [0.91, 2.55]	0.124
HTGW	2.68 [1.68, 4.48]	<0.001	2.24 [1.38, 3.80]	0.002
Decreased GFR				
NTNW	Reference	–	Reference	–
ETNW	2.64 [1.32, 5.21]	0.005	2.25 [1.10, 4.54]	0.024
NTEW	1.63 [1.00, 2.73]	0.056	1.38 [0.84, 2.34]	0.222
HTGW	2.78 [1.71, 4.70]	<0.001	2.21 [1.32, 3.82]	0.003
Elevated UACR				
NTNW	Reference	–	Reference	–
ETNW	2.52 [1.82, 3.48]	<0.001	2.34 [1.68, 3.26]	<0.001
NTEW	1.52 [1.20, 1.94]	0.001	1.33 [1.04, 1.71]	0.023
HTGW	2.53 [1.99, 3.23]	0.001	2.18 [1.69, 2.81]	<0.001
Elevated baPWV				
NTNW	Reference	–	Reference	–
ETNW	1.39 [1.02, 1.90]	0.038	1.37 [0.99, 1.89]	0.056
NTEW	1.69 [1.36, 2.11]	<0.001	1.49 [1.19, 1.88]	0.001
HTGW	1.73 [1.39, 2.16]	<0.001	1.63 [1.28, 2.06]	<0.001
DR				
NTNW	Reference	–	Reference	–
ETNW	1.96 [0.99, 3.82]	0.048	2.02 [1.00, 4.02]	0.046
NTEW	1.25 [0.75, 2.15]	0.402	1.19 [0.70, 2.06]	0.533
HTGW	1.07 [0.62, 1.90]	0.807	1.04 [0.58, 1.90]	0.889

Notes: Model 1: adjust for sex, duration, HbA1c. Molde 2: adjust for history of hypertension, smoking, drinking, education, LDL, HDL, and plus the covariable in model 1.
Abbreviations: NTNW, Normal Triglyceride and Waist; ETNW, Elevated Triglyceride and normal Waist; NTEW, Normal Triglyceride and enlarged Waist; HTGW, Hypertriglyceridemic-waist; DR, Diabetic retinopathy; GFR, Glomerular filtration rate; ABI, ankle brachial index; baPWV, Brachial-ankle pulse wave velocity.

of high academic level, which may be illustrated by a sedentary lifestyle in these people. In addition, the stratified analysis results for ABI and baPWA show differences in patients with a history of hypertension or not, which may contribute to the interaction between d blood pressure and arterial stiffness.[30]

This study also has several limitations. Firstly, due to the cross-sectional study design, we cannot obtain an accurate causal relationship and cannot rule out reverse causality. More cohort studies should be designed to clarify the association between HWP and vascular complications in type 2 diabetes. In future research, we will analyze the association of HWP and vascular complications in a cohort using causal inference methods. Moreover, although a series of sensitivity analyses adjusted the result of the association between HWP and vascular complications, residual confounders still existed, such as the usage of hormones and other drugs. Last, we could not include the patients with type 1 diabetes and gestational diabetes mellitus who have younger ages and morbid states, which should be a reappraisal of the association between HWP and vascular complications.

Therefore, this study found an association between HWP and vascular complications of diabetes. All these results suggest that HWP is a cost-effective screening tool that can be used in clinical practice and health management. Patients of T2DM should monitor the level and trajectory of HWP, which may help to reduce the incidence of serious diabetic vascular complications. For medical researchers, more simple, accurate, and reliable biomarkers should be developed to assess the risk of chronic disease complications.

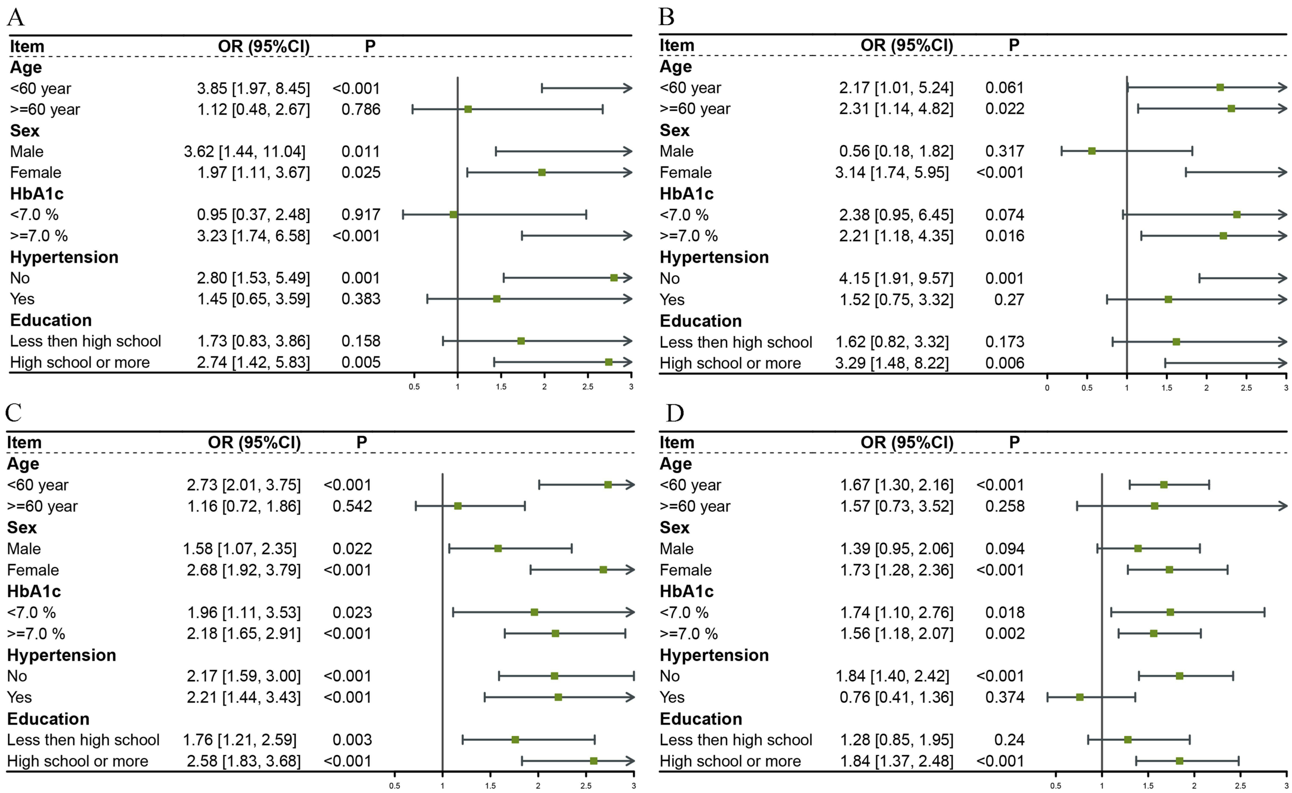

Figure 2 Stratified analysis of associations between the hypertriglyceridemic-waist phenotype and vascular complication index of diabetes. (**A**) ABI (**B**) GFR (**C**) UACR (**D**) baPWV.

Abbreviations: DR, Diabetic retinopathy; GFR, Glomerular filtration rate; ABI, ankle-brachial index; baPWV, Brachial-ankle pulse wave velocity.

Conclusion

In summary, there was an association between HWP and diabetic vascular complications in the Chinese population.

Data Sharing Statement

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

Ethics Approval and Consent to Participate

The Medical Ethics Committee of Beijing Luhe Hospital, Capital Medical University approved the study protocol. This study was performed by the Declaration of Helsinki, and all participants provided written informed consent.

Acknowledgments

We would like to thank the patients for their willingness to participate in these studies.

Funding

This study was supported by grants from Tongzhou District Science and Technology project (No. KJ2022CX030).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Gregory GA, Robinson TIG, Linklater SE, et al; International Diabetes Federation Diabetes Atlas Type 1 Diabetes in Adults Special Interest Group. Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. *Lancet Diabetes Endocrinol*. 2022;10(10):741–760. doi:10.1016/S2213-8587(22)00218-2
2. Sun H, Saeedi P, Karuranga S, et al. IDF diabetes atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183:109119. doi:10.1016/j.diabres.2021.109119
3. Jonas DE, Vander Schaaf EB, Riley S, et al. Screening for prediabetes and type 2 diabetes in children and adolescents: evidence report and systematic review for the US preventive services task force. *JAMA*. 2022;328(10):968–979. doi:10.1001/jama.2022.7957
4. Elafros MA, Andersen H, Bennett DL, et al. Towards prevention of diabetic peripheral neuropathy: clinical presentation, pathogenesis, and new treatments. *Lancet Neurol*. 2022;21(10):922–936. doi:10.1016/S1474-4422(22)00188-0
5. Wang Y, Zhang P, Shao H, Andes LJ, Imperatore G. Medical costs associated with diabetes complications in medicare beneficiaries aged 65 years or older with type 2 diabetes. *Diabetes Care*. 2022;45(11):2570–2576. doi:10.2337/dc21-2151
6. Wu Z, Zhou D, Liu Y, et al. Association of TyG index and TG/HDL-C ratio with arterial stiffness progression in a non-normotensive population. *Cardiovasc Diabetol*. 2021;20(1):134. doi:10.1186/s12933-021-01330-6
7. Shi Y, Yu C, Hu L, et al. Visceral adiposity index and sex differences in relation to peripheral artery disease in normal-weight adults with hypertension. *Biol Sex Differ*. 2022;13(1):22. doi:10.1186/s13293-022-00432-4
8. Lemieux I, Pascot A, Couillard C, et al. Hypertriglyceridemic waist: a marker of the atherogenic metabolic triad (hyperinsulinemia; hyperapolipoprotein B; small, dense LDL) in men? *Circulation*. 2000;102(2):179–184. doi:10.1161/01.cir.102.2.179
9. Janghorbani M, Salamat MR, Aminorroaya A, Amini M. Utility of the visceral adiposity index and hypertriglyceridemic waist phenotype for predicting incident hypertension. *Endocrinol Metab*. 2017;32(2):221–229. doi:10.3803/EnM.2017.32.2.221
10. Lemieux I, Poirier P, Bergeron J, et al. Hypertriglyceridemic waist: a useful screening phenotype in preventive cardiology? *Can J Cardiol*. 2007;23 Suppl B(Suppl B):23B–31B. doi:10.1016/s0828-282x(07)71007-3
11. Gomez-Huelgas R, Bernal-López MR, Villalobos A, et al. Hypertriglyceridemic waist: an alternative to the metabolic syndrome? Results of the IMAP Study (multidisciplinary intervention in primary care). *Int J Obes*. 2011;35(2):292–299. doi:10.1038/ijo.2010.127
12. Wang W, Shen C, Zhao H, et al. A prospective study of the hypertriglyceridemic waist phenotype and risk of incident ischemic stroke in a Chinese rural population. *Acta Neurol Scand*. 2018;138(2):156–162. doi:10.1111/ane.12925
13. Poitout V, Hagman D, Stein R, Artner I, Robertson RP, Harmon JS. Regulation of the insulin gene by glucose and fatty acids. *J Nutr*. 2006;136 (4):873–876. doi:10.1093/jn/136.4.873
14. Unger RH, Zhou YT. Lipotoxicity of beta-cells in obesity and in other causes of fatty acid spillover. *Diabetes*. 2001;50(Suppl 1):S118–S121. doi:10.2337/diabetes.50.2007.s118
15. Zhang Y, Wang W, Ning G. Metabolic management center: an innovation project for the management of metabolic diseases and complications in China. *J Diabetes*. 2019;11(1):11–13. doi:10.1111/1753-0407.12847
16. Wilkinson CP, Ferris FL 3rd, Klein RE, et al. Proposed international clinical diabetic retinopathy and diabetic macular edema disease severity scales. *Ophthalmology*. 2003;110(9):1677–1682. doi:10.1016/S0161-6420(03)00475-5
17. Munakata M. Brachial-ankle pulse wave velocity: background, method, and clinical evidence. *Pulse*. 2016;3(3–4):195–204. doi:10.1159/000443740
18. Li T, Wu XJ, Chen XM, Wang SB, Liu KD, Xing YQ. Ankle-brachial index and brachial-ankle pulse wave velocity are risk factors for ischemic stroke in patients with type 2 diabetes. *Neural Regen Res*. 2017;12(11):1853–1859. doi:10.4103/1673-5374.219046
19. Ohkuma T, Ninomiya T, Tomiyama H, et al. Brachial-ankle pulse wave velocity and the risk prediction of cardiovascular disease: an individual participant data meta-analysis. *Hypertension*. 2017;69:1045–1052. doi:10.1161/HYPERTENSIONAHA.117.09097
20. Hashimoto Y, Tanaka M, Okada H, et al. Metabolically healthy obesity and risk of incident CKD. *Clin J Am Soc Nephrol*. 2015;10(4):578–583. doi:10.2215/CJN.08980914
21. Stevens LA, Claybon MA, Schmid CH, et al. Evaluation of the chronic kidney disease epidemiology collaboration equation for estimating the glomerular filtration rate in multiple ethnicities. *Kidney Int*. 2011;79(5):555–562. doi:10.1038/ki.2010.462
22. Wang SK, Lee MC, Hung CL, Chen HH, Liao CC, Chiu YL. Association between hypertriglyceridemic waist phenotype and hypogonadism in Taiwanese adult men. *PLoS One*. 2022;17(3):e0265629. doi:10.1371/journal.pone.0265629
23. Yan Y, Li S, Liu Y, et al. Associations between life-course lipid trajectories and subclinical atherosclerosis in midlife. *JAMA Netw Open*. 2022;5 (10):e2234862. doi:10.1001/jamanetworkopen.2022.34862
24. Lindberg F, Lund LH, Benson L, et al. Trajectories in New York Heart Association functional class in heart failure across the ejection fraction spectrum: data from the Swedish Heart Failure Registry. *Eur J Heart Fail*. 2022;24(11):2093–2104. doi:10.1002/ejhf.2644
25. Xuan Y, Zhang W, Wang Y, et al. The association between hypertriglyceridemic-waist phenotype and chronic kidney disease in patients with type 2 diabetes: a Cross-Sectional METAL Study. *Diabetes Metab Syndr Obes*. 2022;15:1885–1895. doi:10.2147/DMSO.S359742
26. Kaur R, Kaur M, Singh J. Endothelial dysfunction and platelet hyperactivity in type 2 diabetes mellitus: molecular insights and therapeutic strategies. *Cardiovasc Diabetol*. 2018;17:121. doi:10.1186/s12933-018-0763-3
27. Pekgor S, Duran C, Berberoglu U, Eryilmaz MA. The role of visceral adiposity index levels in predicting the presence of metabolic syndrome and insulin resistance in overweight and obese patients. *Metab Syndr Relat Disord*. 2019;17:296–302. doi:10.1089/met.2019.0005
28. Gunnett CA, Lund DD, McDowell AK, Faraci FM, Heistad DD. Mechanisms of inducible nitric oxide synthase-mediated vascular dysfunction. *Arterioscler Thromb Vasc Biol*. 2005;25(8):1617–1622. doi:10.1161/01.ATV.0000172626.00296.ba
29. Bos G, Dekker JM, Heine RJ; Hoom study. Non-HDL cholesterol contributes to the "hypertriglyceridemic waist" as a cardiovascular risk factor: the Hoorn study. *Diabetes Care*. 2004;27:283–284. doi:10.2337/diacare.27.1.283
30. Liu R, Li D, Yang Y, Hu Y, Wu S, Tian Y. Systolic blood pressure trajectories and the progression of arterial stiffness in Chinese adults. *Int J Environ Res Public Health*. 2022;19(16):10046. doi:10.3390/ijerph191610046