

Association of Type 2 Diabetes and Body Mass Index with Arterial Stiffness: A Carotid Ultrasound Study

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Objective: This study aimed to investigate the joint and independent associations of type 2 diabetes (T2DM) and body mass index (BMI) with arterial stiffness using carotid ultrasound-based measures.

Methods: This retrospective, matched cross-sectional study enrolled 255 participants, including people with T2DM (n=129) and Control group (diabetes-free, n=126). The control group was matched to the T2DM group based on age (± 5 years), sex, and BMI category. People with T2DM were diagnosed according to World Health Organization criteria and classified into three BMI-based categories: lean (BMI < 25 kg/m², n=48), overweight (BMI = 25–29.9 kg/m², n=44) and obese (BMI ≥ 30 kg/m², n=37). Carotid intima-media thickness (IMT) and pulse wave velocity (PWV) were determined using sample images. Univariable and multivariable logistic regression models were used to evaluate the associations between BMI, T2DM and arterial stiffness, adjusted for potential confounders such as age, systolic blood pressure and lipid profiles. Interaction terms tested multiplicative effects.

Results: Compared to people with diabetes-free, those with T2DM had significantly greater IMT and PWV impairments ($P < 0.001$). An increasing BMI category was associated with progressive IMT and PWV increase in people with T2DM ($P < 0.001$). Multi-variable analysis revealed that BMI category had strong associations with carotid IMT (Standardize β 0.715, 95% CI: 113.4, 174.7) and PWV (Standardize β 0.544, 95% CI: 0.81, 1.73), indicating the progressive impact of BMI on arterial stiffness. No interaction was observed between T2DM and BMI (IMT: P -interaction=0.95; PWV: P -interaction=0.56), indicating independent effects.

Conclusion: This study demonstrates additive but non-synergistic effects of T2DM and BMI on arterial stiffness, with BMI driving the majority of vascular impairment. However, the cross-sectional design precludes causal inferences. The findings underscore the clinical relevance of weight management in people with T2DM.

Keywords: type 2 diabetes mellitus, obesity, carotid arteries, body mass index, arterial stiffness

Introduction

The global incidence of type 2 diabetes mellitus (T2DM) continues to rise, with China now home to the largest T2DM population worldwide.^{1,2} This condition, especially when combined with obesity, increases the risk of early atherosclerotic cardiovascular disease (CVD) through mechanisms such as endothelial dysfunction, reduced arterial elasticity and atherosclerosis.³ Type 2 diabetes mellitus and obesity each independently contribute to arterial stiffness and impaired cardiovascular health, but recent findings suggest their combined impact could be even more detrimental.⁴

Arterial stiffness is an early indicator of CVD and is commonly assessed using pulse wave velocity (PWV), a reliable measure of arterial rigidity.⁵ In recent years, studies have shown that PWV reflects arterial stiffness, which is an independent predictor of mortality in people with diabetes and CVD and is also a reliable parameter for assessing global arterial stiffness.⁶ The local PWV can be measured by ultrafast ultrasound imaging, which is an ultrasound-based, non-invasive method for assessing the stiffness of the carotid artery. Pan et al⁷ demonstrated that ultrafast ultrasound imaging is a highly reproducible and effective approach for assessing carotid stiffness by measuring carotid PWV. The quantification of local carotid stiffness holds significant clinical relevance. As the primary conduit arteries supplying the brain, the carotid arteries are directly implicated in cerebrovascular events. Stiffening of the carotid wall not only contributes to increased central pulsatile load but is also a key factor in the pathogenesis of cerebral small vessel disease and cognitive decline. Furthermore, local carotid stiffness assessed by ultrafast PWV has been shown to be a sensitive indicator of early, subclinical atherosclerosis, often preceding overt increases in carotid intima-media thickness (IMT). This makes it a valuable tool for early risk stratification, especially in high-risk populations such as those with T2DM and obesity, allowing for timely interventions aimed at preventing subsequent cardiovascular and cerebrovascular events. Several studies have demonstrated strong correlations between ultrafast carotid PWV and cf-PWV, supporting its validity for assessing vascular function. For instance, a validation study by Couade et al⁸ reported excellent agreement between the two methods in patients with cardiovascular risk factors. However, it is important to note that carotid PWV primarily reflects local arterial stiffness within the carotid segment, whereas cf-PWV provides a more comprehensive assessment of central aortic stiffness. This distinction may limit direct comparability with studies using cf-PWV, particularly when evaluating generalized vascular aging or systemic hemodynamic load. Nevertheless, the reproducibility and feasibility of ultrafast PWV support its utility in clinical research for detecting early vascular changes associated with metabolic disorders. While previous studies have investigated the individual effects of T2DM and BMI on cardiovascular health,^{9–11} few have explored the joint impact of the T2DM and BMI categories on arterial stiffness. Understanding this interaction is critical as it may reveal compounded risks that are not evident when examining T2DM or obesity in isolation.

Despite existing evidence, several critical gaps remain in the literature. First, previous studies have often focused on T2DM or obesity in isolation, rather than investigating their combined and interactive effects within a unified framework^{9,11} Assessing both T2DM and BMI simultaneously requires controlling for various confounders (such as age, blood pressure and lipid levels), which can complicate study designs and statistical analyses. Second, the methodological complexity of concurrently analyzing T2DM and detailed BMI categories, while adequately controlling for key confounders (eg, age, blood pressure, lipid levels), has often been a limiting factor. Third, the use of diverse measurement techniques across studies has hindered direct comparisons and a clear understanding of how T2DM and obesity jointly influence local arterial stiffness assessed by modern ultrasound-based methods like carotid PWV. Therefore, this study was designed to address these gaps. Accordingly, this study aimed to address this gap by investigating the combined effects of T2DM and BMI on arterial stiffness and carotid atherosclerosis, with a specific focus on measuring carotid intima-media thickness (IMT) and PWV.

Materials and Methods

Study Design and Sample Size Calculation

This retrospective, matched cross-sectional study aimed to investigate the combined impact of T2DM and BMI on arterial stiffness and carotid atherosclerosis. The study included 255 people recruited from the Department of Endocrinology and the Physical Examination Department of the hospital. The control group (diabetes-free individuals, n=126) was selected to match the group of people with Type 2 Diabetes (T2DM, n=129) based on the following three criteria:

- Age: ± 5 years
- Sex: 1:1 ratio
- BMI Category: Participants were classified into the same three BMI categories: lean (BMI <25 kg/m²), overweight (BMI 25–29.9 kg/m²), and obese (BMI ≥ 30 kg/m²).

The controls were consecutively recruited from the same hospital's Physical Examination Department during the same study period (January 2020 to December 2022) to ensure they were drawn from a similar population base as the T2DM group, who were recruited from the Department of Endocrinology.

All patient information was obtained from the Medical Ultrasound Department and clinical databases of the hospital over two years. The sample size calculation was performed a priori using GPower software (version 3.1.9.7). Based on a preliminary analysis of the data, a medium effect size (Cohen's $f = 0.25$) for the primary outcome (PWV) among the main groups (T2DM vs control) and BMI categories was anticipated. To achieve 80% statistical power ($\beta = 0.20$) for detecting a significant difference using a one-way Analysis of Variance (ANOVA) at a two-sided alpha level of 0.05, a minimum total sample size of 180 participants was required. Accounting for a potential attrition or data exclusion rate of up to 15%, a total of 210 participants was aimed to be recruited. Ultimately, 255 participants were enrolled, which exceeded the minimum requirement and provided adequate power for the analyses.

Study Population

This retrospective, matched cross-sectional study enrolled 255 participants (129 with T2DM and 126 diabetes-free controls). The T2DM status of patients in the exposed group was confirmed by reviewing their medical records, which documented a diagnosis based on World Health Organization criteria.¹² Similarly, the height and weight measurements used to calculate body mass index (BMI) for all participants were retrieved from their clinical records, taken during the same period as the carotid ultrasound examination. And BMI is recommended by the World Health Organization as such a measurement.¹³ People were consecutively recruited from the Department of Endocrinology and the Physical Examination Department of the hospital between January 2020 and December 2022. Eligible participants who met the inclusion/exclusion criteria were enrolled. People with T2DM ($n=129$) were classified into three BMI-based groups: 48 lean people with T2DM ($\text{BMI} < 25 \text{ kg/m}^2$), 44 overweight people with T2DM ($\text{BMI} = 25\text{--}29.9 \text{ kg/m}^2$) and 37 obese people with T2DM ($\text{BMI} \geq 30 \text{ kg/m}^2$). Diabetes-free controls ($n=126$) were selected to match the T2DM group by age (± 5 years), sex (1:1 ratio) and BMI category (lean, overweight or obese). People with T2DM were compared with 126 people without diabetes. People who were excluded included those with (1) suboptimal ultrasonography images, for example, images with poor resolution or signal dropout in the carotid intima-media layers; (2) specific types of cardiac arrhythmias, including ventricular and supraventricular arrhythmias, which could interfere with consistent PWV measurements; and (3) moderate or severe valvular stenosis or regurgitation (Figure 1).

In addition, we systematically collected the following potential confounding factors from medical records for analysis: smoking status (categorized as current smoker, former smoker, or never smoker); duration of diabetes (from the time of initial diagnosis to enrollment); medication use (including antidiabetic, antihypertensive, and lipid-lowering drugs); and dyslipidemia status (defined according to the 2016 ESC/EAS guidelines¹⁴). The glycemic control status of

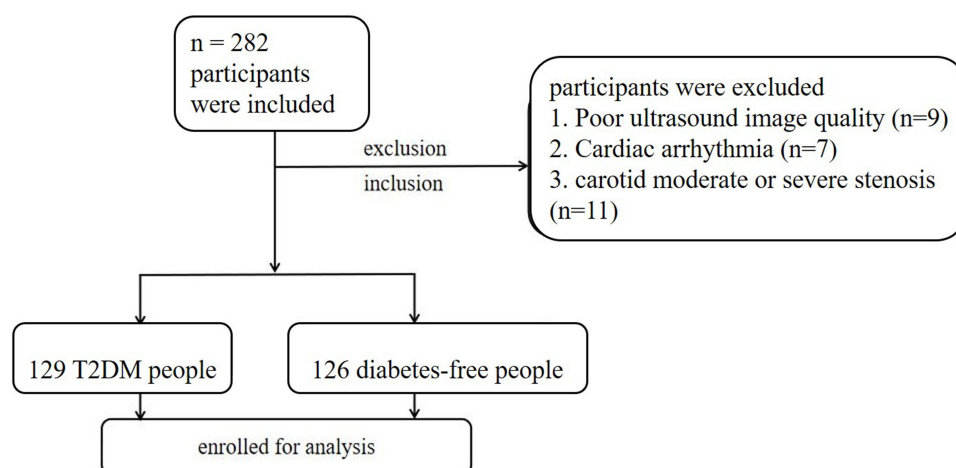


Figure 1 Flow chart of participants inclusion in the T2DM and Control group. T2DM, type 2 diabetes mellitus.

T2DM patients was assessed by HbA1c levels, and their main treatment methods (such as dietary control, oral antidiabetic drugs, or insulin therapy) were recorded.

All people underwent a comprehensive assessment, encompassing a medical history review, physical examination, biochemical analysis and ultrasound imaging of the carotid artery. Resting brachial blood pressure was measured using a calibrated electronic sphygmomanometer after the participant had been seated quietly for at least 10 minutes. The average of two measurements taken at least 5 minutes apart was recorded. The control participants underwent the same standardized carotid ultrasound examination as part of their annual health check-ups to provide baseline vascular data for comparison. The results of the baseline biochemical analyses included the levels of glycated haemoglobin, cholesterol, triacylglycerol, high-density lipoprotein and low-density lipoprotein. All examinations were performed using the same ultrasound device by one of two sonographers who were trained in the study protocol to ensure consistency. All the data were collected by two independent observers who were blinded to the ultrasound results.

This study was approved by the Medical Ethics Committee of the hospital (No. NYSZYEC2024K108R002). Given the retrospective nature of the research, the requirement for informed consent was waived.

Carotid Duplex Ultrasonography

The IMT and PWV measurements obtained from this single examination for each participant constituted the primary dataset for this retrospective analysis. A total of 282 people underwent carotid ultrasound over two years. The examination was offered free of charge as part of a hospital-initiated vascular health screening program. Participants voluntarily enrolled after providing informed consent. Carotid ultrasound examinations were routinely performed as part of cardiovascular risk assessment for people with T2DM, while participants without diabetes underwent the same examination during their annual health check-ups to establish a reference for vascular health. The primary indications included screening for subclinical atherosclerosis and the evaluation of vascular health in high-risk populations. Standardised carotid ultrasound was performed according to the 2017 European Society of Cardiology guidelines for the diagnosis and treatment of peripheral arterial diseases.^{15,16} The participants underwent carotid examination using the Mindray Resona (Shenzhen Mindray Bio-Medical Electronics Co, China) colour Doppler ultrasound system equipped with an L11-3U probe, operating at a frequency range of 3–11 MHz and integrated vascular function analysis software for vascular IMT and local PWV assessment. The people were instructed to assume a supine position, fully expose both sides of the neck and maintain calm breathing for at least 5 minutes in a temperature-controlled room (22°C–25°C). Participants were instructed to refrain from smoking, caffeine consumption and vigorous exercise for at least 12 hours before the examination. The IMT was measured using the RIMT function at a depth of 10–15 mm below the carotid sinus. The real-time IMT (RIMT) function was activated, and the width of the sampling box was set to 10 mm. The RIMT enables the automatic measurement of IMT within 1–6 cardiac cycles, thereby facilitating the calculation of mean and standard deviation values ([Supplementary Figure 1A](#)).

Arterial Stiffness Assessment

The PWV function on the Resona system is capable of automatically detecting the beginning of ejection (BE) and the end of ejection (EE) from the vessel diameter curve, enabling the measurement of PWV at the BE and EE (aortic valve opens and closes, respectively). This is implemented based on wide-beam tracking imaging technology at a very high frame rate (up to thousands of frames per second), where temporal (t) information of the pulse wave reaching different positions (x) of the arterial wall can easily be extracted. Thus, the average PWV within the ultrasound image can be calculated directly by $PWV = dx/dt$. By pressing the “Update” button on the touch screen of the system to start the acquisition, the system automatically calculated the PWV–ES, PWV–EE and standard deviation values. One measurement with a standard deviation less than 1.0 m/s or 20% of the average value was considered a successful measurement. Three successful measurements were taken for each side, and the median value was taken as the final result ([Supplementary Figure 1B](#)).

Reproducibility Analysis

To assess the reliability and reproducibility of the ultrasound measurements, a separate analysis using intraclass correlation coefficients (ICCs) was conducted after the primary data collection. This involved re-analyzing the stored

ultrasound images from a randomly selected subset of 20 participants. For interobserver variability, the differences between two independent sonographers, who were each blinded to the results of the other and analyzed the same set of stored images, were evaluated. For intraobserver variability, the same sonographer re-analyzed the same set of stored images after a 2-week interval to avoid recall bias. The criteria for ICCs were as follows: an ICC greater than 0.75 indicated excellent agreement, 0.60–0.74 indicated good agreement, 0.40–0.59 indicated fair agreement, and less than 0.4 indicated poor agreement.^{17,18}

Observer Training and Blinding

Data were collected by two independent observers who were trained ultrasound technicians with at least 5 years of clinical experience. Both observers underwent additional training sessions specific to this study's protocols to ensure the consistent application of imaging and measurement techniques. Data collection was performed in a blinded manner: observers were unaware of people's diabetes and BMI statuses, reducing observer bias. The two observers collected data at consistent time points for all of the people, with each observer conducting the measurements independently.

Statistical Analysis

The collected data were analysed using the statistical software SPSS 25.0 (IBM SPSS, Statistics, Chicago, IL, United States). Data normality was assessed using the Shapiro–Wilk test. Continuous variables with normal distribution are presented as mean±standard deviation (SD), and those without normal distribution are presented as median (interquartile range). An independent samples *t*-test or Mann–Whitney *U*-test was used for between-group comparisons, while one-way analysis of variance (ANOVA) with Tukey's post hoc test or Kruskal–Wallis test was applied for comparisons among three or more groups, as appropriate. Categorical variables are reported as frequencies and percentages. For comparing categorical variables, the χ^2 test with Yates' correction was used. Pearson correlation analysis was used to assess the linear relationship between two continuous variables, while Spearman correlation analysis was used to assess relationships between one continuous variable and one ordinal variable (eg BMI categories). Additionally, point-biserial correlation analysis was performed to assess the relationships between one continuous variable and one dichotomous variable (eg sex and the presence of diabetes).

One-way ANOVA was initially used to examine the influence of increasing BMI subgroup categories on carotid IMT and PWV in people with T2DM. The variance inflation factor (VIF) was calculated for each independent variable to check for multicollinearity. All VIF values were below 5, indicating no significant multicollinearity. Finally, multiple linear regression analysis was used to determine the independent and additive deleterious effects of an increasing BMI category and diabetes status on carotid IMT and PWV. A two-tailed $P < 0.05$ was considered to indicate statistical significance.

When constructing the multivariate linear regression models to assess the independent effects of BMI and diabetes status on IMT and PWV, we further adjusted for the following potential confounding factors: smoking status (with “never smoker” as the reference), duration of diabetes, antihypertensive medication use (yes/no), lipid-lowering medication use (yes/no), and HbA1c level. This approach was taken to more accurately estimate the independent effects of BMI and T2DM on arterial stiffness.

Data Management and Handling of Missing Data

Data collection was performed using a standardized electronic case report form. Given the retrospective nature of the study and the source of data being structured clinical databases, the occurrence of missing data for the key variables analyzed in this study (demographics, key biochemical parameters, carotid IMT, and PWV) was minimal. Specifically, all enrolled participants had complete data for age, sex, BMI, T2DM status, and the primary outcome measures (carotid IMT and PWV). For the biochemical profile (lipid parameters, HbA1c), missingness was less than 5%. Participants with any missing data in the variables required for a specific analysis were excluded only from that particular analysis (complete-case analysis). No imputation methods were used for missing data due to the low rate of missingness.

Results

Associations of Diabetes Mellitus Status with Carotid Atherosclerosis and Arterial Stiffness

A total of 255 people were included in the analysis: 129 with T2DM and 126 diabetes-free controls. The total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were greater in people with T2DM than in those without T2DM ($P < 0.05$ for both). However, high-density lipoprotein cholesterol (HDL-C) was significantly lower in people with T2DM than in those without T2DM ($P < 0.001$). Clinical characteristics such as age and blood pressure showed no significant between-group differences ($P > 0.05$). However, significant differences were observed in TC, LDL-C and HDL-C levels between the T2DM and Control groups ($P < 0.05$, Table 1). Regarding potential confounding factors, there was no significant difference in smoking status between the two groups ($P = 0.69$). The average duration of diabetes in the T2DM group was 8.5 ± 6.2 years. In terms of medication use, the majority of the T2DM group (72.1%) used oral antidiabetic drugs, 28.7% used insulin, and the usage rates of antihypertensive and lipid-lowering medications were 65.1% and 58.9%, respectively, which were significantly higher than those in the control group (all $P < 0.001$). Additionally, the prevalence of dyslipidemia in the T2DM group (64.3%) was significantly higher than that in the control group (32.5%),

Table 1 Comparison of Clinical and Carotid Ultrasonography Characteristics Between T2DM and Control Group

Variable	T2DM (n = 129)	Control (n = 126)	P-value
Clinical parameters			
Age (Years)	51 ± 9.9	48.3 ± 10.8	0.055
Height (cm)	166 ± 7.9	165 ± 7.2	0.113
Weight (kg)	74 ± 12.3	70 ± 13.1	0.020
BMI (kg/m^2)	26 ± 3.5	25 ± 4.0	0.062
SBP (mm Hg)	133 ± 19	130 ± 17	0.160
DBP (mm Hg)	87 ± 12	81 ± 10	0.286
Biochemical parameters			
HbA1c (%)	7.1 ± 2.0	4.9 ± 0.4	< 0.001
TC (mmol/L)	4.7 ± 1.5	4.2 ± 1.1	0.005
TG (mmol/L)	$1.8 (1.2-3.1)$	$1.5 (1.0-2.3)$	0.317
HDL-C (mmol/L)	1.1 ± 0.3	1.3 ± 0.4	< 0.001
LDL-C (mmol/L)	2.9 ± 1.0	2.6 ± 0.9	0.040
Ultrasonography parameters			
IMT (mm)	0.735 ± 0.155	0.638 ± 0.149	< 0.001
PWV (m/s)	7.7 ± 1.9	7.3 ± 1.7	0.033
Additional confounders			
Smoking status, n (%)			0.690
Current smoker	24 (18.6%)	21 (16.7%)	
Former smoker	31 (24.0%)	28 (22.2%)	
Never smoker	74 (57.4%)	77 (61.1%)	
Diabetes duration (years)	8.5 ± 6.2		
Dyslipidemia, n (%)	83 (64.3%)	41 (32.5%)	< 0.001
Medication use, n (%)			
Antihypertensive	84 (65.1%)	25 (19.8%)	< 0.001
Lipid-lowering	76 (58.9%)	18 (14.3%)	< 0.001
Oral antidiabetic	93 (72.1%)		
Insulin therapy	37 (28.7%)		

Notes: TG used Mann–Whitney *U*-test, and other variables with normal distribution used independent sample *t*-test.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein; IMT, intima-media thickness; LDL-C, low-density lipoprotein; PWV, pulse wave propagation velocity; SBP, systolic blood pressure; TC, cholesterol; TG, triacylglycerol.

$P < 0.001$). The average HbA1c level in T2DM patients ($7.1 \pm 2.0\%$) was significantly higher than that in the control group ($4.9 \pm 0.4\%$, $P < 0.001$).

However, on ultrasonography, carotid IMT thickening was more severe in people with T2DM than in those who did not have T2DM (0.735 ± 0.155 mm vs 0.638 ± 0.149 mm, $P < 0.001$). Furthermore, carotid PWV was higher in people with T2DM than in those who did not have T2DM (7.7 ± 1.9 m/s vs 7.3 ± 1.7 m/s, $P < 0.05$).

For people in the increasing BMI category, there were progressive increases in systolic blood pressure ($P < 0.001$, Table 2). As was anticipated, IMT and PWV in the obesity group with T2DM were the highest among the three groups ($P < 0.001$). Similar results were obtained for the three BMI categories that included people without T2DM ($P < 0.001$). Finally, the increasing BMI category was associated with progressively increasing IMT and PWV (Table 3).

Associations Between the Increasing Body Mass Index Category and Carotid Atherosclerosis and Arterial Stiffness in People with Type 2 Diabetes Mellitus

Univariable analysis revealed that both IMT and PWV significantly correlated with age (standardised β values: 0.435 and 0.389, respectively, both $P < 0.001$; Table 4). Furthermore, IMT and PWV were also found to be correlated with systolic pressure (SBP) (standardised β values of 0.319 and 0.344, respectively; both $P < 0.001$). Moreover, both IMT and PWV

Table 2 Clinical, Biochemical, and Ultrasonically Characteristics of T2DM Group

Variable	Total T2DM population (n = 129)	Lean T2DM (BMI < 25 kg/m ²) (n = 48)	Overweight T2DM (BMI 25–29.9 kg/m ²) (n = 44)	Obesity T2DM BMI (≥ 30 kg/m ²) (n = 37)	P-value
Clinical parameters					
Age (Years)	51 $\pm$ 9.9	47 $\pm$ 10	53 $\pm$ 8.3 [#]	51 $\pm$ 10	0.015
Height (cm)	166 $\pm$ 7.9	167 $\pm$ 7.2	166 $\pm$ 7.4	166 $\pm$ 9.4	0.851
Weight (kg)	74 $\pm$ 12.3	65 $\pm$ 7.8	73 $\pm$ 7.2 [#]	86 $\pm$ 11.3 ^{*#}	< 0.001
BMI (kg/m ²)	26.6 $\pm$ 3.5	23.2 $\pm$ 1.9	26.4 $\pm$ 1.1 [#]	31.2 $\pm$ 1.7 ^{*#}	< 0.001
SBP (mm Hg)	133 $\pm$ 19	127 $\pm$ 17	129 $\pm$ 14	144 $\pm$ 21 ^{*#}	< 0.001
DBP (mmHg)	87 $\pm$ 12	92 $\pm$ 10	81 $\pm$ 12	88 $\pm$ 17	0.714
Biochemical parameters					
HbA1c (%)	7.1 $\pm$ 2.0	6.9 $\pm$ 2.1	7.0 $\pm$ 2.1	7.6 $\pm$ 2.0	0.213
TC (mmol/L)	4.7 $\pm$ 1.5	4.8 $\pm$ 2.0	4.7 $\pm$ 1.2	4.7 $\pm$ 1.0	0.923
TG (mmol/L)	1.8 (1.2–3.1)	2.1 (1.5–4.2)	2.0 (1.3–3.0)	2.3 (1.7–3.5)	0.748
HDL-C (mmol/L)	1.1 $\pm$ 0.3	1.2 $\pm$ 0.3	1.1 $\pm$ 0.3	1.0 $\pm$ 0.3	0.443
LDL-C (mmol/L)	2.9 $\pm$ 1.0	2.8 $\pm$ 1.0	2.9 $\pm$ 1.1	3.0 $\pm$ 0.8	0.675
Ultrasonography parameters					
IMT (mm)	0.735 $\pm$ 0.155	0.595 $\pm$ 0.052	0.769 $\pm$ 0.069 [#]	0.876 $\pm$ 0.144 ^{*#}	< 0.001
PWV (m/s)	7.7 $\pm$ 1.9	6.6 $\pm$ 1.3	7.6 $\pm$ 1.2 [#]	9.3 $\pm$ 2.2 ^{*#}	< 0.001
Additional confounders					
Diabetes duration (years)	8.5 $\pm$ 6.2	7.8 $\pm$ 5.9	8.9 $\pm$ 6.5	9.1 $\pm$ 6.3	0.423
Smoking status, n (%)					0.835
Current smoker	24 (18.6%)	10 (20.8%)	8 (18.2%)	6 (16.2%)	
Former smoker	31 (24.0%)	11 (22.9%)	10 (22.7%)	10 (27.0%)	
Never smoker	74 (57.4%)	27 (56.3%)	26 (59.1%)	21 (56.8%)	
Dyslipidemia, n (%)	83 (64.3%)	28 (58.3%)	29 (65.9%)	26 (70.3%)	0.481
Medication use, n (%)					
Antihypertensive	84 (65.1%)	26 (54.2%)	29 (65.9%)	29 (78.4%)	0.048
Lipid-lowering	76 (58.9%)	25 (52.1%)	26 (59.1%)	25 (67.6%)	0.321
Oral antidiabetic	93 (72.1%)	36 (75.0%)	31 (70.5%)	26 (70.3%)	0.852
Insulin therapy	37 (28.7%)	12 (25.0%)	13 (29.5%)	12 (32.4%)	0.734

Notes: * $P < 0.05$ for Obese T2DM BMI group vs Overweight T2DM group. [#] $P < 0.05$ for Obese T2DM BMI group vs Lean T2DM group or Overweight T2DM group vs Lean T2DM group. P value by one-way ANOVA. TG used Mann–Whitney U-test, and other variables with normal distribution used independent sample t-test.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HbA1c, Glycated hemoglobin; HDL-C, high-density lipoprotein; IMT, intima-media thickness; LDL-C, low-density lipoprotein; PWV, pulse wave propagation velocity; SBP, systolic blood pressure; TC, Total cholesterol; TG, triacylglycerol.

Table 3 Clinical, Biochemical, and Ultrasonography Characteristics of Control Group

Variable	Total Population (n=126)	Lean T2DM Control (BMI<25 kg/m ²) (n=49)	Overweight T2DM Control (BMI 25–29.9 kg/m ²) (n=47)	Obese T2DM Control (BMI≥30 kg/m ²) (n=30)	P-value
Clinical					
Age (years)	48 ± 10.8	43 ± 9.8	50 ± 10	52 ± 10	0.001
Height (cm)	165 ± 7.2	163 ± 6.7	167 ± 6.7	165 ± 7.8	0.011
Weight (kg)	70 ± 13.1	58 ± 8.0	74 ± 7.1	84 ± 8.6	<0.001
BMI (kg/m ²)	25 ± 4.0	21 ± 2.5	26 ± 1.2	30 ± 2.0	<0.001
SBP (mmHg)	130 ± 17	122 ± 12	131 ± 17	139 ± 18	<0.001
DBP (mmHg)	81 ± 10	77 ± 9	82 ± 10	86 ± 9	<0.001
Biochemical					
HbA1c (%)	4.9 ± 0.4	4.8 ± 0.5	5.0 ± 0.3	4.9 ± 0.3	0.130
TC (mmol/L)	4.2 ± 1.1	3.9 ± 1.1	4.4 ± 1.0	4.5 ± 1.1	0.016
TG (mmol/L)	1.8 (1.2–3.1)	1.5 (1.0–2.3)	1.4 (0.9–2.0)	2.8 (1.5–5.5)	0.037
HDL-C (mmol/L)	1.3 ± 0.4	1.5 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	0.015
LDL-C (mmol/L)	2.6 ± 0.9	2.6 ± 0.9	2.9 ± 0.9	2.7 ± 1.0	0.315
Ultrasonography					
IMT (mm)	0.638 ± 0.149	0.500 ± 0.067	0.685 ± 0.100	0.792 ± 0.109	<0.001
PWV (m/s)	7.3 ± 1.7	6.2 ± 0.9	7.3 ± 1.3	9.2 ± 1.5	<0.001
Additional confounders					
Smoking status, n (%)					0.912
Current smoker	21 (16.7%)	9 (18.4%)	7 (14.9%)	5 (16.7%)	
Former smoker	28 (22.2%)	10 (20.4%)	11 (23.4%)	7 (23.3%)	
Never smoker	77 (61.1%)	30 (61.2%)	29 (61.7%)	18 (60.0%)	
Dyslipidemia, n (%)	41 (32.5%)	12 (24.5%)	16 (34.0%)	13 (43.3%)	0.196
Medication use, n (%)					
Antihypertensive	25 (19.8%)	6 (12.2%)	10 (21.3%)	9 (30.0%)	0.127
Lipid-lowering	18 (14.3%)	4 (8.2%)	7 (14.9%)	7 (23.3%)	0.152

Notes: P value by one-way ANOVA. TG used Mann–Whitney *U*-test, and other variables with normal distribution used independent sample *t*-test.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HbA1c, Glycated hemoglobin; HDL-C, high-density lipoprotein; IMT, intima-media thickness; LDL-C, low-density lipoprotein; PWV, pulse wave propagation velocity; SBP, systolic blood pressure; TC, Total cholesterol; TG, triacylglycerol.

were significantly correlated with T2DM status (standardised $\beta=0.303$, 0.133 , $P<0.05$, respectively) and BMI category (standardised $\beta=0.739$, $P<0.001$ and standardised $\beta=0.615$, $P<0.001$, respectively). Multi-variable analysis revealed that BMI category had strong associations with carotid IMT (Standardize β 0.715, 95% CI: 113.4, 174.7) and PWV (Standardize β 0.544, 95% CI: 0.81, 1.73), indicating the progressive impact of BMI on arterial stiffness.

As shown in Figure 2, in the control groups, BMI has a higher explanatory power for IMT and PWV (R^2 value: 0.52 and 0.37, respectively), and both have high significance ($P<0.001$). However, T2DM status has very low explanatory power for IMT and PWV (R^2 value: 0.05 and less than 0.01, respectively). In the T2DM groups, BMI has a medium explanatory power for IMT and PWV (R^2 value: 0.30 and 0.19, respectively), and both have high significance ($P<0.001$).

Table 4 Uni-Variate and Multivariate Analysis for IMT and PWV

Variables	Uni-Variate Analysis			Multi-Variate Analysis		
	Standardized β	95% CI	P-value	Standardize β	95% CI	P-value
Intima-media thickness (IMT)						
Age	0.435	[4.9, 8.4]	< 0.001	0.221	[2.1, 4.6]	< 0.001
SBP	0.319	[1.7, 3.8]	< 0.001	0.034	[-0.3, 0.9]	0.401
Presence of diabetes	0.303	[59.0, 134.3]	< 0.001	0.249	[55.8, 103.1]	< 0.001
BMI categories	0.739	[132.1, 165.7]	< 0.001	0.715	[113.4, 174.7]	< 0.001
Smoking status						
Current vs Never	0.085	[8.2, 45.3]	0.124	0.042	[-5.1, 28.7]	0.167
Former vs Never	0.062	[5.1, 32.8]	0.208	0.031	[-3.8, 21.4]	0.315
Diabetes duration	0.158	[2.1, 8.7]	0.012	0.087	[0.8, 5.2]	0.095
Antihypertensive meds	0.194	[25.3, 78.9]	0.003	0.065	[-8.2, 42.1]	0.184
Lipid-lowering meds	0.167	[18.9, 67.4]	0.008	0.058	[-6.9, 35.2]	0.192
Dyslipidemia	0.142	[15.2, 58.3]	0.023	0.049	[-5.8, 29.7]	0.187
Pulse wave velocity (PWV)						
Age	0.389	[0.04, 0.09]	< 0.001	0.213	[0.02, 0.05]	< 0.001
SBP	0.344	[0.02, 0.04]	< 0.001	0.126	[0.002, 0.023]	0.015
Smoking status						
Current vs Never	0.072	[0.08, 0.52]	0.156	0.035	[-0.06, 0.31]	0.184
Former vs Never	0.054	[0.05, 0.38]	0.237	0.028	[-0.04, 0.25]	0.298
Diabetes duration	0.124	[0.02, 0.11]	0.038	0.072	[-0.01, 0.08]	0.127
Antihypertensive meds	0.158	[0.25, 0.89]	0.009	0.052	[-0.12, 0.48]	0.213
Lipid-lowering meds	0.139	[0.18, 0.76]	0.018	0.046	[-0.10, 0.41]	0.226
Dyslipidemia	0.118	[0.12, 0.65]	0.042	0.041	[-0.08, 0.35]	0.208
Presence of diabetes	0.133	[0.04, 0.94]	0.017	0.067	[-0.11, 0.60]	0.176
BMI categories	0.615	[1.20, 1.66]	< 0.001	0.544	[0.81, 1.73]	< 0.001

Notes: The bold text in the table indicates P-values showing significant differences.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HbA1c, Glycated hemoglobin; HDL-C, high-density lipoprotein; IMT, intima-media thickness; LDL-C, low-density lipoprotein; PWV, pulse wave propagation velocity; SBP, systolic blood pressure; TC, Total cholesterol; TG, triacylglycerol.

Conversely, T2DM status has very low explanatory power for IMT and PWV (R^2 value: both less than 0.01). The explanatory power of age and SBP for IMT and PWV in the two groups was lower, but the significance was higher.

As shown in [Figure 3](#), people with diabetes had significantly increased IMT than those without diabetes across all BMI categories ($P < 0.001$, factorial ANOVA), and there was no significant interaction between the presence of diabetes and BMI categories ($P = 0.95$, factorial ANOVA); Similarly, people with diabetes had more progressive impaired PWV from normal weight to overweight compared with people without diabetes across all BMI categories ($P < 0.001$, factorial ANOVA), and there was no significant interaction between the presence of diabetes and BMI categories ($P = 0.56$, factorial ANOVA) [Figure 4](#).

Repeatability and Reproducibility

As shown in [Table 5](#) and [Supplementary Figure 2](#), the intraobserver and interobserver analyses presented good repeatability and reproducibility for IMT and PWV.

Interaction Analysis

Factorial ANOVA revealed significant main effects of T2DM status and BMI categories on both IMT and PWV ($P < 0.001$ for all) ([Figure 3](#)). However, no significant interaction was observed between the T2DM and BMI categories for either IMT ($P = 0.95$) or PWV ($P = 0.56$) ([Figure 4](#)). This suggests that the detrimental effects of T2DM and obesity on arterial stiffness are independent and additive.

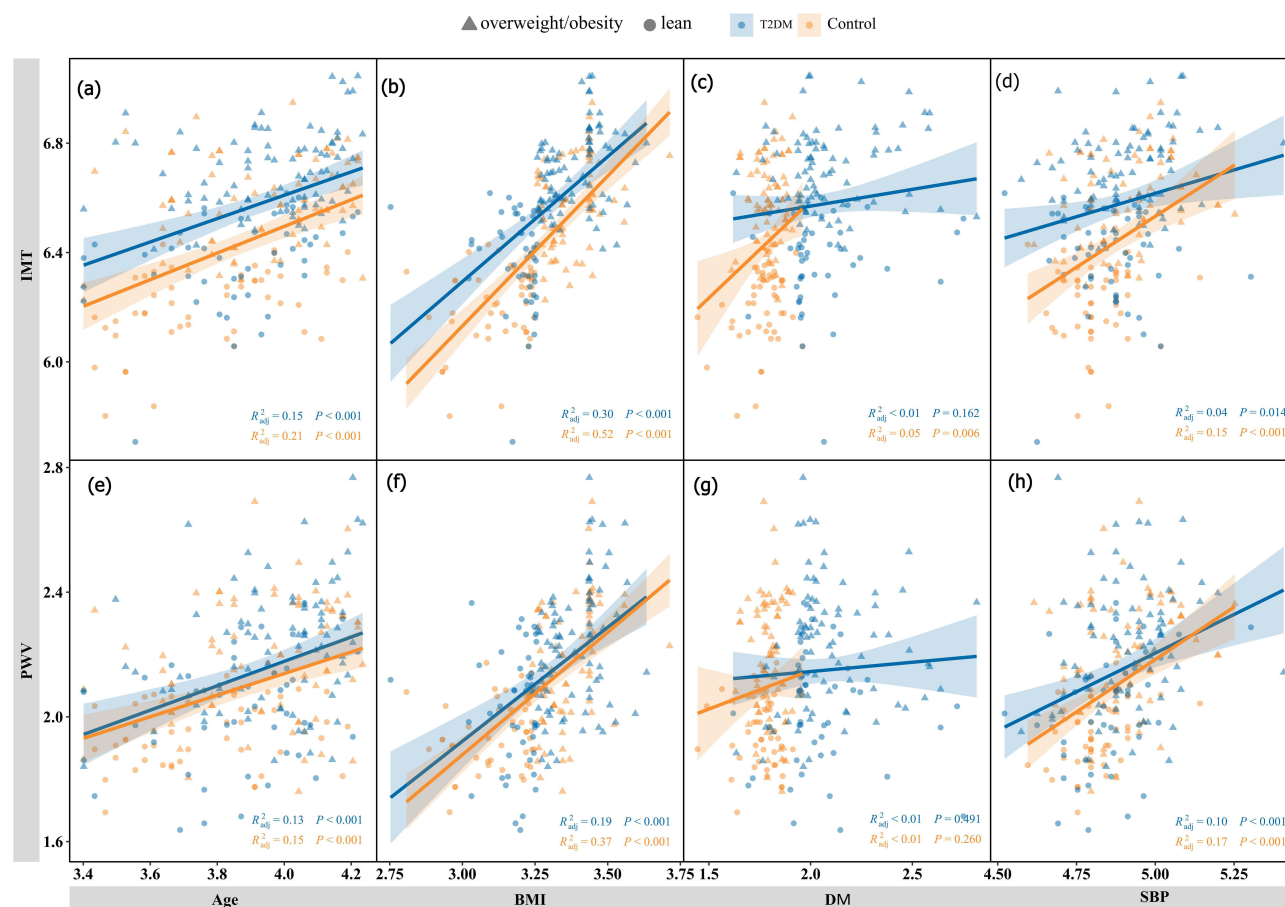


Figure 2 Relationships between IMT&PWV and age (a and e), BMI (b and f), DM (c and g) and SBP (d and h). Blue and yellow symbols represent data of T2DM people and Control people, respectively. The solid cycles and triangles represent data points from lean people (n=97) and overweight+obese people (n=91+67), respectively. The solid line is fitted using ordinary least squares regression, with the shaded area representing the 95% confidence interval. The R^2 value, also known as the coefficient of determination, measures how well the regression model fits the data. The R^2 value ranges from 0 to 1, indicating the proportion of variance in the dependent variable explained by the independent variables.

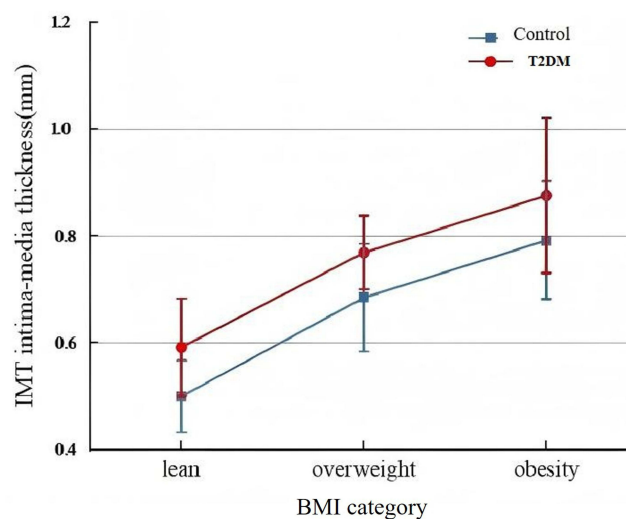


Figure 3 Comparisons of IMT in people with T2DM versus those Control across BMI categories. Increasing BMI was associated with progressive thickness of IMT. People with type 2 diabetes had more thickness of IMT across all BMI categories.

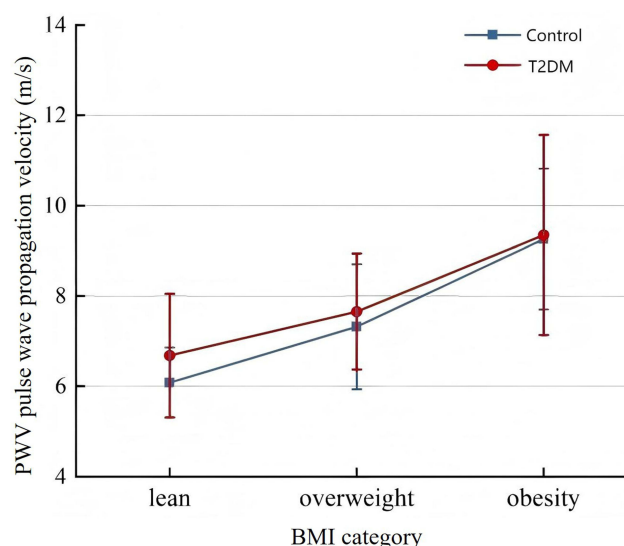


Figure 4 Comparisons of PWV in people with versus those diabetes-free across BMI categories. Increasing BMI was associated with progressive impairment of PWV. People with type 2 diabetes had more impaired PWV across all BMI categories.

Discussion

This study demonstrates that both T2DM and an increasing BMI are independently associated with greater carotid arterial stiffness and atherosclerosis, with BMI showing a particularly strong impact on carotid IMT and PWV. These findings align with previous studies showing that obesity and T2DM each contribute significantly to cardiovascular risk. Few studies have, however, examined their combined effects on arterial stiffness.

Comparing the results with prior studies, this study found both similarities and distinctive findings. Existing research, for example, a study conducted by Bashir et al, reported increased arterial stiffness in people with T2DM, yet the effects of BMI were less emphasised.¹⁹ In contrast, this study uniquely identifies BMI as a more influential factor than T2DM status alone, particularly in multivariable models, where BMI had a greater relative impact on arterial stiffness markers than T2DM. This may have been due to the focus on distinct BMI categories and the use of PWV and IMT, which offer sensitive assessments of arterial changes.

Obesity disrupts systemic homeostasis through adipose tissue dysfunction, characterised by the dysregulated secretion of adipokines (eg leptin resistance, reduced adiponectin), which impairs metabolic signalling and promotes insulin resistance.²⁰ Concurrently, chronic low-grade inflammation driven by adipose macrophage infiltration and elevated circulating cytokines (eg interleukin-6 [IL-6], C-reactive protein [CRP]) further exacerbates metabolic dysregulation.²¹ In recent years, numerous studies have consistently demonstrated a positive correlation between obesity status and impaired carotid artery elasticity. The detrimental effects of obesity may contribute to its concurrent manifestation of metabolic syndrome and endothelial cell damage, which exacerbates the risk of developing carotid atherosclerosis and vascular dysfunction, characterised by increased carotid IMT and vascular stiffness, leading to the development of various CVDs.^{22,23} Frequently, these processes synergistically contribute to the development of carotid atherosclerosis and vascular dysfunction in people with type 2 diabetes, characterised by increased carotid IMT and vascular stiffness, thereby elevating the risk of CVD.²⁴ In addition, obesity exacerbates arterial stiffness through multifaceted biochemical

Table 5 Intra-Observer and Inter-Observer Variability

	ICCs	Intra-Observer Variability	P-value	ICCs	Inter-Observer Variability	P-value
		95%CI			95%CI	
ITM	0.847	0.786–0.966	<0.001	0.834	0.747–0.960	<0.001
PWV	0.900	0.840–0.975	<0.001	0.756	0.642–0.944	<0.001

pathways. Lipotoxicity, driven by ectopic lipid deposition and elevated free fatty acids, induces endothelial dysfunction via oxidative stress and mitochondrial impairment.²⁰ Concurrently, atherogenic dyslipidaemia, characterised by elevated triglycerides, small dense LDL particles and reduced HDL, promotes subendothelial lipoprotein retention and foam cell formation, accelerating atherosclerotic plaque calcification.²¹ Additionally, adipose tissue-derived proinflammatory cytokines (eg IL-6 and Tumor necrosis factor - α [TNF- α]) perpetuate chronic inflammation, activating vascular smooth muscle cells and enhancing extracellular matrix remodelling, thereby increasing arterial rigidity.²⁵ These interconnected mechanisms underscore obesity as a central driver of vascular stiffening, independent of glycaemic status. Furthermore, while some studies have demonstrated the role of BMI in arterial stiffness, the results highlight effect when T2DM coexists with a higher BMI.^{26,27} This may be due to the additive metabolic effects of T2DM and an elevated BMI, which independently contribute to endothelial dysfunction and atherosclerotic processes. While both factors significantly worsen arterial stiffness, this study shows that their effects are not synergistic but cumulative. Differences in methodologies, patient demographics and the types of vascular measurements used could account for variations in findings across studies.

In the present study, both diabetes and the increasing BMI category were associated with IMT and PWV. [Figure 2](#) shows that, compared with other variables, BMI has a higher explanatory power and strong significance for IMT and PWV, while diabetes status has no significant influence on both. This indicates that BMI is the variable that has the greatest influence on IMT and PWV. Numerous carotid ultrasound studies examining diabetes have demonstrated that individuals with T2DM exhibit increased IMT thickness and arterial stiffness compared to healthy individuals.^{28,29} Moreover, several studies have reported that compared with non-obesity, obesity is associated with a greater prevalence of arterial wall stiffness and endothelial dysfunction.³⁰ Although diabetes and obesity frequently coexist, few studies have to date evaluated the combined impact of both diabetes and obesity on arterial stiffness. In a study of 25,020 healthy Chinese adults, Arnold et al³¹ observed that lean body mass was strongly associated with carotid IMT but not with carotid plaque burden. However, this study was limited by the exclusion of people with T2DM and an exclusive focus on adiposis. In contrast, the present study explored the combined impact of T2DM and an increasing BMI on carotid IMT and arterial stiffness. The study demonstrates that the presence of T2DM amplifies the adverse effects of obesity on cardiovascular health, while obesity status exacerbates the metabolic disturbances and vascular complications associated with T2DM. Additionally, significant associations between T2DM and obesity with increased carotid IMT and PWV were observed, indicating the cumulative detrimental impact of T2DM and the increasing BMI category on carotid vascular structure and elastic function. The increasing BMI category was more strongly and independently associated with arterial stiffness compared with T2DM status. Therefore, an elevated BMI may serve as a predictor of progressive increases in IMT and PWV.

One significant strength of this study is that we systematically incorporated a variety of important potential confounding factors into the analysis, including smoking status, duration of diabetes, medication use (antidiabetic, antihypertensive, and lipid-lowering), and glycemic control levels. Despite adjusting for these factors in the multivariate models, the strong association between BMI categories and carotid IMT and PWV remained highly significant, further supporting that obesity is a major independent driver of arterial stiffness. It is worth noting that the higher rates of lipid-lowering and antihypertensive medication use in the T2DM group, which could have potentially attenuated the observed vascular risk in this group, did not diminish the significant impact of BMI. This, in turn, underscores the strength of its effect.

This study has several limitations that should be considered when interpreting the results. First, Notwithstanding the significant associations observed, the interpretation of the findings must be tempered by several important limitations, most notably the inability to infer causality. As a cross-sectional study, the temporal sequence between BMI, T2DM, and arterial stiffness cannot be established. It remains uncertain whether elevated BMI precedes and contributes to vascular stiffening, or whether the pathophysiological state of increased arterial stiffness influences body composition. Therefore, the strong independent association of BMI with IMT and PWV should be interpreted as a robust correlation rather than evidence of a causal relationship. Participants were recruited from a single hospital, which may limit the generalizability of the findings to the broader population. Furthermore, despite the efforts to control for key confounders through multivariable regression, the possibility of residual confounding persists.

Unmeasured or imperfectly accounted for factors, such as detailed dietary habits, physical activity levels, genetic predisposition, and specific medication use, may have influenced both BMI and arterial stiffness, potentially inflating the observed associations. This residual confounding is an inherent limitation of observational studies and means that the true independent effect of BMI might be smaller than reported. Third, the classification of exposure variables has inherent limitations. Using a binary T2DM status oversimplifies the condition's heterogeneity, as factors like disease duration and glycemic control (eg, HbA1c levels) were not fully incorporated due to data availability. Furthermore, BMI was used as a surrogate for adiposity, which does not distinguish between fat and lean mass or account for fat distribution. Fourth, the sample size, particularly in the obese T2DM subgroup ($n=37$), was relatively small. This may have limited the statistical power to detect more subtle associations or potential interactions, and affects the external validity of the subgroup findings. Finally, although the study demonstrated good reproducibility, measurement variability in ultrasonographic assessments (IMT and PWV) is an inherent source of random error. Future studies should address these limitations by employing prospective, longitudinal designs in larger, multi-center cohorts and a key methodological limitation is the use of local carotid PWV instead of the gold-standard carotid-femoral PWV (cf-PWV). While ultrafast carotid PWV has been validated against cf-PWV and is a reliable measure of local arterial stiffness, cf-PWV has a more robust established prognostic value for future cardiovascular events. The findings based on local carotid stiffness may not be directly comparable to studies that used systemic measures like cf-PWV, and the generalizability of the results to overall cardiovascular risk may be constrained. They should incorporate more precise measures of adiposity (eg, DEXA, waist-to-hip ratio), detailed glycemic profiles, and comprehensive data on lifestyle and medication use to better delineate the causal pathways and improve risk stratification. Future longitudinal studies are warranted to establish causality and clarify the temporal relationships. These studies should prioritize large, prospectively designed cohorts with ethnically diverse participants. Critically, such studies must incorporate detailed and standardized documentation of medication use (including antihypertensive, lipid-lowering, and antidiabetic agents), along with comprehensive lifestyle metrics and continuous measures of T2DM severity (eg, HbA1c, diabetes duration), to accurately delineate the independent contributions of BMI and T2DM to arterial stiffening and to refine cardiovascular risk stratification.

Conclusion

In conclusion, within the constraints of a cross-sectional design, this study provides evidence of a compounded association of T2DM and obesity with increased arterial stiffness. BMI showed a stronger correlation with carotid IMT and local carotid PWV than T2DM status. This finding highlights the importance of weight management for cardiovascular health in the overall population, including those with and without T2DM. This supports the clinical emphasis on weight management in patients with T2DM, although the causal nature of this relationship requires verification in longitudinal studies. Future longitudinal research in diverse populations, which includes detailed profiling of medication use, is essential to confirm these associations, understand their causal pathways, and translate these findings into effective personalized prevention strategies.

Data Sharing Statement

The data and supportive information are available within the article.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of Shenzhen Hospital of Southern Medical University (No. NYSZYEC2024K108R002). Due to the nature of retrospective study and anonymized patient's information, informed consent is waived with the approval of Ethics Committee of Shenzhen Hospital of Southern Medical University. All methods were carried out in accordance with relevant guidelines and regulations.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Du YG and Guo YX are employed by Mindray. The authors declare no other competing interests in this work.

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