RESEARCH

Associations of the cardiometabolic index with insulin resistance, prediabetes, and diabetes in U.S. adults: a cross-sectional study

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Abstract

Background The cardiometabolic index (CMI) is a novel metric for assessing cardiometabolic health and type 2 diabetes mellitus (DM), yet its relationship with insulin resistance (IR) and prediabetes (preDM) is not well-studied. There is also a gap in understanding the nonlinear associations between CMI and these conditions. Our study aimed to elucidate these associations.

Methods We included 13,142 adults from the National Health and Nutrition Examination Survey (NHANES) 2007–2020. CMI was calculated by multiplying the triglyceride-to-high density lipoprotein cholesterol (TG/HDL-C) by waist-to-height ratio (WHtR). Using weighted multivariable linear and logistic regression explored the relationships of CMI with glucose metabolism markers, IR, preDM, and DM. Nonlinear associations were assessed using generalized additive models (GAM), smooth curve fittings, and two-piecewise logistic regression.

Results Multivariate regression revealed positive correlations between CMI and glucose metabolic biomarkers, including FBG ($\beta = 0.08$, 95% CI: 0.06–0.10), HbA1c ($\beta = 0.26$, 95% CI: 0.22–0.31), FSI ($\beta = 4.88$, 95% CI: 4.23–5.54), and HOMA-IR ($\beta = 1.85$, 95% CI: 1.56–2.14). There were also significant correlations between CMI and increased risk of IR (OR = 3.51, 95% CI: 2.94–4.20), preDM (OR = 1.49, 95% CI: 1.29–1.71), and DM (OR = 2.22, 95% CI: 2.00-2.47). Inverse nonlinear L-shaped associations were found between CMI and IR, preDM, and DM, with saturation inflection points at 1.1, 1.45, and 1.6, respectively. Below these thresholds, increments in CMI significantly correlated with heightened risks of IR, preDM, and DM.

Conclusions CMI exhibited inverse L-shaped nonlinear relationships with IR, preDM, and DM, suggesting that reducing CMI to a certain level might significantly prevent these conditions.

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Introduction

Insulin resistance (IR) refers to reduced sensitivity of target tissues to insulin, resulting in diminished glucose uptake and utilization, consequently leading to elevated blood glucose levels.The IR is an important characteristic of type 2 diabetes mellitus (DM) and contributes to metabolic syndrome, including hyperglycemia, dyslipidemia, and hypertension [1, 2]. Additionally, IR could influence myocardial metabolism, potentially contributing to subclinical left ventricular dysfunction and heart failure [2, 3]. While the hyperinsulinemic-euglycemic clamp and intravenous glucose tolerance test serve as gold standards for assessing IR [4, 5], their expense and limited accessibility restrict their clinical utility. Currently, the homeostatic model assessment of insulin resistance (HOMA-IR) is widely adopted for evaluating IR [6].

Prediabetes (preDM) increases the risk of cardiovascular diseases (CVD) and type 2 DM [7]. The preDM is characterized by impaired glucose tolerance (IGT) or impaired fasting glucose (IFG), and elevated HbA1c levels [8]. The global burden of preDM is substantial and rising [7], with an estimated 352 million individuals affected worldwide in 2017 [9]. In the United States (U.S.), preDM affects 25% of adolescents [8]. Globally, the incidence and mortality of DM are on the rise due to the aging population, lifestyle changes, industrialization, and urbanization [10]. There were 463 million people with type 2 DM in 2019, and by 2045 that number is expected to rise to 548 million, according to the International Diabetes Federation (IDF) [11].

Studies have indicated correlations between obesity, waist circumference, dyslipidemia, and IR [12, 13]. The waist-to-height ratio (WHtR) serves as a comprehensive indicator, surpassing single measures in identifying obesity and assessing risks for hypertension, CVD, and DM [14, 15]. IR can be distinguished in non-obese women with normal glucose levels using the TG/HDL-C [16]. Moreover, TG/HDL-C is linked to a higher likelihood of developing DM and is believed to have a linear relationship with IR [17–19].

Wakabayashi et al. presented a new measure called the cardiometabolic index (CMI), calculated by multiplying WHtR by TG/HDL-C, that effectively predicts DM [20]. CMI integrates parameters of adiposity and lipids parameters and exhibits associations with non-alcoholic fatty liver disease (NAFLD), hyperuricemia, chronic kidney disease (CKD), CVD, and stroke [21–25]. CMI heightens the risk of cardiometabolic multimorbidity and may synergistically contribute to this risk with sarcopenia [26]. Higher CMI is linked to greater odds of DM prevalence and could serve as a cost-effective screening tool for the general population [27]. CMI is associated with ischemic stroke, and this relationship is stronger in women [25, 28]. Additionally, in peripheral arterial disease patients, CMI is linked to the degree of atherosclerosis in the common carotid artery and leg artery ischemia [29].

However, the potential links of CMI with IR, and preDM, and the relationship between CMI and DM warrants further expansion. Consequently, this study examines the connections and nonlinear associations of CMI with IR, preDM, and DM using cross-sectional analysis on a large sample.

Methods

Data source and study population

The National Health and Nutrition Examination Survey (NHANES), administered by the National Center for Health Statistics (NCHS), is a cross-sectional survey that gathers comprehensive data every two years for a cycle. NHANES evaluates the health of non-institutionalized U.S. civilians through sophisticated sampling methods (stratified, multistage, probability cluster). Data from NHANES that includes demographics, physical examinations, laboratory results, and disease-related questionnaires. The Institutional Review Board of the NCHS granted permission for the survey, and all participants gave written informed consent prior to taking part. More information about NHANES can be found at https://www.cdc.gov/nchs/nhanes/index.htm.

Data from seven consecutive NHANES database cycles were used in this cross-sectional study (2007–2008, 2009–2010, 2011–2012, 2013–2014, 2015–2016, 2017–2018, and 2019–2020), encompassing 75,402 participants. Following exclusion criteria, including individuals aged < 18, pregnant participants, those with missing variables (exposure, outcome, and covariates), and outliers in CMI, the final sample size amounted to 13,142 participants.

Exposure variable and outcome variables

CMI was the exposure variable, which was defined as WHtR*(TG/HDL-C), where WHtR represented waist circumference (cm) divided by height (cm), and TG/HDL-C was ratio of triglycerides (mmol/L) to high-density lipoprotein cholesterol (mmol/L) [20]. Using an encircling tape measure, the waist circumference was measured above the tops of the bilateral iliac bones at the waist [30].

Outcome variables comprised biochemical markers of glucose metabolism, IR, preDM, and DM.

Biochemical markers of glucose metabolism serve as risk indicators for preDM and DM, including HOMA-IR, fasting serum insulin (FSI, pmol/L), glycosylated

hemoglobin (HbA1c, %), and fasting blood glucose (FBG, mmol/L). To calculate HOMA-IR, the formula is: [FBG (mmol/L) * FSI (μU/ml)] / 22.5 [6]. Notably, FBG levels were measured in the morning after a 9-hour fast using venous blood samples. The samples were sent to Fairview Medical Center laboratories at the University of Minnesota for analysis in NHANES 2007–2013, and to the University of Missouri at Columbia for analysis in NHANES 2013–2020. Detailed information on specimen collection and processing, could be seen in the Biospecimen Program of NHANES [31].

Based on previous studies, IR in the general U.S. population was defined as HOMA-IR > 2.6 [32, 33]. In this study, preDM was defined based on laboratory testing and related questionnaires, encompassing any of the following criteria: 5.7% ≤ HbA1c < 6.5%, FBG levels from 5.6 mmol/L to 6.9 mmol/L, Oral Glucose Tolerance Test (OGTT) with blood glucose levels between 7.8 and 11.0 mmol/L at 2 h, or self-reported preDM status. DM was defined as FBG ≥ 7.0 mmol/L, HbA1c ≥ 6.5%, OGTT with blood glucose ≥ 11.1 mmol/L at 2 h, self-reported DM, or current use of glucose-lowering therapy [7, 34, 35].

Covariates

We included covariates potentially influencing both the exposure and outcome variables, drawn from demographic data and clinical expertise. Covariates in the study encompassed age, sex, ethnicity, body mass index (BMI), poverty-to-income ratio (PIR), blood pressure, education, smoking status, marital status, alcohol use, physical activity, total cholesterol (TC, mmol/L), γ-glutamyl transferase (γ-GGT, IU/L), alanine aminotransferase (ALT, IU/L), aspartate aminotransferase (AST, IU/L), serum uric acid (SUA, mg/dL), serum creatinine (SCR, mg/dL), and hemoglobin (Hb, g/dL), as well as disease including hypertension, CVD, and CKD.

Age was categorized into three groups: young (< 40 years), middle-aged (≥ 40 to < 65 years), and old (≥ 65 years). Participants self-reported their gender (male and female), ethnicity (Mexican American, Non-Hispanic White, Non-Hispanic Black, Other), marital status (married/living with partner, widowed/divorced/single), level of education (high school or below, college or above), PIR, and smoking status (never, former, and current). BMI, calculated as weight divided by the height square (kg/m^2), was categorized into normal (< 25), overweight (≥ 25 to < 30), and obese (≥ 30). Alcohol use was characterized by consuming three or more beverages daily for females or four or more beverages daily for males, along with engaging in heavy drinking at least five times per month. Physical activity was assessed based on questionnaires regarding work or recreational activity, with individuals engaging in vigorous or both moderate to vigorous levels considered active. Hypertension was

characterized by systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg, or taking antihypertensive drugs [36]. CVD was identified by self-reported angina, heart attack, coronary heart disease, stroke, or heart failure [37]. CKD was diagnosed as an estimated glomerular filtration rate (eGFR) of < 60 mL/min/1.73 m^2 or an albumin-to-creatinine ratio of ≥ 30 mg/g, with eGFR determined using the CKD Epidemiology Collaboration (CKD-EPI) equation derived from SCR values [38].

Statistical analysis

To obtain unbiased estimates from the complex NHANES design, all analyses incorporate sampling weights and we use Taylor series (linearization) to estimate standard errors (SE). The study utilized R (version 4.2.1) and EmpowerStats (version 2.0) for all analyses. A two-tailed p-value < 0.05 was considered statistically significant.

Baseline characteristics of participants were categorized into four groups based on quartiles of CMI levels (Q1: 0.027–0.28, Q2: 0.28–0.49, Q3: 0.49–0.86, Q4: 0.86–3.52). Categorical variables were displayed as frequencies and percentages (weighted %), while continuous variables were described using means (SE). Statistical differences between continuous variables were evaluated through the one-way Analysis of Variance (ANOVA), while distinctions among categorical variables were analyzed using the chi-square test.

Weighted multivariate linear regression was utilized to assess the associations between CMI and various biochemical indicators of glucose metabolism, including FBG, HbA1c, FSI, and HOMA-IR. Weighted multivariate logistic regression was employed to evaluate the associations of CMI with IR, preDM, and DM. In accordance with the guidelines outlined in the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement [39], three adjustment models were utilized in this research. Model 1 utilized a univariate logistic regression model, while Model 2 was adjusted for age, gender, race, and BMI. Model 3 further adjusted for PIR, smoking status, alcohol use, marital status, education, physical activity, hypertension, CVD, CKD, ALT, AST, γGGT, SUA, Hb, and TC. Additionally, sensitivity analyses were performed. We excluded individuals with preDM and DM to assess the association between CMI and biochemical markers of glucose metabolism, and evaluated the association between CMI and IR in different glucose metabolism status participants. We also included DM treatment (antidiabetic drugs or insulin) data to explore the association between CMI and IR in DM participants.

Furthermore, considering the potential nonlinear metabolic patterns in biomedicine, and previous findings of

nonlinear links between CMI and disease [40–42], we explored possible nonlinear associations. Generalized Additive Models (GAM) were utilized to analyze the nonlinear associations of CMI and IR, preDM, and DM through smooth curve fitting. When nonlinearities were detected, inflection points for the associations of CMI with IR, preDM, and DM were calculated using a two-piecewise recursive algorithm. Threshold effect analysis was conducted using log likelihood ratio test to compare the overall logistic regression model and two-piecewise logistic regression models. Additionally, subgroup smooth curve fitting based on age groups, gender, race, and BMI groups was performed to assess the robustness and possible differences of the results.

Results

Baseline characteristics of the study population

A total of 13,142 adult participants were ultimately included in this study, among whom 5,851 had preDM and 2,701 had DM (Fig. 1). The baseline characteristics of participants were outlined based on the quartiles of CMI (Table 1). Compared to participants in the lowest quartile of CMI (Q1), individuals in the highest quartile (Q4) were older, predominantly male, increasing proportion of Mexican American, had lower PIR, higher prevalence of obesity, higher marriage rate, lower education, higher prevalence of current or past smoking, higher proportion of alcohol use, more inactive in physical activity, and higher levels of FBG, HbA1c, FSI, HOMA-IR, TC, ALT, AST, γGGT, SCR, SUA, and Hb, as well as higher prevalence of hypertension, CVD, and CKD (all $P < 0.05$). Importantly, participants with higher CMI levels exhibited higher prevalence of IR, preDM, and DM (all $P < 0.05$) (Fig. 2A).

Associations between CMI and biochemical markers of glucose metabolism

We investigated the relationships between CMI and preDM/DM risk markers (Table 2). Multivariate linear regression analyses, adjusted for confounders (Model 3), revealed CMI was positively associated with FBG ($\beta = 0.53$, 95% CI: 0.43–0.63), HbA1c ($\beta = 0.26$, 95% CI: 0.22–0.31), FSI ($\beta = 4.88$, 95% CI: 4.23–5.54), and HOMA-IR ($\beta = 1.85$, 95% CI: 1.56–2.14). CMI quartile increments (Q3 and Q4) were consistently linked to elevated levels of these markers (all P for trend < 0.001). Sensitivity analyses, excluding patients with preDM/DM ($n = 8,555$), confirmed these findings (**Supplementary file: Table** S1).

Associations of CMI with IR, preDM, and DM

In all three logistic regression models, there was a positive correlation between CMI and the prevalence of IR (Model 1: OR = 8.27, 95% CI: 6.88–9.93; Model 2: OR = 3.76, 95% CI: 3.18–4.44; Model 3: OR = 3.51, 95% CI: 2.94–4.20). Notably, after adjusting for potential confounders (Model 3), the odds of IR become 2.51 times
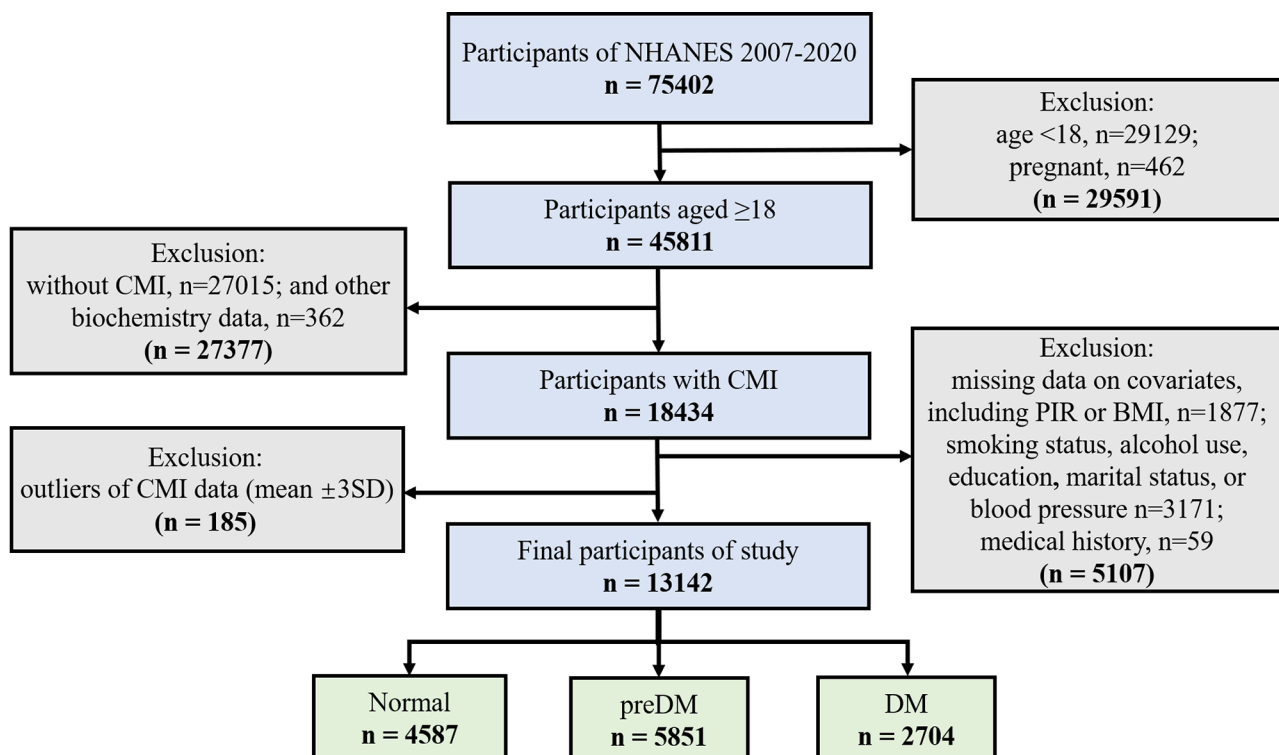
**Fig. 1** Participants selection of the study from the NHANES 2007–2020

Table 1 Baseline demographic and clinical characteristics of participants according to the CMI quartiles

Characteristics	Overall	Quartiles of CMI				*P*-value
		Q1	Q2	Q3	Q4	
		(0.027, 0.28)	(0.28, 0.49)	(0.49, 0.86)	(0.86, 3.52)	
N	13,142	3286	3285	3285	3286	
Age (years)	47.46(0.28)	43.85(0.54)	47.99(0.42)	48.67(0.40)	49.55(0.34)	< 0.001
Age group, N (%)						< 0.001
Young	4327(35.55)	1448(45.64)	1047(35.23)	958(32.85)	874(27.90)	
Middle	2984(18.04)	593(14.49)	792(19.79)	834(19.93)	765(18.17)	
Old	5831(46.41)	1241(39.87)	1453(44.98)	1488(47.23)	1649(53.93)	
Gender, N (%)						< 0.001
Female	6580(50.17)	1985(61.69)	1724(51.89)	1541(47.63)	1330(38.82)	
Male	6562(49.83)	1297(38.31)	1568(48.11)	1739(52.37)	1958(61.18)	
Race/Ethnicity, N (%)						< 0.001
Mexican American	1913(8.19)	291(5.48)	400(6.77)	577(9.91)	645(10.82)	
Non-Hisp. White	5648(69.25)	1301(67.60)	1421(70.76)	1346(66.49)	1580(72.08)	
Non-Hisp. Black	2661(9.72)	960(14.01)	788(10.94)	590(8.97)	323(4.70)	
Other Race	2920(12.85)	730(12.91)	683(11.53)	767(14.63)	740(12.40)	
PIR	3.08(0.04)	3.27(0.04)	3.14(0.05)	2.99(0.05)	2.92(0.05)	< 0.001
SBP (mmHg)	120.89(0.23)	116.47(0.38)	120.49(0.36)	121.77(0.40)	125.05(0.39)	< 0.001
DBP (mmHg)	70.52(0.21)	68.08(0.26)	69.73(0.31)	70.99(0.34)	73.44(0.31)	< 0.001
BMI (kg/m^2)	28.98(0.10)	24.60(0.11)	28.12(0.14)	30.60(0.16)	32.86(0.18)	< 0.001
BMI group, N (%)						< 0.001
Normal	3783 (28.79)	1891 (57.55)	1024 (31.17)	572 (17.41)	296 (9.01)	
Overweight	4371 (33.26)	923 (28.09)	1254 (38.17)	1158 (35.25)	1036 (31.53)	
Obesity	4988 (37.95)	472 (14.36)	1007 (30.65)	1555 (47.34)	1954 (59.46)	
Height (cm)	169.10(0.12)	168.00(0.24)	169.16(0.23)	169.14(0.22)	170.15(0.25)	< 0.001
Waist circumference (cm)	99.29(0.24)	86.93(0.26)	97.22(0.35)	103.68(0.38)	110.08(0.40)	< 0.001
Marital status, N (%)						< 0.001
Married/Living with Partner	7918(64.17)	1772(60.36)	1963(63.07)	2053(65.24)	2130(68.22)	
Widowed/Divorced/Singled	5224(35.83)	1510(39.64)	1329(36.93)	1227(34.76)	1158(31.78)	
Education, N (%)						< 0.001
High school or below	5837(36.98)	1177(29.22)	1373(34.74)	1561(39.73)	1726(44.72)	
College or above	7305(63.02)	2105(70.78)	1919(65.26)	1719(60.27)	1562(55.28)	
Smoking status, N (%)						< 0.001
Never	7290(55.61)	2062(61.97)	1908(59.30)	1743(52.54)	1577(48.18)	
Former	3214(25.83)	658(22.64)	747(23.82)	884(27.46)	925(29.61)	
Now	2638(18.57)	562(15.40)	637(16.88)	653(20.00)	786(22.20)	
Alcohol use, N (%)	2792(21.57)	655(19.93)	670(20.98)	717(23.03)	750(22.47)	< 0.001
Physical activity, N (%)						< 0.001
Inactive	8063(56.70)	1708(45.38)	1978(56.06)	2169(61.59)	2208(64.49)	
Active	5079(43.30)	1574(54.62)	1314(43.94)	1111(38.41)	1080(35.51)	
Laboratory data						
FBG (mmol/L)	5.91(0.02)	5.45(0.02)	5.70(0.02)	5.96(0.03)	6.56(0.06)	< 0.001
HbA1c (%)	5.62(0.01)	5.37(0.01)	5.51(0.01)	5.65(0.02)	5.95(0.03)	< 0.001
FSI (µU/ml)	12.91(0.17)	7.17(0.20)	10.20(0.20)	14.44(0.36)	20.16(0.45)	< 0.001
HOMA-IR	3.66(0.06)	1.82(0.08)	2.69(0.07)	3.97(0.11)	6.25(0.19)	< 0.001
ALT (IU/L)	24.83(0.20)	20.74(0.41)	22.92(0.31)	26.09(0.40)	29.83(0.38)	< 0.001
AST (IU/L)	24.67(0.18)	24.27(0.35)	24.12(0.33)	24.37(0.30)	25.93(0.38)	0.002
γGGT (IU/L)	27.51(0.34)	21.64(0.57)	24.88(0.58)	28.13(0.59)	35.72(0.73)	< 0.001
SUA (mg/dL)	5.48(0.02)	4.82(0.03)	5.32(0.03)	5.71(0.03)	6.11(0.04)	< 0.001
Hb (g/dL)	14.36(0.03)	14.00(0.04)	14.29(0.04)	14.45(0.03)	14.74(0.04)	< 0.001
SCR (mg/dL)	0.87(0.00)	0.84(0.01)	0.87(0.01)	0.88(0.01)	0.90(0.01)	< 0.001
eGFR (mL/min/1.73m^2)	95.18(0.36)	99.34(0.67)	94.61(0.45)	93.76(0.51)	92.76(0.53)	< 0.001
TC (mmol/L)	4.97(0.02)	4.75(0.03)	4.88(0.02)	5.01(0.03)	5.25(0.03)	< 0.001

Table 1 (continued)

Characteristics	Overall	Quartiles of CMI				P-value
		Q1	Q2	Q3	Q4	
		(0.027, 0.28)	(0.28, 0.49)	(0.49, 0.86)	(0.86, 3.52)	
TG (mmol/L)	1.30(0.01)	0.63(0.00)	0.97(0.01)	1.35(0.01)	2.31(0.02)	<0.001
HDL-C (mmol/L)	1.41(0.01)	1.81(0.01)	1.47(0.01)	1.27(0.01)	1.06(0.00)	<0.001
Hypertension, N (%)	5400(36.80)	920(22.46)	1294(33.97)	1500(41.64)	1686(50.01)	<0.001
CVD, N (%)	1377(8.47)	200(5.14)	339(7.58)	354(8.23)	484(13.07)	<0.001
CKD, N (%)	2211(13.06)	397(10.13)	527(11.78)	545(12.71)	742(17.76)	<0.001
IR, N (%)	6322(45.21)	523(13.70)	1265(35.32)	1948(57.49)	2586(76.36)	<0.001
preDM, N (%)	5851(44.71)	1220(34.93)	1513(45.13)	1566(48.66)	1552(50.71)	<0.001
DM, N (%)	2704(15.35)	279(5.35)	511(10.51)	781(17.98)	1133(28.16)	<0.001
DM treatment, N (%)	1578(8.92)	160(3.09)	289(5.43)	490(10.84)	639(16.70)	<0.001
WHtR	0.59(0.00)	0.52(0.00)	0.58(0.00)	0.61(0.00)	0.65(0.00)	<0.001
TG/HDL-C	1.08(0.01)	0.36(0.00)	0.67(0.00)	1.07(0.00)	2.24(0.02)	<0.001
CMI	0.65(0.01)	0.18(0.00)	0.38(0.00)	0.65(0.00)	1.43(0.01)	<0.001

CMI, Cardiometabolic index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; PIR, Poverty-to-income ratio; BMI, Body mass index; FBG, Fasting blood glucose; HbA1c, Hemoglobin A1c; FSI, Fasting serum insulin; HOMA-IR, Homeostasis model assessment of insulin resistance; ALT, Alanine aminotransferase, AST, Aspartate aminotransferase; γGGT, Gama-glutamyl transpeptidase; SUA, Serum uric acid; Hb, hemoglobin; SCR, Serum creatinine; eGFR, Estimated glomerular filtration rate; TC, Total cholesterol; TG, Triglyceride; HDL-C, High-density lipoprotein cholesterol; CVD, Cardiovascular disease; CKD, Chronic kidney disease; IR, Insulin resistance; preDM, Prediabetes; DM, Diabetes mellitus; WHtR, Ratio of waist circumference to height
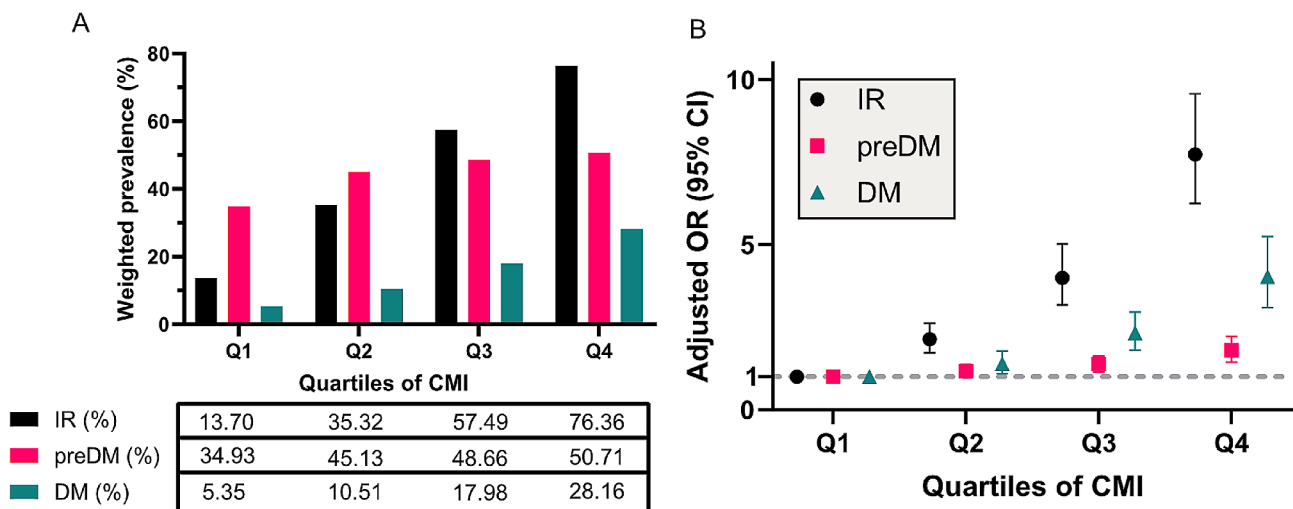
Fig. 2 The weighted (%) prevalence of IR, preDM, and DM by quartiles of CMI (A). Associations between quartiles of CMI and the prevalence of IR, preDM, and DM (B). The OR (95% CI) adjusted age, gender, race, BMI, PIR, education, marital status, smoking status, alcohol use, physical activity, hypertension, CVD, CKD, ALT, AST, γGGT, SUA, Hb, and TC

higher for each unit increase in CMI. Moreover, the statistical significance of the positive trend in relation to increased risk of IR remained when CMI was divided into quartiles, showing a progressive association with higher quartiles of CMI (P for trend<0.001) (Table 3). We also stratified the analysis of the correlation between CMI and IR according to glucose metabolism status into normal, preDM, and DM subgroups (the mean of HOMA-IR was 2.13, 3.56, and 7.95, respectively), and the positive correlation persisted after multivariable adjustments (Supplementary file: Table S2). Notably, in DM participants, the risk between CMI and IR was lower in group with DM treatment than without DM treatment (OR: 3.74 vs. 5.82) (Supplementary file: Table S3).

The relationship between CMI and the prevalence of preDM was positively correlated across all three logistic regression models (Model 1: OR=2.68, 95% CI: 2.37–3.03; Model 2: OR=1.74, 95% CI: 1.54–1.96; Model 3: OR=1.49, 95% CI: 1.29–1.71). It is noteworthy that when accounting for potential confounders (Model 3), per one unit rise in CMI was inked to a 49% rise in the risk of preDM. Furthermore, the statistical significance of the trend remained when CMI was divided into quartiles, showing a consistent increase in the risk of preDM with higher quartiles of CMI (P<0.001 for trend) (Table 3).

Similarly, the link between CMI and the prevalence of DM was positively correlated in all three logistic regression models (Model 1: OR=2.53, 95% CI:

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Table 2 The associations between CMI and biochemical markers of glucose metabolism

Outcomes	β (95% CI)					P-trend
	CMI (continuous)	Quartiles of CMI (categorical)				
		Q1	Q2	Q3	Q4	
FBG (mmol/L)						
Model 1	0.77(0.67,0.87)	Ref	0.25(0.19,0.30)	0.51(0.44,0.58)	1.12(1.00,1.23)	< 0.001
Model 2	0.53(0.43, 0.62)	Ref	0.01(-0.05, 0.08)	0.15(0.07, 0.23)	0.64(0.52, 0.76)	< 0.001
Model 3	0.53(0.43, 0.63)	Ref	0.04(-0.03, 0.10)	0.19(0.10, 0.28)	0.65(0.51, 0.79)	< 0.001
HbA1c (%)						
Model 1	0.39(0.34,0.44)	Ref	0.14(0.11,0.18)	0.29(0.25,0.32)	0.58(0.52,0.64)	< 0.001
Model 2	0.28(0.23, 0.32)	Ref	0.02(-0.02, 0.06)	0.1(0.06, 0.14)	0.35(0.30, 0.41)	< 0.001
Model 3	0.26(0.22, 0.31)	Ref	0.03(-0.01, 0.06)	0.11(0.07, 0.15)	0.34(0.27, 0.40)	< 0.001
FSI (μU/ml)						
Model 1	8.76(7.93,9.59)	Ref	3.03(2.55, 3.51)	7.27(6.42, 8.13)	12.99(11.95,14.03)	< 0.001
Model 2	5.05(4.37, 5.73)	Ref	0.31(-0.25, 0.87)	2.57(1.72, 3.42)	6.57(5.74, 7.39)	< 0.001
Model 3	4.88(4.23, 5.54)	Ref	0.24(-0.31, 0.79)	2.33(1.47, 3.20)	6.09(5.22, 6.96)	< 0.001
HOMA-IR						
Model 1	3.08(2.75,3.42)	Ref	0.86(0.67,1.06)	2.14(1.83,2.45)	4.43(3.99,4.86)	< 0.001
Model 2	1.84(1.55, 2.13)	Ref	-0.11(-0.35, 0.13)	0.49(0.14, 0.83)	2.18(1.83, 2.52)	< 0.001
Model 3	1.85(1.56, 2.14)	Ref	-0.08(-0.32, 0.15)	0.5(0.16, 0.84)	2.12(1.71, 2.53)	< 0.001

Model 1 was univariate linear regression model

Model 2 adjusted for age, gender, race, and BMI.

Model 3 adjusted for age, gender, race, BMI, PIR, education, marital status, smoking status, alcohol use, physical activity, hypertension, CVD, CKD, ALT, AST, γGGT, SUA, Hb, and TC.

Table 3 The associations of CMI with IR, preDM, and DM

Outcomes	OR (95% CI)					P-trend
	CMI (continuous)	Quartiles of CMI (categorical)				
		Q1	Q2	Q3	Q4	
IR						
Model 1	8.27(6.88,9.93)	Ref	3.44(2.84, 4.17)	8.52(7.01,10.35)	20.35(16.98,24.38)	< 0.001
Model 2	3.76(3.18,4.44)	Ref	2.17(1.76,2.68)	4.15(3.36,5.13)	8.15(6.76,9.83)	< 0.001
Model 3	3.51(2.94,4.20)	Ref	2.14(1.72,2.67)	3.99(3.17,5.02)	7.73(6.24,9.57)	< 0.001
preDM						
Model 1	2.68(2.37,3.03)	Ref	1.74(1.52,1.99)	2.49(2.19,2.84)	4.10(3.55,4.74)	< 0.001
Model 2	1.74(1.54,1.96)	Ref	1.25(1.06,1.47)	1.57(1.34,1.84)	2.27(1.90,2.71)	< 0.001
Model 3	1.49(1.29,1.71)	Ref	1.17(0.99,1.38)	1.36(1.14,1.62)	1.80(1.45,2.23)	< 0.001
DM						
Model 1	2.53(2.34,2.74)	Ref	2.08(1.67,2.59)	3.88(3.19,4.73)	6.94(5.72,8.42)	< 0.001
Model 2	2.15(1.97,2.35)	Ref	1.40(1.11,1.77)	2.31(1.86,2.86)	3.99(3.19,5.00)	< 0.001
Model 3	2.22(2.00,2.47)	Ref	1.39(1.09,1.78)	2.32(1.81,2.96)	4.03(3.09,5.25)	< 0.001

Model 1 was univariate logistic regression model
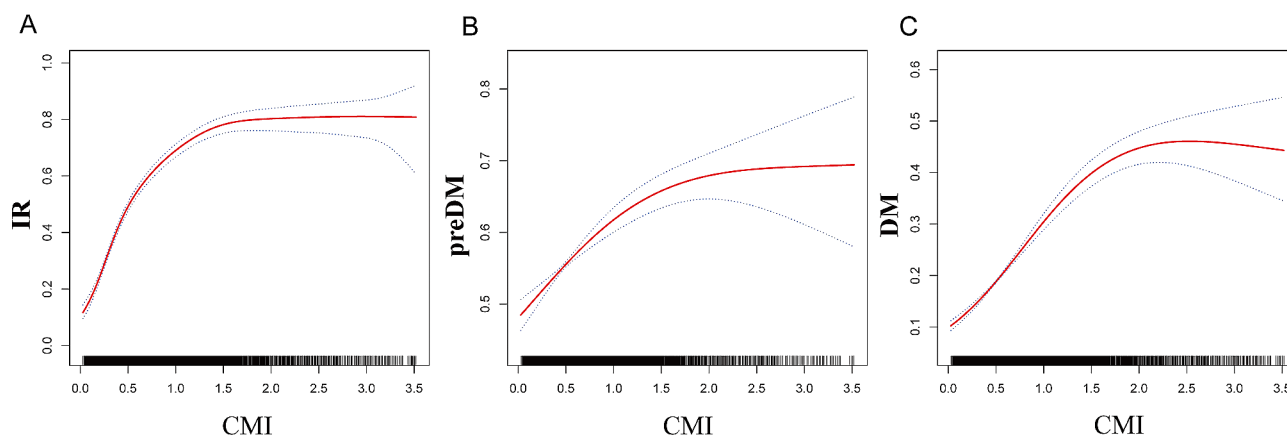
Model 2 adjusted for age, gender, race, and BMI.

Model 3 adjusted for age, gender, race, BMI, PIR, education, marital status, smoking status, alcohol use, physical activity, hypertension, CVD, CKD, ALT, AST, γGGT, SUA, Hb, and TC.

2.34–2.74; Model 2: OR = 2.15, 95% CI: 1.97–2.35; Model 3: OR = 2.22, 95% CI: 2.00–2.47). Specifically, following the adjustment for potential confounders (Model 3), an increment of one unit in CMI was linked to 1.22 times higher in the risk of DM. Moreover, when CMI was categorized into quartiles, statistical significance remained, with higher quartiles of CMI progressively associated with greater risk of DM (P for trend < 0.0001) (Table 3).

Adjusted Model 3, incorporating all other covariates, presents the ORs and their 95% CIs for the associations of CMI quartiles with the risk of IR, preDM, and DM, depicted in a forest plot (Fig. 2B).

Nonlinear associations
To visually assess the dose-response effect of CMI, we used GAM and smooth curve fitting to examine the nonlinear associations of CMI with the risks of IR, preDM,

Fig. 3 Smooth curve fitting using GAM to evaluate the associations between CMI and the prevalence of IR (A), preDM (B), and DM (C). The nonlinear inverse L-shaped curves between CMI and the prevalence of IR, preDM, and DM were found (P for log likelihood ratio < 0.05). The solid red line and dashed blue line represent the estimated values and their corresponding 95% CI. Adjustment factors included age, gender, race, BMI, PIR, education, marital status, smoking status, alcohol use, physical activity, hypertension, CVD, CKD, ALT, AST, γGGT, SUA, Hb, and TC

Table 4 Threshold effect analysis of CMI on IR, preDM, and DM using a two-piecewise logistic regression model

	Inflection point	Adjusted OR (95% CI), *P* value (per 0.1 increase of CMI)	*P* for log-likelihood ratio test
IR			
Total		1.16 (1.14, 1.17) < 0.0001	
Fitting by two-piecewise logistic regression model	1.1		< 0.001
CMI < 1.1		1.27 (1.25, 1.29) < 0.0001	
CMI > 1.1		1.01 (0.99, 1.03) 0.2553	
preDM			
Total		1.04 (1.03, 1.05) < 0.0001	
Fitting by two-piecewise logistic regression model	1.45		0.022
CMI < 1.45		1.05 (1.04, 1.07) < 0.0001	
CMI > 1.45		1.01 (0.98, 1.04) 0.5562	
DM			
Total		1.08 (1.07, 1.09) < 0.0001	
Fitting by two-piecewise logistic regression model	1.6		< 0.001
CMI < 1.6		1.12 (1.10, 1.14) < 0.0001	
CMI > 1.6		1.01 (0.98, 1.03) 0.5517	

Adjusted OR (95% CI) represented results for adjustment of model 3, including age, gender, race, BMI, PIR, education, marital status, smoking status, alcohol use, physical activity, hypertension, CVD, CKD, ALT, AST, γGGT, SUA, Hb, and TC.

and DM, further confirming our findings. In Model 3 adjusted for covariates, nonlinear and inverse L-shaped associations were detected between CMI and IR, preDM, and DM (Fig. 3). Threshold effect analysis revealed inflection points at 1.1, 1.45, and 1.6, respectively (Table 4). Prior to the inflection points, CMI exhibited significant positive correlations with all three outcome variables, with ORs (95% CI) of 1.27 (1.25, 1.29), 1.05 (1.04, 1.07), and 1.12 (1.10, 1.14) with per 0.1 CMI increase. However, beyond the inflection points, although the risks of IR, preDM, and DM remained elevated, the associations of CMI with these outcomes were not significant and tended to plateau.

In subgroup analyses based on impaired glucose metabolism status, similar nonlinear inverse L-shaped associations were found between CMI and IR in the normal, preDM, and DM subgroups (**Supplementary file: Figure** S1). Stratified subgroup analyses by age, sex, race, and BMI groups revealed persistent nonlinear relationships between CMI and IR risk (Supplementary file: Figure S1). However, the nonlinear associations of CMI with preDM and DM seemed partially inconsistent. The linear positive correlations of CMI with preDM, could be found in the old age group, male, and Mexican American ethnicity. While, the inverted U-shaped curve association of CMI with DM, could be found in Non-Hisp.

Black ethnicity, and normal BMI group (Supplementary file: Figures S3-S4). In DM participants categorized by treatment, the inflection point and plateau of CMI and IR risk inverted L-shape curves were lower in the treatment group (Supplementary file: Figures S5).

Summary of results

To get an overview of main results, we summarize the presentation of study variables and correlations (Fig. 4). In 13,142 U.S. participants, we investigated the associations between CMI and glucose metabolism markers (FBG, HbA1c, FSI, HOMA-IR), IR, preDM, and DM. The main results for Model 3 (continuous or categorical CMI) in Tables 2 and 3 are presented visually in the form of forest plots. Furthermore, CMI has nonlinear correlations with IR, preDM, and DM with inflection points of 1.1, 1.45 and 1.6 respectively.

Discussion

We sought to fill the knowledge gap by studying the connections between CMI, and glucose metabolism markers, IR, preDM, and DM. This cross-sectional study of U.S. adults showed a positive association between CMI and biochemical markers of glucose metabolism after adjusting for confounding factors. Additionally, we identified correlations between CMI and higher risk of IR, preDM and DM. Notably, the relationships between CMI and these conditions followed nonlinear inverted-L shapes, with inflection points of 1.1, 1.45 and 1.6 respectively. Below these thresholds, CMI demonstrated a significant

positive correlation with IR, preDM, and DM. However, when CMI is higher than inflection point, their correlation is not significant. It is suggested that CMI may act as a surveillance parameter for impaired glucose metabolism and provide evidence for risk assessment of IR, preDM and DM. This study could potentially be applied in the general population or clinical practice based on the inverted L-shaped dose-response relationships.

Men and older adults had relatively higher prevalence of metabolic syndrome [43]. Obesity is associated with increased risk of metabolic issues like high waist circumference, high TG, and low HDL-C [44]. Similarly, our results suggest that participants in the highest quartile group Q4 of CMI were older, male, and obese. The CMI, derived from TG/HDL-C and WHtR, reflects CVD risk factors including dyslipidemia, DM, and hypertension [20, 21, 45]. Previous studies have linked TG/HDL-C to increased risk of IR and DM [17, 18]. WHtR is recognized as a predictor for DM and CVD, with a recommended threshold below 0.5 [46]. WHtR is linked to dyslipidemia (such as high TG, high LDL-C, and low HDL-C), and is a risk factor for CVD [47]. The CMI combines WHtR and TG/HDL-C, suggesting a potential role in CVD.

Based on a retrospective study of 15,453 Japanese adults, Zhao et al. found a nonlinear association between CMI and DM, with an inflection point at 1.01 [40]. While, our cross-sectional study revealed an inflection point at 1.6 between CMI and DM. Wu et al. observed in patients with type 2 DM that increased CMI was significantly correlated with IR in a nonlinear relationship [48].
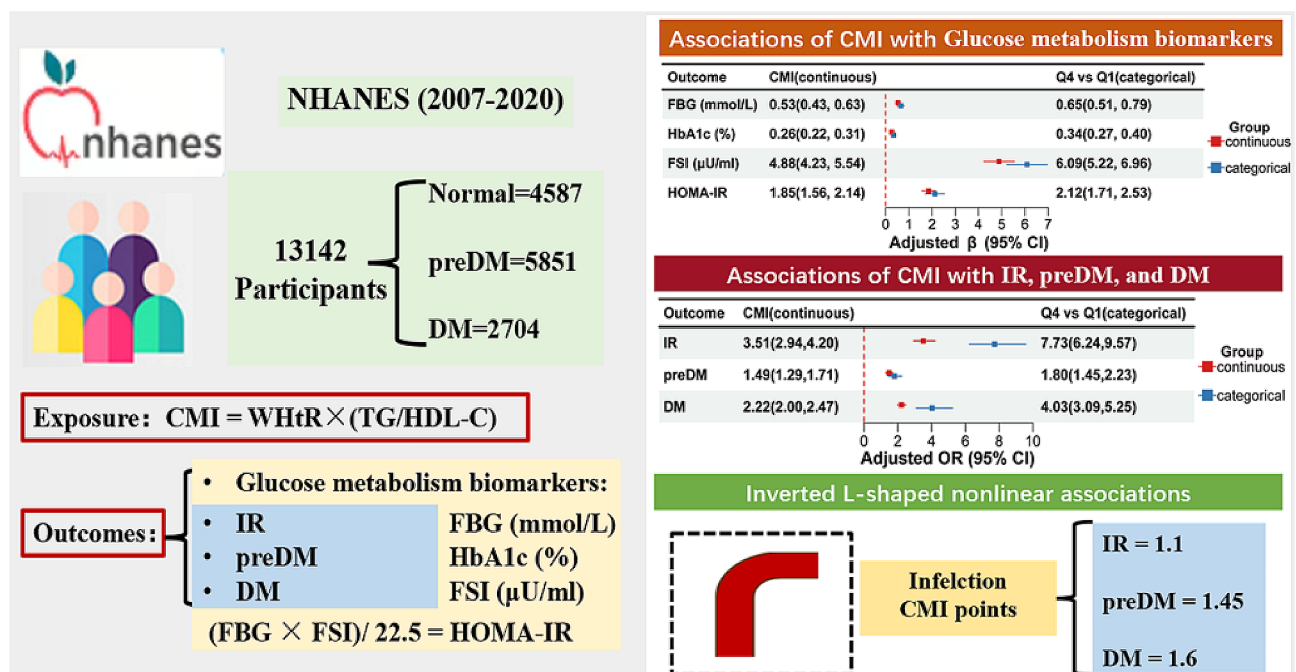
Fig. 4 Overview of study results. The left side mainly describes the study population and variables, and the right side shows the main results of correlations

Our research expands upon this by identifying a similar nonlinear association between CMI and IR across normal and preDM participants, not limited to DM participants. Notably, as far as we know, no reports were found regarding the association between CMI and preDM. Similarly, Liu et al. reported TG/HDL-C to be linked with IR, impaired fasting glucose (IFG), and DM [33], with IFG being encompassed within the preDM criteria [7, 8]. In summary, our study underscored the positive correlation of CMI with FBG, HbA1c, FSI, and the HOMA-IR, establishing independent nonlinear inverted L-shaped correlations between CMI and IR, preDM, and DM.

One study suggested a link between central body fat accumulation and the pathogenesis of IR and DM [49]. Furthermore, WHtR has been proposed as a better indicator than BMI for identifying CVD risk factors or metabolic syndrome, including DM and IR [15, 46, 50]. Additionally, TG/HDL-C has been identified as a useful marker for DM and IR [17, 19]. Interestingly, log (TG/HDL-C) as an atherogenic index of plasma (AIP), is a marker of CVD. Study findings showed nonlinear positive associations between AIP and IR and DM, and in women, there was a significant relationship between AIP and preDM and DM [32, 51]. The TG/HDL-C, reflecting lipid levels indirectly, demonstrates potential associations with IR, preDM, and DM. Similar to our study, a longitudinal study of Chinese middle-aged and elderly population found a 78% increased risk of type 2 DM among those with high baseline CMI [52].

Elevated CMI, indicative of higher WHtR and/or TG/HDL-C, suggesting the potential presence of abdominal obesity and dysregulated lipid metabolism. Obesity is linked to increased risk of IR and type 2 DM [53, 54]. Extra fat tissue releases increased levels of pro-inflammatory cytokines, free fatty acids, glycerol, and other factors that contribute to IR, hindering glucose uptake into tissue cells and impairing insulin's metabolic function, thereby raising blood glucose levels [55]. Additionally, individuals with abdominal obesity exhibit reduced insulin receptor numbers and affinity in target tissues, leading to decreased glucose utilization efficiency. Lower levels of HDL-C may adversely affect β-cell function, reducing insulin output and sensitivity [53, 56]. Notably, postprandial plasma TG levels significantly increase in patients with preDM and DM when IR is present [57]. These findings intricately connect obesity and dyslipidemia with IR, preDM, and DM, suggesting CMI as a potentially valuable indicator.

Nonlinear associations between CMI and IR, preDM, and DM have been underexplored [40, 48]. Our study found that CMI was associated with IR, preDM and DM in a nonlinear inverted-L shape, with inflection points of 1.1, 1.45 and 1.6, respectively. This threshold saturation effect is beneficial for clinical practice reference, i.e. when CMI is below the inflection point, the risk of IR, preDM and DM increases with increasing CMI. However, mitigating obesity and lipid levels to lower CMI did not significantly reduce the risk of IR, preDM, and DM when CMI exceeded the inflection point. The inverted L-shaped phenomenon of CMI with IR, preDM and DM reflects an increase in risk followed by a slowdown and a plateau. This could be caused by metabolic abnormalities (increased CMI), visceral obesity, and excess fat leading to cardiovascular and endocrine adaptive changes, in line with the obesity paradox in epidemiology [58, 59]. Additionally, our study found gender differences of CMI-preDM curve, which was linear for men. This may be due to estrogen in women may protect against preDM and DM [60]. Addressing other DM risk factors, such as high-sugar diet, sedentary lifestyle, smoking, and comorbidities like hypertension, hyperuricemia, and polycystic ovary syndrome, may be necessary to reduce risk [34, 61]. Furthermore, in the U.S., CMI is associated with NAFLD, fibrosis, CKD, microalbuminuria, depression, and is vital for predicting all-cause mortality in the elderly [24, 41, 42, 62, 63]. CMI may represent a significant modifiable risk factor for cardiometabolic diseases, playing a critical role in public health and prevention strategies.

Our study has several strengths. Firstly, it benefits from a large, nationally representative sample size that underwent weighted analysis, providing estimates for the U.S. adults. Secondly, our definition of preDM and DM extended beyond FBG and self-reported condition, but included 2-hour OGTT and HbA1c measurements to minimize potential misdiagnoses. Thirdly, CMI, compared to HOMA-IR, integrates obesity and lipid parameters, offering a more accessible, cost-effective, and clinically practical measure. Fourthly, we examined both categorical and continuous CMI as independent variables, adjusting for multiple covariates to assess their associations with glucose metabolic markers, IR, preDM, and DM risk. Additionally, we explored the nonlinear relationship between continuous CMI and IR, preDM, and DM, identifying inflection points in the inverse L-shaped relationship. Finally, sensitivity analyses were conducted, including analyses in relationships of CMI with glucose metabolic biochemical markers and IR after excluding preDM and DM, ensured the robustness of our findings.

Some limitations we should be aware of. Firstly, the definition of DM in our research pertains to type 2 DM, and the results may not be generalizable to type 1 DM. Moreover, the nonlinear associations and their inflection points identified in the U.S. adult population may not be universally applicable to other regions globally. Secondly, despite adjusting for various covariates, potential biases from uncontrolled or unmeasured confounding factors, such as dietary habits and family history of DM, cannot

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be ruled out. Given the nature of cross-sectional study, causal relationships between CMI and various outcome variables cannot be established, only associations can be inferred. Despite these limitations, our findings expand the understanding of the link between abnormal glucose metabolism and CMI, providing insights and clues for clinical practice in risk management of IR, preDM, and DM. Furthermore, research has shown that alterations over time in CMI could be indicative of future risk in DM [52]. Hence, future research could explore the role of baseline CMI and its variability in predicting IR, preDM, and DM. Moreover, the inclusion of more metabolic indicators through machine learning will help in the early detection, prevention and management of DM in the future [64].

Conclusions

In conclusion, CMI is linked to abnormal glucose metabolism. Importantly, CMI demonstrates inverse L-shaped nonlinear relationships with IR, preDM, and DM, with inflection points at 1.1, 1.45, and 1.6, respectively. Below these thresholds, higher CMI is significantly linked to elevated risks of IR, preDM, and DM. These results imply that lowering CMI within a specific range might potentially benefit the prevention and management of IR, preDM, and DM.

Abbreviations

AIP	atherogenic index of plasma
ALB	Albumin
ALT	Alanine aminotransferase
ANOVA	Analysis of Variance
AST	Aspartate aminotransferase
BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CI	Confidence interval
CKD	Chronic kidney disease
CKD-EPI	Chronic kidney disease-epidemiology collaboration
CMI	Cardiometabolic index
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DM	Diabetes mellitus
eGFR	Estimated glomerular filtration rate
FBG	Fasting blood glucose
FSI	Fasting serum insulin
GAM	Generalized additive model
γGGT	γGlutamyl transpeptidase
HbA1c	Glycosylated hemoglobin A1c
HDL-C	High-density lipoprotein cholesterol
HOMA-IR	Homeostatic Model Assessment of Insulin Resistance
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IGT	impaired glucose tolerance
IR	Insulin resistance
NAFLD	Non-alcoholic fatty liver disease
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
OGTT	Oral glucose tolerance test
PIR	Poverty-income ratio
preDM	Prediabetes
SBP	Systolic blood pressure
SCR	Serum creatinine
SE	Standard error
SUA	Serum uric acid
TC	Total cholesterol
TG	Triglyceride
U.S.	United States
WHtR	Waist-to-Height Ratio

Declarations

Statement of ethics and consent to participate
This study was conducted in accordance with the principles of the Declaration of Helsinki. The investigation was approved by the NCHS research ethics review board. The NHANES database used in this study did not contain identifiable nor protected health information, and was publicly available for download. All participants have provided written informed consent to the NHANES.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Conflict of interest
No disclosures were reported.

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References

1. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, Fruchart JC, James WP, Loria CM, Smith SC Jr. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009, 120(16):1640–1645.
2. Tune JD, Goodwill AG, Sassoon DJ, Mather KJ. Cardiovascular consequences of metabolic syndrome. Transl Res. 2017;183:57–70.
3. Hirose K, Nakanishi K, Daimon M, Sawada N, Yoshida Y, Iwama K, Yamamoto Y, Ishiwata J, Hirokawa M, Koyama K, et al. Impact of insulin resistance on subclinical left ventricular dysfunction in normal weight and overweight/obese Japanese subjects in a general community. Cardiovasc Diabetol. 2021;20(1):22.
4. Park SE, Park CY, Sweeney G. Biomarkers of insulin sensitivity and insulin resistance: past, present and future. Crit Rev Clin Lab Sci. 2015;52(4):180–90.
5. Tam CS, Xie W, Johnson WD, Cefalu WT, Redman LM, Ravussin E. Defining insulin resistance from hyperinsulinemic-euglycemic clamps. Diabetes Care. 2012;35(7):1605–10.
6. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27(6):1487–95.
7. Rooney MR, Fang M, Ogurtsova K, Ozkan B, Echouffo-Tcheugui JB, Boyko EJ, Magliano DJ, Selvin E. Global prevalence of Prediabetes. Diabetes Care. 2023;46(7):1388–94.
8. Andes LJ, Cheng YJ, Rolka DB, Gregg EW, Imperatore G. Prevalence of Prediabetes among adolescents and young adults in the United States, 2005–2016. JAMA Pediatr. 2020;174(2):e194498.
9. Standl E, Khunti K, Hansen TB, Schnell O. The global epidemics of diabetes in the 21st century: current situation and perspectives. Eur J Prev Cardiol. 2019;26(2suppl):7–14.
10. Balooch Hasankhani M, Mirzaei H, Karamoozian A. Global trend analysis of diabetes mellitus incidence, mortality, and mortality-to-incidence ratio from 1990 to 2019. Sci Rep. 2023;13(1):21908.
11. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: results from the International Diabetes Federation Diabetes Atlas, 9(th) edition. Diabetes Res Clin Pract. 2019;157:107843.
12. Abbasi F, Malhotra D, Mathur A, Reaven GM, Molina CR. Body mass index and waist circumference associate to a comparable degree with insulin resistance and related metabolic abnormalities in south Asian women and men. Diab Vasc Dis Res. 2012;9(4):296–300.
13. Abbasi F, McLaughlin T, Lamendola C, Yeni-Komshian H, Tanaka A, Wang T, Nakajima K, Reaven GM. Fasting remnant lipoprotein cholesterol and triglyceride concentrations are elevated in nondiabetic, insulin-resistant, female volunteers. J Clin Endocrinol Metab. 1999;84(11):3903–6.
14. Tomas Ž, Škarić-Jurić T, Zajc Petranović M, Jalšovec M, Rajić Šikanjić P. Smolej Narančić N: Waist to height ratio is the anthropometric index that most appropriately mirrors the lifestyle and psychological risk factors of obesity. Nutr Diet. 2019;76(5):539–45.
15. Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. Obes Rev. 2012;13(3):275–86.
16. He J, He S, Liu K, Wang Y, Shi D, Chen X. The TG/HDL-C ratio might be a surrogate for Insulin Resistance in Chinese nonobese women. Int J Endocrinol. 2014;2014:105168.
17. Kim JS, Kang HT, Shim JY, Lee HR. The association between the triglyceride to high-density lipoprotein cholesterol ratio with insulin resistance (HOMA-IR) in the general Korean population: based on the National Health and Nutrition Examination Survey in 2007–2009. Diabetes Res Clin Pract. 2012;97(1):132–8.
18. Chen Z, Hu H, Chen M, Luo X, Yao W, Liang Q, Yang F, Wang X. Association of Triglyceride to high-density lipoprotein cholesterol ratio and incident of
19. Lim TK, Lee HS, Lee YJ. Triglyceride to HDL-cholesterol ratio and the incidence risk of type 2 diabetes in community dwelling adults: a longitudinal 12-year analysis of the Korean Genome and Epidemiology Study. Diabetes Res Clin Pract. 2020;163:108150.
20. Wakabayashi I, Daimon T. The cardiometabolic index as a new marker determined by adiposity and blood lipids for discrimination of diabetes mellitus. Clin Chim Acta. 2015;438:274–8.
21. Cai X, Hu J, Wen W, Wang J, Wang M, Liu S, Zhu Q, Hong J, Dang Y, Yao X et al. Associations of the Cardiometabolic Index with the Risk of Cardiovascular Disease in Patients with Hypertension and Obstructive Sleep Apnea: Results of a Longitudinal Cohort Study. *Oxid Med Cell Longev* 2022, 2022:4914791.
22. Zuo YQ, Gao ZH, Yin YL, Yang X, Feng PY. Association between the Cardiometabolic Index and Hyperuricemia in an Asymptomatic Population with normal body Mass Index. Int J Gen Med. 2021;14:8603–10.
23. Liu Y, Wang W. Sex-specific contribution of lipid accumulation product and cardiometabolic index in the identification of nonalcoholic fatty liver disease among Chinese adults. Lipids Health Dis. 2022;21(1):8.
24. Guo Q, Wang Y, Liu Y, Wang Y, Deng L, Liao L, Lin X, Wu M, Sun M, Liao Y. Association between the cardiometabolic index and chronic kidney disease: a cross-sectional study. Int Urol Nephrol 2023.
25. Li FE, Luo Y, Zhang FL, Zhang P, Liu D, Ta S, Yu Y, Guo ZN, Yang Y. Association between Cardiometabolic Index and Stroke: a Population- based cross-sectional study. Curr Neurovasc Res. 2021;18(3):324–32.
26. He L, Lin C, Tu Y, Yang Y, Lin M, Tu H, Li J. Correlation of cardiometabolic index and sarcopenia with cardiometabolic multimorbidity in middle-aged and older adult: a prospective study. Front Endocrinol (Lausanne). 2024;15:1387374.
27. Shi WR, Wang HY, Chen S, Guo XF, Li Z, Sun YX. Estimate of prevalent diabetes from cardiometabolic index in general Chinese population: a community-based study. Lipids Health Dis. 2018;17(1):236.
28. Wang H, Chen Y, Guo X, Chang Y, Sun Y. Usefulness of cardiometabolic index for the estimation of ischemic stroke risk among general population in rural China. Postgrad Med. 2017;129(8):834–41.
29. Wakabayashi I, Sotoda Y, Hirooka S, Orita H. Association between cardiometabolic index and atherosclerotic progression in patients with peripheral arterial disease. Clin Chim Acta. 2015;446:231–6.
30. Centers for Disease Control and Prevention. National Center for Health Statistics. NHANES 2007–2020, Examination, Anthropometry (Body Measures). pdf (3.4.8, page 3–19 to 3–20). [https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/manuals.aspx?Cycle=2011-2012]
31. Centers for Disease Control and Prevention. National Center for Health Statistics. NHANES 2007–2020, Biospecimen Program. [https://www.cdc.gov/nchs/nhanes/biospecimens/serum_plasma_urine.htm]
32. Yin B, Wu Z, Xia Y, Xiao S, Chen L, Li Y. Non-linear association of atherogenic index of plasma with insulin resistance and type 2 diabetes: a cross-sectional study. Cardiovasc Diabetol. 2023;22(1):157.
33. Liu Y, Gong R, Luo G, Li J, Li Q, Yang L, Wei X. Associations of Triglycerides/High-Density lipoprotein cholesterol ratio with insulin resistance, impaired glucose tolerance, and diabetes in American adults at different vitamin D3 levels. Front Endocrinol (Lausanne). 2021;12:735736.
34. 2. Classification and diagnosis of diabetes: standards of Medical Care in Diabetes-2019. Diabetes Care. 2019;42(Suppl 1):S13–28.
35. Zhang Q, Xiao S, Jiao X, Shen Y. The triglyceride-glucose index is a predictor for cardiovascular and all-cause mortality in CVD patients with diabetes or pre-diabetes: evidence from NHANES 2001–2018. Cardiovasc Diabetol. 2023;22(1):279.
36. Muntner P, Hardy ST, Fine LJ, Jaeger BC, Wozniak G, Levitan EB, Colantonio LD. Trends in blood pressure control among US adults with hypertension, 1999–2000 to 2017–2018. JAMA. 2020;324(12):1190–200.
37. Liu AB, Zhang D, Meng TT, Zhang Y, Tian P, Chen JL, Zheng Y, Su GH. Association of Chronic Kidney Disease with Cardiovascular Disease in Cancer patients: a cross-sectional study. Cardiorenal Med. 2023;13(1):344–53.
38. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150(9):604–12.
39. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, Poole C, Schlesselman JJ, Egger M. Strengthening the reporting of Observational studies in Epidemiology (STROBE): explanation and elaboration. Epidemiology. 2007;18(6):805–35.

40. Zha F, Cao C, Hong M, Hou H, Zhang Q, Tang B, Hu H, Han Y, Zan Y, Wang Y, et al. The nonlinear correlation between the cardiometabolic index and the risk of diabetes: a retrospective Japanese cohort study. Front Endocrinol (Lausanne). 2023;14:1120277.

41. Zhou X, Tao XL, Zhang L, Yang QK, Li ZJ, Dai L, Lei Y, Zhu G, Wu ZF, Yang H, et al. Association between cardiometabolic index and depression: National Health and Nutrition Examination Survey (NHANES) 2011–2014. J Affect Disord. 2024;351:939–47.

42. Miao M, Deng X, Wang Z, Jiang D, Lai S, Yu S, Yan L. Cardiometabolic index is associated with urinary albumin excretion and renal function in aged person over 60: data from NHANES 2011–2018. Int J Cardiol. 2023;384:76–81.

43. Tang X, Liu Q. Prediction of the development of metabolic syndrome by the Markov model based on a longitudinal study in Dalian City. BMC Public Health. 2018;18(1):707.

44. Abbasi F, Blasey C, Reaven GM. Cardiometabolic risk factors and obesity: does it matter whether BMI or waist circumference is the index of obesity? Am J Clin Nutr. 2013;98(3):637–40.

45. Wang H, Chen Y, Sun G, Jia P, Qian H, Sun Y. Validity of cardiometabolic index, lipid accumulation product, and body adiposity index in predicting the risk of hypertension in Chinese population. Postgrad Med. 2018;130(3):325–33.

46. Browning LM, Hsieh SD, Ashwell M. A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0·5 could be a suitable global boundary value. Nutr Res Rev. 2010;23(2):247–69.

47. Zhu Q, Wang XB, Yao Y, Ning CX, Chen XP, Luan FX, Zhao YL. Association between anthropometric measures and cardiovascular disease (CVD) risk factors in Hainan centenarians: investigation based on the Centenarian's health study. BMC Cardiovasc Disord. 2018;18(1):73.

48. Wu L, Xu J. Relationship between cardiometabolic index and Insulin Resistance in patients with type 2 diabetes. Diabetes Metab Syndr Obes. 2024;17:305–15.

49. Livingston EH. Lower body subcutaneous fat accumulation and diabetes mellitus risk. Surg Obes Relat Dis. 2006;2(3):362–8.

50. Adil SO, Musa KI, Uddin F, Shafique K, Khan A, Islam MA. Role of anthropometric indices as a screening tool for predicting metabolic syndrome among apparently healthy individuals of Karachi, Pakistan. Front Endocrinol (Lausanne). 2023;14:1223424.

51. Shi Y, Wen M. Sex-specific differences in the effect of the atherogenic index of plasma on prediabetes and diabetes in the NHANES 2011–2018 population. Cardiovasc Diabetol. 2023;22(1):19.

52. Qiu Y, Yi Q, Li S, Sun W, Ren Z, Shen Y, Wu Y, Wang Z, Xia W, Song P. Transition of cardiometabolic status and the risk of type 2 diabetes mellitus among middle-aged and older Chinese: a national cohort study. J Diabetes Investig. 2022;13(8):1426–37.

53. Zeyda M, Stulnig TM. Obesity, inflammation, and insulin resistance–a mini-review. Gerontology. 2009;55(4):379–86.

54. Barazzoni R, Gortan Cappellari G, Ragni M, Nisoli E. Insulin resistance in obesity: an overview of fundamental alterations. Eat Weight Disord. 2018;23(2):149–57.

55. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444(7121):840–6.

56. Tataranni PA. Pathophysiology of obesity-induced insulin resistance and type 2 diabetes mellitus. Eur Rev Med Pharmacol Sci. 2002;6(2–3):27–32.

57. Leon-Acuña A, Alcala-Diaz JF, Delgado-Lista J, Torres-Peña JD, Lopez-Moreno J, Camargo A, Garcia-Rios A, Marin C, Gomez-Delgado F, Caballero J, et al. Hepatic insulin resistance both in prediabetic and diabetic patients determines postprandial lipoprotein metabolism: from the CORDIOPREV study. Cardiovasc Diabetol. 2016;15:68.

58. Ailhaud G, Reach G. [Does obesity protect against diabetes? A new controversy]. Ann Endocrinol (Paris). 2001;62(4 Pt 2):S43–54.

59. Bastien M, Poirier P, Lemieux I, Després JP. Overview of epidemiology and contribution of obesity to cardiovascular disease. Prog Cardiovasc Dis. 2014;56(4):369–81.

60. Stefanska A, Cembrowska P, Kubacka J, Kuligowska-Prusinska M, Sypniewska G. Gonadotropins and Their Association with the Risk of Prediabetes and Type 2 Diabetes in Middle-Aged Postmenopausal Women. *Dis Markers* 2019, 2019:2384069.

61. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. JAMA. 2007;298(22):2654–64.

62. Yan L, Hu X, Wu S, Cui C, Zhao S. Association between the cardiometabolic index and NAFLD and fibrosis. Sci Rep. 2024;14(1):13194.

63. Xu B, Wu Q, La R, Lu L, Abdu FA, Yin G, Zhang W, Ding W, Ling Y, He Z, et al. Is systemic inflammation a missing link between cardiometabolic index with mortality? Evidence from a large population-based study. Cardiovasc Diabetol. 2024;23(1):212.

64. Nguyen LP, Tung DD, Nguyen DT, Le HN, Tran TQ, Binh TV, Pham DTN. The Utilization of Machine Learning Algorithms for assisting Physicians in the diagnosis of diabetes. Diagnostics (Basel) 2023, 13(12).

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