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Exploring the nonlinear association between cardiometabolic index and hypertension in U.S. Adults: an NHANES-based study

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Abstract

Background Hypertension is a prevalent chronic disease affecting over 1.2 billion people worldwide, representing a major modifiable risk factor for cardiovascular diseases. The Waist-to-Height Ratio (WHtR) and Triglyceride to High-Density Lipoprotein Cholesterol (TG/HDL-C) ratio are established metabolic indicators linked to the risk of cardiovascular and metabolic diseases. Recently, a Cardiometabolic Index (CMI), combining WHtR and TG/HDL-C ratios, has been proposed to provide a comprehensive assessment of metabolic health. This study investigates the association between CMI and hypertension using data from the National Health and Nutrition Examination Survey (NHANES).

Methods The study utilized NHANES data from nine cycles spanning 2001 to 2018, encompassing 20,049 participants aged over 20. Exclusions were made for individuals with incomplete CMI or hypertension data, and pregnant women. CMI was calculated by multiplying the WHtR by the TG/HDL-C ratio. Hypertension was defined according to American Heart Association guidelines. The relationship between CMI and hypertension was evaluated using multivariate logistic regression analyses, with additional subgroup analyses conducted based on demographic factors. Nonlinear relationships were analyzed using smoothing curve fitting techniques.

Results The study identified a significant positive correlation between CMI and hypertension risk, with an increase of one unit in CMI associated with a 9% heightened risk of hypertension (OR: 1.09, 95% CI: 1.05, 1.13). The association remained significant across various demographic subgroups. A nonlinear relationship was observed, with a critical CMI threshold of 2.64. Below this threshold, higher CMI values were associated with a progressively higher prevalence of hypertension, whereas beyond this threshold, further increases in CMI did not significantly correlate with an elevated risk of hypertension.

Conclusion The study demonstrates that CMI is significantly associated with hypertension risk and may serve as a valuable tool for early screening and risk assessment, particularly in identifying individuals at higher risk before reaching the critical CMI threshold. These results underscore the importance of addressing metabolic health in the prevention and management of hypertension. Future research should focus on longitudinal studies to establish

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causality, explore the clinical utility of CMI in hypertension screening, and examine its applicability in diverse populations.

Keywords Hypertension, Cardiometabolic Index, Waist-to-Height Ratio, Triglyceride to High-Density Lipoprotein Cholesterol (TG/HDL-C) ratio, Metabolic health

Introduction

Hypertension stands as one of the most prevalent chronic conditions globally, impacting more than 1.2 billion individuals, which accounts for one-third of the adult population [1]. It has emerged as one of the most significant and costly public health challenges, and also serves as a primary modifiable risk factor for cardiovascular diseases. Premature deaths due to hypertension have increased by 56.1% in the last decade [2]. Identifying and understanding potential metabolic risk factors are essential for its prevention and management [3]. Common indicators of metabolic abnormalities include the waist-to-height ratio (WHtR) and the triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-C) [4, 5]. WHtR reflects central obesity and is a dependable predictor of cardiovascular and metabolic disease risk, whereas the TG/HDL-C ratio indicates lipid metabolism disorders [6]. Elevated TG/HDL-C ratios are linked to a higher risk of atherosclerosis and cardiovascular events [7]. Recently, a new Cardiometabolic Index (CMI) has been proposed to provide a more comprehensive assessment of an individual's metabolic health by combining the WHtR and TG/HDL-C ratios [8, 9]. The CMI integrates two relevant risk factors, abdominal obesity and dyslipidemia, by multiplying the WHtR by the TG/HDL-C ratio, theoretically providing stronger predictive power for risk.

Given the importance of both central obesity and lipid imbalances in predicting metabolic health, combining WHtR and TG/HDL-C into a single composite index (CMI) offers the potential for a more comprehensive risk assessment. While WHtR serves as a reliable marker for central obesity [10, 11], TG/HDL-C reflects lipid metabolism disturbances commonly associated with cardiovascular diseases [12]. Their combination into the CMI may provide a more robust and integrated understanding of metabolic health. Previous studies have demonstrated that composite indices, which integrate multiple metabolic risk factors, can outperform single metrics in predicting outcomes such as cardiovascular events and diabetes [13, 14]. These findings suggest that composite indices like CMI could provide superior risk stratification, enhancing their clinical utility.

This study employed data from the National Health and Nutrition Examination Survey (NHANES) database to explore the association between CMI and hypertension. The onset of hypertension is frequently linked to a range of metabolic abnormalities, such as insulin resistance, lipid metabolism disorders, and elevated visceral fat [15–17]. Therefore, examining the relationship between CMI and hypertension may help reveal the metabolic basis of hypertension and provide new perspectives and tools for early prevention and management. We hypothesized that CMI, as a composite measure of WHtR and the TG/HDL-C ratio, is significantly associated with hypertension risk. By analyzing the correlation between CMI and hypertension in different populations, we aim to determine the value of CMI in early screening and risk assessment of hypertension, thereby supporting clinical practice. This research will enhance the comprehension of the link between metabolic health and hypertension, and assist in the timely identification and treatment of those at high risk for hypertension.

Methods

Study population

This research utilized data from the NHANES, a survey designed to represent the U.S. population, conducted by the Centers for Disease Control and Prevention [18, 19]. Approval for study procedures was granted by the Research Ethics Review Board of the National Center for Health Statistics (NCHS). Informed consent in writing was obtained from all participants at enrollment [20]. The survey covered nine cycles over 18 years, from 2001 to 2018. We excluded individuals under 20 years old (41,150 participants), those with incomplete or missing CMI data (29,536 participants), those without hypertension data (89 participants), and pregnant women (527 participants). Pregnant women were excluded because the physiological changes during pregnancy could significantly affect metabolic parameters such as blood pressure, lipid profiles, and increased waist circumference, all of which could confound the relationship between the CMI and hypertension [21, 22]. Individuals under 20 years old were excluded because hypertension in younger individuals is less common and may be influenced by different pathophysiological factors. Including them could distort the results and misrepresent the relationship between CMI and hypertension in adults. Consequently, the study comprised 20,049 participants (Fig. 1).

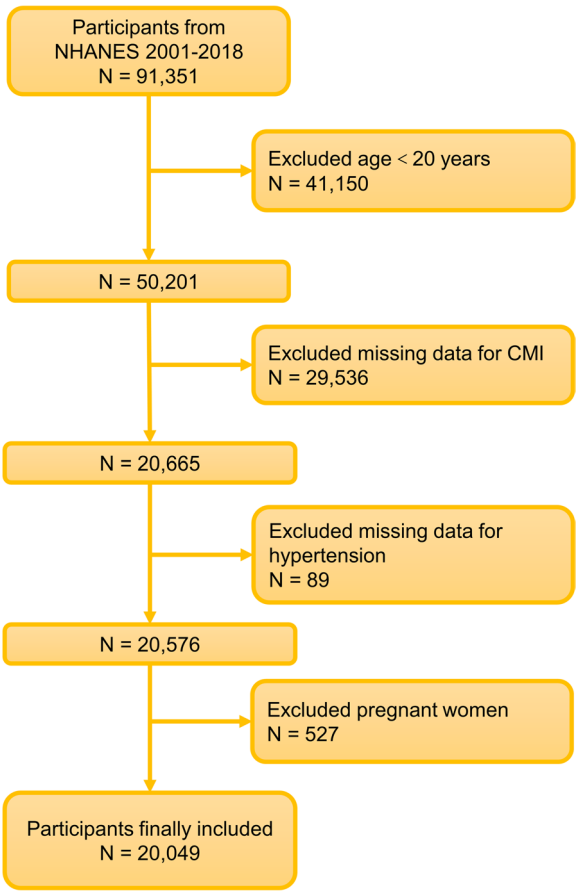

Fig. 1 Flowchart of participant selection

Assessment of CMI

The CMI was the primary independent variable in our exposure assessment. The determination of CMI followed a previously established method. Specifically, the Waist-to-Height Ratio (WHtR), calculated by dividing the waist circumference (in centimeters) by height (in centimeters), is a well-established indicator of central obesity. It has been shown to predict cardiovascular risk and metabolic disturbances more effectively than other anthropometric measures, such as BMI [23]. Additionally, the Triglyceride to High-Density Lipoprotein Cholesterol (TG/HDL-C) ratio serves as a reliable marker of dyslipidemia and lipid metabolism disorders, both of which are strongly linked to hypertension and other cardiovascular conditions [24]. These two indices were selected because, together, they provide a comprehensive assessment of metabolic health, integrating both obesity-related and lipid-related risk factors [25]. The CMI was calculated by multiplying the WHtR by the TG/HDL-C ratio, resulting in a unitless index that reflects combined metabolic health [26]. The CMI has been previously used in studies evaluating metabolic health and cardiovascular risks. The formula for CMI is: CMI = WHtR × (TG/HDL-C ratio).

Definition of hypertension

Blood pressure measurements were taken by trained examiners following the American Heart Association guidelines, as detailed on the NHANES website. The average blood pressure was determined from three readings taken consecutively in a calm environment. Hypertension was defined according to any of the following criteria: an average systolic blood pressure (SBP) of 140 mmHg or higher, an average diastolic blood pressure (DBP) of 90 mmHg or higher, self-reported hypertension, or the use of antihypertensive medication. We relied on clinic-based blood pressure measurements for the definition of hypertension, as per the guidelines of the American Heart Association [27]. While ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM) would provide a more accurate and continuous assessment of blood pressure, clinic-based measurements remain a common practice in large-scale epidemiological studies like NHANES [28, 29]. We acknowledge that clinic-based measurements may either underestimate or overestimate hypertension in some cases. Specifically, clinic measurements might overestimate the true prevalence of hypertension due to the "white coat effect," where individuals' blood pressure may be elevated temporarily due to anxiety in a clinical setting [30]. On the other hand, they could also underestimate hypertension by failing to capture isolated instances of elevated blood pressure that occur intermittently or under specific conditions, which might not be reflected in a single clinic measurement. These measurement inconsistencies could lead to misclassification of hypertension status, potentially diluting or exaggerating the observed association between CMI and hypertension [31, 32]. Therefore, while clinic-based measurements are widely used and practical in large-scale studies, the potential for error should be considered when interpreting the results.

Covariables

Various demographic and health-related factors were included as covariates in the study. These factors included age, race, gender, education level, income-to-poverty ratio (PIR), smoking and alcohol consumption habits, and the presence of conditions such as diabetes, coronary heart disease (CHD), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD). Additional covariates included hemoglobin A1c (HbA1c) levels, Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) levels, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and body

mass index (BMI). Self-reported variables such as smoking and alcohol consumption were obtained from participant questionnaires, which may be subject to recall bias and inaccuracies. Clinically measured variables such as BMI, cholesterol levels, and HbA1c were obtained from NHANES laboratory assessments, which are generally more reliable. However, some measurement errors might still occur due to differences in equipment calibration or testing protocols. Despite these limitations, we believe that the comprehensive approach used in NHANES data collection minimizes such biases.

Statistical analysis

The relationship between CMI quartiles and demographic characteristics was examined using t-tests and chi-square tests. Multivariate linear and logistic regression analyses were employed to assess the association between CMI and hypertension, identifying linear correlations. Additionally, CMI was categorized into quartiles, and a trend test was performed to examine its linear relationship with hypertension. Subgroup analyses were conducted to explore this relationship across various demographics, including gender, age, race, BMI, and diabetes status. Interaction tests were performed to evaluate the consistency of associations across these subgroups. Nonlinear relationships were analyzed using smoothing curve fitting techniques. All statistical analyses were performed using R (version 4.3.3) and EmpowerStats (version 6.0), with statistical significance defined as a two-sided *p*-value of less than 0.05.

Results

Baseline characteristics

The study encompassed 20,049 participants aged over 20, with an average age of 49.95 ± 17.74 years. The cohort consisted of 50.27% females and 44.78% non-Hispanic whites. The mean CMI was 0.79 ± 1.13, with distribution across quartiles as follows: Quartile 1: 0.20 ± 0.06, Quartile 2: 0.41 ± 0.06, Quartile 3: 0.70 ± 0.12, and Quartile 4: 1.87 ± 1.85. Hypertension was diagnosed in 42.45% of the participants. Individuals in the highest CMI quartile were predominantly male, non-Hispanic White, with lower educational levels and higher PIR. Additionally, these participants had a higher prevalence of CHD, diabetes, COPD, CKD, and hypertension compared to those in the lowest CMI quartile. Elevated CMI values correlated with increases in HbA1c, ALT, AST, TG, TC, and LDL-C, as outlined in Table 1.

Association between CMI and hypertension

As presented in Table 2, multivariate logistic regression analyses identified a significant positive association between CMI and hypertension risk across all three models. After full adjustment, each unit increase in CMI was linked to a 9% higher risk of hypertension (OR: 1.09, 95% CI: 1.05, 1.13). Each unit increase in CMI represents a significant shift in the likelihood of developing hypertension, and this association holds clinical relevance. A 9% increased risk per unit change suggests that even modest increases in CMI may be important indicators for healthcare providers to monitor, as it could signify a need for early interventions to prevent the onset of hypertension. This highlights the potential of CMI as a simple, practical tool for early risk stratification. When CMI was analyzed by quartiles, participants in the highest quartile had a 50% higher risk of hypertension compared to those in the lowest quartile (OR: 1.50, 95% CI: 1.34, 1.68). A sensitivity analysis was also performed by adjusting the diagnostic threshold for hypertension from 140/90 mmHg to 130/80 mmHg. The results of this analysis, presented in Supplementary Table 1, demonstrate that the association between CMI and hypertension remains consistent, reinforcing the robustness of our findings. A generalized model using smooth curve fitting demonstrated a nonlinear relationship between CMI and hypertension, as depicted in Fig. 2. Further analysis using a two-piece logistic regression model confirmed this nonlinear association (p = 0.006 for the log-likelihood ratio test), identifying a CMI threshold of 2.64 (Table 3). Below this threshold, hypertension prevalence increased with CMI (OR: 1.32; 95% CI: 1.22–1.42) Conversely, for CMI values of 2.64 or higher, further increases in CMI were not associated with a higher prevalence of hypertension (OR: 0.75; 95% CI: 0.52,1.08). This threshold effect may be explained by the physiological processes underlying metabolic health [33]. Below the threshold, increases in CMI reflect rising levels of central obesity and lipid abnormalities, which are known to contribute to hypertension through mechanisms such as insulin resistance, inflammation, and endothelial dysfunction [34]. However, beyond this threshold, compensatory mechanisms, such as improved lipid metabolism or metabolic adaptations, may attenuate the impact of further increases in CMI [35]. Future research should explore these potential biological mechanisms, including how genetic factors or other comorbidities might influence this nonlinear relationship.

Subgroup analyses

Subgroup analyses and interaction tests were conducted to evaluate the consistency of the CMI-hypertension association across various demographic groups, including age, gender, race, BMI, and diabetes status (Fig. 3). However, this association is not consistent in terms of findings. Significant interactions were observed for race (P for interaction = 0.0145)

Table 1 Weighted baseline characteristics of the study population according to CMI Quartiles

Characteristics	CMI				P-value
	Q1 (N = 5012)	Q2 (N = 5012)	Q3 (N = 5012)	Q4 (N = 5013)	
Age (years)	45.80 ± 18.14	50.15 ± 18.12	51.92 ± 17.54	51.94 ± 16.37	< 0.001
Gender, (%)					< 0.001
Male	1952 (38.95%)	2391 (47.71%)	2586 (51.60%)	3041 (60.66%)	
Female	3060 (61.05%)	2621 (52.29%)	2426 (48.40%)	1972 (39.34%)	
Race/Ethnicity, (%)					< 0.001
Non-Hispanic White	2103 (41.96%)	2203 (43.95%)	2175 (43.40%)	2496 (49.79%)	
Mexican American	512 (10.22%)	759 (15.14%)	977 (19.49%)	1115 (22.24%)	
Non-Hispanic Black	1448 (28.89%)	1155 (23.04%)	884 (17.64%)	521 (10.39%)	
Other races	949 (18.93%)	895 (17.86%)	976 (19.47%)	881 (17.57%)	
Education level, (%)					< 0.001
Some college or above	3050 (60.85%)	2638 (52.63%)	2403 (47.94%)	2147 (42.83%)	
High school	1040 (20.75%)	1155 (23.04%)	1184 (23.62%)	1229 (24.52%)	
Less than high school	922 (18.40%)	1219 (24.32%)	1425 (28.43%)	1637 (32.66%)	
PIR, (%)					< 0.001
≤ 1.3	1645 (32.82%)	1493 (29.79%)	1342 (26.78%)	1253 (25.00%)	
> 1.3, < = 3.5	2161 (43.12%)	2171 (43.32%)	2269 (45.27%)	2144 (42.77%)	
> 3.5	1206 (24.06%)	1348 (26.90%)	1401 (27.95%)	1616 (32.24%)	
Smoke, (%)					< 0.001
Never Smoker	3054 (60.93%)	2803 (55.93%)	2610 (52.08%)	2305 (45.98%)	
Former Smoker	1027 (20.49%)	1209 (24.12%)	1309 (26.12%)	1496 (29.84%)	
Current Smoker	931 (18.58%)	1000 (19.95%)	1093 (21.81%)	1212 (24.18%)	
Alcohol Use, (%)					< 0.001
Never	602 (12.01%)	645 (12.87%)	642 (12.81%)	639 (12.75%)	
Former	521 (10.40%)	756 (15.08%)	882 (17.60%)	1004 (20.03%)	
Mild	2137 (42.64%)	2031 (40.52%)	1991 (39.72%)	1836 (36.62%)	
Moderate	897 (17.90%)	664 (13.25%)	589 (11.75%)	557 (11.11%)	
Heavy	855 (17.06%)	916 (18.28%)	908 (18.12%)	977 (19.49%)	
Hypertension, (%)					< 0.001
No	3529 (70.41%)	2990 (59.66%)	2663 (53.13%)	2357 (47.02%)	
Yes	1483 (29.59%)	2022 (40.34%)	2349 (46.87%)	2656 (52.98%)	
CHD, (%)					< 0.001
No	4888 (97.53%)	4841 (96.59%)	4764 (95.05%)	4701 (93.78%)	
Yes	124 (2.47%)	171 (3.41%)	248 (4.95%)	312 (6.22%)	
Diabetes, (%)					< 0.001
No	4594 (91.66%)	4253 (84.86%)	3867 (77.15%)	3356 (66.95%)	
Yes	418 (8.34%)	759 (15.14%)	1145 (22.85%)	1657 (33.05%)	
COPD, (%)					< 0.001
No	4841 (96.59%)	4795 (95.67%)	4776 (95.29%)	4751 (94.77%)	
Yes	171 (3.41%)	217 (4.33%)	236 (4.71%)	262 (5.23%)	
CKD, (%)					< 0.001
No	4384 (87.47%)	4215 (84.10%)	4046 (80.73%)	3819 (76.18%)	
Yes	628 (12.53%)	797 (15.90%)	966 (19.27%)	1194 (23.82%)	
BMI (Kg/m2)					< 0.001
< = 25	674 (13.45%)	1486 (29.65%)	2216 (44.21%)	2822 (56.29%)	
> 25, < = 30	1392 (27.77%)	1853 (36.97%)	1880 (37.51%)	1702 (33.95%)	
> 30	2946 (58.78%)	1673 (33.38%)	916 (18.28%)	489 (9.75%)	
CMI	0.20 ± 0.06	0.41 ± 0.06	0.70 ± 0.12	1.87 ± 1.85	< 0.001
HbA1c (%)	5.43 ± 0.65	5.63 ± 0.90	5.83 ± 1.14	6.09 ± 1.39	< 0.001

Table 1 (continued)

Characteristics	CMI				P-value
	Q1 (N = 5012)	Q2 (N = 5012)	Q3 (N = 5012)	Q4 (N = 5013)	
ALT (IU/L)	21.54 ± 33.70	23.13 ± 16.35	25.99 ± 16.97	31.01 ± 34.22	< 0.001
AST (IU/L)	25.06 ± 31.38	24.65 ± 20.72	25.03 ± 15.29	27.19 ± 18.97	< 0.001
Triglyceride (mmol/L)	0.67 ± 0.20	1.03 ± 0.25	1.45 ± 0.35	2.81 ± 2.14	< 0.001
Total cholesterol (mmol/L)	4.76 ± 0.96	4.92 ± 1.02	5.04 ± 1.06	5.35 ± 1.22	< 0.001
HDL- cholesterol(mmol/L)	1.79 ± 0.43	1.46 ± 0.29	1.26 ± 0.25	1.04 ± 0.22	< 0.001
LDL- cholesterol(mmol/L)	2.66 ± 0.79	2.99 ± 0.88	3.11 ± 0.94	3.09 ± 0.96	< 0.001

Mean ± SD for continuous variables: the P value was calculated by the weighted linear regression model. (%) for categorical variables: the P value was calculated by the weighted chi-square test

Abbreviation: *BMI* body mass index, *PIR* poverty income ratio, *CKD* chronic kidney disease, *COPD* Chronic Obstructive Pulmonary Disease, *CHD* coronary heart disease, *CMI* cardiometabolic index, *HbA1c* Hemoglobin A1c, *ALT* Alanine Aminotransferase, *AST* Aspartate Aminotransferase, *Triglyceride* Triglycerides, *Total cholesterol* Total Cholesterol, *HDL-cholesterol* High-Density Lipoprotein Cholesterol, *LDL-cholesterol* Low-Density Lipoprotein Cholesterol

Table 2 Association between CMI and hypertension

Exposure	Model 1 [OR (95% CI)]	Model 2 [OR (95% CI)]	Model 3 [OR (95% CI)]
Continuous CMI	1.26 (1.21, 1.30) < 0.0001	1.32 (1.27, 1.37) < 0.0001	1.09 (1.05, 1.13) < 0.0001
CMI classification			
Quartile 1	Reference	Reference	Reference
Quartile 2	1.61 (1.48, 1.75) < 0.0001	1.49 (1.36, 1.64) < 0.0001	1.15 (1.04, 1.27) 0.0067
Quartile 3	2.10 (1.93, 2.28) < 0.0001	2.02 (1.84, 2.22) < 0.0001	1.26 (1.13, 1.40) < 0.0001
Quartile 4	2.68 (2.47, 2.91) < 0.0001	3.04 (2.76, 3.35) < 0.0001	1.50 (1.34, 1.68) < 0.0001

Model 1: no covariates were adjusted

Model 2: age, gender, and race were adjusted

Model 3: age, gender, race, education level, PIR, smoking behavior, drinking behavior, CHD, Diabetes, COPD, CKD, HbA1c, ALT, AST, and BMI were adjusted

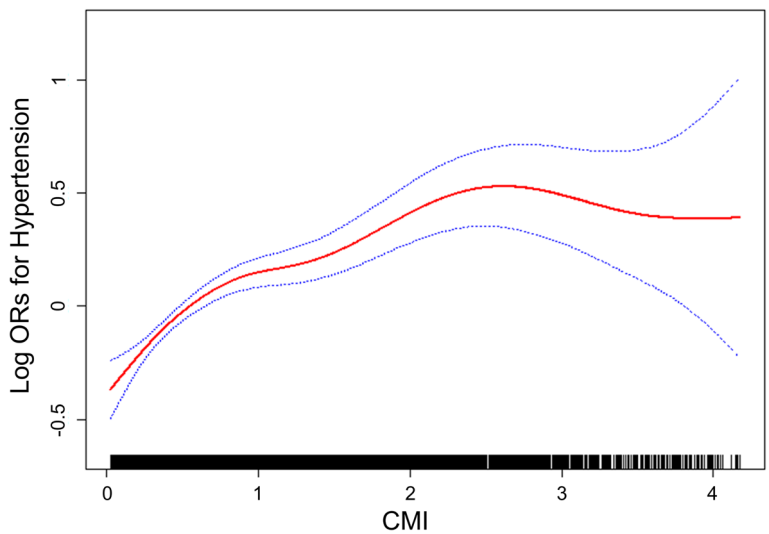

Fig. 2 Nonlinear association between CMI and hypertension. The figure shows the relationship between the Cardiometabolic Index (CMI) and the prevalence of hypertension, as analyzed using a smoothing curve fitting technique. The solid red line represents the smoothed curve fit, illustrating the nonlinear association between CMI and hypertension risk. The shaded blue area around the curve indicates the 95% confidence interval, which provides an estimate of the uncertainty in the relationship. The figure highlights a critical CMI threshold of 2.64, below which the risk of hypertension increases with higher CMI values. Beyond this threshold, the relationship between CMI and hypertension weakens, as indicated by the plateau of the curve

Table 3 Results of two-piecewise logistic-regression model

Outcome: HYPERTENSION (dichotom)
Risk factor of interest: CMI (Index, dimensionless)
* Inflection point (K) of CMI 2.64
* Effect size OR (95% CI) for CMI < K 1.32 (1.22, 1.42)
* Effect size OR (95% CI) for CMI ≥ K 0.75 (0.52, 1.08)
P for log likelihood ratio test 0.006

Two-piecewise logistic-regression model was used to calculate the threshold effect of the CMI. If the log likelihood ratio test > 0.05, it means the two-piecewise logistic regression model is not superior to the single-line logistic regression model

Adjustment Model was adjusted for age, gender, race, education level, PIR, smoking behavior, drinking behavior, CHD, Diabetes, COPD, CKD, HbA1c, ALT, AST, and BMI

and diabetes status (P for interaction = 0.0011). In individuals without diabetes, the risk of hypertension increased by 14% per 1 unit increase in CMI. In contrast, among those with diabetes, the association between CMI and hypertension became a non-significant positive relationship. Similarly, in both Non-Hispanic White and Non-Hispanic Black populations, the risk of hypertension increased by 15% per 1 unit increase in CMI, whereas in Mexican American and Other races, the association was not statistically significant. However, the relationship between CMI and hypertension remained consistent across age, sex, and BMI subgroups (P > 0.05 for interaction).

Discussion

Our analysis of NHANES data revealed a significant positive association between CMI and the risk of hypertension, which remained strong even after adjusting for confounding factors. Subgroup analyses confirmed this association across various demographics. We also found a nonlinear relationship, with a critical threshold at a CMI of 2.64. Our results endorse the use of CMI as an effective tool for early hypertension screening and risk evaluation, integrating measures of central obesity and lipid metabolism disorders to inform targeted preventive strategies.

As far as we know, this study is the first to investigate the connection between CMI and hypertension. Previous studies have demonstrated that the WHtR [36, 37] and the TG/HDL-C [38] are independently associated with cardiovascular and metabolic disease risks. Notably, an elevated WHtR has been linked with a heightened likelihood of developing coronary heart disease, diabetes, and increased overall mortality [39, 40]. Conversely, the TG/HDL-C ratio serves as an indicator of lipid metabolism disorders and has been associated with a higher risk of atherosclerosis and cardiovascular events [41, 42]. An elevated TG/HDL-C ratio is recognized as an indicator of insulin resistance, which is strongly associated with metabolic syndrome and cardiovascular diseases [43]. Although these studies have respectively highlighted the links between WHtR and TG/HDL-C with cardiovascular diseases, our research is the first to combine these two indices into a comprehensive measure, the CMI,

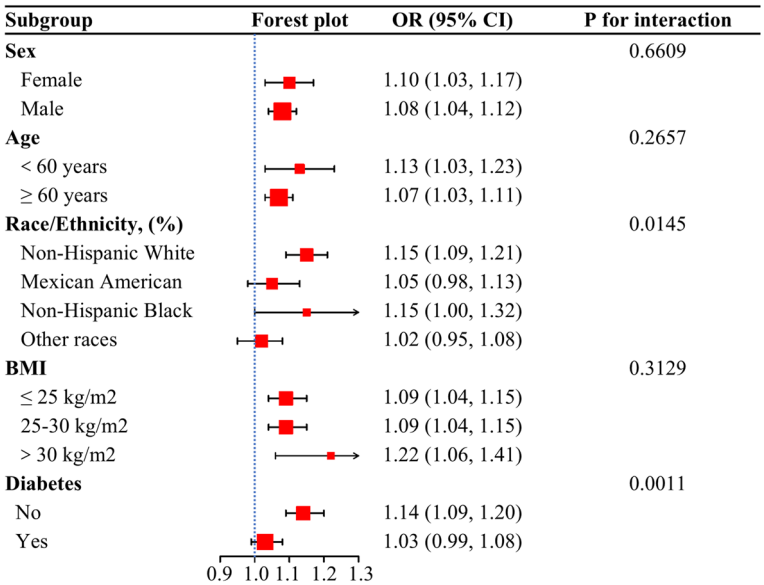

Fig. 3 Subgroup analysis of the association between CMI and hypertension. Age, gender, race, education level, PIR, smoking behavior, drinking behavior, CHD, Diabetes, COPD, CKD, HbA1c, ALT, AST, and BMI were adjusted. In the subgroup analyses, the model is not adjusted for the stratification variable itself

potentially enhancing the predictive power for hypertension risk. Currently, several established risk prediction models, such as the Framingham Risk Score [44] and Arteriosclerotic Cardiovascular Disease (ASCVD) Risk Calculator [45], are commonly used to assess the likelihood of hypertension and cardiovascular events. These models primarily consider factors like age, gender, blood pressure, and cholesterol levels to predict risk. Additionally, hypertension management guidelines, such as those from the American Heart Association (AHA) [46] and the European Society of Cardiology (ESC) [47], focus on controlling blood pressure through lifestyle modifications and pharmacotherapy, based on these traditional risk factors. However, these models may not fully account for the complex interplay between multiple metabolic pathways and their combined effect on hypertension risk. Incorporating CMI into existing risk prediction models could enhance their ability to identify individuals at high risk of hypertension earlier, particularly those whose metabolic disturbances may not be captured by traditional single-factor models. Unlike the use of WHtR or TG/HDL-C ratio alone, CMI integrates two critical metabolic abnormalities-central obesity and lipid metabolism disorders-providing a more comprehensive assessment of metabolic health [48, 49]. Through this comprehensive evaluation method, we can more accurately identify high-risk individuals, supporting early intervention and management in clinical practice. In contrast, previous studies that focused solely on single metabolic indicators might underestimate or overlook the impact of interactions between different metabolic pathways on hypertension risk [50, 51]. Therefore, our study has significant methodological advantages, contributing to a more comprehensive understanding of the complexity of metabolic health and its impact on hypertension. Integrating CMI into hypertension management guidelines could lead to more personalized treatment strategies, enabling clinicians to identify patients who might benefit from early interventions targeting multiple metabolic risk factors, rather than focusing on blood pressure alone. This approach could ultimately improve patient outcomes by addressing the root causes of hypertension in a more holistic manner.

Additionally, CMI not only integrates two important metabolic indicators but also considers their potential interactions, making it more sensitive and specific in predicting hypertension risk [4]. In contrast, previous studies that focused solely on single metabolic indicators might underestimate or overlook the impact of interactions between different metabolic pathways on hypertension risk. Therefore, our study has significant methodological advantages, contributing to a more comprehensive understanding of the complexity of metabolic health and its impact on hypertension. By considering these interactions, CMI can offer a more nuanced approach to managing hypertension, providing a clearer pathway for clinicians to address the underlying metabolic factors contributing to the disease.

Further analyses identified a non-linear correlation between CMI and hypertension, demonstrating that when CMI values were below 2.64, the prevalence of hypertension rose as CMI values increased. However, when CMI values exceeded 2.64, the association between increasing CMI and hypertension risk was not significant. This finding provides a new perspective on the complex relationship between metabolic health and hypertension. Our results lay the foundation for future research, suggesting further investigation into the application of CMI in different populations and assessing whether combining CMI with other metabolic indices can improve predictive accuracy. Additionally, longitudinal studies are needed to better understand the causal relationship between CMI and hypertension, providing more robust evidence for clinical practice. Several mechanisms may explain the positive association identified between CMI and hypertension in our study. First, a higher WHtR reflects central obesity, which is closely associated with increased visceral fat [52]. Visceral fat contributes to insulin resistance and metabolic syndrome, both recognized as significant risk factors for hypertension [53–55]. Similarly, a higher TG/HDL-C ratio signals lipid metabolism disorders, linked to a heightened risk of atherosclerosis and ensuing cardiovascular events [56, 57]. The combination of these factors in CMI may more comprehensively reflect metabolic health, thereby enhancing its predictive power for hypertension. Chronic inflammation and oxidative stress associated with central obesity, lipid metabolism disorders, and thyroid dysfunction may collectively promote the development and progression of hypertension. These interconnected metabolic disturbances, including the impaired thyroid function that often contributes to dyslipidemia and metabolic slowdowns, can amplify the risk of hypertension [58]. Thus, utilizing CMI as a comprehensive index can more effectively identify and manage individuals at high risk. Central obesity is not only related to hypertension but also associated with various cardiovascular diseases and metabolic disorders [59, 60]. Excess visceral adipose tissue can lead to adipocyte hypertrophy and dysfunction, triggering a cascade of inflammatory responses [61]. Adipocytes release pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which trigger systemic inflammation, ultimately affecting vascular function and raising the risk of hypertension [62]. Moreover, the accumulation of visceral fat is directly linked to fatty liver and insulin resistance, which are fundamental aspects

of metabolic syndrome and important risk factors for hypertension [63, 64]. Conversely, a higher TG/HDL-C ratio indicates dyslipidemia, characterized by elevated triglyceride levels and reduced high-density lipoprotein cholesterol. Dyslipidemia is intimately associated with the progression of atherosclerosis, the fundamental pathological underpinning of hypertension and cardiovascular diseases [65]. High triglyceride levels contribute to the generation of small, dense low-density lipoprotein (LDL) particles, which tend to deposit within arterial walls, leading to the formation of atherosclerotic plaques [66]. Meanwhile, low high-density lipoprotein levels reduce the protective effects on arterial walls, further increasing the risk of atherosclerosis [67]. Additionally, lipid metabolism disorders may affect blood pressure regulation through oxidative stress and endothelial dysfunction [68]. Oxidative stress arises from an imbalance between the generation of reactive oxygen species and their clearance, resulting in cellular and tissue damage [69]. Lipid peroxidation is a major manifestation of oxidative stress, which not only directly damages vascular endothelial cells but also promotes inflammatory responses and the progression of atherosclerosis, indirectly affecting blood pressure regulation [70]. Research has demonstrated a significant correlation between elevated triglyceride levels, reduced high-density lipoprotein levels, and markers of oxidative stress, which may contribute to the increased risk of hypertension associated with the TG/HDL-C ratio [71]. Furthermore, central obesity and lipid metabolism disorders are often accompanied by insulin resistance, which has a complex interaction with hypertension [72]. Insulin resistance can lead to elevated plasma insulin levels, which not only increase blood volume through renal sodium retention but also directly influence blood pressure by activating the sympathetic nervous system and promoting vascular smooth muscle cell proliferation [73]. Moreover, insulin resistance leads to an increase in insulin-like growth factor-1 (IGF-1) levels, which are intimately linked to vascular remodeling and atherosclerosis, thereby further elevating the risk of hypertension [74]. It is noteworthy that the predictive power of CMI for hypertension comes not only from the additive effects of single metabolic abnormalities but also from the potential interactions between these indices. Central obesity and lipid metabolism disorders may synergize through shared metabolic pathways and pathological mechanisms, contributing to the development and progression of hypertension. For example, chronic inflammation induced by central obesity may exacerbate lipid metabolism disorders, while lipid metabolism disorders may further worsen insulin resistance and oxidative stress [75, 76]. These interacting factors ultimately lead to elevated blood pressure. Therefore, CMI as a comprehensive index can more fully reflect an individual's metabolic health status and, by integrating multiple metabolic abnormalities, improve the accuracy of hypertension prediction. In summary, the relationship between CMI and hypertension may be mediated through multiple complex mechanisms, including central obesity, lipid metabolism disorders, chronic inflammation, oxidative stress, and insulin resistance. These mechanisms not only independently contribute to the development of hypertension but also interact to further exacerbate the risk. Our study highlights the importance of CMI as a comprehensive metabolic health assessment index, providing new perspectives and methods for future hypertension prevention and treatment strategies.

This study exhibits several key strengths. Firstly, the utilization of a large, nationally representative sample from NHANES significantly enhances the generalizability and representativeness of the findings. Secondly, extensive adjustments for multiple potential confounders were conducted, thereby improving the reliability of the results. The identification of a nonlinear relationship between CMI and hypertension provides more nuanced insights into the impact of metabolic health on hypertension risk. Nonetheless, this study is subject to certain limitations. Given its cross-sectional design, causal inferences between CMI and hypertension cannot be established. Additionally, some potential confounders, such as dietary habits, physical activity levels, and other unmeasured variables, were not fully controlled, which may have influenced the observed associations. The potential for residual confounding remains a concern, as these unmeasured factors could affect the relationship between CMI and hypertension. Future studies could address these limitations by incorporating longitudinal data to better capture causal pathways and by including additional covariates such as physical activity and diet, which may provide a more comprehensive understanding of the factors influencing hypertension risk.

Conclusion

In conclusion, our study suggests that the CMI is significantly associated with the risk of hypertension and may be a useful tool for early screening and risk assessment. Given the findings from a nationally representative sample, incorporating CMI into clinical practice could aid in identifying individuals at risk for hypertension at an earlier stage, allowing for timely interventions. Promoting the use of CMI in public health initiatives could help address hypertension on a broader scale. Future research should focus on longitudinal studies to further establish the causal relationship between CMI and hypertension and explore its applicability across different populations.

Institutional review board statement
Not applicable.

Authors' contributions
Huatao Zhou: Writing – original draft, Visualization, Software, Methodology, Formal analysis, Conceptualization. Yu Mao: Methodology, Investigation, Data curation, Conceptualization. Muyao Ye: Visualization, Software. Zhongkun Zuo: Writing – review & editing, Supervision, Methodology, Conceptualization.

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Data availability
The datasets used in this study were extracted from the NHANES (http://wwwn.cdc.gov/nchs/nhanes/).

Declarations

Ethics approval and consent to participate
The study protocol was approved by the NHANES Institutional Review Board, and was performed in accordance with the Declaration of Helsinki, with all NHANES participants providing signed informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Rahimi K, Emdin CA, MacMahon S. The epidemiology of blood pressure and its worldwide management. Circ Res. 2015;116(6):925–36.
2. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart Disease and Stroke Statistics-2020 Update: A Report From the American Heart Association. Circulation. 2020;141(9):e139–596.
3. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1223–49.
4. 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.
5. Lin D, Qi Y, Huang C, Wu M, Wang C, Li F, et al. Associations of lipid parameters with insulin resistance and diabetes: A population-based study. Clin Nutr. 2018;37(4):1423–9.
6. Sheng G, Lu S, Xie Q, Peng N, Kuang M, Zou Y. The usefulness of obesity and lipid-related indices to predict the presence of Non-alcoholic fatty liver disease. Lipids Health Dis. 2021;20(1):134.
7. Liao LP, Wu L, Yang Y. The relationship between triglyceride/high-density lipoprotein cholesterol ratio and coronary microvascular disease. BMC Cardiovasc Disord. 2023;23(1):228.
8. Liu X, Wu Q, Yan G, Duan J, Chen Z, Yang P, et al. Cardiometabolic index: a new tool for screening the metabolically obese normal weight phenotype. J Endocrinol Invest. 2021;44(6):1253–61.
9. Wang J, Su Z, Feng Y, Xi R, Liu J, Wang P. Comparison of several blood lipid-related indexes in the screening of non-alcoholic fatty liver disease in women: a cross-sectional study in the Pearl River Delta region of southern China. BMC Gastroenterol. 2021;21(1):482.
10. Hamulka J, Wadolowska L, Hoffmann M, Kowalkowska J, Gutkowska K. Effect of an Education Program on Nutrition Knowledge, Attitudes toward Nutrition, Diet Quality, Lifestyle, and Body Composition in Polish Teenagers. The ABC of Healthy Eating Project: Design, Protocol, and Methodology. Nutrients. 2018;10(10):1439.
11. 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.
12. Kosmas CE, Rodriguez Polanco S, Bousvarou MD, Papakonstantinou EJ, Peña Genao E, Guzman E, et al. The Triglyceride/High-Density Lipoprotein Cholesterol (TG/HDL-C) Ratio as a Risk Marker for Metabolic Syndrome and Cardiovascular Disease. Diagnostics (Basel). 2023;13(5):929.
13. He H-M, Xie Y-Y, Chen Q, Li Y-K, Li X-X, Fu S-J, et al. The synergistic effect of the triglyceride-glucose index and a body shape index on cardiovascular mortality: the construction of a novel cardiovascular risk marker. Cardiovasc Diabetol. 2025;24(1):69.
14. Yang Y, Li S, Ren Q, Qiu Y, Pan M, Liu G, et al. The interaction between triglyceride-glucose index and visceral adiposity in cardiovascular disease risk: findings from a nationwide Chinese cohort. Cardiovasc Diabetol. 2024;23(1):427.
15. Sun Q, Ren Q, Du L, Chen S, Wu S, Zhang B, et al. Cardiometabolic Index (CMI), Lipid Accumulation Products (LAP), Waist Triglyceride Index (WTI) and the risk of acute pancreatitis: a prospective study in adults of North China. Lipids Health Dis. 2023;22(1):190.
16. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol. 2018;17(1):122.
17. Zafar U, Khaliq S, Ahmad HU, Manzoor S, Lone KP. Metabolic syndrome: an update on diagnostic criteria, pathogenesis, and genetic links. Hormones (Athens). 2018;17(3):299–313.
18. Cheng TD, Ferderber C, Kinder B, Wei YJ. Trends in Dietary Vitamin A Intake Among US Adults by Race and Ethnicity, 2003–2018. JAMA. 2023;329(12):1026–9.
19. Paulose-Ram R, Graber JE, Woodwell D, Ahluwalia N. The National Health and Nutrition Examination Survey (NHANES), 2021–2022: Adapting Data Collection in a COVID-19 Environment. Am J Public Health. 2021;111(12):2149–56.
20. Mei Z, Addo OY, Jefferds ME, Sharma AJ, Flores-Ayala RC, Brittenham GM. Physiologically based serum ferritin thresholds for iron deficiency in children and non-pregnant women: a US National Health and Nutrition Examination Surveys (NHANES) serial cross-sectional study. Lancet Haematol. 2021;8(8):e572–82.
21. Gootjes DV, Posthumus AG, Wols DF, de Rijke YB, Roeters Van Lennep JE, Steegers EAP. Maternal lipid profile in pregnancy and embryonic size: a population-based prospective cohort study. BMC Pregnancy Childbirth. 2022;22(1):333.
22. Jovandaric MZ, Babic S, Raus M, Medjo B. The Importance of Metabolic and Environmental Factors in the Occurrence of Oxidative Stress during Pregnancy. Int J Mol Sci. 2023;24(15):11964.
23. Ashwell M, Gibson S. Waist-to-height ratio as an indicator of "early health risk": simpler and more predictive than using a "matrix" based on BMI and waist circumference. BMJ Open. 2016;6(3): e010159.
24. Deng Q-W, Li S, Wang H, Lei L, Zhang H-Q, Gu Z-T, et al. The Short-term Prognostic Value of the Triglyceride-to-high-density Lipoprotein Cholesterol Ratio in Acute Ischemic Stroke. Aging Dis. 2018;9(3):498–506.
25. Alberti KGMM, Zimmet P, Shaw J. The metabolic syndrome–a new worldwide definition. Lancet. 2005;366(9491):1059–62.
26. Xu B, Wu Q, Yin G, Lu L, La R, Zhang Y, et al. Associations of cardiometabolic index with diabetic statuses and insulin resistance: the mediating role of inflammation-related indicators. BMC Public Health. 2024;24(1):2736.
27. Tan L, Liu Y, Liu J, Zhang G, Liu Z, Shi R. Association between insulin resistance and uncontrolled hypertension and arterial stiffness among US adults: a population-based study. Cardiovasc Diabetol. 2023;22(1):311.
28. Hou X-Z, Lv Y-F, Li Y-S, Wu Q, Lv Q-Y, Yang Y-T, et al. Association between different insulin resistance surrogates and all-cause mortality in patients with coronary heart disease and hypertension: NHANES longitudinal cohort study. Cardiovasc Diabetol. 2024;23(1):86.

29. Zhang X, Wei R, Wang X, Zhang W, Li M, Ni T, et al. The neutrophil-to-lymphocyte ratio is associated with all-cause and cardiovascular mortality among individuals with hypertension. Cardiovasc Diabetol. 2024;23(1):117.
30. Kario K, Thijs L, Staessen JA. Blood Pressure Measurement and Treatment Decisions. Circ Res. 2019;124(7):990–1008.
31. Hall EM, Acevedo J, López FG, Cortés S, Ferreccio C, Smith AH, et al. Hypertension among adults exposed to drinking water arsenic in Northern Chile. Environ Res. 2017;153.
32. van Ballegooijen AJ, Kestenbaum B, Sachs MC, de Boer IH, Siscovick DS, Hoofnagle AN, et al. Association of 25-hydroxyvitamin D and parathyroid hormone with incident hypertension: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol. 2014;63(12):1214–22.
33. Kang YM, Jung CH, Jang JE, Hwang JY, Kim EH, Park J-Y, et al. The association of incident hypertension with metabolic health and obesity status: definition of metabolic health does not matter. Clin Endocrinol (Oxf). 2016;85(2):207–15.
34. Tanner M. Antihypertensive drugs reduced risk for new-onset type 2 diabetes; effect varies by antihypertensive class. Ann Intern Med. 2022;175(4):JC44.
35. Dozio E, Maffioli E, Vianello E, Nonnis S, Grassi Scalvini F, Spatola L, et al. A Wide-Proteome Analysis to Identify Molecular Pathways Involved in Kidney Response to High-Fat Diet in Mice. Int J Mol Sci. 2022;23(7):3809.
36. General and abdominal adiposity and hypertension in eight world regions: a pooled analysis of 837 population-based studies with 7·5 million participants. Lancet. 2024;404(10455):851–63.
37. Quetglas-Llabrés MM, Monserrat-Mesquida M, Bouzas C, Gómez C, Mateos D, Ripoll-Vera T, et al. Inflammatory and Oxidative Stress Markers Related to Adherence to the Mediterranean Diet in Patients with Metabolic Syndrome. Antioxidants (Basel). 2022;11(5):901.
38. Che B, Zhong C, Zhang R, Pu L, Zhao T, Zhang Y, et al. Triglyceride-glucose index and triglyceride to high-density lipoprotein cholesterol ratio as potential cardiovascular disease risk factors: an analysis of UK biobank data. Cardiovasc Diabetol. 2023;22(1):34.
39. Chandramouli C, Tay WT, Bamadhaj NS, Tromp J, Teng T-HK, Yap JJL, et al. Association of obesity with heart failure outcomes in 11 Asian regions: A cohort study. PLoS Med. 2019;16(9):e1002916.
40. Liu Y, Liu X, Zhang S, Zhu Q, Fu X, Chen H, et al. Association of Anthropometric Indices With the Development of Diabetes Among Hypertensive Patients in China: A Cohort Study. Front Endocrinol. 2021;12: 736077.
41. Perla FM, Prelati M, Lavorato M, Visicchio D, Anania C. The Role of Lipid and Lipoprotein Metabolism in Non-Alcoholic Fatty Liver Disease. Children (Basel). 2017;4(6):46.
42. Sultani R, Tong DC, Peverelle M, Lee YS, Baradi A, Wilson AM. Elevated Triglycerides to High-Density Lipoprotein Cholesterol (TG/HDL-C) Ratio Predicts Long-Term Mortality in High-Risk Patients. Heart Lung Circ. 2020;29(3):414–21.
43. Nie G, Hou S, Zhang M, Peng W. High TG/HDL ratio suggests a higher risk of metabolic syndrome among an elderly Chinese population: a cross-sectional study. BMJ Open. 2021;11(3): e041519.
44. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743–53.
45. Yang X, Li J, Hu D, Chen J, Li Y, Huang J, et al. Predicting the 10-Year Risks of Atherosclerotic Cardiovascular Disease in Chinese Population: The China-PAR Project (Prediction for ASCVD Risk in China). Circulation. 2016;134(19):1430–40.
46. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71(6):1269–324.
47. McEvoy JW, McCarthy CP, Bruno RM, Brouwers S, Canavan MD, Ceconi C, et al. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. Eur Heart J. 2024;45(38):3912–4018.
48. Shi W-R, Wang H-Y, Chen S, Guo X-F, Li Z, Sun Y-X. Estimate of prevalent diabetes from cardiometabolic index in general Chinese population: a community-based study. Lipids Health Dis. 2018;17(1):236.
49. Zhu Y, Huang Y, Sun H, Chen L, Yu H, Shi L, et al. Novel anthropometric indicators of visceral obesity predict the severity of hyperlipidemic acute pancreatitis. Lipids Health Dis. 2024;23(1):120.
50. Lv D, Liu Z, Wu X, Xie F, Shang Q, Xie W, et al. Novel metabolic indicators and the risk of cardiovascular disease in patients with hypertension: A primary-care cohort study. Nutr Metab Cardiovasc Dis. 2024.
51. Tanaka A, Node K. Associations of metabolic disorders with hypertension and cardiovascular disease: recent findings and therapeutic perspectives. Hypertens Res. 2024;47(12):3338–44.
52. Li X, Sun M, Yang Y, Yao N, Yan S, Wang L, et al. Predictive Effect of Triglyceride Glucose-Related Parameters, Obesity Indices, and Lipid Ratios for Diabetes in a Chinese Population: A Prospective Cohort Study. Front Endocrinol (Lausanne). 2022;13: 862919.
53. Muir LA, Neeley CK, Meyer KA, Baker NA, Brosius AM, Washabaugh AR, et al. Adipose tissue fibrosis, hypertrophy, and hyperplasia: Correlations with diabetes in human obesity. Obesity (Silver Spring). 2016;24(3):597–605.
54. Verboven K, Wouters K, Gaens K, Hansen D, Bijnen M, Wetzels S, et al. Abdominal subcutaneous and visceral adipocyte size, lipolysis and inflammation relate to insulin resistance in male obese humans. Sci Rep. 2018;8(1):4677.
55. Das R, Giri J, P KP, Froelich N, Chinnadurai R, McCoy S, et al. A STAT5-Smad3 dyad regulates adipogenic plasticity of visceral adipose mesenchymal stromal cells during chronic inflammation. NPJ Regen Med. 2022;7(1):41.
56. Li F, Jiang M, Ma M, Chen X, Zhang Y, Zhang Y, et al. Anthelmintics nitazoxanide protects against experimental hyperlipidemia and hepatic steatosis in hamsters and mice. Acta Pharm Sin B. 2022;12(3):1322–38.
57. Naiemian S, Naeemipour M, Zarei M, Lari Najafi M, Gohari A, Behroozikhah MR, et al. Serum concentration of asprosin in new-onset type 2 diabetes. Diabetol Metab Syndr. 2020;12:65.
58. Pangrazzi L, Naismith E, Miggitsch C, Carmona Arana JA, Keller M, Grubeck-Loebenstein B, et al. The impact of body mass index on adaptive immune cells in the human bone marrow. Immun Ageing. 2020;17:15.
59. Chang L, Xiong W, Zhao X, Fan Y, Guo Y, Garcia-Barrio M, et al. Bmal1 in Perivascular Adipose Tissue Regulates Resting-Phase Blood Pressure Through Transcriptional Regulation of Angiotensinogen. Circulation. 2018;138(1):67–79.
60. Prola A, Blondelle J, Vandestienne A, Piquereau J, Denis RGP, Guyot S, et al. Cardiolipin content controls mitochondrial coupling and energetic efficiency in muscle. Sci Adv. 2021;7(1):eabd6322.
61. Van Herck MA, Vonghia L, Kwanten WJ, Julé Y, Vanwolleghem T, Ebo DG, et al. Diet Reversal and Immune Modulation Show Key Role for Liver and Adipose Tissue T Cells in Murine Nonalcoholic Steatohepatitis. Cell Mol Gastroenterol Hepatol. 2020;10(3):467–90.
62. Aljafary MA, Al-Suhaimi EA. Adiponectin System (Rescue Hormone): The Missing Link between Metabolic and Cardiovascular Diseases. Pharmaceutics. 2022;14(7).
63. Sun Y, Liu B, Snetselaar LG, Wallace RB, Caan BJ, Rohan TE, et al. Association of Normal-Weight Central Obesity With All-Cause and Cause-Specific Mortality Among Postmenopausal Women. JAMA Netw Open. 2019;2(7): e197337.
64. Duell PB, Welty FK, Miller M, Chait A, Hammond G, Ahmad Z, et al. Nonalcoholic Fatty Liver Disease and Cardiovascular Risk: A Scientific Statement From the American Heart Association. Arterioscler Thromb Vasc Biol. 2022;42(6):e168–85.
65. Mundal LJ, Igland J, Svendsen K, Holven KB, Leren TP, Retterstol K. Association of Familial Hypercholesterolemia and Statin Use With Risk of Dementia in Norway. JAMA Netw Open. 2022;5(4): e227715.
66. Aday AW, Lawler PR, Cook NR, Ridker PM, Mora S, Pradhan AD. Lipoprotein Particle Profiles, Standard Lipids, and Peripheral Artery Disease Incidence. Circulation. 2018;138(21):2330–41.
67. Kimura T, Kobiyama K, Winkels H, Tse K, Miller J, Vassallo M, et al. Regulatory CD4(+) T Cells Recognize Major Histocompatibility Complex Class II Molecule-Restricted Peptide Epitopes of Apolipoprotein B. Circulation. 2018;138(11):1130–43.
68. Amaral AL, Batista JP, Mariano IM, Goncalves LF, Tavares JB, de Souza AV, et al. Redox Status of Postmenopausal Women with Single or Multiple

Cardiometabolic Diseases Has a Similar Response to Mat Pilates Training. Antioxidants (Basel). 2022;11(8).
69. Wang R, Lu J, Yin J, Chen H, Liu H, Xu F, et al. A TEMPOL and rapamycin loaded nanofiber-covered stent favors endothelialization and mitigates neointimal hyperplasia and local inflammation. Bioact Mater. 2023;19:666–77.
70. Masenga SK, Kabwe LS, Chakulya M, Kirabo A. Mechanisms of Oxidative Stress in Metabolic Syndrome. Int J Mol Sci. 2023;24(9).
71. Min B-K, Oh CJ, Park S, Lee J-M, Go Y, Park B-Y, et al. Therapeutic effect of dichloroacetate against atherosclerosis via hepatic FGF21 induction mediated by acute AMPK activation. Exp Mol Med. 2019;51(10).
72. Tai H, Tong YJ, Yu R, Yu Y, Yao SC, Li LB, et al. A possible new activator of PI3K-Huayu Qutan Recipe alleviates mitochondrial apoptosis in obesity rats with acute myocardial infarction. J Cell Mol Med. 2022;26(12):3423–45.
73. Agbaje AO. Mediating role of body composition and insulin resistance on the association of arterial stiffness with blood pressure among adolescents: The ALSPAC study. Front Cardiovasc Med. 2022;9: 939125.
74. De Giorgi A, Marra AM, Iacoviello M, Triggiani V, Rengo G, Cacciatore F, et al. Insulin-like growth factor-1 (IGF-1) as predictor of cardiovascular mortality in heart failure patients: data from the T.O.S.CA. registry. Intern Emerg Med. 2022;17(6):1651–60.
75. Fang J, Wang F, Song H, Wang Z, Zuo Z, Cui H, et al. AMPKalpha pathway involved in hepatic triglyceride metabolism disorder in diet-induced obesity mice following Escherichia coli Infection. Aging (Albany NY). 2018;10(11):3161–72.
76. Hou B, He P, Ma P, Yang X, Xu C, Lam SM, et al. Comprehensive Lipidome Profiling of the Kidney in Early-Stage Diabetic Nephropathy. Front Endocrinol (Lausanne). 2020;11:359.

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