Lipids in Health and Disease

RESEARCH

Open Access

Association between metabolic score for insulin resistance (METS-IR) and hypertension: a cross-sectional study based on NHANES 2007–2018

Zhen Guo[1†], Xia Guo[1†], Hanchi Xu[1], Haoxuan Chu[1], Yulin Tian[1], Shipeng Wang[1] and Yushi Wang[1*]

Abstract

Background Insulin resistance (IR) reduces insulin efficacy and heightens the danger of cardiovascular diseases including hypertension. The Metabolic Score for Insulin Resistance (METS-IR), which is based on triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C), body mass index (BMI), and fasting glucose levels, provides a simpler way to assess IR. As the hypertension's prevalence increases, particularly in those with metabolic disorders, exploring the relationship between hypertension and METS-IR has become crucial.

Methods 16,310 individuals from the 2007–2018 National Health and Nutrition Examination Survey dataset was included. Hypertension was defined by asking participants about their medical history and blood pressure measurements. METS-IR was calculated as follows: ln([HDL-C (mg/dL)] × [2 × fasting glucose (mg/dL)] + TG (mg/dL) × BMI (kg/m^2)). The study adjusted for covariates like sex; age; race; poverty-income ratio; marital status; educational background; total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and serum creatinine levels; smoking; stroke; alcohol consumption; diabetes; and coronary heart disease (CHD). This study was conducted using a multi-factor regression model.

Results This research demonstrated a significant positive relationship between hypertension and METS-IR. Each 1-unit rise in METS-IR corresponds to a 3% higher chance of hypertension (odds ratio [OR], 1.03; 95% confidence interval [CI], 1.03–1.04). In model 3, METS-IR exhibited a notable correlation with hypertension (OR, 3.31; 95% CI, 2.64–4.14; $P < 0.001$). A threshold effect analysis demonstrated a nonlinear association. Finally, subgroup analyses supported the stability of the relationship between METS-IR and factors such as sex, race, alcohol consumption, CHD, smoking, and stroke ($P > 0.05$).

Conclusions METS-IR showed a strong relationship with hypertension and may be an important marker for evaluating metabolic health and the early hypertension danger.

†Zhen Guo and Xia Guo contributed equally to this work and should be considered co-first authors.

*Correspondence:
Yushi Wang
yushi@jlu.edu.cn

Full list of author information is available at the end of the article

Keywords METS-IR, Hypertension, NHANES, Cross-sectional study, HDL-C

Background

Insulin resistance (IR) is a tolerance state in which insulin loses its effectiveness in peripheral tissues. This can result in hyperinsulinemia and disrupt the balance between lipid and glucose metabolisms. IR is present in patients with metabolic syndrome and diabetes mellitus. In fact, IR is increasingly acknowledged as a major predictor of cardiovascular complications associated with diabetes, including autonomic heart disease, coronary heart disease (CHD), and diabetic cardiomyopathy. Recent research has highlighted that IR not only exacerbates these cardiovascular risks but contributes to a more complex interplay of metabolic disturbances, suggesting that its treatment could be pivotal in preventing diabetes-related heart disease and improving overall patient outcomes. Several prospective studies have demonstrated that both metabolic syndrome and Homeostatic Model Assessment for IR (HOMA-IR) are independent predictors of cardiovascular disease (CVD) [1–4]. Additionally, incorporating the Metabolic Score for Insulin Resistance (METS-IR) markedly enhanced the forecasting of CVD risk events compared to several conventional risk factors.

The prevalence of hypertension, one of the most important risk factors for CVD, has gradually increased in recent years. Beyond traditional hypertension risk factors, like high-salt and low-potassium diets, age, smoking, alcohol intake, and metabolism-related factors (e.g., being overweight or obese), psychological influences and other contributors are increasingly acknowledged as significant in its onset and advancement [5]. A Mendelian randomization analysis revealed a notable correlation between increased body mass index (BMI) and hypertension risk, suggesting a 49% increase in risk with every 5 kg/m² increase in BMI [6, 7]. Moreover, IR marked by hyperinsulinemia can enhance the multiplication of vascular smooth muscle cells and increase vascular stiffness, thereby accelerating aortic sclerosis and predisposing individuals to hypertension [8]. Moreover, insulin may directly or indirectly impair vasodilation while increasing oxidative stress and inflammatory processes in the vascular wall [9, 10]. Given that hypertension has a low prevalence threshold in which prehypertension and first-degree hypertension often go unnoticed, identifying additional metabolism-related indicators is crucial for understanding the complex etiology of hypertension and formulating multidimensional diagnostic and therapeutic approaches.

Bello-Chavolla et al. introduced a novel substitution index the METS-IR, to estimate insulin action, which was validated against the Euglycemic-Hyper insulinemic Clamp (EHC) [5]. This model was calculated using readily available parameters from routine tests, including BMI and triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and fasting glucose levels. Because it does not require a fasting insulin assessment, this method serves as a valuable tool for predicting diabetes events. Consequently, METS-IR is a relatively indirect yet simple measure that can also detect IR associated with the pathological elements of metabolic syndrome, such as visceral, intrahepatic, and intrapancreatic lipids [5]. Previous studies investigating the association between hypertension and METS-IR primarily focused on Asian populations [11, 12]; by increasing the sample size and confounders, the research sought to study the link pertaining to METS-IR and hypertension in U.S. individuals from the 2007–2018 National Health and Nutrition Examination Survey (NHANES) dataset.

Methods

Research cohort

Data was collected from the NHANES database, which evaluates nutritional and health conditions in the US. Comprehensive information pertaining to NHANES research design and data can be found on the Centers for Disease Control and Prevention (CDC) website.

The research utilized data from the 2007–2018 NHANES survey cycle, encompassing all information related to hypertension, along with the complete variables (BMI and HDL-C, TG, and fasting glucose levels) used to calculate the METS-IR. The preliminary analysis included 59,842 participants. However, participants for whom METS-IR data were lacking ($n = 41,950$) or for whom incomplete information on hypertensive disease was available ($n = 1,582$) were excluded, resulting in a final count of 16,310 participants. Further exclusion criteria included lack of data regarding diabetes ($n = 215$), smoking ($n = 8$), alcohol consumption ($n = 5,608$), marital status ($n = 5$), education ($n = 1,536$), CHD ($n = 22$), and stroke ($n = 14$). The analysis included 8,902 participants (Fig. 1).

METS-IR and hypertension defined

METS-IR was calculated as follows: ln [(2 × fasting glucose (mg/dL)) + TG (mg/dL)] × BMI (kg/m^2))/(ln[HDL-C (mg/dL)] (5). Later, the participants were categorized into four distinct groups based on METS-IR quartile: Group Q1 (< 33.77), Group Q2 (33.77–40.79), Group Q3 (40.79–49.52), and Group Q4 (> 49.52). This classification enables a comprehensive analysis of metabolic health across varying IR levels. For detailed information on the quality control measures applied to the laboratory tests, please refer to the NHANES guidelines available on the

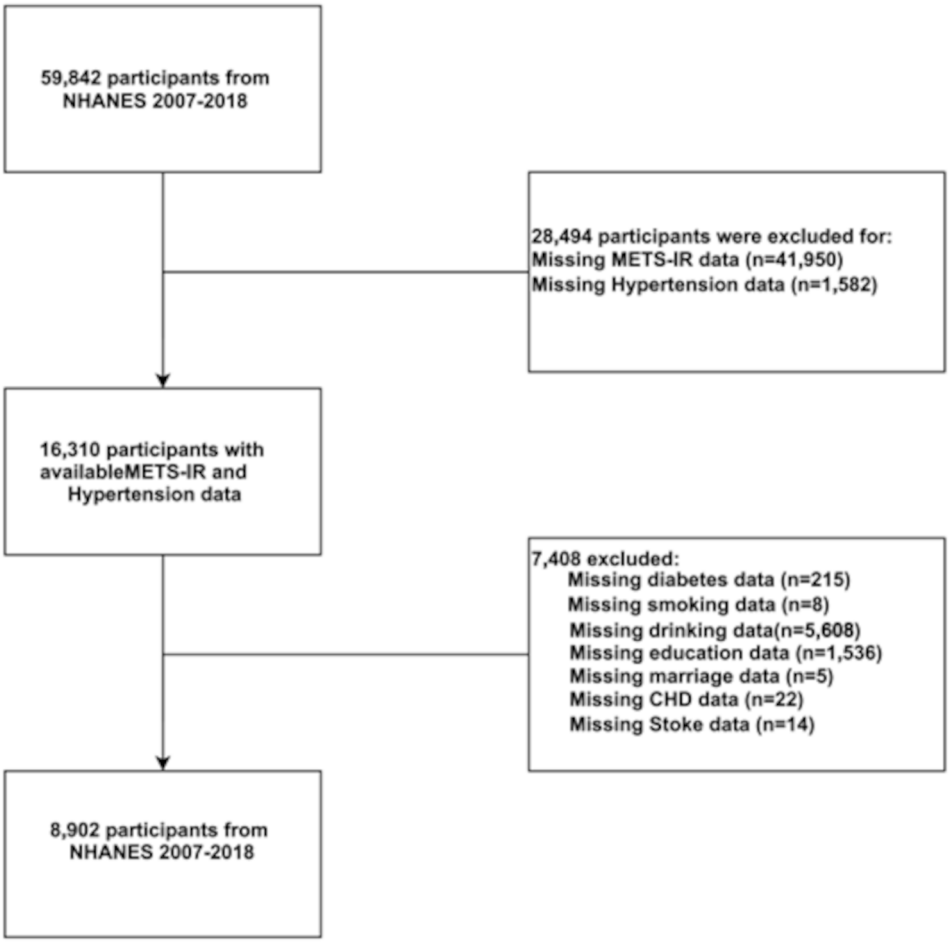

Fig. 1 Flowchart of participant selection process
CHD, coronary heart disease; METS-IR, Metabolic Score for Insulin Resistance; NHANES, National Health and Nutrition Examination Survey

CDC website. Hypertension was calculated according to the average of three consecutive blood pressure measurements and based on the participants' responses to a particular inquiry related to their medical history, i.e., "Has a doctor ever diagnosed you with hypertension?" If they gave an affirmative response and had a systolic blood pressure (SBP) ≥ 130 mmHg and/or a diastolic blood pressure (DBP) ≥ 80 mmHg, they were classified as having hypertension.

Covariates

This study examined the following covariates: sex (male/female), race, age (years), education level, HDL-C (mg/dL), BMI (kg/m^2), TG (mg/dL), fasting glucose (mg/dL), total cholesterol ([TC]; mg/dL), serum creatinine (mg/dL), low-density lipoprotein cholesterol ([LDL-C], mg/dL) and diabetes (defined using the query, "Has a doctor ever diagnosed you with diabetes?"), CHD (determined using the query, "Has a doctor ever diagnosed you with CHD?"), stroke (determined using the query, "Has a doctor ever diagnosed you with stroke?"), and smoking (identified through the query, "Have you smoked 100 or more cigarettes throughout your life?"), and alcohol consumption (characterized through the query, "In the past year, on the days when you consumed alcoholic beverages, what was your average number of drinks?"). Each participant's status was obtained through home interviews and categorized as never, former, current, or unknown. Comprehensive data collection methods for the variables are listed at www.cdc.gov/nchs/nhanes/.

Statistical analysis

Given the complexity of the NHANES sampling design, it is essential to incorporate sample weights, stratification, and clustering into all analyses of NHANES data. Owing to the oversampling of minority populations, each model was weighted using CDC-recommended weights to ensure an accurate representation. To obtain the most unbiased and accurate estimates of the effects on the population, the weights for the 2-year cycle were divided by six to generate new weights.

METS-IR metrics were used as independent variables to stratify the characteristics of the research population and relevant clinical indicators. One-way analysis of variance was used for the baseline variables. The means and standard deviations were computed for continuous variables, and categorical variables were expressed as frequencies and percentages. Furthermore, the study cohort was categorized into hypertensive and non-hypertensive groups based on participants' outcomes, and the baseline features of each population were compared using the statistical methods outlined above.

Results

Patients' baseline characteristics

The research enrolled 8,902 patients in total (Fig. 1), of whom 1,846 had hypertension. Baseline characteristics of cohort participants by hypertensive and nonhypertensive outcomes are shown in Table 1. The sample population's mean age was 45.9 ± 0.3 years; 52.1% of them were men. The mean METS-IR score was 42.4 ± 0.2. Older individuals; men; smokers; those with a high BMI, elevated triglycerides, or increased fasting glucose level; those with diabetes mellitus, CHD, or stroke; and those with lower education levels were found to have a higher probability of developing hypertension than their non-hypertensive counterparts($P < 0.05$). Importantly, the hypertensive group had notably elevated METS-IR levels compared to the non-hypertensive group (47.1 vs. 41.4, respectively; $P < 0.001$).

Association between METS-IR and hypertension

This research revealed a notable positive relationship between hypertension and METS-IR. In continuous variable analysis, each 1-unit rise in METS-IR corresponded to 3% higher risk of hypertension (odds ratio [OR], 1.03; 95% confidence interval [CI], 1.03–1.04). The fully adjusted model revealed a 3% increased risk (OR, 1.03; 95% CI, 1.03–1.04). Statistically significant results were found in all trend tests across Models 1, 2, and 3. For the sensitivity analysis, METS-IR was categorized into quartiles (Table 2). In Model 1 (unadjusted), individuals in the upper quartile had a 3.67 times greater likelihood of developing hypertension compared to individuals in the lowest quartile (OR, 3.67; 95% CI, 2.95–4.55; $P < 0.001$). In Model 2, the OR increased to 3.66 after the control for sex, age, and race (95% CI, 2.91–4.60; $P < 0.001$). Furthermore, in Model 3, adding educational background, marriage, drinking, smoking, history of CHD, stroke and diabetes, revealed a compelling link between increased METS-IR levels and an enhanced chance of hypertension (OR, 3.31; 95% CI, 2.64–4.14; $P < 0.001$).

Nonlinearity and threshold effect analysis of METS-IR and hypertension

This research applied a smoothed curve fit to illustrate the nonlinear relationship between hypertension and METS-IR (Fig. 2). All variables adjusted in the analysis were sex, age, ethnicity, marital status, educational background, poverty-to-income ratio (PIR), serum creatinine, LDL-C, TC, CHD, diabetes mellitus, stroke, alcohol consumption, and smoking status. Figure 2 illustrates the curve trends at varying METS-IR levels. Within the lower METS-IR range, the likelihood of hypertension increased as METS-IR level increased. In the high range (> 65.13), the risk plateaus or exhibits a decreasing tendency. Moreover, the CI were significantly wider, possibly because of the decrease in sample size or increased variability in the data distribution.

Finally, further analyses were conducted using various models (standard and segmented linear models) (Table 3). A positive relationship between hypertension and METS-IR was consistently observed; however, nonlinear characteristics were also evident. In the standard linear model, the adjusted OR was 1.03 (95% CI, 1.03–1.04; $P < 0.001$). Each 1-level rise in METS-IR corresponded to a 3% greater chance of developing hypertension.

In the segmented model, the inflection points were identified at 45.12 and 75.65. When METS-IR was < 65.13, the OR of 1.04 (95% CI, 1.03–1.05) and $P < 0.001$ revealed a positive connection with hypertension. For the range of METS-IR ≥ 65.13, the P-value of 0.536 implied that the relationship lacked statistical significance. When the METS-IR exceeds a specific threshold (e.g., 81.67), its marginal effect on hypertension diminishes or even disappears. Thus, the segmented model outperformed the standard linear model ($P < 0.001$).

Subgroup analysis

Finally, subgroup analyses were performed to determine whether the association between hypertension risk and METS-IR was stable under various demographic circumstances. The data demonstrated the robustness of METS-IR and various other factors, including sex, race, CHD, stroke, smoking, and drinking ($P > 0.05$) (Table 4). Nevertheless, METS-IR was significantly correlated with hypertension with respect to age, diabetes, PIR, education level, and marital status ($P < 0.05$).

Discussion

By examining the data of 8,902 participants, this retrospective study observed a notable positive relationship between METS-IR and hypertension. Notably, sex, race, alcohol consumption, CHD, smoking, and stroke were not associated with this correlation.

Table 1 Weighted baseline characteristics of hypertensive versus non-hypertensive groups

Variable	Overall (*N* = 8,902)	Hypertensive (*n* = 1,846)	Non-hypertensive (*n* = 7,056)	*P*-value
Age (years), mean ± SD	45.93 ± 0.29	55.88 ± 0.40	43.78 ± 0.31	< 0.001
Sex, n (%)				0.007
Male	4,622 (51.89%)	1,017 (55.62%)	3,605 (51.09%)	
Female	4,280 (48.11%)	829 (44.38%)	3,451 (48.91%)	
Race, n (%)				< 0.001
Mexican-American	714 (8.03%)	101 (5.24%)	613 (8.63%)	
Other Hispanic	492 (5.53%)	79 (4.25%)	413 (5.81%)	
Non-Hispanic White	6,244 (70.15%)	1,320 (71.63%)	4,924 (69.82%)	
Non-Hispanic Black	872 (9.78%)	255 (14.22%)	617 (8.82%)	
Other, including multiple	580 (6.52%)	91 (4.67%)	489 (6.91%)	
Education level, n (%)				< 0.001
< 9th grade	283 (3.18%)	64 (3.51%)	219 (3.11%)	
9-11th grade (includes 12th grade with no diploma)	828 (9.30%)	187 (10.16%)	641 (9.12%)	
High school diploma/GED	1,921 (21.58%)	448 (24.29%)	1,473 (21.00%)	
Some college or 2-year degree	2,879 (32.33%)	637 (34.56%)	2,242 (31.84%)	
College degree or beyond	2,991 (33.61%)	510 (27.48%)	2,481 (34.94%)	
Marital status, n (%)				< 0.001
Married	4,924 (55.32%)	1,056 (57.67%)	3,868 (54.82%)	
Widowed	350 (3.91%)	149 (8.85%)	201 (2.85%)	
Divorced	961 (10.80%)	222 (12.25%)	739 (10.48%)	
Separated	181 (2.03%)	50 (2.82%)	131 (1.86%)	
Never married	1,671 (18.78%)	219 (10.48%)	1,452 (20.58%)	
Living with partner	815 (9.15%)	150 (7.93%)	665 (9.41%)	
PIR	3.12 ± 0.04	3.12 ± 0.07	3.12 ± 0.04	0.993
BMI (kg/m^2)	28.73 ± 0.11	31.02 ± 0.22	28.23 ± 0.12	< 0.001
HDL-C (mg/dL)	55.11 ± 0.33	53.84 ± 0.65	55.39 ± 0.34	0.018
TG (mg/dL)	122.07 ± 1.45	144.75 ± 3.19	117.16 ± 1.57	< 0.001
Fasting glucose (mg/dL)	105.17 ± 0.42	116.88 ± 1.29	102.64 ± 0.40	< 0.001
METS-IR	42.44 ± 0.22	47.08 ± 0.41	41.43 ± 0.24	< 0.001
SBP (mmHg)	120.42 ± 0.25	134.92 ± 0.65	117.28 ± 0.22	< 0.001
DBP (mmHg)	70.16 ± 0.22	75.36 ± 0.44	69.03 ± 0.22	< 0.001
Serum creatinine (mg/dL)	126.80 ± 1.37	124.01 ± 1.47	127.41 ± 1.47	0.229
TC (mg/dL)	193.39 ± 0.26	193.40 ± 0.78	193.39 ± 0.23	0.980
LDL-c (mg/dL)	113.86 ± 0.53	114.18 ± 1.24	113.80 ± 0.60	0.785
Diabetes, n (%)				< 0.001
Yes	706 (7.61%)	322 (17.52%)	384 (5.47%)	
No	8,196 (92.39%)	1,524 (82.48%)	6,672 (94.53%)	
CHD, n (%)				< 0.001
Yes	269 (2.89%)	119 (6.41%)	150 (2.12%)	
No	8,633 (97.11%)	1,727 (93.59%)	6,906 (97.88%)	
Stroke, n (%)				< 0.001
Yes	175 (1.88%)	77 (4.15%)	98 (1.38%)	
No	8,727 (98.12%)	1,769 (95.85%)	6,958 (98.62%)	
Smoking, n (%)				< 0.001
Yes	4,244 (47.27%)	1,031 (55.62%)	3,213 (45.46%)	
No	4,658 (52.73%)	815 (44.38%)	3,843 (54.54%)	
Alcohol consumption (drinks/day), n (%)				0.345
≤ 5	8,088 (90.83%)	1,692 (91.61%)	6,396 (90.66%)	
> 5	814 (9.17%)	154 (8.39%)	660 (9.34%)	

BMI, body mass index; CHD, coronary heart disease; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; METS-IR, metabolic score for insulin resistance; PIR, poverty-to-income ratio; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides

Continuous variables are described as weighted mean ± standard deviation, while categorical variables are presented as unweighted n (%)

Table 2 Weighted association of METS-IR with hypertension in different models among all participants

Exposure	Model 1	Model 2	Model 3
	OR (95% CI), *P*-value	**OR (95% CI), *P*-value**	**OR (95% CI), *P*-value**
Continuous	1.50 (1.40–1.60), < 0.001	1.52 (1.41–1.63), < 0.001	1.46 (1.36–1.58), < 0.001
METS-IR quartile			
Q1	Reference	Reference	Reference
Q2	1.86 (1.49–2.34), < 0.001	1.64 (1.28–2.11), < 0.001	1.61 (1.27–2.06), < 0.001
Q3	2.30 (1.84–2.87), < 0.001	2.07 (1.63–2.64), < 0.001	2.01 (1.57–258), < 0.001
Q4	3.67 (2.95–4.55), < 0.001	3.66 (2.91–4.60), < 0.001	3.31 (2.64–4.14), < 0.001
P for trend	1.03 (1.03–1.04), < 0.001	1.04 (1.03–1.04), < 0.001	1.03 (1.03–1.04), < 0.001

CI, confidence interval; METS-IR, Metabolic Score for Insulin Resistance; OR, odds ratio

Note: In the multivariate analysis, the visceral adiposity index was converted from a continuous for categorical variables (tertiles)

Model 1: no covariates adjusted

Model 2: adjusted for age, sex, and race

Model 3: adjusted for the covariates in Model 2 as well as education level, marital status, poverty-to-income ratio, serum creatinine, total cholesterol, low-density lipoprotein cholesterol, smoking, alcohol consumption, stroke, coronary heart disease, and diabetes

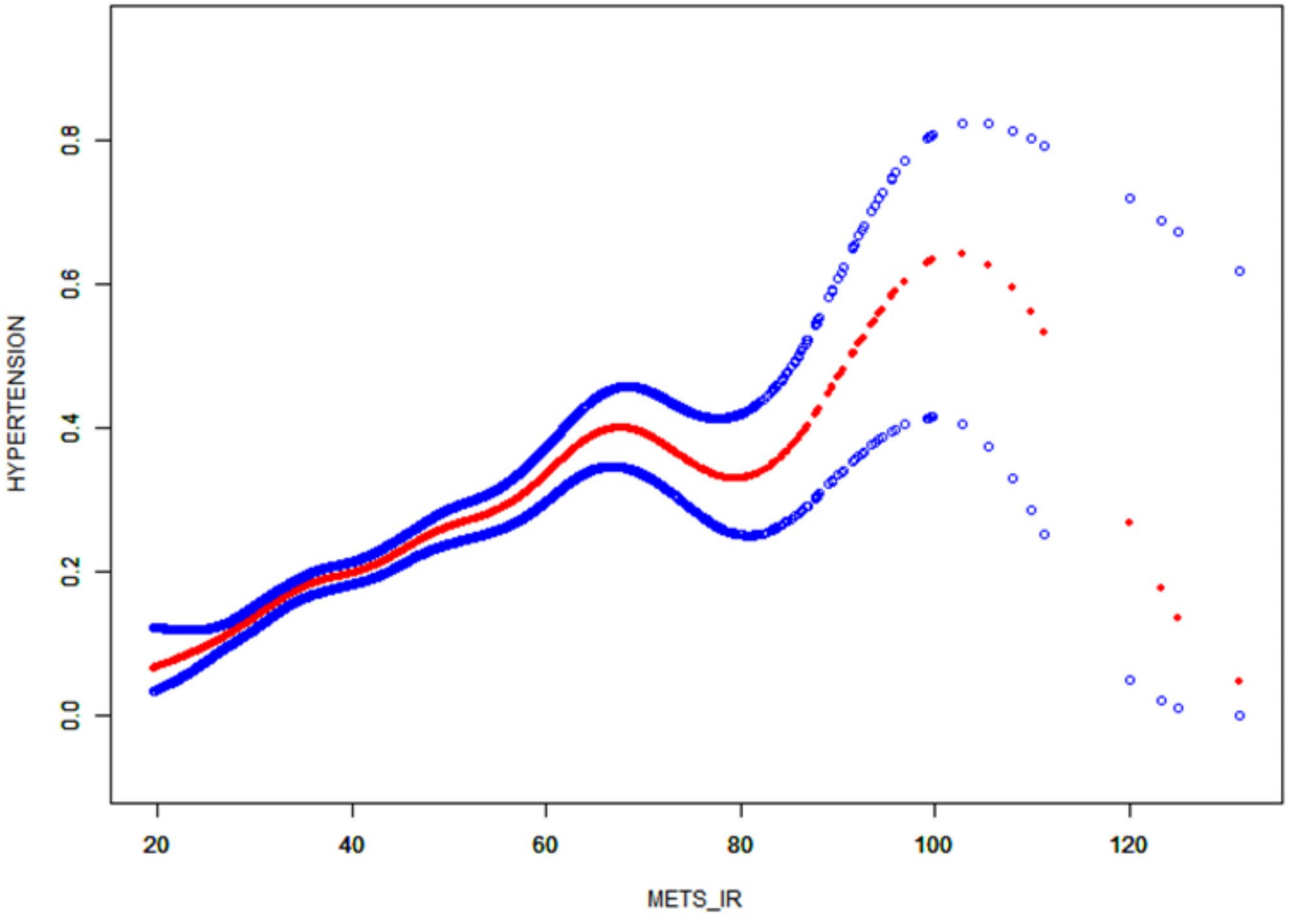

Fig. 2 Association between METS-IR and hypertension
METS-IR, Metabolic Score for Insulin Resistance
Note: The solid red line represents the fit between the variables, while the blue bands represent the 95% confidence intervals. The smooth curve was adjusted for covariates including age, sex, race, education level, marital status, poverty-to-income ratio, serum creatinine level, total cholesterol level, low-density lipoprotein cholesterol level, smoking, alcohol consumption, stroke, coronary heart disease, and diabetes status

Table 3 Threshold effect analysis of METS-IR and hypertension

METS-IR	Adjusted OR (95% CI), *P*-value
Fitting by the standard linear model	1.03 (1.03–1.04), < 0.001
Fitting by the three-piecewise model	
Inflection point	65.13–81.67
METS-IR < 65.13	1.04 (1.03–1.05), < 0.001
65.13 ≤ METS-IR < 81.67	0.99 (0.96–1.02), < 0.536
METS-IR ≥ 81.67	1.01 (0.97–1.06), 0.610
P for log-likelihood ratio	< 0.001

CI, confidence interval; METS-IR, Metabolic Score for Insulin Resistance; OR, odds ratio

Note: The data were adjusted for age, sex, race, educational level, marital status, poverty-to-income ratio, serum creatinine, total cholesterol, low-density lipoprotein cholesterol, smoking, alcohol consumption, coronary heart disease, angina, stroke, and diabetes

The HOMA-IR, benchmarked against the EHC, is widely adopted approach to evaluating IR in both clinical and epidemiological contexts. While HOMA-IR provides a practical approach to estimating IR, its reliance on fasting insulin levels may limit its precision compared to EHC. Nonetheless, EHC remains an invasive procedure whose practical application is constrained by high cost. Therefore, alternative indicators of IR based on fasting insulin and non-insulin measures are required [12–14]. The METS-IR has gained widespread recognition for its role in assessing cardiovascular health. Its utility across diverse populations underscores its potential to enhance early detection and preventive care in cardiovascular health management. Here the research demonstrated the robustness of the primary findings concerning METS-IR and various variables like race, sex, marriage, PIR, CHD, stroke, drinking and smoking ($P > 0.05$) (Table 4).

Previous research has explored how METS-IR is related to CVD and whether METS-IR has the potential to predict adverse cardiovascular outcomes. In a cross-sectional study involving 14,653 people, Duan et al. identified a notable connection between METS-IR and all-cause together with cardiovascular mortality, noting that this relationship exhibited a nonlinear, U-shaped trend [15]. Moreover, the Su et al. cross-sectional study involving 14,772 people, further demonstrated a notable positive relationship between heart failure (HF) and METS-IR (each 1-unit increase: OR, 2.44; 95% CI, 1.38–4.32). Through a smoothing curve-fitting analysis, they identified the saturation effect between HF and METS-IR, presenting as a J-shaped curve [16]. This finding suggests that, while an initial rise in METS-IR is linked to a higher HF danger, there may be a threshold beyond which the risk stabilizes or decreases, indicating a complex interplay between metabolic health and cardiovascular outcomes.

Such insights align with the recent literature emphasizing the need for a nuanced understanding of how metabolic indices influence heart health and highlighting the

Table 4 Weighted subgroup analysis of association between METS-IR and hypertension

Variable	OR (95% CI), *P*-value	*P*-interaction
Age (years)		< 0.001
≤ 40	1.05 (1.04–1.06), < 0.001	
> 40 to ≤ 60	1.02 (1.01–1.04), < 0.001	
> 60	1.02 (1.01–1.04), < 0.001	
Sex		0.646
Male	1.04 (1.03–1.05), < 0.001	
Female	1.03 (1.03–1.04), < 0.001	
Race		0.430
Mexican-American	1.04 (1.02–1.06), < 0.001	
Other Hispanic	1.04 (1.02–1.05), < 0.001	
Non-Hispanic White	1.04 (1.03–1.04), < 0.001	
Non-Hispanic Black	1.03 (1.02–1.04), < 0.001	
Other, including multiple	1.05 (1.03–1.07), < 0.001	
Education level		< 0.001
< 9th grade	1.04 (1.02–1.06), < 0.001	
9–11th grade (Includes 12th grade without diploma)	1.03 (1.01–1.05), 0.004	
High school graduate/GED	1.01 (1.00–1.03), 0.058	
Some college or 2-year degree	1.04 (1.03–1.05), < 0.001	
College degree or beyond	1.05 (1.04–1.06), < 0.001	
Marital status		0.037
Married	1.04 (1.03–1.05), < 0.001	
Widowed	1.00 (0.98–1.03), 0.702	
Divorced	1.03 (1.01–1.05), < 0.001	
Separated	1.02 (0.99–1.04), 0.219	
Never married	1.03 (1.02–1.04), < 0.001	
Living with partner	1.03 (1.01–1.05), 0.006	
Poverty-to-income ratio		0.009
≤ 1	1.02 (1.01–1.03), 0.005	
> 1 to ≤ 3	1.03 (1.02–1.04), < 0.001	
> 3	1.04 (1.03–1.05), < 0.001	
Diabetes		0.030
Yes	1.02 (1.00–1.04), 0.024	
No	1.05 (1.04–1.05), < 0.001	
Coronary heart disease		0.612
Yes	1.04 (1.02–1.06), < 0.001	
No	1.03 (1.03–1.04), < 0.001	
Stroke		0.508
Yes	1.02 (0.99–1.06), 0.119	
No	1.04 (1.03–1.04), < 0.001	
Smoking		0.337
Yes	1.02 (1.00–1.05), < 0.001	
No	1.04 (1.03–1.04), < 0.001	
Alcohol consumption, drinks/day		0.09
≤ 5	1.05 (1.04–1.05), < 0.001	
> 5	1.03 (1.01–1.05), 0.012	

CI, confidence interval; METS-IR, Metabolic Score for Insulin Resistance; OR, odds ratio

potential for tailored interventional strategies aimed at optimizing METS-IR to ensure better cardiovascular outcomes. Furthermore, a wealth of research suggests that METS-IR can predict hypertension [17, 18]. Using data from the 2007–2018 NHANES database, the research is the first to demonstrate that hypertensive individuals exhibit significantly higher METS-IR levels than non-hypertensive individuals. This finding supports previous research [19, 20] and further supports METS-IR as a promising instrument for heart-related risk evaluations in hypertensive populations.

The fully adjusted model demonstrated a notable positive link between METS-IR and hypertension, pointing that increased METS-IR levels contribute to a higher risk of hypertension, which may involve several mechanisms. Blood pressure is influenced by three primary factors: blood volume, vascular wall tone, and kinetic energy generated by the cardiac ejection. In most individuals, a reduction in vascular wall tone with age coupled with various other risk factors is the main mechanism underlying the development of hypertension [21]. High METS-IR levels indicate a response to this reduction in vascular wall tone. IR contributes to hyperinsulinemia, overstimulation of the sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS), adverse inflammatory responses, increased oxidative stress, dyslipidemia, obesity, and adipocyte dysfunction. The increase in adipocyte-derived inflammatory cytokines in the circulation in turn increases vascular IR, which recruits and activates pro-inflammatory immune cells within the vasculature, ultimately contributing to increased arterial stiffness.

Visceral adipose tissue (VAT) is a type of fat that surrounds the internal organs. The latest research has demonstrated its relationship with inflammation, metabolic abnormalities [22], and residual risk of CVD (i.e., the remaining danger of CVD after accounting for predisposing causes). An increase in VAT can lead to the dysregulated secretion of various biologically active molecules and pro-inflammatory cytokines including leptin, aldosterone, angiotensinogen, interleukin 6, tumor necrosis factor alpha, and resistin [22]. These imbalances contribute to systemic inflammation, IR, and cardiovascular dysfunction, exacerbating metabolic disorders and increasing the risk of related complications. The IR and hypertensive groups tended to have high VAT levels, increased IR, and enhanced lipolytic activity within the VAT that generated more free fatty acids, which could further harm the endothelium and promote endothelial dysfunction and vascular stiffness. Therefore, the negative effects of VAT on cardiovascular health may be exacerbated. Furthermore, the perivascular adipose tissue, which provides structural support to most arteries and secretes paracrine molecules that affect the vasculature, can become dysfunctional, leading to extracellular matrix remodeling, local RAAS activation, and, ultimately, vascular stiffness. This dysfunction is central to the progression of CVD and chronic kidney diseases [23–26].

Other studies indicated that electron transport chain function in the submuscular mitochondria is significantly impaired in individuals with IR. This reduction affects crucial cellular processes such as such as the transport of glucose, oxidation of fatty acids, and maintenance of insulin signaling, contributing to metabolic dysfunction [27–31]. The combined impact of these alterations disrupts autoregulation of the vascular tone and heightens vascular resistance. Meanwhile, insulin's antidiuretic effects the kidney's ability to retain sodium and water, promote fluid overload, and subsequently contribute to hypertension [32].

Additionally, the threshold effect analysis provided deeper insight into the link between hypertension and METS-IR. This study found a positive link between the hypertension development and METS-IR; however, this relationship exhibited nonlinear characteristics. The influence of IR on hypertension was more significant at lower and moderate METS-IR levels but attenuated at higher levels, likely due to inadequate sample size compensation by other metabolic mechanisms. Individuals with a high METS-IR may have other concurrent risk factors (e.g., abnormal renal function, severe obesity, or medication use) [33]. Thus, METS-IR may offer significant insight into a patient's risk of hypertension during the pre-disease phase.

Strengths and limitations

The study has several advantages. A key strength of this study is the utilization of NHANES database repository gathered through a stratified, multistage probability sampling technique that provides a substantial sample size and strong national representativeness. Furthermore, potential confounding factors were controlled such as sex, years, race, marital status, degree of education, tobacco and alcohol consumption, and the presence of brain attack, CHD, and glycemic disorder to minimize confounding effects and obtain more reliable results. Finally, the consistency of the relationship in different populations was assessed by subgroup analysis.

Although this study provided valuable insights, it has some limitations. First, as the NHANES data were cross-sectional, causal relationships could not be established. Second, while some confounding factors were controlled for, the potential impact of unrecognized or unmeasured confounders could not be completely excluded. Third, because of database limitations, the study was confined to a US population, and data on hypertension grades were not available. Therefore, this study could not value

the link pertaining to METS-IR and the degree or stage of hypertension, indicating a need for further investigation.

Conclusions

The research found a strong positive relationship between hypertension and METS-IR. These results highlight the importance of managing and monitoring METS-IR components, including BMI and HDL-C, TG, and fasting glucose levels, to enhance hypertension risk assessments and optimize interventions to help guide early lifestyle interventions, such as dietary modifications and physical activity, and develop prevention strategies in populations with metabolic disorders and IR to prevent the hypertension's progression.

Abbreviations

BMI	Body mass index
CDC	Centers for Disease Control and Prevention
CHD	Coronary heart disease
CI	Confidence interval
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
EHC	Euglycemic-hyperinsulinemic clamp
HDL-C	High-density lipoprotein cholesterol
HF	Heart failure
HOMA-IR	Homeostatic Model Assessment for Insulin Resistance
IR	Insulin resistance
LDL-C	Low-density lipoprotein cholesterol
METS	Metabolic syndrome
METS-IR	Metabolic Score for Insulin Resistance
NHANES	National Health and Nutrition Examination Survey
OR	Odds radio
PIR	Poverty-to-income ratio
SBP	Systolic blood pressure
TC	Total cholesterol
TG	Triglycerides
RAAS	Renin-angiotensin-aldosterone system
VAT	Visceral adipose tissue

Acknowledgements

The authors acknowledge the assistance of other individuals and organizations in the data collection and analysis processes and in terms of technical expertise. Finally, we express our gratitude to friends and family for their constant support and understanding throughout this study.

Author contributions

The authors' roles are outlined as follows: ZG and XG oversaw the overall research design and the presentation of the final manuscript; HC and XH performed data analyses and drafted the initial version of the paper; SW and YT were responsible for designing the figures and revising the study manuscript. All authors consented to the final version of the article.

Funding

Neither this study nor the authors of this paper were funded.

Data availability

The data involved in this research are listed in publicly accessible online repositories. Detailed access information can be found in www.cdc.gov/nchs/nhanes/.

Declarations

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Cardiovascular Medicine, The First Hospital of Jilin University, Changchun 130021, China

Received: 17 December 2024 / Accepted: 16 February 2025
Published online: 21 February 2025

References

1. Gast KB, Tjeerdema N, Stijnen T, Smit JWA, Dekkers OM. Insulin resistance and risk of incident cardiovascular events in adults without diabetes: Meta-analysis. Hernandez AV, editor. PLoS ONE. 2012;7:e52036.
2. Jeppesen J, Hansen TW, Rasmussen S, Ibsen H, Torp-Pedersen C, Madsbad S. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease. J Am Coll Cardiol. 2007;49:2112–9.
3. Tenenbaum A, Adler Y, Boyko V, Tenenbaum H, Fisman EZ, Tanne D, et al. Insulin resistance is associated with increased risk of major cardiovascular events in patients with preexisting coronary artery disease. Am Heart J. 2007;153:559–65.
4. Yun JE, Won S, Sung J, Jee SH. Impact of metabolic syndrome independent of insulin resistance on the development of cardiovascular disease. Circ J. 2012;76:2443–8.
5. Bello-Chavolla OY, Almeda-Valdes P, Gomez-Velasco D, Viveros-Ruiz T, Cruz-Bautista I, Romo-Romo A, et al. METS-IR, a novel score to evaluate insulin sensitivity, is predictive of visceral adiposity and incident type 2 diabetes. Eur J Endocrinol. 2018;178:533–44.
6. Kim MS, Kim WJ, Khera AV, Kim JY, Yon DK, Lee SW, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and mendelian randomization studies. Eur Heart J. 2021;42:3388–403.
7. Zhao M, Bovet P, Xi B. Weight status change from adolescence to young adulthood and the risk of hypertension and diabetes mellitus. Hypertension. 2020;76:583–8.
8. McEniery CM, Wilkinson IB, Johansen NB, Witte DR, Singh-Manoux A, Kivimaki M, et al. Nondiabetic glucometabolic status and progression of aortic stiffness: the whitehall II study. Diabetes Care. 2017;40:599–606.
9. Anfossi G, Russo I, Doronzo G, Trovati M. Contribution of insulin resistance to vascular dysfunction. Arch Physiol Biochem. 2009;115:199–217.
10. Potenza MA, Addabbo F, Montagnani M. Vascular actions of insulin with implications for endothelial dysfunction. Endocrinol Metab. 2009;297.
11. Liu XZ, Fan J, Pan SJ. METS-IR, a novel simple insulin resistance indexes, is associated with hypertension in normal-weight Chinese adults. J Clin Hypertens. 2019;21:1075–81.
12. Han K-Y, Gu J, Wang Z, Liu J, Zou S, Yang C-X, et al. Association between METS-IR and prehypertension or hypertension among normoglycemia subjects in Japan: a retrospective study. Front Endocrinol. 2022;13:851338.
13. Manley SE, Stratton IM, Clark PM, Luzio SD. Comparison of 11 human insulin assays: implications for clinical investigation and research. Clin Chem. 2007;53:922–32.
14. Roberts LD, Koulman A, Griffin JL. Towards metabolic biomarkers of insulin resistance and type 2 diabetes: progress from the metabolome. Lancet Diabetes Endocrinol. 2014;2:65–75.
15. Duan M, Zhao X, Li S, Miao G, Bai L, Zhang Q, et al. Metabolic score for insulin resistance (METS-IR) predicts all-cause and cardiovascular mortality in the general population: evidence from NHANES 2001–2018. Cardiovasc Diabetol. 2024;23:243.
16. Su X, Zhao C, Zhang X. Association between METS-IR and heart failure: a cross-sectional study. Front Endocrinol. 2024;15:1416462.
17. Zhang Z, Zhao L, Lu Y, Meng X, Zhou X. Association between non-insulin-based insulin resistance indices and cardiovascular events in patients undergoing percutaneous coronary intervention: a retrospective study. Cardiovasc Diabetol. 2023;22:161.
18. Yoon J, Jung D, Lee Y, Park B. The metabolic score for insulin resistance (METS-IR) as a predictor of incident ischemic heart disease: a longitudinal study among Korean without diabetes. J Pers Med. 2021;11:742.
19. Yang W, Cai X, Hu J, Wen W, Mulalibieke H, Yao X, et al. The metabolic score for insulin resistance (METS-IR) predicts cardiovascular disease and its subtypes in patients with hypertension and obstructive sleep apnea. CLEP. 2023;15:177–89.
20. Bello-Chavolla OY, Antonio-Villa NE, Vargas-Vázquez A, Martagón AJ, Mehta R, Arellano-Campos O, et al. Prediction of incident hypertension and arterial

stiffness using the non–insulin-based metabolic score for insulin resistance (METS-IR) index. J Clin Hypertens. 2019;21:1063–70.
21. Antonopoulos AS, Margaritis M, Coutinho P, Shirodaria C, Psarros C, Herdman L et al. Adiponectin as a link between type 2 diabetes mellitus and vascular NADPH-oxidase activity in the human arterial wall: the regulatory role of perivascular adipose tissue.
22. Cesaro A, De Michele G, Fimiani F, Acerbo V, Scherillo G, Signore G, et al. Visceral adipose tissue and residual cardiovascular risk: a pathological link and new therapeutic options. Front Cardiovasc Med. 2023;10:1187735.
23. Aroor AR, Whaley-Connell A, Sowers JR. Utility of obesity and metabolic dyslipidemia (a non-insulin based determinate of the metabolic syndrome and insulin resistance) in predicting arterial stiffness. J Clin Hypertens. 2019;21:1071–4.
24. DeMarco VG, Aroor AR, Sowers JR. The pathophysiology of hypertension in patients with obesity. Nat Rev Endocrinol. 2014;10:364–76.
25. Jia G, Jia Y, Sowers JR. Contribution of maladaptive adipose tissue expansion to development of cardiovascular disease. In: Terjung R, editor. Comprehensive Physiology [Internet]. 1st ed. Wiley; 2016 [cited 2024 Oct 14]. pp. 253–62. Available from: https://onlinelibrary.wiley.com/doi/https://doi.org/10.1002/cphy.c160014
26. Lastra G, Manrique C. Perivascular adipose tissue, inflammation and insulin resistance: link to vascular dysfunction and cardiovascular disease. Horm Mol Biol Clin Investig. 2015;22:19–26.
27. Hood DA. Invited review: contractile activity-induced mitochondrial biogenesis in skeletal muscle. J Appl Physiol. 2001;90:1137–57.
28. Kelley DE, He J, Menshikova EV, Ritov VB. Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. Diabetes. 2002;51:2944–50.
29. Petersen KF, Dufour S, Befroy D, Garcia R, Shulman GI. Impaired mitochondrial activity in the insulin-resistant offspring of patients with type 2 diabetes. N Engl J Med. 2004;350:664–71.
30. Ritov VB, Menshikova EV, He J, Ferrell RE, Goodpaster BH, Kelley DE. Deficiency of subsarcolemmal mitochondria in obesity and type 2 diabetes. Diabetes. 2005;54:8–14.
31. Savage DB, Petersen KF, Shulman GI. Disordered lipid metabolism and the pathogenesis of insulin resistance. Physiol Rev. 2007;87:507–20.
32. Nakamura M, Satoh N, Suzuki M, Kume H, Homma Y, Seki G, et al. Stimulatory effect of insulin on renal proximal tubule sodium transport is preserved in type 2 diabetes with nephropathy. Biochem Biophys Res Commun. 2015;461:154–8.
33. Himanshu Garg N, Batra G, Singh A, Mujral. Hypertension and diabetes mellitus: coprediction and time trajectories. Indian J Public Health Res Dev. 2022;13:102–6.

Publisher's note