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Cardiovascular anthropometry for large scale population studies

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Cardiovascular anthropometry for large scale population studies

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Editorial: Cardiovascular anthropometry for large scale population studies

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Editorial on the Research Topic
Cardiovascular anthropometry for large scale population studies

Obesity and overweight are associated with development of cardiovascular diseases (CVD) such as hypertension, diabetes mellitus (DM), and the metabolic syndrome, as well as clinical conditions resulting from the consequent atherosclerotic cardiovascular diseases like stroke, heart attacks and peripheral artery disease. According to the World Health Organization (WHO), obesity, and overweight refer to abnormal or excessive fat accumulating in the body, which in turn impact negatively on health. This realization that overweight and obesity have an adverse effect on health has been recognized as far back as the 6th century BC. The WHO therefore came up with the body mass index (BMI) as measure of overweight and obesity for use in epidemiological studies.

This issue of Frontiers in Cardiovascular Medicine is dedicated to articles in Cardiovascular anthropometry and simple affordable non-anthropometric measures that tend to refine the age long WHO recommended measure, BMI making it more predictive of cardiometabolic diseases.

Whereas Agbo et al. (1) came up with a new index called the Abdominal Height which they recommended for wide scale use in sub-Saharan Africa, several other workers have, utilizing existing anthropometric measures come up with indices predictive of cardiovascular disease risk.

One is the weight adjusted waist circumference index, a quotient of waist circumference and square root of weight. It is a simple surrogate for fat mass accumulation. Applying it to the NHANES data of 1999–2018, Zhang et al. were able to show a linear and significant association with prevalence of heart failure. This has been known and as stated by Koparkar and Biswas (2) cardiomyopathy results as a direct consequence of fat in what has been called adipositas cordis.

Vascular calcification, a measure of severity of atherosclerotic cardiovascular disease is becoming of high utility in predicting higher cardiovascular disease burden. This is most evident with coronary artery disease (3). In this issue, Li et al. used an anthropometric index a body surface index (ABSI) derived from height body mass index and weight circumference to interrogate abdominal aortic calcification (AAC). They showed that ABSI correlated positively with AAC and that its discriminant ability superseded those of the different anthropometric indices from which it was derived.

The body roundedness index (BRI) is another novel anthropometric index that predicts body fat distribution better than BMI. It has been shown to better predict metabolic syndrome and cardiometabolic diseases than other common anthropometric indices (4) as it predicts both body fat and visceral adiposity. In this issue, Ding et al. applying this index in a Chinese middle age to elderly population showed that BRI in the higher trajectory was significantly related to all cause and cardiovascular mortality.

Atrial fibrillation (AF), the commonest arrhythmia in clinical practice is known to be a cause of increased all cause and cardiovascular mortality in the population. It has been shown to be related to body fat (5). From anthropometry, blood chemistry and some life style factors Woo et al. derived more precise cardiovascular disease indices: predicted body fat mass index and predicted lean body mass index. They found that the risk of AF rises with these indices except in those underweight by the BMI classification.

Non-alcoholic fatty disease is known to be a manifestation of metabolic syndrome, a forerunner to cardiometabolic diseases (6). Fatty Liver Index (FLI) derived from certain anthropometric and blood chemistry measures was used by Niu et al. to detect ischemic heart disease (IHD) using data from the 1999–2016 NHANES. This study published in this issue showed a linear and positive relationship between FLI and prevalent IHD.

Using R analysis Li et al. in this issue tried to determine risk factors for hypertension in an overweight and obese population. Seven such factors were identified but age and uric acid exhibited synergistic interaction making them a potential reference standard for initiation of preventive and curative action in overweight and obese hypertensives.

Weight management has been stressed as key in preventing cardiovascular diseases in diabetics (7). Li et al. in this issue interrogating a population of Chinese diabetics found that the burden of cardiovascular disease risk factors changed for the better with weight reduction. This means that for reduction in cardiovascular disease morbidity in diabetics, every effort must be made to normalize body weight.

Quality of diet has a bearing on prevalent cardiovascular diseases (8), hence the impact of dietary modification in the management of cardiovascular diseases. Mohamadi et al. in this issue utilized the diet quality index (DQI) to study overweight and obese women for cardiometabolic risk factors. They were able to show a relationship giving fillip to the need for good quality diet in prevention of cardiometabolic diseases.

Finally Peng et al. using NHANES 1999–2018 data looked at weight change and predicted 10 year risk for atherosclerotic vascular disease in an American population of the elderly. They were able to show that stable weight rather than flux in weight was more beneficial for maintaining cardiovascular health

On the whole, the various contributions in this issue show that though relevant BMI is not very precise in predicting risk of cardiometabolic diseases and new paradigms tracking fat mass and fat location in the body rather than overall weight which includes bone and muscle would be the way to go. This is where the novel anthropometric index, Abdominal Height stands out. It does not require more anthropometric measures for inclusion into an equation to derive, neither does it involve blood sampling and biochemical analyses which introduce inconvenience and cost.

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References

1. Agbo HA, Zoakah AI, Isichei CO, Sagay AS, Achenbach CJ, Okeahialam BN. Cardiovascular anthropometry: What is best suited for large-scale population screening in sub-saharan Africa? *Front Cardiovasc Med*). 2020 7:522123. doi: 10.3389/fcvm.2020.522123

2. Koparkar G, Biswas DA. Adiposity and cardiac defects: pathophysiology and aetiology. *Cureus*. (2023) 15(1):e34026. doi: 10.7759/cureus.34026

3. Shreya D, Zamora DI, Patel GS, Grossman I, Rodriguez K, Soni M, et al. Coronary artery calcium score: a reliable indicator of coronary artery disease? *Cureus*. (2021) 13 (12):e20149. doi: 10.7759/cureus.20149

4. Rico-Martin S, Calderon-Garcia JF, Sanchez-Ray P, Franco-Antonio C, Alvarez MM, Munoz-Torrero JFS. Effectiveness of body roundedness index in predicting metabolic syndrome: a systematic review and metaanalysis. *Obese Rev*. (2020) 21(7): e13023. doi: 10.1111/obr.13023

5. Anaszewicz M, Banas W, Wawrizenczyk A, Brudznski J. Body composition in patients with atrial fibrillation. *Acta Cardiol Sin*. (2019) 35(5):484–92. doi: 10.6515/ACS.201909_35(5).20190323A

6. Asslan U, Yenevong M. Relationship between non-alcoholic fatty liver disease and coronary heart disease. *World J. Clin Cases*. (2020) 8(20):4688–99. doi: 10.12998/wjcc.v8.i20.4688

7. Wang C, Ye D, Xie Z, Huang K, Wang Z, Haiyan S, et al. Assessment of cardiovascular risk factors and their interactions in the risk of coronary heart disease in patients with type 2 diabetes with different weight levels. *Diab Metab. Synd Obes.* (2021) 14:4253–62. doi: 10.2147/DMSO.S335017

8. Diab A, Dastmalchi LN, Gulati M, Michos ED. A heart healthy diet for cardiovascular disease prevention. Where are we now? *Vasc Hlth Risk Mgt*. (2023) 19::237–53. doi: 10.2147/VHRM.S379874

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Association between weight-adjusted-waist index and heart failure: Results from National Health and Nutrition Examination Survey 1999–2018

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Background: Weight-adjusted waist circumference index (WWI) is a novel index positively associated with excessive fat accumulation. The current study aims to evaluate the association between WWI and the prevalent heart failure (HF), and to assess the value of WWI to improve the detection of HF in the general population.

Methods: A total of 25,509 subjects from National Health and Nutrition Examination Survey 1999–2018 were included into our study. WWI was calculated as WC (cm) divided by the square root of weight (kg). HF was identified according to the subjects' reports.

Results: The prevalence of reported HF was 2.96%. With adjustment of demographic, anthropometric, laboratory, and medical history data, one SD increment of WWI could cast an additional 19.5% risk for prevalent HF. After separating WWI into quartiles, the fourth quartile had a 1.670 times risk of prevalent HF compared to the first quartile. Furthermore, smooth curve fitting suggested that the association was linear in the entire range of WWI. Moreover, the association was robust to subgroups of age, sex, race, obesity, hypertension, and diabetes. Additionally, ROC analysis revealed a significant improvement for the detection of prevalent HF from WWI (0.890 vs. 0.894, $P < 0.001$); And continuous net reclassification index (0.225, $P < 0.001$) and integrated discrimination index (0.004, $P < 0.001$) also supported the improvement from WWI.

Conclusion: Our data demonstrated a significant, linear, and robust association between WWI, a simple surrogate for fat mass accumulation, and

the risk for prevalent HF in a representative population. Moreover, our results also suggested the potential value of WWI to refine the detection of prevalent HF in the general population.

KEYWORDS

epidemiology, heart failure, fat mass accumulation, weight-adjusted waist circumference index, obesity

Introduction

Heart failure (HF) is a complicated syndrome developed at the end stage of various cardiovascular diseases (1). The prevalence of HF remains a continuous rising trend, and is estimated to be more than 37.7 million individuals globally (2). Until 2011, an estimated 5.7 million patients suffered from HF and 870,000 new cases were diagnosed per year in the United States (3). In many developing countries, the burden of cardiovascular diseases, including HF, is also under a rapid increasing stage (4). Under this grim situation, it is essential to improve the early diagnosis of HF in the general population.

Obesity is one of the major risk factors for the development of HF, both heart failure with persevered ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF) (5). In the Framingham Heart Study, obesity was identified to independently associate with HF risk with the adjustment of other cardiovascular risk factors (6). Later, the association between obesity and HF risk was confirmed in a study with larger population (7). Furthermore, a similar association between increased body mass index (BMI) and the risk of HF was also observed in non-US population (8, 9). More importantly, distribution of adiposity could play a pivotal role in the impact of obesity on HF incidence and prevalence; a magnetic resonance imaging study demonstrated that visceral but not subcutaneous adipose tissue was related to adverse cardiac remodeling (10). However, the widely used indicator of obesity, BMI and waist circumference (WC), were unable to differentiate between muscle mass and fat mass (11).

In 2018, Park et al. proposed a novel anthropometric index named weight-adjusted-waist index (WWI) (12). WWI has been demonstrated to positively correlated with fat mass but negatively associated with muscle mass (13). Later studies have identified that WWI is associated with cardiovascular diseases and mortality (14–16). However, the association between WWI and the prevalent HF remains unclear. Therefore, the current study aims to evaluate the association between WWI and the risk of prevalent WWI, and to assess whether WWI could improve the detection of prevalent HF in the general population.

Materials and methods

Subjects

Our current analysis was a secondary analysis of the National Health and Nutrition Examination Survey (NHANES) 1999–2018. The NHANES survey refers to a series of cross-sectional survey conducted by the National Center for Health Statistics (NCHS), an affiliated department of the Centers for Disease Control and Prevention. The survey was conducted in the United States for every 2 years in the past two decades. The survey adopted a multistage, stratified, and clustered probability sampled pattern to maintain its representativity. The data from different circle of survey could be appended together for integrated analysis. More detailed information about the NHANES design and conduction is available to the public at the NHANES official website.[1] In the current analysis, the inclusion criterion was subjects aged $\geq$ 20 and $\leq$85 years old. The exclusion criteria were subjects with incomplete data used in the current analysis. A total of 25,509 subjects were finally enrolled into our study (**Supplementary Figure 1**). The protocol of NHANES survey was approved by the NCHS institutional Ethics Review Board, and our current study did not contain any person identifying material. Therefore, the current study did not require further ethic review. All data used in our study could be downloaded from the NHANES official website.

Data collection and measurements

Interviews were conducted at subjects' home during the data collection process, and laboratory examinations were performed at the Mobile Examination Center (MEC). Demographic data were collected by trained stuffs through a computer-assisted interviewing system. For subjects who could not answer the question by themselves, a family member would answer the questions instead. Drink for at least 12 times during the past year before enrollment was regarded as current drinking. Subjects answered "some days" or "every day" to the question

1 https://www.cdc.gov/nchs/nhanes/index.htm

"Do you now smoke cigarettes" were determined as current smoking subjects. The poverty-to-income ratio (PIR) was used to estimate the socioeconomic status, and it was calculated by family income ratio to the federal poverty threshold. The definition of HF is based on the question "Someone ever told you had congestive heart failure" from the questionnaire. Similarly, coronary heart disease (CHD) was defined as answering "yes" to the question "Someone ever told you had coronary heart disease."

Anthropometric parameters were collected with a standard operation procedure. Waist circumference (WC) and height were quantified to the nearest 0.1 cm; weight was quantified to the nearest 0.1 kg. Blood pressure was measured after sitting and resting quietly for at least 5 min. The mean value of three blood pressure recordings was used in the current analysis. More detailed information about the blood pressure measurement is available in the "Physician Examination Procedures Manual" on the NHANES official website.

Laboratory examinations were conducted at laboratories certified by the CDC. Fasting plasma glucose (FPG) was measured by the oxygen rate method on the Modular Chemistry side of the Beckman DxC800; Blood lipids were quantified by enzymatic assay on the Roche modular P and Roche Cobas 60,000 chemistry analyzers. Serum creatinine (Scr) was determined by DxC800 modular chemistry side through the Jaffe rate method.

Definition

Body mass index was calculated as weight (kg) ratio to height (m) squared. Answering "Yes" to the question "Take diabetic pills to lower blood sugar" or "Taking insulin now" was regarded as anti-diabetic therapy; FPG $\geq$ 7 mmol/L and/or self-reported use of anti-diabetic therapy was defined as diabetes (17). Answering "Yes" to the question "Now

TABLE 1 Subjects' characteristics.

Variables	Total (25,509)	Reported HF (n = 754)	Without reported HF (n = 24755)	P-value
Age (years)	46.77 (46.18–47.26)	65.66 (64.41–66.90)	46.34 (45.85–46.83)	< 0.001
Male (%)	48.84 (48.28–49.39)	54.82 (50.18–59.38)	48.70 (48.13–49.28)	0.006
Race (%)				0.013
Non-hispanic white	73.60 (71.16–75.90)	78.90 (75.59–81.87)	73.48 (71.02–75.80)	
Non-hispanic black	8.50 (7.54–9.55)	6.54 (4.47–9.46)	8.54 (7.58–9.61)	
Mexican American	9.54 (8.28–10.96)	9.90 (7.78–12.52)	9.53 (8.27–10.96)	
Other hispanic	6.74 (5.52–8.22)	3.30 (2.01–5.35)	6.82 (5.58–8.31)	
Others	1.63 (1.35–1.95)	1.36 (0.52–3.54)	1.63 (1.36–1.96)	
Current drinking (%)	26.73 (25.41–28.10)	32.79 (29.28–36.50)	26.60 (25.26–27.97)	< 0.001
Current smoking (%)	17.36 (16.48–18.28)	18.46 (15.23–22.21)	17.34 (16.43–18.29)	0.548
PIR	3.02 (2.94–3.09)	2.29 (2.13–2.45)	3.03 (2.96–3.10)	< 0.001
Height (cm)	168.98 (168.78–169.18)	167.33 (166.41–168.25)	169.02 (168.81–169.22)	0.119
Weight (kg)	82.36 (81.89–82.82)	89.40 (86.87–91.94)	82.20 (81.74–82.65)	< 0.001
BMI (kg/m^2)	28.76 (28.59–28.93)	31.81 (30.92–92.71)	28.69 (28.53–28.85)	< 0.001
WC (cm)	98.76 (98.33–99.19)	109.51 (107.56–111.45)	98.51 (98.09–98.93)	< 0.001
SBP (mmHg)	121.97 (121.59–122.35)	129.08 (127.33–130.84)	121.80 (121.43–122.18)	< 0.001
DBP (mmHg)	70.43 (70.02–70.83)	66.53 (65.33–67.74)	70.51 (70.11–70.92)	< 0.001
FPG (mmol/L)	5.47 (5.44–5.51)	6.58 (6.32–6.84)	5.45 (5.42–5.48)	< 0.001
TC (mmol/L)	5.07 (5.04–5.09)	4.65 (4.51–4.78)	5.07 (5.05–5.10)	< 0.001
HDL-c (mmol/L)	1.40 (1.38–1.41)	1.26 (1.22–1.29)	1.40 (1.39–1.41)	< 0.001
Scr (μmol/L)	78.78 (78.31–79.26)	105.33 (99.83–110.82)	78.18 (77.73–78.64)	< 0.001
Anti-hypertension therapy (%)	25.59 (24.61–26.61)	72.06 (67.84–75.91)	24.54 (23.59–25.53)	< 0.001
Anti-diabetic therapy (%)	6.92 (6.53–7.34)	29.81 (25.79–34.16)	6.41 (6.03–6.80)	< 0.001
Lipid-lowering therapy (%)	16.04 (15.31–16.80)	53.35 (48.32–58.31)	15.20 (14.47–15.96)	< 0.001
Hypertension (%)	32.73 (31.68–33.79)	77.85 (73.70–81.50)	31.71 (30.68–81.50)	< 0.001
Diabetes (%)	10.91 (10.39–11.45)	36.92 (32.30–41.80)	10.32 (9.82–10.84)	< 0.001
CHD history (%)	3.28 (2.97–3.63)	40.74 (36.11–45.53)	2.44 (2.17–2.73)	< 0.001
WWI (cm/$\sqrt{}$kg)	10.94 (10.91–10.96)	11.66 (11.58–11.75)	10.92 (10.90–10.94)	< 0.001

Data were summarized as mean (95% confidence intervals) or numbers (95% confidence intervals) according to their data type.
HF, heart failure; PIR, poverty-to-income ratio; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; HDL-c, high density lipoprotein cholesterol; Scr, serum creatinine; CHD, coronary heart disease; WWI, weight-adjusted waist circumference.

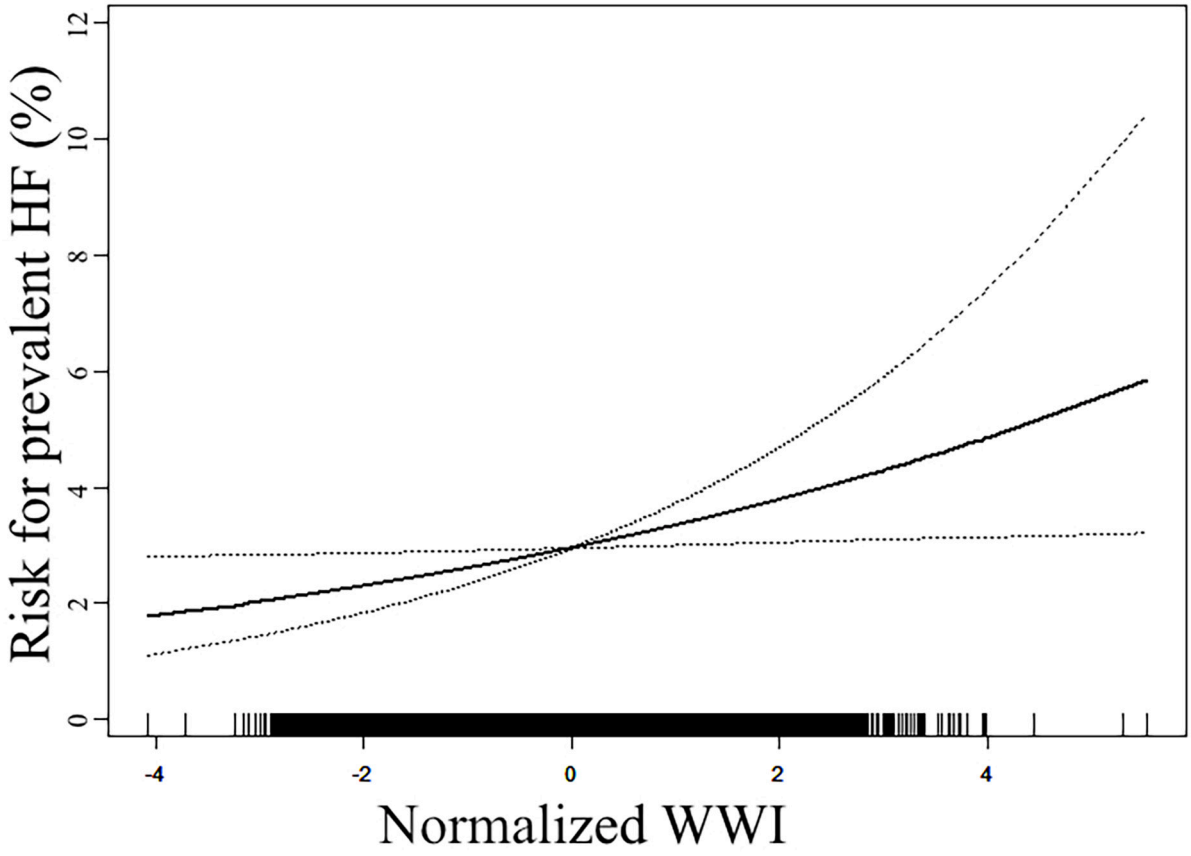

FIGURE 1
Smooth curve fitting to evaluate the linearity of the association between weight-adjusted waist circumference index (WWI) and the reported heart failure (HF). The model was adjusted for age, sex, race, current smoking, current drinking, poverty-to-income ratio (PIR), body mass index (BMI), waist circumference (WC), serum creatinine (Scr), fasting plasma glucose (FPG), total cholesterol (TC), high-density lipoprotein (HDL), systolic blood pressure (SBP), anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy, and coronary heart disease (CHD) history (The same as Model 2 in **Table 2**). The solid line in the plot referred to the estimated risk of prevalent reported HF, and the dotted lines indicated the pointwise 95% CI. The association followed a linear pattern in the entire range of WWI.

taking prescribed medicine for hypertension" was determined as anti-hypertensive therapy; A mean systolic blood pressure (SBP) $\geq$ 140 mmHg, a mean diastolic blood pressure (DBP) $\geq$ 90 mmHg, and/or anti-hypertensive therapy were indicated as hypertension (18). Answering "Yes" to the question "Now taking prescribed medicine for cholesterol" during the interview was defined as lipid-lowering therapy. WWI was calculated as WC (cm) divided by the square root of weight (kg) (12).

Statistical analysis

In our study, statistical data were weighted because of the survey design of NHANES.[2] Categorical variates were also summarized as frequency and 95% CI. Continuous variates were listed as the mean value with 95% confidence intervals (CI). Comparison of categorical variates and continuous variates were conducted by Chi-square test and *t*-test, respectively. Association between WWI and the risk of prevalent HF was assessed by multivariate logistic regression analysis. The results were displayed as odds ratios (ORs) and 95% CI. Furthermore, A generalized addictive model with a spline smooth-fitting function was conducted to investigate whether the association was linear in the entire range of WWI. Finally, receiver-operating characteristic (ROC) curve and reclassification analysis (continuous net reclassification index, NRI and integrated discrimination index, IDI) were conducted to assess the potential value of WWI to improve the detection of prevalent HF. All the statistical analysis was conducted by s Stata Statistical Software (version 15.0; StataCorp. LLC., College Station, TX, USA), statistical software packages R[3] (The R

2 https://wwwn.cdc.gov/nchs/nhanes/tutorials/module3.aspx

3 http://www.R-project.org

Foundation) and EmpowerStats[4] (X&Y Solutions, Inc., Boston, MA, USA). A two-tailed *P*-value less than 0.05 was regarded as statistical significance.

Results

Subjects characteristics

The characteristics of enrolled subjects were summarized in **Table 1**. The prevalence of HF was 2.96% (754/25509). Regarding the demographic data, HF patients had a significantly higher age level, larger percentages of male sex, white race, and current drinking status, and a subsequently lower PIR level than subjects without HF. For the anthropometric data, weight, BMI, WC, SBP levels were significantly higher in HF patients, while DBP level was lower in HF patients. Laboratory exams revealed that FPG, total cholesterol (TC), and Scr were higher in HF patients and HDL-c was higher in subjects without HF. Medical history data showed that the percentages of receiving anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy, and CHD history were remarkably higher in HF patients than their counterparts. Accordingly, the prevalence of hypertension and diabetes were subsequent lower in subjects without HF. Finally, the level of WWI was significantly higher in HF patients than in subjects without HF.

Linear association between weight-adjusted waist circumference index and the prevalent heart failure

Logistic regression analysis was conducted to assess the association between WWI and the prevalent HF. The results were showed in **Table 2**. In the crude model, each SD increase of WWI could cast a 2.484 times risk of prevalent HF. After adjustment of demographic covariates, including age, sex, race, current smoking and drinking status, and PIR, the additional risk for each SD increase of WWI diminished to 66.9%. With the further adjustment of BMI, WC, Scr, FPG, TC, high-density lipoprotein (HDL), SBP, anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy, and CHD history, the additional risk reduced to 19.5%. When separating WWI values into quartiles, the risk for prevalent HF increased significantly alone with the elevation of WWI quartiles (*P* for trend = 0.040), and the top quartile had a 1.670 times risk of prevalent HF when compared to the first quartile.

Our study also employed a generalized additive model with a smooth curve fitting function to assess the linearity of the association between WWI and the prevalent HF (**Figure 1**). The model was adjusted for all covariates used in Model 2 of **Table 2**. The results displayed that the association was linear in the entire range of WWI. The risk for prevalent HF increased from around 2% at the lowest end of WWI to more than 4% at the highest end of WWI.

Robustness of the association between weight-adjusted waist circumference index and the prevalent heart failure

To investigate whether the association between WWI and the prevalent HF was robust among several conventional cardiovascular subpopulations, we conducted subgroup analysis with interaction test (**Figure 2**). The model was adjusted for all covariates in Model 2 of **Table 2**, except for the covariates used to define subgroups. The figure showed that our main finding was robust in subgroups of age (<60 or ≥ 60), sex, race (white or others), obesity, hypertension, and diabetes, with all *P* for interaction > 0.05.

Significant value of weight-adjusted waist circumference index to refine the detection of prevalent heart failure

Receiver-operating characteristic and reclassification analysis were employed to assess the value of WWI to refine the detection of prevalent HF (**Table 3** and **Supplementary Table 1**). The AUC of WWI for the detection of prevalent HF was 0.709 (0.704–0.715), significantly higher than that of BMI (0.598, 95% CI: 0.592–0.604) and WC (0.659, 95% CI: 0.653–0.665). When adding WWI into conventional risk factors (including BMI and WC), the AUC for prevalent HF significantly increased from 0.890 (0.886–0.893) to 0.894 (0.890–0.897). About the reclassification analysis, both continuous NRI (0.225, 95% CI: 0.152–0.297) and IDI (0.004, 95% CI: 0.002–0.007) revealed a significant improvement for the detection of prevalent HF when adding WWI into conventional cardiovascular risk factors.

Discussion

In the current study, our data demonstrated a significant and positive association between WWI, a novel, easy-acquired indicator of adipose obesity, and the prevalent HF in a representative American population. Furthermore, the association was linear in the entire range of WWI, suggesting risk of prevalent HF increased proportionally with the elevation of WWI. Moreover, the association was robust in several conventional cardiovascular subpopulations. Finally, results from both ROC and reclassification analysis demonstrated the significant value of WWI to refine the detection of

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TABLE 2 Association between weight-adjusted waist circumference index (WWI) and the reported heart failure (HF).

Variables	Odds ratio (95% CI)					
	Crude	*P*-value	Model 1	*P*-value	Model 2	*P*-value
WWI (Per SD increase)	2.484 (2.265–2.725)	< 0.001	1.669 (1.472–1.893)	< 0.001	1.195 (1.036–1.379)	0.015
Quartiles of WWI						
Quartile 1	Reference		Reference		Reference	
Quartile 2	3.222 (2.153–4.821)	< 0.001	1.883 (1.255–2.825)	0.003	1.361 (0.877–2.111)	0.167
Quartile 3	7.171 (5.197–9.896)	< 0.001	2.763 (1.942–3.931)	< 0.001	1.545 (1.027–2.323)	0.037
Quartile 4	15.231 (10.873–21.335)	< 0.001	4.039 (2.781–5.865)	< 0.001	1.670 (1.059–2.634)	0.028
P for trend		< 0.001		< 0.001		0.040

Crude: no adjustment; Model 1: age, sex, race, current smoking, current drinking, PIR; Model 2: model 1 + BMI, WC, Scr, FPG, TC, HDL-c, SBP, anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy, and coronary heart disease history.

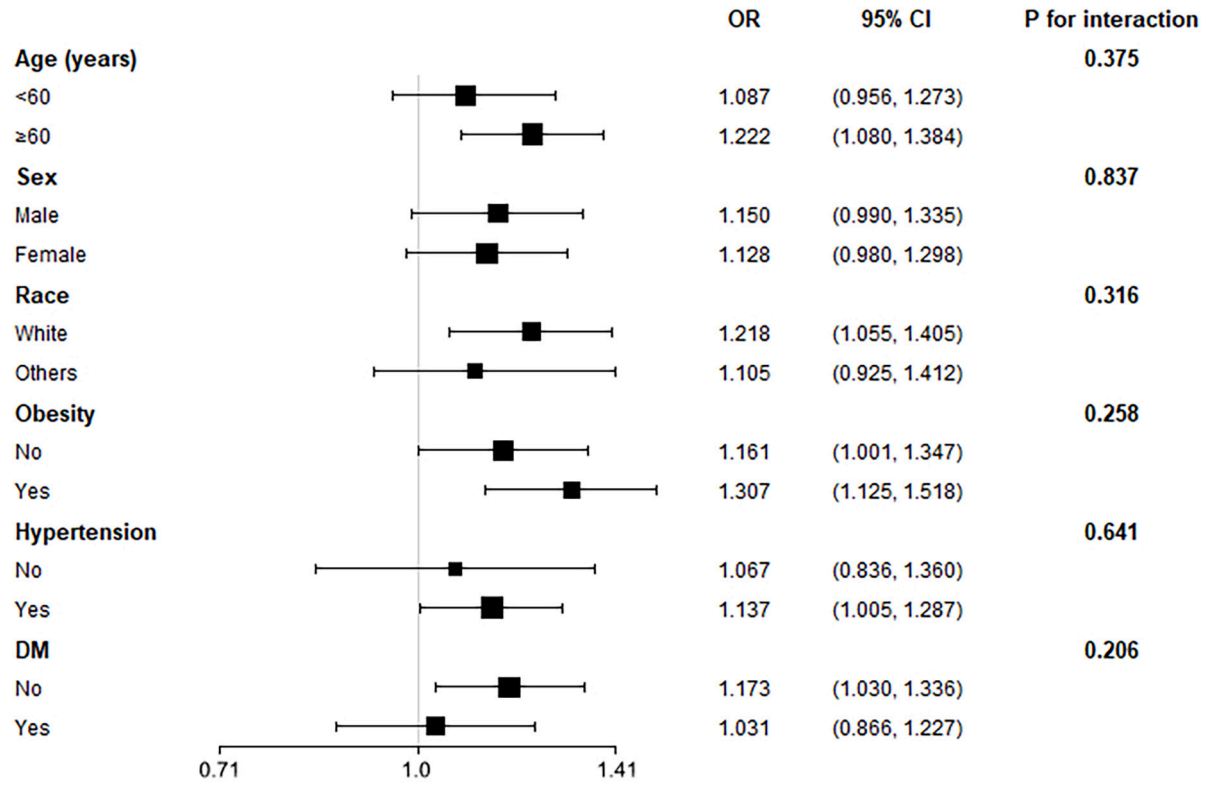

FIGURE 2
Subgroup analysis for the association between weight-adjusted waist circumference index (WWI) and the prevalent reported heart failure (HF). The multivariate logistic model adjusted for all variates in used in Model 2 of Table 2, except for the variate that used to define subgroups. None of the stratified variables, including age, sex, race, obesity (BMI ≥ 30 kg/m^2), hypertension, and diabetes, significantly modified the association between WWI and the reported HF (all *P* for interaction > 0.05).

prevalent HF. Therefore, our analysis suggests the potential association between WWI and the risk of prevalent HF in the general population, and our findings also support the potential incremental value of WWI to optimize the detection of prevalent HF in the general population.

Our results confirmed the association between WWI and the risk of prevalent HF in the general population. In multivariate logistic regression analysis, WWI showed a significant and positive association with the prevalent HF even after adjusting for demographic, anthropometric, laboratory, and medical history covariates. It is necessary to mention that the adjusted covariates included BMI and WC. Therefore, the association between WWI and prevalent HF is independent from the confounding effect of general obesity and simple abdominal obesity, suggesting the impact of fat mass on the risk of prevalent HF. Furthermore, we also observed a significant and

TABLE 3 Receiver-operating characteristic (ROC) and reclassification analysis for weight-adjusted waist circumference index (WWI) to improve the identification of reported heart failure (HF).

Model	AUC (95% CI)	*P*-value	*P* for comparison	NRI (continuous)	*P*-value	IDI	*P*-value
WWI	0.709 (0.704–0.715)	< 0.001	–	–	–	–	–
BMI	0.598 (0.592–0.604)	< 0.001	< 0.001	–	–	–	–
WC	0.659 (0.653–0.665)	< 0.001	< 0.001	–	–	–	–
Clinical risk factors*	0.890 (0.886–0.893)	< 0.001	–	–	–	–	–
Clinical risk factors + WWI	0.894 (0.890–0.897)	< 0.001	0.002	0.225 (0.152–0.297)	<0.001	0.004 (0.002–0.007)	0.002

*Clinical risk factors: age, sex, race, current smoking, current drinking, PIR, BMI, WC, Scr, FPG, TC, HDL, SBP, anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy, and coronary heart disease history.

linear trend toward higher risk of prevalent HF. Moreover, smooth curve fitting also confirmed the linear trend; the risk for prevalent HF increased proportionally with the elevation of WWI value, without any threshold or saturation effect. These results implicate that WWI could serve as an independent and linear indicator for the risk of prevalent HF in the general population.

The results from the subgroup analysis demonstrated that the significant association between WWI and the prevalent HF was consistent among several conventional cardiovascular subpopulations. Results displayed in **Figure 2** revealed that the association was robust to age, sex, race, obesity, hypertension, and diabetes subgroups. The ORs in these subgroups were similar to the OR observed in the entire population. Some subgroups showed difference, such as sex subgroups, race subgroups, and obesity subgroups; However, the none of the *P*-value for interaction reached statistical significance. Importantly, we observed a difference in OR value between subjects with and without obesity. Subjects with obesity had a higher risk increase for prevalent HF for each SD increase of WWI than subjects without obesity, suggesting obesity subjects could be more vulnerable to the increase of WWI, and the underlying fat mass. However, the difference did not achieve statistical significance. Hence, this finding still requires more study to validate.

Receiver-operating characteristic and reclassification analysis revealed the potential role of WWI in detecting prevalent HF. The AUC of WWI was significantly higher than that of BMI and WC, suggesting the superior value of WWI in HF identification. Furthermore, when introducing WWI into conventional cardiovascular risk factors, we observed a significant improvement for the identification of prevalent HF. Nevertheless, ROC analysis still has its limitation even if it is the most common approach to assess the diagnosis ability of novel markers. ROC analysis possesses a low sensitivity to identify the usefulness of a new index to improve the risk identification of prevalent diseases (19). Rather than detecting the value of an index itself to improve risk identification, ROC only compares the ability of different models (20). Therefore, ROC analysis alone may be insufficient to evaluate the impact of a new index to refine the risk identification of prevalent diseases. Accordingly, statisticians have proposed reclassification analysis to investigate the incremental value of new indexes for refining risk identification of prevalent diseases (21–23). In the current analysis, both continuous NRI and IDI were significant, implicating a significant and incremental value of WWI to optimize the risk identification of prevalent HF. In general, both ROC and reclassification analysis reported an incremental value of WWI to refine the risk identification of prevalent HF. Therefore, clinicians may achieve more precise identification of patients with high risk of prevalent HF from the general population by applying WWI into primary care settings.

Our findings were consistent with established data. In a recent published article, Huynh et al. demonstrated that increased intramuscular thigh muscle fat accumulation is independently associated with HF, suggesting excessive adiposity deposition, especially the intramuscular fat, contributes to the elevation of HF risk (24). From the view of pathophysiology, excessive adipose accumulation could lead to HF through multiple pathways, including altered hemodynamics, cardiac structure remodeling, inflammation, and neurohumoral and cellular dysfunction (25). Our current study suggests that WWI, a simple estimate of fat mass, may associate with the risk of prevalent HF. Therefore, our study provides a clue to transform the pathophysiological association between fat accumulation and HF into clinical practice.

Except of some novel findings, our study still has some disadvantages. First, the cross-sectional design of the NHANES did not allow us to assess the value of WWI to predict the occurrence of HF. Therefore, the goal of our current study focused on the association between WWI and the presence of HF, and we also aimed to evaluate whether WWI could improve the detection or identification of the presence of HF in the general population. Studies with longitudinal design is required to confirm our findings. Second, we excluded a number of NHANES participants due to lack of related variates, which could introduce bias into our results. Third, some variables, such as the medication history and the self-reported HF, relied on the recall of the participants, and we could not categorize the subtypes of HF. This could introduce information bias into our current study. However, these variables are naturally difficult to define according to objective criteria in large sample size

studies, and the NHANES was conducted strictly to its protocol. Therefore, we believe the information bias was still acceptable in our current study, but we still need more studies to confirm our findings. Fourth, the NHANES study was conducted only in the United States, whether our findings are applicable to other populations remains unclear. Last, we have adjusted for demographic data, anthropometric data, laboratory data, and medication data in our current study. Nevertheless, many factors associated with HF could confound the association between WWI and HF. However, due to the limited data provided by NHANES, we could not adjust all confounders in the current study. This is a natural limitation of observation studies. Accordingly, more studies with more detailed data collection are needed to validate our results. Based on above four points, more longitudinal studies with more detailed information are needed to confirm our findings.

Data availability statement

Publicly available datasets were analyzed in this study. The dataset supporting the conclusions of this article is available from the corresponding authors on appropriate request. All the data could be downloaded from the NHANES official website.

Ethics statement

The NCHS Institutional Ethics Review Board approved the study protocol of NHANES. The patients/participants provided their written informed consent to participate in this study.

Author contributions

DZ and WS designed the current study. WS, ZD, and JP integrated and analyzed the data. DZ, WS, and SW drafted the manuscript. JZ revised the manuscript and proofread it for publication. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2022.1069146/full#supplementary-material

References

1. Ziaeian B, Fonarow G. Epidemiology and aetiology of heart failure. *Nat Rev Cardiol.* (2016) 13:368–78. doi: 10.1038/nrcardio.2016.25

2. Vos T, Flaxman A, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (Ylds) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the global burden of disease study 2010. *Lancet.* (2012) 380:2163–96. doi: 10.1016/s0140-6736(12)61729-2

3. Mozaffarian D, Benjamin E, Go A, Arnett D, Blaha M, Cushman M, et al. Heart disease and stroke statistics-2016 update: a report from the American heart association. *Circulation.* (2016) 133:e38–360. doi: 10.1161/cir.0000000000000350

4. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the global burden of disease study 2013. *Lancet.* (2015) 385:117–71. doi: 10.1016/s0140-6736(14)61682-2

5. Horwich T, Fonarow G, Clark A. Obesity and the obesity paradox in heart failure. *Prog Cardiovasc Dis.* (2018) 61:151–6. doi: 10.1016/j.pcad.2018.05.005

6. Kenchaiah S, Evans J, Levy D, Wilson P, Benjamin E, Larson M, et al. Obesity and the risk of heart failure. *N Engl J Med.* (2002) 347:305–13. doi: 10.1056/NEJMoa020245

7. Kenchaiah S, Sesso H, Gaziano J. Body mass index and vigorous physical activity and the risk of heart failure among men. *Circulation.* (2009) 119:44–52. doi: 10.1161/circulationaha.108.807289

8. Hu G, Jousilahti P, Antikainen R, Katzmarzyk P, Tuomilehto J. Joint effects of physical activity, body mass index, waist circumference, and waist-to-hip ratio on the risk of heart failure. *Circulation.* (2010) 121:237–44. doi: 10.1161/circulationaha.109.887893

9. Levitan E, Yang A, Wolk A, Mittleman M. Adiposity and incidence of heart failure hospitalization and mortality: a population-based prospective study. *Circ Heart Fail.* (2009) 2:202–8. doi: 10.1161/circheartfailure.108.794099

10. Neeland I, Gupta S, Ayers C, Turer A, Rame J, Das S, et al. Relation of regional fat distribution to left ventricular structure and function. *Circ Cardiovasc Imaging.* (2013) 6:800–7. doi: 10.1161/circimaging.113.000532

11. Romero-Corral A, Somers V, Sierra-Johnson J, Thomas R, Collazo-Clavell M, Korinek J, et al. Accuracy of body mass index in diagnosing obesity in the adult general population. *Int J Obes.* (2008) 32:959–66. doi: 10.1038/ijo.2008.11

12. Park Y, Kim N, Kwon T, Kim S. A novel adiposity index as an integrated predictor of cardiometabolic disease morbidity and mortality. *Sci Rep.* (2018) 8:16753. doi: 10.1038/s41598-018-35073-4

13. Kim N, Park Y, Kim N, Kim S. Weight-adjusted waist index reflects fat and muscle mass in the opposite direction in older adults. *Age Ageing.* (2021) 50:780–6. doi: 10.1093/ageing/afaa208

14. Li Q, Qie R, Qin P, Zhang D, Guo C, Zhou Q, et al. Association of weight-adjusted-waist index with incident hypertension: the rural Chinese cohort study. *Nutr Metab Cardiovasc Dis.* (2020) 30:1732–41. doi: 10.1016/j.numecd.2020.05.033

15. Xie F, Xiao Y, Li X, Wu Y. Association between the weight-adjusted-waist index and abdominal aortic calcification in united states adults: results from the national health and nutrition examination survey 2013-2014. *Front Cardiovasc Med.* (2022) 9:948194. doi: 10.3389/fcvm.2022.948194

16. Ding C, Shi Y, Li J, Li M, Hu L, Rao J, et al. Association of weight-adjusted-waist index with all-cause and cardiovascular mortality in china: a prospective cohort study. *Nutr Metab Cardiovasc Dis.* (2022) 32:1210–7. doi: 10.1016/j.numecd.2022.01.033

17. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care.* (2003) 26 Suppl. 1:S5–20. doi: 10.2337/diacare.26.2007.s5

18. Chobanian A, Bakris G, Black H, Cushman W, Green L, Izzo J Jr., et al. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension.* (2003) 42:1206–52. doi: 10.1161/01.HYP.0000107251.49515.c2

19. Cook N. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation.* (2007) 115:928–35. doi: 10.1161/circulationaha.106.672402

20. Pickering J, Endre Z. New metrics for assessing diagnostic potential of candidate biomarkers. *Clin J Am Soc Nephrol.* (2012) 7:1355–64. doi: 10.2215/cjn.09590911

21. Pencina M, D'Agostino R Sr., D'Agostino R Jr., Vasan R. Evaluating the added predictive ability of a new marker: from area under the roc curve to reclassification and beyond. *Stat Med.* (2008) 27:157–72; discussion 207–12. doi: 10.1002/sim.2929

22. Pencina M, D'Agostino R Sr., Steyerberg E. Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. *Stat Med.* (2011) 30:11–21. doi: 10.1002/sim.4085

23. Grunkemeier G, Jin R. Net reclassification index: measuring the incremental value of adding a new risk factor to an existing risk model. *Ann Thorac Surg.* (2015) 99:388–92. doi: 10.1016/j.athoracsur.2014.10.084

24. Huynh K, Ayers C, Butler J, Neeland I, Kritchevsky S, Pandey A, et al. Association between thigh muscle fat infiltration and incident heart failure: the health Abc study. *JACC Heart Fail.* (2022) 10:485–93. doi: 10.1016/j.jchf.2022.04.012

25. Lavie C, Alpert M, Arena R, Mehra M, Milani R, Ventura H. Impact of obesity and the obesity paradox on prevalence and prognosis in heart failure. *JACC Heart Fail.* (2013) 1:93–102. doi: 10.1016/j.jchf.2013.01.006

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Association between a body shape index and abdominal aortic calcification in general population: A cross-sectional study

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Background: The association between a body shape index (ABSI) and abdominal aortic calcification (AAC) is still unclear, so we tried to prove the association between ABSI and AAC in the general population in this cross-sectional study.

Materials and methods: After excluding participants with missing data on height, weight, waist circumference (WC), and AAC, we finally selected 3,140 participants aged 40–80 years from the 2013–2014 National Health and Nutrition Examination Survey. Using multivariate logistic regression and receiver operating characteristic (ROC) curves to test the association between ABSI and AAC.

Results: Participants (median age: 58.0 years; 48.3% men) were divided into two groups by the optimal cutoff point of ABSI: higher ABSI ($>$ 0.84) and lower ABSI ($\leq$ 0.84). Participants with higher ABSI showed significantly higher proportion of AAC than those with lower ABSI (39.8 vs. 23.7%, $P < 0.001$). Participants with higher ABSI had an increased risk of developing AAC in crude model (ABSI as a continuous variable: OR = 2.485, 95% CI: 2.099–2.942, $P < 0.001$; as a categorical variable: OR = 2.132, 95% CI: 1.826–2.489, $P < 0.001$), and ABSI was still independently associated with AAC in all adjusted models (all $P < 0.05$). Further subgroup analyses showed that higher ABSI was consistently associated with AAC in subgroups with sex (male or female), age ($\leq$ 65 or $>$ 65 years), smoking history (yes or no), hypertension (yes or no), diabetes (yes or no), sleep disorder (yes or no), body mass index (BMI) ($<$ 23 or $\geq$ 23 kg/m^2), systolic blood pressure ($<$ 140 or $\geq$ 140 mmHg),

diastolic blood pressure (< 90 or ≥ 90 mmHg), fasting plasma glucose (< 126 or ≥ 126 mg/dL), and low-density lipoprotein cholesterol (≤ 130 or > 130 mg/dL) (*P* for interaction > 0.05). While in other subgroups, the association was no longer synchronized. The ROC showed that the area under the curve of ABSI was significantly higher than height, weight, BMI, WC, and waist-to-height ratio (WHtR).

Conclusion: Higher ABSI was closely associated with higher risk of AAC, and discriminant ability of ABSI for AAC was significantly higher than height, weight, BMI, WC, and WHtR.

KEYWORDS

a body shape index, body mass index, waist circumference, waist-to-height ratio, abdominal aortic calcification

Background

Abdominal aortic calcification (AAC) refers to vascular calcification in the abdominal aorta, which has been proved by previous studies to be related to coronary artery calcification and the severity of cardiovascular diseases (CVDs) (1–3). Calcium deposits may occur in all layers of blood vessels, including intima, media, and adventitia (4, 5). The mechanism of vascular calcification has not been fully elucidated. It has been reported that chronic inflammation, insulin resistance, oxidative stress, vascular smooth muscle cell transdifferentiation, mitochondrial dysfunction, apoptosis, autophagy and DNA damage are involved in the occurrence of vascular calcification (4, 6–8). And in clinical practice, it has been reported that advanced age, smoking, obesity, diabetes, dyslipidemia and low relative lean mass may be the risk factors of AAC (4, 9–12). However, there may be other risk factors for AAC, such as nutritional and metabolic disorders. Further elucidation of other risk factors of AAC and targeted intervention are beneficial to prevent the occurrence and development of AAC, thereby reducing the occurrence of cardiovascular events.

For decades, with the improvement of living conditions, obesity, especially central obesity, has become an increasingly serious global health problem (13). In contrast to subcutaneous fat, visceral fat accumulation has been shown to be closely associated with dyslipidemia, insulin resistance, diabetes and hypertension, all of which increase the risk of CVDs (13–15). Hence, it is of great significance to find a propagable and simple clinical tool for detecting visceral fat and diagnosing central obesity. At present, the traditional anthropometric indicators mainly include height, weight, body mass index (BMI), waist circumference (WC), hip circumference andwaist-to-height ratio (WHtR). However, these indicators have some limitations. For instance, BMI can't reflect the fat distribution (14). Although WC is generally considered to be a sign of central obesity, it still has some limitations, such as being disturbed by race and gender (16, 17). Therefore, in order to overcome these limitations, Krakauer et al. developed a new nutritional index, namely a body shape index (ABSI), which is calculated from height, weight and WC (18). And their study confirmed that ABSI was positively associated with visceral fat or central obesity, and they also found that the association between ABSI and premature death was higher than that of BMI and WC (18). Since then, ABSI has received more and more attention. Subsequent studies revealed the association between ABSI and arterial stiffness (19), carotid atherosclerosis (20), hypertension (21), metabolic syndrome (22), diabetes, and CVDs (23–27). For example, Ma et al. showed in a large cross-sectional study that ABSI was closely related to subclinical carotid atherosclerosis in participants without cardio-cerebrovascular disease and hypertension, diabetes, and hyperlipidemia (28). In addition, Otaki et al. found an independent association between ABSI and deaths associated with aortic disease in a large cohort study of 630,842 participants (29).

However, as far as we know, data about the association between ABSI and AAC is currently lacking. Furthermore, there are no related studies to compare the predictive efficiency of traditional anthropometric indicators and ABSI for AAC.

Abbreviations: ABSI, A body shape index; AAC, Abdominal aortic calcification; ROC, Receiver operating characteristic; CVD, Cardiovascular disease; BMI, Body mass index; WC, Waist circumference; WHtR, Waist-to-height ratio; NHANES 2013–2014, 2013–2014 National Health and Nutrition Examination Survey; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; FPG, Fasting plasma glucose; HbA1c, Hemoglobin A1c; DXA, Dual-energy X-ray absorptiometry; LDL-C, Low-density lipoprotein cholesterol; AUC, Area under the curve; TG, Triglycerides; BUN, Blood urea nitrogen; GGT, γ-glutamyl transpeptidase; ALP, Alkaline phosphatase; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; OR, Odds ratio; CI, Confidence interval.

Therefore, the present study was to explore the association between ABSI and AAC. Besides, we also tried to test the predictive ability of ABSI and anthropometric indicators for AAC in the general population aged 40–80 years from the 2013–2014 National Health and Nutrition Examination Survey (NHANES 2013–2014).

Materials and methods

Study population

National Health and Nutrition Examination Survey (NHANES) is a regular survey of representative samples of the general population in the United States, which aimed to investigate the health and disease status of the general population in the United States and provide perfect health guidance, the contents and survey data of which have been described in detail in other literatures (30). After excluding participants with missing data on height, weight, WC, and AAC, we finally selected 3,140 participants aged 40–80 years from the NHANES 2013–2014 for this cross-sectional study. The protocol of NHANES 2013–2014 was approved by the National Center for Health Statistics of the Center for Disease Control and Prevention Institutional Review Board (Protocol #2011-17), all participants of the present study provided written informed consent at the time of enrollment, and the study was consistent with the principles of the Declaration of Helsinki. Flow chart of participant selection of the present study was shown in the figure below (**Figure 1**).

Survey and measurement

The demographic characteristics of all participants were obtained by standardized family interview questionnaire, including age, sex, race, smoking history, history of diabetes, hypertension, osteoporosis, and sleep disorder. The race was divided into five groups: non-Hispanic White, non-Hispanic Black, Mexican American, other Hispanic and others. Smoking history was divided into two groups: yes and no. Height, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), and WC were measured by medical trained professionals according to measurement procedures and standards, and the calculation method of the BMI was: weight (kg) divided into the square of the height (meter). The WHtR was defined as the ratio of WC to height. The parameter values of blood samples of participants were determined strictly according to operational procedures by medically trained technicians in standard basic laboratory, including blood lipid profile, fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), serum electrolytes, kidney function, etc.

For the calculation of ABSI, we used the formula described by Krakauer et al. based on height, BMI and WC (18), that is:

$$\mathrm{ABSI} = \frac{\mathrm{WC}}{\mathrm{height}^{\frac{1}{2}} \times \mathrm{BMI}^{\frac{2}{3}}}$$

In our study, we divided participants into two groups based on the optimal cutoff point of ABSI: higher ABSI ($>$ 0.84; n = 1,264) and lower ABSI ($\leq$ 0.84; n = 1,876).

Abdominal aortic calcification (AAC) was gained by transverse scanning of the lumbar spine (vertebrae L1–L4) with dual-energy X-ray absorptiometry (DXA) (Densitometer Discovery A, Hologic, Marlborough, MA, USA) and semi-quantified by the Kauppila score system, with scores ranging from 0 to 24, and the specific scoring rules of AAC have been described in detail elsewhere, that is, as shown in **Figure 2**, the severity of calcification of the anterior and posterior walls of the abdominal aorta in each segment from L1-L4 was evaluated separately, and a score of 1 ($<$ 1/3), 2 (1/3∼2/3) or 3 ($>$ 2/3) was given according to the extent of calcification involvement in that segment, and the total score for each segment involved was the AAC score (0–24) for that patient (31–33). We divided AAC into two groups: no calcification (AAC = 0) and calcification (AAC $>$ 0).

Statistical analysis

All Statistical tests were performed with SPSS 19.0 (SPSS Inc., Chicago, IL, USA), MedCalc version 19.1 (MedCalc Software, Belgium) and R Programming Language (version 3.6.3, R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as mean ± standard deviation or median (quartiles: Q1, Q3) depending on whether the data was normal distribution, and the independent-sample t-test or Mann-Whitney U test was used to examined the differences between the two groups. Categorical variables were presented as numbers (percentages), and chi-square test or fisher's exact test was used to tested the differences between groups. The effect of ABSI on AAC was evaluated by the multivariate logistic regression in different models, including crude model and adjusted models. Crude model: unadjusted; Model 1: adjusted for age, smoking history, hypertension, diabetes, and osteoporosis; Model 2: adjusted for variables included in Model 1 and BMI, SBP; Model 3: adjusted for variables included in Model 2 and triglycerides (TG), total cholesterol (TC), creatinine, FPG. In multivariate logistic regression analysis, four models (crude model and Model 1–3) including covariables with $P < 0.1$ for avoiding missing some important factors and clinical significance were established to assess the predictive significance of ABSI for AAC. Further subgroup analyses were performed to test the consistence of the predictive significance of ABSI for AAC according to sex (male or female), age ($\leq$ 65 or $>$ 65 years), smoking

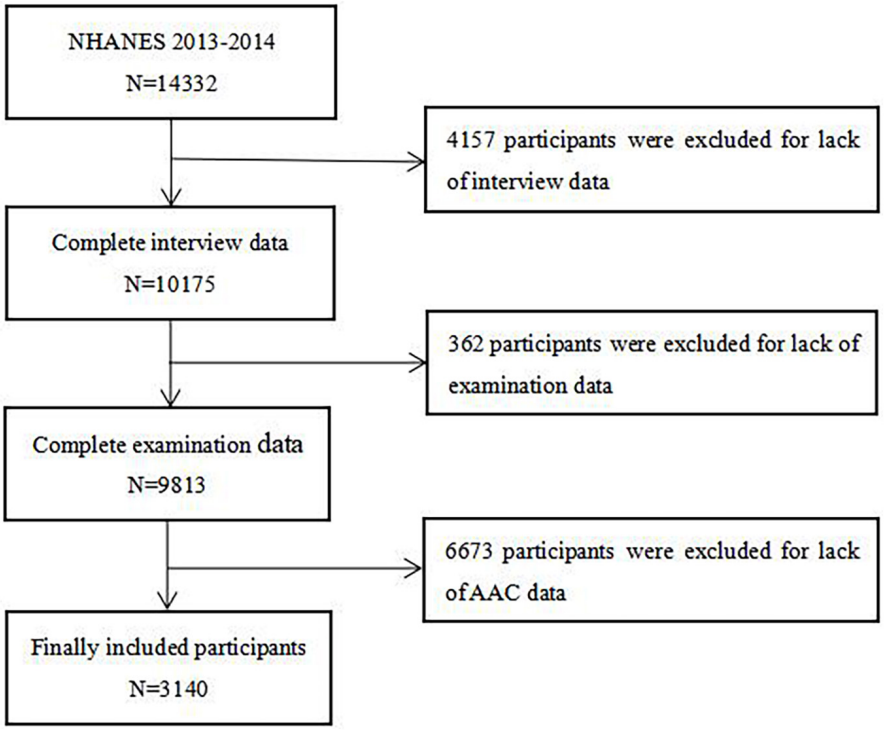
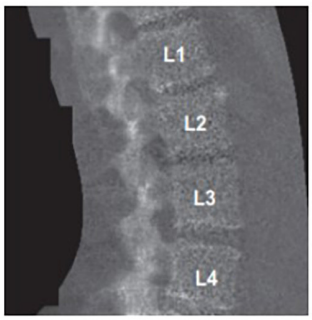


FIGURE 1
Flow chart of the study population enrollment. NHANES 2013–2014, 2013–2014 National Health and Nutrition Examination Survey; AAC, abdominal aortic calcification.



24-Point Score: 0-24							
L1		L2		L3		L4	
Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
0-3	0-3	0-3	0-3	0-3	0-3	0-3	0-3

24-Point Score: 0 (Left picture)							
L1		L2		L3		L4	
Anterior	Posterior	Anterior	Posterior	Anterior	Posterior	Anterior	Posterior
0	0	0	0	0	0	0	0

FIGURE 2
24-point semi-quantitative AAC scale and image by DXA (33). AAC, abdominal aortic calcification; DXA, dual-energy X-ray absorptiometry.

history (yes or no), hypertension (yes or no), diabetes (yes or no), osteoporosis (yes or no), sleep disorder (yes or no), BMI (< 23 or ≥ 23 kg/m^2), SBP (< 140 or ≥ 140 mmHg), DBP (< 90 or ≥ 90 mmHg), FPG (< 126 or ≥ 126 mg/dL), HbA1c (< 6.5 or ≥ 6.5%), and low-density lipoprotein cholesterol (LDL-C) (≤ 130 or > 130 mg/dL). The model used in the subgroup analyses did not contain other covariates. Besides, possible modifications of the association between ABSI and AAC were also assessed by interaction tests. C-statistics derived from receiver-operating characteristic (ROC) curve analysis was used to test the predictive potential of ABSI and traditional anthropometric indicators for AAC, and examine the incremental effects of ABSI on the predictive potential of the baseline risk model that including age, smoking history, diabetes, hypertension, osteoporosis, SBP, TG, TC, FPG, HbA1c, creatinine, uric acid, alkaline phosphatase (ALP), total calcium, and 25-OH-VitD3. DeLong's test was performed to compare the area under the curve (AUC) of each prediction model. The optimal cutoff point of ABSI for predicting AAC was determine by ROC curve analysis. A two-tailed P value < 0.05 was regarded as statistically significant.

Results

The 3,140 participants [age: 58.0 (48.0, 68.0) years; 48.3% men] enrolled in the present study were divided into two groups based on the optimal cutoff point of ABSI: higher ABSI (> 0.84; $n = 1{,}264$) and lower ABSI (≤ 0.84; $n = 1{,}876$). Baseline characteristics of total population and participants stratified by the ABSI of 0.84 were displayed in **Table 1** and **Figure 3**. Compared with participants in lower ABSI group, those with higher ABSI appeared to be older, displayed higher levels of WC, WHtR, SBP, and AAC score, and higher percentage of male, non-Hispanic White and smoker, and higher prevalence of diabetes, hypertension, osteoporosis, sleep disorder, and AAC, while lower BMI. Laboratory indices including FPG, TG, blood urea nitrogen (BUN), uric acid, creatinine, HbA1c, γ-glutamyl transpeptidase (GGT), and ALP were significantly higher in participants with higher ABSI, while TC, LDL-C, and high-density lipoprotein cholesterol (HDL-C) levels were comparatively lower ($P < 0.05$).

In multivariate logistic regression analysis, with the increase of confounding factors, higher ABSI remained to be an independent risk predictor of AAC, whether ABSI was regarded as a categorical or continuous variable (all $P < 0.05$ in Model 1–3) (**Table 2**). Further subgroup analyses (**Figure 4**) showed higher ABSI (regarding lower ABSI as reference) was consistently correlated with AAC in eleven subgroups, including sex, age, smoking history, hypertension, diabetes, sleep disorder, BMI, SBP, DBP, FPG, and LDL-C (P for interaction > 0.05). However, in the osteoporosis and HbA1c subgroups, the association was no longer synchronized (P for interaction < 0.05). Interestingly, the risk of participants with higher ABSI developing into AAC seemed to be more noticeable in participants without osteoporosis [OR (95% CI): 2.157 (1.829–2.542), $P < 0.001$] and with HbA1c $< 6.5\%$ [OR (95% CI): 2.251 (1.898–2.669), $P < 0.001$].

The ROC curve analysis showed that the discriminant ability of ABSI for AAC was significantly higher than that of other univariate predictive models, including height, weight, BMI, WC, and WHtR (all P for comparison < 0.001). However, the addition of ABSI had no significant increasing effect on the AUC obtained by the baseline risk model composed of age, smoking history, diabetes, hypertension, osteoporosis, SBP, TG, TC, FPG, HbA1c, creatinine, uric acid, ALP, total calcium, and 25-OH-VitD3 (AUC: baseline risk model, 0.726 vs. baseline risk model + ABSI, 0.728, P for comparison = 0.098) (**Table 3**, **Figure 5**).

Discussion

As far as we know, the present study was the first report on the association between ABSI and AAC. In the present study, we retrospectively explored the predictive importance of ABSI for AAC. The main findings were as follows: (1) compared with participants in lower ABSI group, those with higher ABSI showed higher AAC score and higher prevalence of AAC; (2) higher ABSI increased the risk of AAC by 20–30% compared with lower ABSI, although after adjusting for possible interference factors; (3) the risk of participants with higher ABSI developing into AAC seemed to be more noticeable in participants without osteoporosis and with HbA1c $< 6.5\%$; (4) the discriminant ability of ABSI for predicting AAC was significantly higher than height, weight, BMI, WC, and WHtR. These results suggested that ABSI may be essential for risk management of AAC.

Abdominal aortic calcification (AAC) has been widely considered as an important risk factor for CVDs, and it is very common in patients with CVDs. Some studies have shown that AAC is significantly associated with incident myocardial infarction (2), stroke (34), osteoporosis (35), fracture (36), CVDs mortality (2), and all-cause mortality (3). Therefore, the identification of pathogenic factors of AAC is of great clinical significance for primary and secondary prevention of CVDs. Several studies showed that advanced age, smoking, diabetes, obesity, and dyslipidemia may be the risk factors of AAC (4, 9–11). However, there may be other risk factors for AAC, such as nutrition indices.

At present, BMI and WC are the most commonly used anthropometric indicators in clinical practice, but both of them have some limitations in fat distribution. First, BMI not only can't distinguish between adipose and non-adipose tissue, but also can't reflect the distribution of fat (37). In fact, people with excess visceral fat or central obesity are more likely to develop CVDs and metabolic syndrome (14, 15). Unlike BMI, WC has always been regarded as an alternative indicator of central obesity (38). Previous studies have shown that WC could predict the risk of death better than BMI (39, 40), but a comparative study showed that WC was weakly or negatively correlated with subclinical CVDs (19). This suggests that the ability of WC to predict metabolic-related diseases may be overrated. The reason for this may be that the WC can't distinguish between subcutaneous fat and visceral fat, and can't reflect the difference of height and race (17). Therefore, WC may not be enough to fully represent central obesity. In addition, although there is evidence that WHtR derived from WC and height can predict metabolic disorders (41), it fails to reflect differences of weight between individuals. Therefore, it is essential to develop a better tool to assess central obesity. It is reported that imaging technology is the gold standard for the evaluation of central obesity, but it is difficult to be widely popularized because of its high cost, complex operation, and radiation. Therefore, a simple evaluation method comes into being, that is, ABSI developed by Krakauer et al. in 2012 (18).

The association between a body shape index (ABSI) is a recently developed nutritional index composed of height, weight, and WC, which is reported to be positively associated

TABLE 1 Participants characteristics stratified by the optimal cutoff point of a body shape index (ABSI).

Variables	Total population (n = 3,140)	Lower ABSI (≤ 0.84; n = 1,876)	Higher ABSI (> 0.84; n = 1,264)	P value
Age, years	58.0 (48.0, 68.0)	53.0 (46.0, 63.0)	64.0 (56.0, 73.0)	< 0.001
Sex, male, n (%)	1518 (48.3)	821 (43.8)	697 (55.1)	< 0.001
Race, n (%)				< 0.001
Non-Hispanic white	1375 (43.8)	724 (38.6)	651 (51.5)	
Non-Hispanic black	620 (19.7)	439 (23.4)	181 (14.3)	
Mexican-American	412 (13.1)	253 (13.5)	159 (12.6)	
Other Hispanic	298 (9.5)	187 (10.0)	111 (8.8)	
Others	435 (13.9)	273 (14.6)	162 (12.8)	
Smoking history, n (%)	1452 (46.2)	765 (40.8)	687 (54.4)	< 0.001
Diabetes, n (%)	648 (20.6)	290 (15.5)	358 (28.3)	< 0.001
Hypertension, n (%)	1486 (47.3)	782 (41.7)	704 (55.7)	< 0.001
Osteoporosis, n (%)	258 (8.2)	127 (6.8)	131 (10.4)	< 0.001
Sleep disorder, n (%)	336 (10.7)	166 (8.8)	170 (13.4)	< 0.001
Body mass index, kg/m^2	28.4 ± 5.6	28.8 ± 5.8	28.0 ± 5.1	< 0.001
Waist circumference, cm	99.3 ± 13.6	96.2 ± 13.0	103.9 ± 13.0	< 0.001
WHtR	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.1	< 0.001
SBP, mmHg	127.2 ± 18.3	125.1 ± 17.1	130.4 ± 19.4	< 0.001
DBP, mmHg	71.3 ± 10.8	72.0 ± 10.2	70.3 ± 11.5	0.221
Laboratory results				
Triglycerides, mg/dL	132.0 (86.0, 192.8)	121.0 (80.0, 176.0)	144.0 (97.0, 211.8)	< 0.001
Total cholesterol, mg/dL	196.0 ± 42.7	198.0 ± 41.9	193.2 ± 43.7	0.002
LDL-C, mg/dL	114.8 ± 36.0	117.0 ± 35.2	111.4 ± 37.1	0.004
HDL-C, mg/dL	54.1 ± 16.5	55.6 ± 16.9	51.8 ± 15.6	< 0.001
Blood urea nitrogen, mg/dL	14.3 ± 6.2	13.6 ± 5.3	15.3 ± 7.1	< 0.001
Creatinine, mg/dL	0.9 (0.7, 1.0)	0.9 (0.7, 1.0)	0.9 (0.8, 1.1)	< 0.001
Uric acid, mg/dL	5.5 ± 1.4	5.3 ± 1.3	5.6 ± 1.4	< 0.001
FPG, mg/dL	98.0 (90.0, 110.0)	96.0 (89.0, 109.0)	102.0 (91.0, 119.0)	< 0.001
Hemoglobin A1c, %	5.7 (5.4, 6.0)	5.6 (5.3, 5.9)	5.8 (5.4, 6.2)	< 0.001
Total bilirubin, mg/dL	0.6 ± 0.3	0.6 ± 0.3	0.6 ± 0.3	0.663
GGT, U/L	21.0 (15.0, 30.0)	20.0 (14.0, 30.0)	21.0 (15.0, 31.0)	0.002
Alkaline phosphatase, IU/L	65.0 (53.0, 77.0)	64.0 (53.0, 75.0)	67.0 (54.0, 80.0)	< 0.001
Total calcium, mg/dL	9.5 ± 0.4	9.4 ± 0.4	9.5 ± 0.3	0.226
Phosphorus, mg/dL	3.8 ± 0.6	3.8 ± 0.6	3.8 ± 0.6	0.164
25-OH-VitD3, nmol/L	63.8 (45.9, 81.0)	63.3 (46.2, 79.6)	64.9 (45.7, 83.1)	0.065
AAC, n (%)	947 (30.2)	444 (23.7)	503 (39.8)	< 0.001

ABSI, a body shape index; WHtR, waist-to-height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; GGT, γ-glutamyl transpeptidase; AAC, abdominal aortic calcification.

with central obesity, metabolic related diseases and death risk (18, 22). A subsequent study found that among teenagers, ABSI was better in identifying hypertension than BMI and WC (42). And in Chinese adults, ABSI is a better predictor of diabetes and metabolic syndrome than BMI and WC (25). Recent studies have also found that ABSI had a stronger association with all-cause mortality and CVDs mortality than WC, BMI, and WHtR, and it might be an important marker

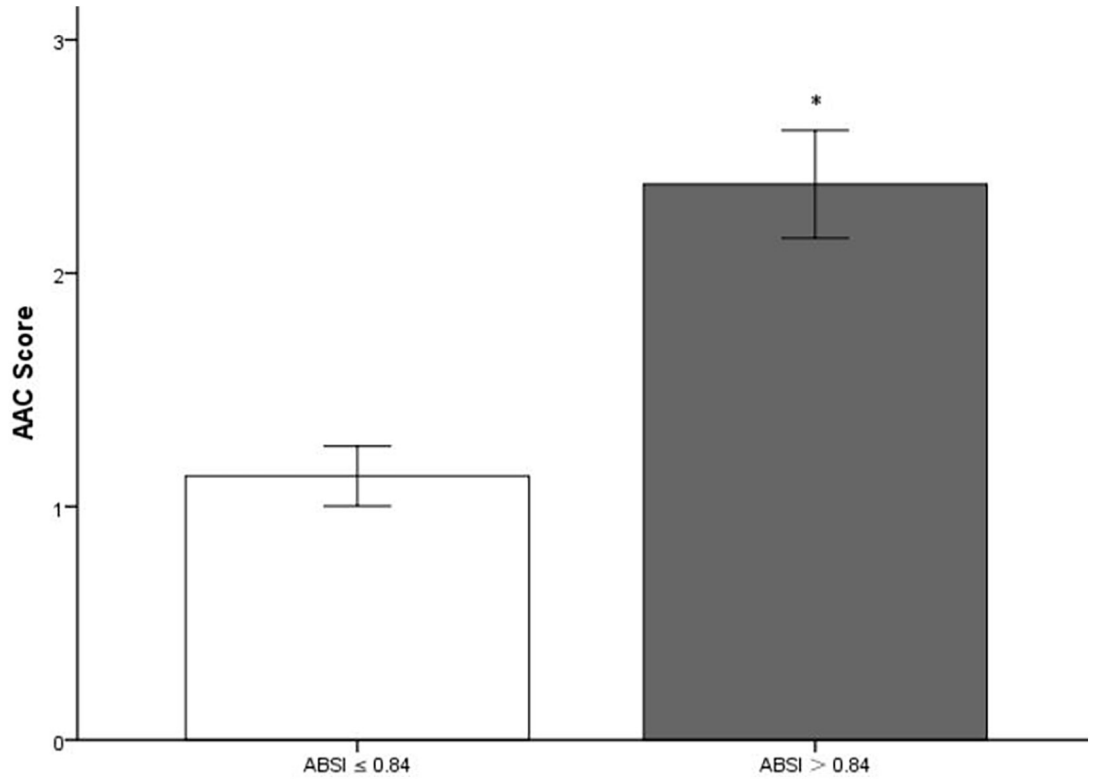


FIGURE 3
Bar graph of mean value of AAC score stratified by a body shape index (ABSI). AAC, abdominal aortic calcification. *Compared with lower a body shape index (ABSI) group, participants in higher ABSI group had significantly higher AAC score ($P < 0.001$).

TABLE 2 Univariable and multivariable logistic regression analyses of associations between a body shape index (ABSI) and abdominal aortic calcification (AAC).

	ABSI as a continuous variable[a]			ABSI as a categorical variable[b]		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Crude model	2.485	2.099–2.942	< 0.001	2.132	1.826–2.489	< 0.001
Model 1	1.378	1.150–1.653	0.001	1.257	1.057–1.494	0.010
Model 2	1.287	1.070–1.547	0.007	1.220	1.025–1.453	0.025
Model 3	1.259	1.046–1.516	0.015	1.201	1.008–1.430	0.041

Crude model: unadjusted.
Model 1: adjusted for age, smoking history, hypertension, diabetes, and osteoporosis.
Model 2: adjusted for variables included in Model 1 and body mass index, systolic blood pressure.
Model 3: adjusted for variables included in Model 2 and triglycerides, total cholesterol, creatinine, and fasting plasma glucose.
ABSI, a body shape index; AAC, abdominal aortic calcification; OR, odds ratio; CI, confidence interval.
[a]The OR was examined by per 1-unit increase of ABSI.
[b]The OR was examined regarding lower ABSI as reference (stratified by the optimal cutoff point of ABSI determined by ROC curve analysis).

of atherosclerosis in patients with type 2 diabetes (43, 44). Similarly, a study by Geraci et al. has also shown that ABSI might be a better predictor of carotid atherosclerosis in patients with hypertension than traditional nutrition indexes, including WC and BMI (20). However, some studies have found that ABSI is not superior to BMI and WC in predicting the risk of related disease or death. For example, two studies coincidentally found that in Chinese children, adolescents or adults and the elderly, the association between ABSI and pre-hypertension or hypertension was not higher than WC, BMI and WHtR, and the WHtR had the highest predictive power (21, 45). In addition, another study found that although ABSI was positively associated with arterial stiffness, its AUC value was significantly lower than WHtR in differentiating arterial stiffness, suggesting that ABSI might not be a better predictor of arterial stiffness in Chinese population (19). Besides, A large European cohort study

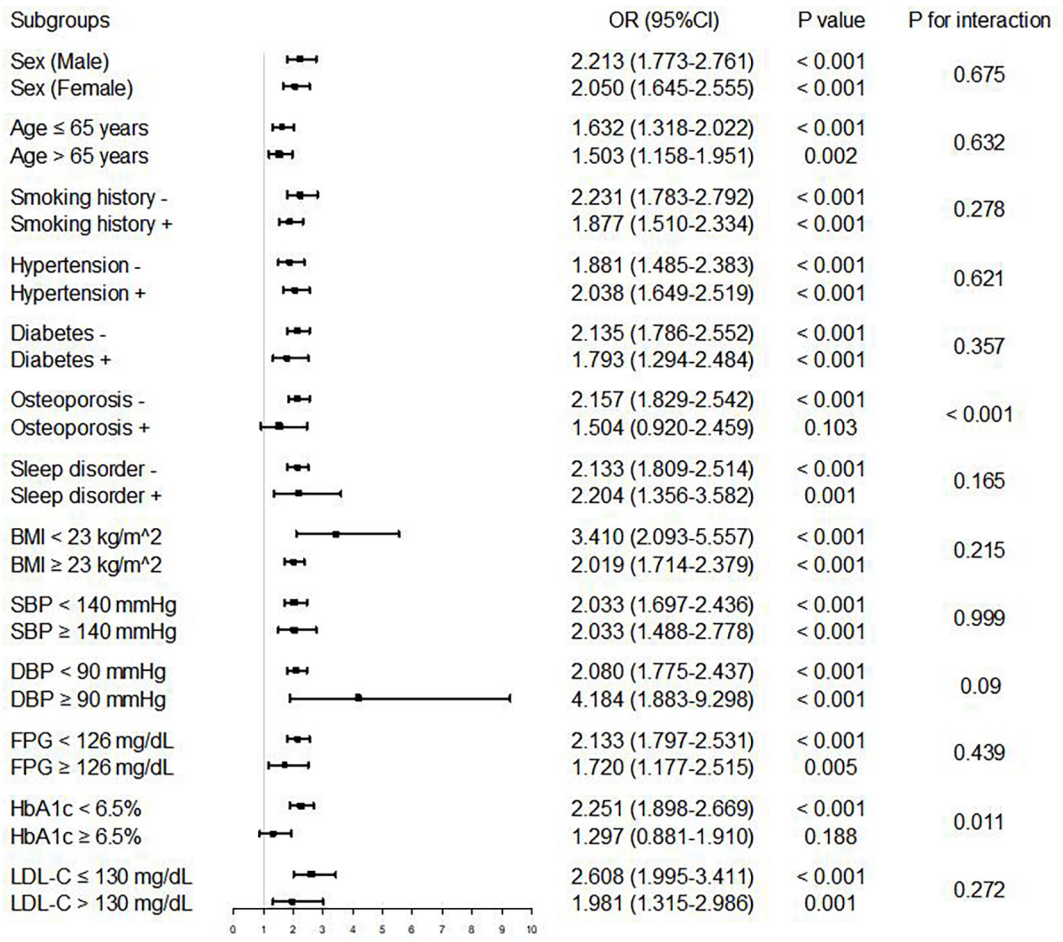


FIGURE 4
Logistic regression analysis of associations between ABSI and AAC in different subgroups. The OR was examined regarding lower ABSI as reference (stratified by the optimal cutoff point of ABSI determined by ROC curve analysis). *P* value < 0.05 and *P* for interaction < 0.05 were regarded as statistically significant. ABSI, a body shape index; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; CI, confidence interval.

TABLE 3 C-statistics for discrimination ability of different models.

Variables	AUC	95% CI	*P* value	*Z* value	*P* for comparison
Univariate model					
ABSI	0.625	0.608–0.642	< 0.001	Reference	Reference
Height	0.532	0.514–0.549	0.005	5.710	< 0.001
Weight	0.562	0.545–0.580	< 0.001	4.217	< 0.001
BMI	0.548	0.530–0.565	< 0.001	5.385	< 0.001
WC	0.505	0.487–0.523	0.652	6.841	< 0.001
WHtR	0.512	0.494–0.529	0.284	8.687	< 0.001
Combined variable model					
Baseline risk model[a] without ABSI	0.726	0.710–0.741	< 0.001	Reference	Reference
Baseline risk model[a] with ABSI	0.728	0.712–0.744	< 0.001	1.657	0.098

ABSI, a body shape index; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio; AUC, area under the curve; CI, confidence interval. [a]The baseline risk model included age, smoking history, diabetes, hypertension, osteoporosis, systolic blood pressure, triglycerides, total cholesterol, fasting plasma glucose, hemoglobin A1c, creatinine, uric acid, alkaline phosphatase, total calcium, and 25-OH-VitD3.

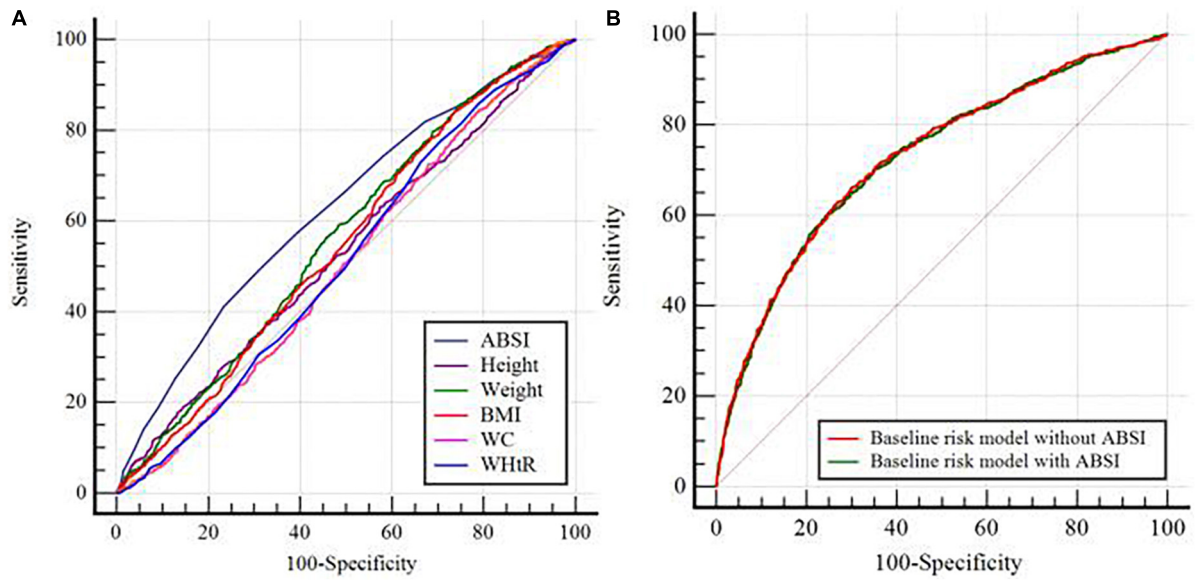


FIGURE 5
C-statistics evaluating incremental effect of different models. **(A)** ABSI vs. Height or Weight or BMI or WC or WHtR; **(B)** Baseline risk model without ABSI vs. Baseline risk model with ABSI. ABSI, a body shape index; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio. The baseline risk model included age, smoking history, diabetes, hypertension, osteoporosis, systolic blood pressure, triglycerides, total cholesterol, fasting plasma glucose, hemoglobin A1c, creatinine, uric acid, alkaline phosphatase, total calcium, and 25-OH-VitD3.

found that WC, BMI and WHtR were J-shaped correlated with all-cause mortality, while ABSI was positively associated with all-cause mortality, and BMI was superior to ABSI in predicting CVDs mortality (46). Furthermore, a meta-analysis of 30 clinical studies showed that higher ABSI was associated with increased risks of hypertension, type 2 diabetes, CVDs and all-cause death, which increased by 13, 35, 21, and 55%, respectively, and ABSI was superior to WC and BMI in predicting all-cause mortality, but it performed poorly in predicting chronic diseases (23). And a previous study has found that ABSI was associated with depression and anxiety, but this correlation existed only in men (47). In addition to these diseases, Zhang et al. have shown that higher ABSI was closely associated with higher urinary albumin-creatinine ratio (48). However, the studies mentioned above are aimed at exploring the association between ABSI and other diseases, and there is little evidence to compare ABSI with other anthropometric indicators in predicting the risk of AAC. Our study was the first to determine the ability of ABSI to recognize AAC. The results showed that higher ABSI increased the risk of AAC by 20–30% compared with lower ABSI. Additionally, we found that ABSI was a better indicator of AAC than BMI, WC and WHtR, and it showed similar predictive power to baseline risk models in the American population. Moreover, we also found for the first time that participants with higher ABSI had a higher risk of developing AAC in the subgroups with HbA1c $< 6.5\%$ and non-osteoporosis. The reason for this might be that osteoporosis and HbA1c ≥ 6.5 were the interference factors of ABSI risk prediction model, which was also the focus of our future research. The homogenization and differentiation of the above studies may be explained by the differences in race, sample size and population characteristics.

Innovatively, our findings added to the evidence between ABSI and CVDs from clinical to subclinical diseases. Moreover, we compared the predictive value of ABSI and other nutrition indexes for AAC for the first time. Therefore, this study provided additional information that the evaluation of ABSI might be of clinical significance in primary prevention to identify people at risk of CVDs. In spite of this, our study still had several limitations. Firstly, the present study was a cross-sectional study, which could not identify the causal association between ABSI and AAC. Secondly, in multivariate logistic regression analysis, we only controlled for several meaningful confounding factors, but there might be other confounding factors not included in our study, such as inflammatory indicators, menopause of women and use of medications. Thirdly, ABSI with a very small variance was highly concentrated around the mean value, which made it difficult to define the best critical value of ABSI in clinical practice. Fourthly, since the hip circumference of the participants was not measured during NHANES 2013–2014, we were unable to calculate the WHR, which means that we can't conduct a comparative analysis of ABSI, hip circumference and WHR. Finally, the data of this study only came from the general population of NHANES 2013–2014, so the findings may not be applicable more populations broadly.

Conclusion

Taken together, our results showed that WC, BMI, WHtR, and ABSI were significantly associated with AAC and found ABSI was superior to BMI, WC, and WHtR in predicting the risk of AAC. However, whether ABSI is suitable for clinical practice needed to be further studied in different populations.

Preprint statement

A preprint has previously been published (49).

Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by National Center for Health Statistics of the Center for Disease Control and Prevention Institutional Review Board. The patients/participants provided their written informed consent to participate in this study.

Author contributions

ZW conceived and designed the study. WL and ZW collected, analyzed and interpreted the data, and drafted the manuscript. WL was responsible for the management and retrieval of data, contributed to initial data analysis and interpretation, revised the article, and embellished the entire article for grammar when the manuscript was revised. WL, ML, JX, JG, and NL revised the manuscript. NL was the designer of the manuscript and approved to submit the manuscript finally. All authors agreed with the order of the author list, the description of the author contributions, read, and approved the final version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Schousboe J, Claflin D, Barrett-Connor E. Association of coronary aortic calcium with abdominal aortic calcium detected on lateral dual energy X-ray absorptiometry spine images. *Am J Cardiol.* (2009) 104:299–304. doi: 10.1016/j.amjcard.2009.03.041

2. Criqui MH, Denenberg JO, McClelland RL, Allison MA, Ix JH, Guerci A, et al. Abdominal aortic calcium, coronary artery calcium, and cardiovascular morbidity and mortality in the multi-ethnic study of atherosclerosis. *Arterioscler Thromb Vasc Biol.* (2014) 34:1574–9. doi: 10.1161/ATVBAHA.114.303268

3. Wilson PW, Kauppila LI, O'Donnell CJ, Kiel DP, Hannan M, Polak JM, et al. Abdominal aortic calcific deposits are an important predictor of vascular morbidity and mortality. *Circulation.* (2001) 103:1529–34. doi: 10.1161/01.cir.103.11.1529

4. Golledge J. Abdominal aortic calcification: clinical significance, mechanisms and therapies. *Curr Pharm Des.* (2014) 20:5834–8. doi: 10.2174/1381612820666140212195309

5. Szulc P. Abdominal aortic calcification: a reappraisal of epidemiological and pathophysiological data. *Bone.* (2016) 84:25–37. doi: 10.1016/j.bone.2015.12.004

6. Leopold J. Vascular calcification: mechanisms of vascular smooth muscle cell calcification. *Trends Cardiovasc Med.* (2015) 25:267–74. doi: 10.1016/j.tcm.2014.10.021

7. Phadwal K, Vrahnas C, Ganley IG, MacRae VE. Mitochondrial dysfunction: cause or consequence of vascular calcification? *Front Cell Dev Biol.* (2021) 9:611922. doi: 10.3389/fcell.2021.611922

8. Li M, Zhu Y, Jaiswal SK, Liu N. Mitochondria homeostasis and vascular medial calcification. *Calcif Tissue Int.* (2021) 109:113–20. doi: 10.1007/s00223-021-00828-1

9. Yang S, Yang H, Chen Y, Chen W. Unraveling the link between metabolic syndrome and abdominal aortic calcification. *Nutr Metab Cardiovasc Dis.* (2021) 31:464–71. doi: 10.1016/j.numecd.2020.10.003

10. Yuan M, Hsu F, Bowden DW, Xu J, Smith SC, Wagenknecht LE, et al. Relationships between measures of adiposity with subclinical atherosclerosis in patients with type 2 diabetes. *Obesity.* (2016) 24:1810–8. doi: 10.1002/oby.21540

11. Bendix EF, Johansen E, Ringgaard T, Wolder M, Starup-Linde J. Diabetes and abdominal aortic calcification-a systematic review. *Curr Osteoporos Rep.* (2018) 16:42–57. doi: 10.1007/s11914-018-0418-z

12. Rodríguez AJ, Scott D, Khan B, Khan N, Hodge A, English DR, et al. Low relative lean mass is associated with increased likelihood of abdominal aortic calcification in community-dwelling older Australians. *Calcif Tissue Int.* (2016) 99:340–9. doi: 10.1007/s00223-016-0157-z

13. Bray GA, Heisel WE, Afshin A, Jensen MD, Dietz WH, Long M, et al. The science of obesity management: an endocrine society scientific statement. *Endocr Rev.* (2018) 39:79–132. doi: 10.1210/er.2017-00253

14. Fox C, Massaro J, Hoffmann U, Pou K, Maurovich-Horvat P, Liu C, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the framingham heart study. *Circulation.* (2007) 116:39–48. doi: 10.1161/CIRCULATIONAHA.106.675355

15. Britton KA, Massaro JM, Murabito JM, Kreger BE, Hoffmann U, Fox CS. Body fat distribution, incident cardiovascular disease, cancer, and all-cause mortality. *J Am Coll Cardiol.* (2013) 62:921–5. doi: 10.1016/j.jacc.2013.06.027

16. Zhou B. Cooperative meta-analysis group of the working group on obesity in China. predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults–study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomed Environ Sci.* (2002) 15:83–96.

17. Misra A, Wasir J, Vikram N. Waist circumference criteria for the diagnosis of abdominal obesity are not applicable uniformly to all populations and ethnic groups. *Nutrition.* (2005) 21:969–76. doi: 10.1016/j.nut.2005.01.007

18. Krakauer N, Krakauer JC. A new body shape index predicts mortality hazard independently of body mass index. *PLoS One.* (2012) 7:e39504. doi: 10.1371/journal.pone.0039504

19. Zhang J, Fang L, Qiu L, Huang L, Zhu W, Yu Y. Comparison of the ability to identify arterial stiffness between two new anthropometric indices and classical obesity indices in Chinese adults. *Atherosclerosis.* (2017) 263:263–71. doi: 10.1016/j.atherosclerosis.2017.06.031

20. Geraci G, Zammuto M, Gaetani R, Mattina A, D'Ignoto F, Geraci C, et al. Relationship of a body shape index and body roundness index with carotid atherosclerosis in arterial hypertension. *Nutr Metab Cardiovasc Dis.* (2019) 29:822–9. doi: 10.1016/j.numecd.2019.04.013

21. Hu L, Hu G, Huang X, Zhou W, You C, Li J, et al. Different adiposity indices and their associations with hypertension among Chinese population from Jiangxi province. *BMC Cardiovasc Disord.* (2020) 20:115. doi: 10.1186/s12872-020-01388-2

22. Wu L, Zhu W, Qiao Q, Huang L, Li Y, Chen L. Novel and traditional anthropometric indices for identifying metabolic syndrome in non-overweight/obese adults. *Nutr Metab.* (2021) 18:3. doi: 10.1186/s12986-020-00536-x

23. Ji M, Zhang S, An R. Effectiveness of a body shape index (ABSI) in predicting chronic diseases and mortality: a systematic review and meta-analysis. *Obes Rev.* (2018) 19:737–59. doi: 10.1111/obr.12666

24. Zhao Q, Zhang K, Li Y, Zhen Q, Shi J, Yu Y, et al. Capacity of a body shape index and body roundness index to identify diabetes mellitus in han Chinese people in Northeast China: a cross-sectional study. *Diabet Med.* (2018) 35:1580–7. doi: 10.1111/dme.13787

25. Wei J, Liu X, Xue H, Wang Y, Shi Z. Comparisons of visceral adiposity index, body shape index, body mass index and waist circumference and their associations with diabetes mellitus in adults. *Nutrients.* (2019) 11:1580. doi: 10.3390/nu11071580

26. Cho H, Chung W, Moon S, Ryu O, Kim MK, Kang JG. Effect of sarcopenia and body shape on cardiovascular disease according to obesity phenotypes. *Diabetes Metab J.* (2021) 45:209–18. doi: 10.4093/dmj.2019.0223

27. Tang J, Zhao S, Yu S, Chi C, Ji H, Xiong J, et al. Association between hypertension-mediated organ damage and obesity defined by novel anthropometric indices in community-dwelling elderly individuals. *Clin Nutr.* (2021) 40:4473–80. doi: 10.1016/j.clnu.2020.12.035

28. Ma X, Chen L, Hu W, He L. Association between a body shape index and subclinical carotid atherosclerosis in population free of cardiovascular and cerebrovascular diseases. *J Atheroscler Thromb.* (2022) 29:1140–52. doi: 10.5551/jat.62988

29. Otaki Y, Watanabe T, Konta T, Watanabe M, Fujimoto S, Sato Y, et al. A body shape index and aortic disease-related mortality in Japanese general population. *J Atheroscler Thromb.* (2022). doi: 10.5551/jat.63753 [Epub ahead of print].

30. Burt V, Harris T. The third national health and nutrition examination survey: contributing data on aging and health. *Gerontologist.* (1994) 34:486–90. doi: 10.1093/geront/34.4.486

31. Kauppila LI, Polak JF, Cupples LA, Hannan MT, Kiel DP, Wilson PW. New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. *Atherosclerosis.* (1997) 132:245–50. doi: 10.1016/s0021-9150(97)00106-8

32. Schousboe J, Wilson K, Kiel D. Detection of abdominal aortic calcification with lateral spine imaging using DXA. *J Clin Densitom.* (2006) 9:302–8. doi: 10.1016/j.jocd.2006.05.007

33. Reid S, Schousboe J, Kimelman D, Monchka B, Jafari Jozani M, Leslie W. Machine learning for automated abdominal aortic calcification scoring of DXA vertebral fracture assessment images: a pilot study. *Bone.* (2021) 148:115943. doi: 10.1016/j.bone.2021.115943

34. Hollander M, Hak AE, Koudstaal PJ, Bots ML, Grobbee DE, Hofman A, et al. Comparison between measures of atherosclerosis and risk of stroke: the rotterdam study. *Stroke.* (2003) 34:2367–72. doi: 10.1161/01.STR.0000091393.32060.0E

35. Zhou R, Zhou H, Cui M, Wang Y, Tan J, Sawmiller D, et al. Association between aortic calcification and the risk of osteoporosis in a Chinese cohort: the chongqing osteoporosis study. *Calcif Tissue Int.* (2013) 93:419–25. doi: 10.1007/s00223-013-9776-9

36. Szulc P, Blackwell T, Kiel DP, Schousboe JT, Cauley J, Hillier T, et al. Abdominal aortic calcification and risk of fracture among older women - the SOF study. *Bone.* (2015) 81:16–23. doi: 10.1016/j.bone.2015.06.019

37. Nevill AM, Stewart AD, Olds T, Holder R. Relationship between adiposity and body size reveals limitations of BMI. *Am J Phys Anthropol.* (2006) 129:151–6. doi: 10.1002/ajpa.20262

38. Balkau B, Deanfield JE, Després J, Bassand J, Fox KA. International day for the evaluation of abdominal obesity (IDEA) a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168 000 primary care patients in 63 countries. *Circulation.* (2007) 116:1942–51. doi: 10.1161/CIRCULATIONAHA.106.676379

39. Pischon T, Boeing H, Hoffmann K, Bergmann M, Schulze MB, Overvad K, et al. General and abdominal adiposity and risk of death in Europe. *N Engl J Med.* (2008) 359:2105–20. doi: 10.1056/NEJMoa0801891

40. Seidell J. Waist circumference and waist/hip ratio in relation to all-cause mortality, cancer and sleep apnea. *Eur J Clin Nutr.* (2010) 64:35–41. doi: 10.1038/ejcn.2009.71

41. Zhu Q, Shen F, Ye T, Zhou Q, Deng H, Gu X. Waist-to-height ratio is an appropriate index for identifying cardiometabolic risk in Chinese individuals with normal body mass index and waist circumference. *J Diabetes.* (2014) 6:527–34. doi: 10.1111/1753-0407.12157

42. Duncan MJ, Mota J, Vale S, Santos MP, Ribeiro JC. Associations between body mass index, waist circumference and body shape index with resting blood pressure in Portuguese adolescents. *Ann Hum Biol.* (2013) 40:163–7. doi: 10.3109/03014460.2012.752861

43. Bouchi R, Asakawa M, Ohara N, Nakano Y, Takeuchi T, Murakami M, et al. Indirect measure of visceral adiposity 'a body shape index' (ABSI) is associated with arterial stiffness in patients with type 2 diabetes. *BMJ Open Diabetes Res Care.* (2016) 4:e000188. doi: 10.1136/bmjdrc-2015-000188

44. Dhana K, Kavousi M, Ikram MA, Tiemeier HW, Hofman A, Franco OH. Body shape index in comparison with other anthropometric measures in prediction of total and cause-specific mortality. *J Epidemiol Community Health.* (2016) 70:90–6. doi: 10.1136/jech-2014-205257

45. Tong Y, Han E. Associations between body shape, body adiposity and other indices: a case study of hypertension in Chinese children and adolescents. *Ann Hum Biol.* (2019) 46:460–6. doi: 10.1080/03014460.2019.1688864

46. Song X, Jousilahti P, Stehouwer CD, Söderberg S, Onat A, Laatikainen T, et al. Cardiovascular and all-cause mortality in relation to various anthropometric measures of obesity in Europeans. *Nutr Metab Cardiovasc Dis.* (2015) 25:295–304. doi: 10.1016/j.numecd.2014.09.004

47. Lotfi K, Hassanzadeh Keshteli A, Saneei P, Afshar H, Esmaillzadeh A, Adibi PA. Body shape index and body roundness index in relation to anxiety, depression, and psychological distress in adults. *Front Nutr.* (2022) 9:843155. doi: 10.3389/fnut.2022.843155

48. Zhang Y, Gao W, Li B, Liu Y, Chen K, Wang A, et al. The association between a body shape index and elevated urinary albumin-creatinine ratio in Chinese community adults. *Front Endocrinol.* (2022) 13:955241. doi: 10.3389/fendo.2022.955241

49. Zhenwei W, Min L, Jing X, Jing G, Naifeng L. Association between a body shape index and abdominal aortic calcification in the general population: national health and nutrition examination survey 2013-2014. *Res Squ.* [Preprint]. (2022). doi: 10.21203/rs.3.rs-812288/v1

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Association of body roundness index and its trajectories with all-cause and cardiovascular mortality among a Chinese middle-aged and older population: A retrospective cohort study

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Objectives: The body roundness index (BRI) is a novel anthropometric index that is a better indicator for predicting fat distribution than the body mass index (BMI). The longitudinal study can repeatedly collect measured results for the variables to be studied and then consider the potential effects of intraindividual changes in measurement. However, few population-based, longitudinal studies of BRI have been conducted, especially among the Chinese population. The study aimed to investigate the association of BRI and its longitudinal trajectories with all-cause and cardiovascular mortality.

Methods: A total of 71,166 participants with four times BRI measurements between January 2010 and December 2019 were included in this longitudinal study, with a median follow-up was 7.93years, and 11,538 deaths were recorded, of which 5,892 deaths were due to cardiovascular disease (CVD). A latent class growth mixture modeling (LCGMM) was used to identify BRI trajectories. Cox proportional hazard models were used to estimate associations between BRI trajectories and the risk of all-cause and cardiovascular mortality.

Results: In the restricted cubic spline regression models, a U-shaped relationship between BRI and all-cause and cardiovascular mortality was observed. Three BRI longitudinal trajectories of low-stable (mean BRI=2.59), moderate-stable (mean BRI=3.30), and high-stable (mean BRI=3.65) were identified by LCGMM. After being adjusted for potential confounders, the HRs for all-cause mortality were 1.18 (1.13–1.24) for the moderate-stable group and 1.74 (1.66–1.82) for the high-stable group compared to the low-stable group. The HRs for cardiovascular mortality were 1.12 (1.05–1.18) for the moderate-stable group and 1.64 (1.53–1.75) for the high-stable group compared to the low-stable group.

Conclusion: A nonlinear association of BRI with all-cause and cardiovascular mortality was observed, and participants in the higher BRI longitudinal trajectory group were significantly associated with an increased risk of all-cause and cardiovascular mortality.

KEYWORDS

cardiovascular risk, body roundness index, trajectories, retrospective cohort study, obesity

Introduction

With a rapidly aging global population and epidemiologic changes in disease, cardiovascular disease remains a significant cause of both morbidity and mortality globally, especially for middle-aged and older adults (1, 2), which also causes a substantial economic burden on society (3, 4). Obesity is a well-known independent risk factor for CVD and mortality (5). Most previous work has focused on the relationship between BMI with CVD and mortality (5, 6). However, studies in recent years have revealed that because BMI is not sufficient to distinguish between muscle and fat mass, it may not adequately reflect the fat distribution (7–9), mainly when abdominal fat is strongly associated with CVD (10, 11). As a complement to BMI, the BRI, which combines height and waist circumference (WC) measurements, is a new anthropometric index that is a better indicator to describe fat distribution (12).

Prior studies have suggested that BRI is a valuable predictor of cardiovascular disease in men and women in the Chinese population, but most of them are based on a cross-sectional design (13, 14). The longitudinal study design provides the opportunity to collect measured results for the variables to be studied repeatedly and then take the potential effects of intraindividual changes in measurement into account (15–17). Group-based trajectory modeling techniques such as LCGMM are a universal approach to illustrate the development of the variable over time and can be used to disentangle underlying population heterogeneity (18, 19). However, very few studies were conducted on the longitudinal trajectory of BRI, especially among the middle-aged and older Chinese population. A study focused on trajectories of BMI prior to CVD diagnosis identified three distinct BMI trajectories, probably due to the small number of study participants(n = 6,126), and the results suggested that BMI alone is not sufficient to identify people at high risk for CVD in middle-aged and older adults (20). Besides, a recent study based on a longitudinal trajectory model found that higher levels of BRI over time were statistically related to a higher risk of CVD and mortality. However, this study seemed to be restricted by a short follow-up time and almost a 4:1 male-to-female ratio (21). Therefore, our study aimed to examine the association of BRI with all-cause and cardiovascular mortality, identify longitudinal trajectories in BRI, and then estimate the associations of BRI trajectories with all-cause and cardiovascular mortality based on a sizeable dynamical cohort study.

Method

Study population

This retrospective cohort study was performed in a dynamic population based on an annual health check-up project, and it has been carried out since 2010 in Xin Zheng, Henan Province. All participants were asked to complete a questionnaire and to take anthropometric and laboratory measurements at baseline and follow-up. Details of this dynamic cohort have been described previously (22–24). The data were analyzed from residents' electronic health records in the Xin Zheng Hospital Information System from January 2010 to December 2019. To ensure the quality of the cohort and trajectories, the records with missing data for BRI were removed, and each study participant kept one health examination record per year. Between January 2010 and December 2019, 102,797 participants with four or more medical records were enrolled. We excluded 31,631 individuals who met with any one of the following circumstances: a history of CVD at baseline (n = 18,704); aged less than 45 years old (n = 7,981); missing information (n = 1,682) on BMI at baseline; missing information (n = 3,264) on smoking, drinking, physical activity, and Marital status at baseline. The records and times of the four examinations of the participants are presented in Supplemental Table S1. Finally, in the study, we have data from 71,166 participants with four recordings, including when the outcome occurred.

Data collection

Data were collected through a standardized questionnaire, as well as from physical and laboratory examinations. Standardized questionnaire of the National Norms for Basic Public Health Services (Third Edition), which included their sociodemographic characteristics (age, sex), medical history (coronary heart disease (CHD) and stroke), smoking, drinking, and physical activity, were administered by trained research staff. Based on self-reported marital status, smoking, and drinking, participants were classified as follows: living with a partner or without a partner; nonsmokers (including previous smokers) or current smokers; and never, occasionally, or daily drinkers. The frequency of physical activity was described as never, occasionally, and daily (25).

Standing height and weight were measured to the nearest 0.1 cm and 0.1 kg with the participant standing erect on bare feet, and the results were recorded by the mean of two replicate measurements. BMI was calculated as weight (kg) divided by height squared (m). Waist circumference was measured to the nearest 0.1 cm at the midpoint between the lowest rib margin and the iliac crest following a standard protocol. Blood pressure was measured at least twice using an automatic sphygmomanometer (OMRON HEM-7125, Kyoto, Japan), and the mean of the two measurements qualified was used in the analysis.

Assessment of BRI

BRI was calculated as follows: (12).

$$BRI = 364.2 - 365.5 \times \sqrt{1 - \frac{(WC/2\pi)^2}{(0.5height)^2}}$$, and then the quartiles of BRI and its trajectories were used to statistical analysis.

Assessment of outcomes

The primary outcomes in the study were all-cause and CVD mortality, where CVD death was defined as death from CHD and death from stroke. For mortality surveillance, participants' mortality information was obtained from the Xinzheng Center for Disease Control and Prevention from the baseline survey to October 7, 2022. The causes of death were recorded using codes from the International Classification of Diseases (ICD-10), in which death from CVD was defined as I20eI25 and I60eI69.

Statistical analyzes

For non-normal distribution, continuous variables are characterized by the median (interquartile range (IQR)), while categorical variables are expressed as frequency (%). The Kruskal-Wallis test was used to compare continuous variables and the Chi-square test for categorical variables.

Latent BRI trajectories identification

The latent class growth mixture modeling (LCGMM) was used to explore heterogeneity in the dynamic course of BRI to distinguish subgroups of similar underlying BRI trajectories as experienced over time. Models were fit using the package "LCMM" (version 2.0.0.) in R to group participants with a similar trajectory of BRI development from the first examination to the fourth (18). Three possible polynomial specifications were allowed to describe the longitudinal BRI response as a function of time: a linear, quadratic, and a cubic specification, and every polynomial model (order 1 to 3) was, respectively, modeled as a 1 to 4 class solution. Given that no clear standard exists, the choice of the best model was evaluated by the following composite criteria: (1) observing improvement in the Bayesian information criterion (BIC); (2) at least 5% participants in each trajectory class; (3) values of mean posterior class membership probabilities (>70%); (4) confirming visually distinct trajectories. (21, 26) For ease of interpretation, we have assigned labels to these trajectories based on their modeled graphic patterns.

Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) between all-cause and cardiovascular mortality and BRI trajectories, quartiles of BRI at baseline, and per 1sd increment in BRI after inspection of Schoenfeld residuals. Model 1 was unadjusted; Model 2 was adjusted for sex and age; Model 3 was adjusted for sex, age, smoking status, alcohol drinking level, and physical activity. We performed tests for linear trends by modeling BRI quartiles as ordinal variables. To assess nonlinearity, we performed a restricted cubic spline to the multivariable cox proportional hazards models, and then the cut-off value was estimated by trying all possible values and choosing the cut-off point with the highest likelihood. We performed subgroup analyzes based on sex. To verify the robustness of the results, we conducted an additional sensitivity analysis, excluding those participants with less than 3 years of follow-up. Besides, we similarly analyzed the trajectories of BMI and waist circumference of the participants in our study.

$p < 0.05$ for a two-sided test was regarded as statistically significant. All analyzes were performed using R version 4.1.3 (R Foundation for Statistical Computing).

Results

Baseline characteristics

The baseline characteristics of the study sample, stratified by all-cause and cardiovascular mortality, are summarized in Table 1. A total of 71,166 study participants (women: 36,503) were included in the present study. The median age (interquartile range) for women and men was 61.75 (56.78–69.13) and 61.97 (57.38–68.56), respectively. During the 512,131 person-years of follow-up (median follow-up time 7.93 years), 11,538 deaths were recorded, of which 5,892 deaths were due to CVD, and 4,065 and 2,108 cases of CHD and stroke, respectively. Compared with participants who survived to the end of the study, the decedents were older, were more likely to be male, living with a partner, and had a higher proportion of smokers. Similar demographic characteristics were observed in participants who died from cardiovascular disease, except for the proportion of smoking.

Associations of BRI and its trajectories with all-cause and cardiovascular mortality

Based on the BIC, class membership posterior probabilities, and classification to assess the goodness-of-fit of the competing LCGMM models, the model with 3 BRI trajectories among the 71,166 participants was identified as the best-fit model: there were low-stable (mean BRI = 2.59, $n = 12{,}972$), moderate-stable (mean BRI = 3.30, $n = 26{,}796$), and high-stable (mean BRI = 3.65, $n = 31{,}398$) trajectories (Supplemental Tables S2, S3; Figure 1). Though several identified latent classes had a low proportion of participants (<20%), they were highly discriminated with high mean posterior probabilities and posterior probabilities. The proportion of men was higher in the "high-stable" and "moderate-stable" trajectory groups, but the "low-stable" group contained more women. Compared with participants in the low-stable class, counterparts in the other two groups were more likely in higher BMI and waist circumference values.

The estimated risk for all-cause and cardiovascular mortality by BRI quartile and its trajectories were presented in Table 2. After adjusting for potential confounders, as compared with quartile 1 of BRI, with quartiles 2, 3, and 4, the HRs for all-cause mortality were 0.96(0.92–1.01), 0.91(0.86–0.96) and 0.95(0.89–0.99), respectively (P trend =0.010); the HRs for cardiovascular mortality were 0.92(0.86–0.98), 0.93(0.87–0.99) and 0.98(0.91–1.05), respectively (P trend =0.617). Further, compared with the low-stable category, counterparts in the other two groups had a significantly higher risk of all-cause and CVD mortality. After being adjusted for potential confounders, the HRs for all-cause mortality were 1.18 (1.13–1.24) for the moderate-stable group and 1.74 (1.66–1.82) for the high-stable group. The HRs for cardiovascular mortality were 1.12 (1.05–1.18) for the moderate-stable group and 1.64 (1.53–1.75) for the high-stable group. The dose–response relationships between the BRI and all-cause and cardiovascular mortality by restricted cubic spline models in the middle-aged and elderly population were presented in Figures 2, 3. The cut-off values of all-cause and cardiovascular mortality were 3.60 and 3.42, respectively, and while BRI < 3.60, the HR for all-cause mortality was 0.93 (0.89–0.96) as per 1 SD BRI increased, $p < 0.001$. As BRI was more than 3.60, the HR for all-cause mortality was 1.05 (1.01–1.10) as per 1 SD BRI increased, $p = 0.026$. Similar results were observed for cardiovascular disease mortality.

Subgroup analyzes and sensitivity analyzes

The results of the subgroup analysis by sex were generally consistent with the primary analysis in Supplemental Figures S1, S2. In all-cause and cardiovascular mortality, there was a U-shaped

TABLE 1 Baseline characteristics of the study population stratified by outcome.

Variables	All-cause mortality		*p* value	Cardiovascular disease mortality		*P* value
	No (*n*=59,628)	Yes (*n*=11,538)		No (*n*=65,274)	Yes (*n*=5,892)	
Age (years)	60.75 (56.48, 66.11)	71.81 (63.99, 77.78)	<0.001	61.31 (56.76, 67.56)	71.95 (64.28, 77.85)	<0.001
Gender (%)			<0.001			<0.001
Women	31,366 (52.60)	5,137 (44.52)		33,781 (51.75)	2,722 (46.20)	
Men	28,262 (47.40)	6,401 (55.48)		31,493 (48.25)	3,170 (53.80)	
Marital status (%)			<0.001			<0.001
Living without partner	8,767 (14.70)	3,906 (33.85)		10,591 (16.23)	2,082 (35.34)	
Living with partner	50,861 (85.30)	7,632 (66.15)		54,683 (83.77)	3,810 (64.66)	
Smoking (%)			0.0075			0.1496
Never or previous	52,055 (87.30)	9,967 (86.38)		56,923 (87.21)	5,099 (86.54)	
Current	7,573 (12.70)	1,571 (13.62)		8,351 (12.79)	793 (13.46)	
Drinking (%)			<0.001			<0.001
Never	55,271 (92.69)	10,702 (92.75)		60,539 (92.75)	5,434 (92.23)	
Occasionally	3,513 (5.89)	566 (4.91)		3,781 (5.79)	298 (5.06)	
Daily	844 (1.42)	270 (2.34)		954 (1.46)	160 (2.72)	
Physical activity (%)			<0.001			0.0015
Never	48,389 (81.15)	9,584 (83.06)		5,3,107 (81.36)	4,866 (82.59)	
Occasionally	5,212 (8.74)	1,016 (8.81)		5,700 (8.73)	528 (8.96)	
Daily	6,027 (10.11)	938 (8.13)		6,467 (9.91)	498 (8.45)	
WC	80.00 (75.00, 85.32)	80.00 (74.70, 85.00)	<0.001	80.00 (75.00, 85.00)	80.00 (74.00, 85.00)	<0.001
BMI	23.66 (22.23, 25.54)	23.19 (21.48, 24.97)	<0.001	23.62 (22.20, 25.46)	23.31 (21.60, 25.15)	<0.001
BRI	3.25 (2.72, 3.88)	3.14 (2.62, 3.78)	<0.001	3.24 (2.71, 3.87)	3.19 (2.62, 3.83)	<0.001
Time of follow-up	8.08 (6.08, 8.93)	5.94 (4.07, 7.36)	<0.001	8.00 (5.96, 8.92)	5.99 (4.17, 7.81)	<0.001

Data are presented, median (interquartile range), or number (percentage). BMI, body mass index; WC, waist circumference; BRI, body roundness index.

relationship for both sexes, but differences in cutoff values emerged. For cardiovascular mortality, the BRI cutoff value was higher in women than in men, while in all-cause mortality, it was higher in men than in women. Furthermore, a sensitivity analysis showed similar results to the primary analysis. When excluding those participants with less than 3 years of follow-up, the parameters of the LCGMM model were also much optimized, and similar results of the association of BRI and its trajectories with all-cause and cardiovascular mortality were observed in Supplementary Tables S4, S5. From Supplementary Figures S3, S4, it can be found that both BMI and WC trajectories appear crossed and do not have a good differentiation ability compared to BRI, and the details of the trajectory models of BMI and WC are presented in Supplementary Tables S6, S7. Besides, after comparing the results of the Cox regression models, it was found that only the results of BRI are statistically significant. (Supplementary Tables S8, S9).

Discussion

The median follow-up of the study was 7.93 years (range 5.86–8.92), with four examinations in all participants. A U-shaped trend in the association between BRI and all-cause and cardiovascular mortality was observed in the study. The all-cause and cardiovascular mortality were lowest when the BRI was 3.60 and 3.42, respectively. During the follow-up period, according to the BRI trajectory of the study participants, we divided them into three groups, namely, low-stable, moderate-stable, and high-stable. Overall, the BRI of the study subjects showed a steady ascending trend during the entire study follow-up.

As a universal indicator of obesity, BMI has always been a hot spot for research. Several epidemiological studies have found a U-shaped association between BMI and all-cause and cardiovascular mortality, including in the middle-aged and elderly population. (27–29) At the same time, a J-shaped association has also been found between BMI and all-cause and cardiovascular mortality. (28, 30) Previous research suggested that this debate may lie in the fact that BMI does not discriminate well between fat mass and lean body mass. (31) Meanwhile, an association between BRI and cardiovascular mortality was observed (13, 32, 33), including a U-shaped relationship (34), especially when BRI was able to better distinguish the proportion between total fat and abdominal fat. (12) The proliferation and hypertrophy of adipocytes can affect the integrity and functionality of adipose tissue, which further affects the risk of cardio metabolism. (35, 36) Adipose tissue causes damage to cardio metabolism by affecting metabolic homeostasis, which in turn creates a state of low-grade systemic inflammation and insulin resistance. (37) Furthermore, the expansion of adipose tissue can cause a series

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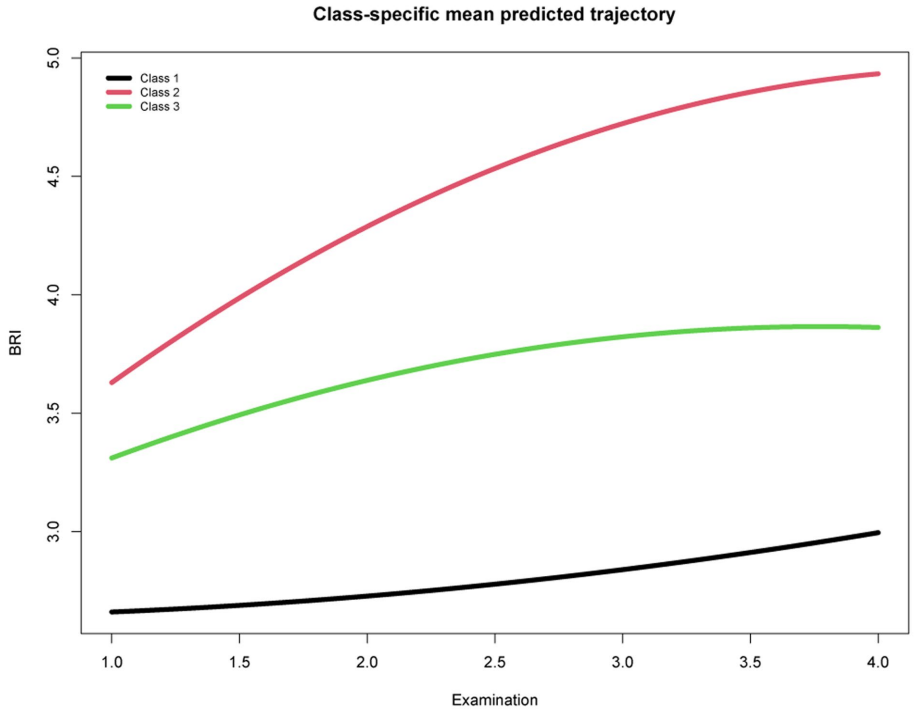

FIGURE 1
Trajectories of body roundness index from the first physical examination to the fourth.

TABLE 2 Cox regression analysis between BRI and all-cause mortality and cardiovascular mortality.

	Model 1			Model 2			Model 3		
	HR	95%CI	*P*	HR	95%CI	*P*	HR	95%CI	*P*
All-cause mortality									
Q1(2.03–2.54)	1(Ref)			1(Ref)			1(Ref)		
Q2(2.82–3.11)	0.87	0.83, 0.92	<0.001	0.97	0.92, 1.02	0.214	0.96	0.92, 1.01	0.158
Q3(3.36–3.67)	0.79	0.75, 0.84	<0.001	0.91	0.86, 0.96	<0.001	0.91	0.86, 0.96	<0.001
Q4(4.09–4.91)	0.87	0.83, 0.92	<0.001	0.95	0.90, 0.99	0.036	0.95	0.89, 0.99	0.039
P_{trend}			<0.001			0.008			0.010
Low-stable	1(Ref)			1(Ref)			1(Ref)		
Moderate-stable	1.17	1.12, 1.23	<0.001	1.18	1.13, 1.23	<0.001	1.18	1.13, 1.24	<0.001
High-stable	2.09	1.99, 2.19	<0.001	1.74	1.66, 1.82	<0.001	1.74	1.66, 1.82	<0.001
CVD mortality									
Q1(2.03–2.54)	1(Ref)			1(Ref)			1(Ref)		
Q2(2.82–3.11)	0.83	0.77, 0.89	<0.001	0.92	0.86, 0.99	0.027	0.92	0.86, 0.98	0.018
Q3(3.36–3.67)	0.81	0.76, 0.87	<0.001	0.93	0.87, 1.01	0.056	0.93	0.87, 0.99	0.043
Q4(4.09–4.91)	0.91	0.84, 0.97	0.006	0.98	0.91, 1.05	0.597	0.98	0.91, 1.05	0.532
P_{trend}			0.009			0.675			0.617
Low-stable	1(Ref)			1(Ref)			1(Ref)		
Moderate-stable	1.09	1.03, 1.16	0.004	1.11	1.05, 1.18	<0.001	1.12	1.05, 1.18	<0.001
High-stable	1.94	1.82, 2.07	<0.001	1.64	1.53, 1.75	<0.001	1.64	1.53, 1.75	<0.001

Data were showed by HR, 95% CI and *P* value. Model 1: Unadjusted. Model 2: Adjusted for age and gender. Model 3: Adjusted for age, gender, smoking, alcohol consumption, and physical activity. Q1: 1st Quartiles; Q2: 2nd Quartiles; Q3: 3rd Quartiles; Q4: 4th Quartiles. Q1 to Q4 are the quartiles of BRI at baseline.

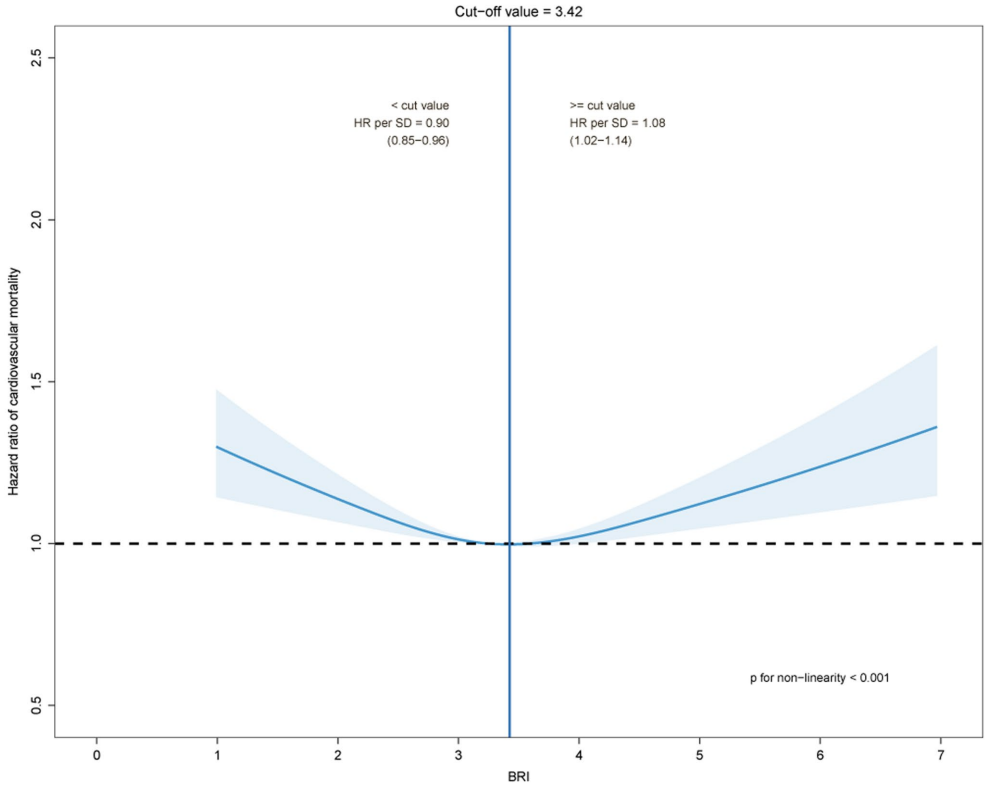

FIGURE 2
The dose−response relationships between the body roundness index and cardiovascular mortality by restricted cubic spline models.

of bodily reactions, such as fibrosis (38), hypoxia (39), inflammation (40), dysregulated adipokine secretion (41), a pro-inflammatory and pro-thrombotic state and endothelial dysfunction, all of which would be cardiovascular risk factors. (42) Especially for the middle-aged and elderly population, BRI was related to malnutrition, fatigue, decreased activity tolerance, and muscle atrophy, all of these were risk factors for death in the elderly. (43, 44)

Although previous studies were abundant, most classified variables into predefined categories, such as based on established criteria or quartiles. It has been reported that this classification method may lead to the misclassification of those individuals close to the classification cutoff point. (20) Whereas, in the LGCMM model in this study, it was assumed that there was no single developmental curve in the study population and that individuals belonged to different subgroups with different developmental trajectories. The pattern of BRI changes during the follow-up period was modeled based on population heterogeneity. In recent years, many studies on the trajectory analysis of obesity indicators and cardiovascular disease have been reported. For instance, Marie-Jeanne Buscot (2018) and Kim Blond (2020) have investigated the association between distinct BMI trajectories in childhood and cardiovascular risk factors in adulthood. (18, 45) By analyzing BMI trajectories, Klodian Dhana et al. found that BMI alone is insufficient to identify high-risk subjects for cardiovascular disease in the middle-aged and elderly population. (20) A recent study of BRI trajectories conducted by Wu et al. found that higher BRI levels were significantly associated with an increased risk of CVD over time. (21) Our conclusions are consistent with these findings. In our middle-aged and elderly cohort, we identified three BRI trajectories that slowly increased over time and found that higher BRI levels were significantly associated with an increased risk of cardiovascular mortality.

Few studies, based on a large population, have assessed the association between BRI trajectories and cardiovascular disease risk. In fact, our study has important implications for the primary prevention of cardiovascular mortality in the middle-aged and elderly and public health. First, because of the U-shaped trend in the association between BRI and all-cause and cardiovascular mortality, from an individual level, maintaining the BRI at around 3.30 has the lowest risk. It is noteworthy that although no U-shaped association has been observed in waist circumference, it is also an important indicator of obesity signs. If more evidence becomes available in the future, it would be helpful for people to choose an optimal control range when managing body shape. Second, recent studies have revealed that the cardiovascular risk of obesity is cumulative and that the duration of obesity may substantially impact CVD outcomes. (18, 46) When participants with less than 3 years of follow-up were excluded, the model was enhanced, though the results remained robust, suggesting that the long-term patterns of BRI may have a potential additional impact on all-cause and cardiovascular mortality. Considering that cardiovascular disease prevention is long-term and dynamic, especially with increasing age and accumulation of co-morbidities, based on population considerations, our results emphasize that dynamic surveillance and multi-level prevention should be implemented on a long-term or even lifetime basis.

Strengths of this study include the cohort study design, the availability of repeated measurements of BRI, and identify groups of

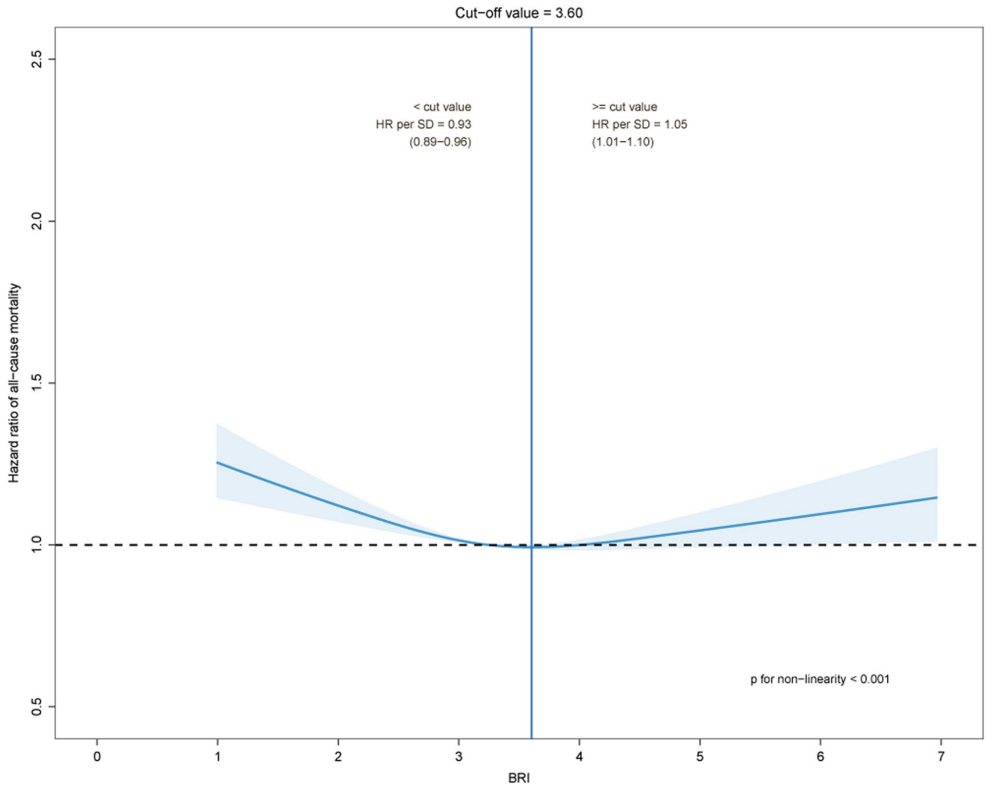

FIGURE 3
The dose−response relationships between the body roundness index and all-cause mortality by restricted cubic spline models.

individuals with similar patterns of BRI trajectories based on long-term follow-up and repeated measurement. On the other hand, several limitations of the study are worth mentioning for future improvements. First, the study was conducted among middle-aged and elderly Chinese individuals with an average age of approximately 63.06 years, making it difficult to generalize to all populations. Second, although we have adjusted for some confounders as far as possible, the possibility of bias still existed, such as the use of antidiabetic, antihypertension drugs and other medications, dietary factors, genetic factors, and unavoidable recall bias. Then, only four physical examination records were kept for each participant during the follow-up period, which may have limited the ability to investigate potential effects.

Conclusion

Overall, as an easily accessible anthropometric indicator of obesity, a U-shaped association between BRI and all-cause and cardiovascular mortality was observed in the study. In addition, the long-term trajectory study found that higher BRI levels were associated with an increased risk of all-cause and cardiovascular mortality over time, while there may be some potential effects of long-term patterns of BRI. Longitudinal trajectory models made up for some of the limitations of cross-sectional studies, but in the future, the potential impact caused by follow-up time needs to be examined further.

Sharing statement of data

Due to third-party requirements for confidentiality, the raw data in the study are not currently available to the public but can be requested from the corresponding authors upon reasonable request.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: Due to third-party requirements for confidentiality, the raw data in the study are not currently available to the public but can be requested from the corresponding authors upon reasonable request. Requests to access these datasets should be directed to Songhe Shi, ssh@zzu.edu.cn

Ethics statement

Study procedures were performed in accordance with the Declaration of Helsinki ethical principles for medical research involving human subjects. The study was approved by the Ethics Committee of Zhengzhou University, and written informed consent was obtained from all participants (Reference Number: ZZUIRB2019-019).

Author contributions

JD performed primary research design, statistical analysis, and wrote first draft. KB, ZS, and XC contributed to the analysis and interpretation of the data. SS planned overall, supervised the data analysis, and revised it critically. All authors approved the final version submitted and published and are responsible for all aspects of the study.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1107158/full#supplementary-material

References

1. Roth GA, Forouzanfar MH, Moran AE, Barber R, Nguyen G, Feigin VL, et al. Demographic and epidemiologic drivers of global cardiovascular mortality. *N Engl J Med*. (2015) 372:1333–41. doi: 10.1056/NEJMoa1406656

2. Ren J, Zhang Y. Targeting autophagy in aging and aging-related cardiovascular diseases. *Trends Pharmacol Sci*. (2018) 39:1064–76. doi: 10.1016/j.tips.2018.10.005

3. Shaw LJ, Goyal A, Mehta C, Xie J, Phillips L, Kelkar A, et al. 10-year resource utilization and costs for cardiovascular care. *J Am Coll Cardiol*. (2018) 71:1078–89. doi: 10.1016/j.jacc.2017.12.064

4. Liu S, Li Y, Zeng X, Wang H, Yin P, Wang L, et al. Burden of cardiovascular diseases in China, 1990-2016: findings from the 2016 global burden of disease study. *JAMA Cardiol*. (2019) 4:342–52. doi: 10.1001/jamacardio.2019.0295

5. 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. doi: 10.1093/eurheartj/ehab454

6. Aune D, Sen A, Norat T, Janszky I, Romundstad P, Tonstad S, et al. Body Mass index, abdominal fatness, and heart failure incidence and mortality: a systematic review and dose-response meta-analysis of prospective studies. *Circulation*. (2016) 133:639–49. doi: 10.1161/CIRCULATIONAHA.115.016801

7. Cespedes Feliciano EM, Chen WY, Bradshaw PT, Prado CM, Alexeeff S, Albers KB, et al. Adipose tissue distribution and cardiovascular disease risk among breast cancer survivors. *J Clin Oncol*. (2019) 37:2528–36. doi: 10.1200/JCO.19.00286

8. Chandramouli C, Tay WT, Bamadhaj NS, Tromp J, Teng TK, Yap JJL, et al. Association of Obesity with heart failure outcomes in 11 Asian regions: a cohort study. *PLoS Med*. (2019) 16:e1002916. doi: 10.1371/journal.pmed.1002916

9. Piche ME, Tchernof A, Despres JP. Obesity phenotypes, diabetes, and cardiovascular diseases. *Circ Res*. (2020) 126:1477–500. doi: 10.1161/CIRCRESAHA.120.316101

10. van't Klooster CC, Ridker PM, Hjortnaes J, van der Graaf Y, Asselbergs FW, Westerink J, et al. The relation between systemic inflammation and incident cancer in patients with stable cardiovascular disease: a cohort study. *Eur Heart J*. (2019) 40:3901–9. doi: 10.1093/eurheartj/ehz587

11. Koenen M, Hill MA, Cohen P, Sowers JR. Obesity, adipose tissue and vascular dysfunction. *Circ Res*. (2021) 128:951–68. doi: 10.1161/CIRCRESAHA.121.318093

12. Thomas DM, Bredlau C, Bosy-Westphal A, Mueller M, Shen W, Gallagher D, et al. Relationships between body roundness with body fat and visceral adipose tissue emerging from a new geometrical model. *Obesity (Silver Spring)*. (2013) 21:2264–71. doi: 10.1002/oby.20408

13. Xu J, Zhang L, Wu Q, Zhou Y, Jin Z, Li Z, et al. Body roundness index is a superior indicator to associate with the cardio-metabolic risk: evidence from a cross-sectional study with 17,000 eastern-China adults. *BMC Cardiovasc Disord*. (2021) 21:97. doi: 10.1186/s12872-021-01905-x

14. Rico-Martin S, Calderon-Garcia JF, Sanchez-Rey P, Franco-Antonio C, Martinez Alvarez M, Sanchez Munoz-Torrero JF. Effectiveness of body roundness index in predicting metabolic syndrome: a systematic review and meta-analysis. *Obes Rev*. (2020) 21:e13023. doi: 10.1111/obr.13023

15. Becque MD, Katch VL, Rocchini AP, Marks CR, Moorehead C. Coronary risk incidence of obese adolescents: reduction by exercise plus diet intervention. *Pediatrics*. (1988) 81:605–12. doi: 10.1542/peds.81.5.605

16. Zheng Y, Song M, Manson JE, Giovannucci EL, Hu FB. Group-based trajectory of body shape from ages 5 to 55 years and cardiometabolic disease risk in 2 us cohorts. *Am J Epidemiol*. (2017) 186:1246–55. doi: 10.1093/aje/kwx188

17. Nagin DS. Group-based trajectory modeling: An overview. *Ann Nutr Metab*. (2014) 65:205–10. doi: 10.1159/000360229

18. Buscot MJ, Thomson RJ, Juonala M, Sabin MA, Burgner DP, Lehtimäki T, et al. Distinct child-to-adult body Mass index trajectories are associated with different levels of adult Cardiometabolic risk. *Eur Heart J*. (2018) 39:2263–70. doi: 10.1093/eurheartj/ehy161

19. Lee J, Song RJ, Musa Yola I, Shrout TA, Mitchell GF, Vasan RS, et al. Association of Estimated Cardiorespiratory Fitness in midlife with Cardiometabolic outcomes and mortality. *JAMA Netw Open*. (2021) 4:e2131284. doi: 10.1001/jamanetworkopen.2021.31284

20. Dhana K, van Rosmalen J, Vistisen D, Ikram MA, Hofman A, Franco OH, et al. Trajectories of body Mass index before the diagnosis of cardiovascular disease: a latent class trajectory analysis. *Eur J Epidemiol*. (2016) 31:583–92. doi: 10.1007/s10654-016-0131-0

21. Wu M, Yu X, Xu L, Wu S, Tian Y. Associations of longitudinal trajectories in body roundness index with mortality and cardiovascular outcomes: a cohort study. *Am J Clin Nutr*. (2022) 115:671–8. doi: 10.1093/ajcn/nqab412

22. Bai K, Chen X, Shi Z, He K, Hu X, Song R, et al. Hypertension modifies the associations of body Mass index and waist circumference with all-cause mortality among older Chinese: a retrospective cohort study. *BMC Geriatr*. (2022) 22:441. doi: 10.1186/s12877-022-03057-9

23. He K, Zhang WL, Hu XQ, Zhao H, Guo BX, Shi Z, et al. Relationship between multimorbidity, disease cluster and all-cause mortality among older adults: a retrospective cohort analysis. *BMC Public Health*. (2021) 21:1080. doi: 10.1186/s12889-021-11108-w

24. Song R, Chen X, He K, Hu X, Bai K, Shi W, et al. Associations of Bmi with all-cause mortality in Normoglycemia, impaired fasting glucose and type 2 diabetes mellitus among an elderly Chinese population: a cohort study. *BMC Geriatr*. (2022) 22:690. doi: 10.1186/s12877-022-03382-z

25. He K, Zhang W, Hu X, Zhao H, Song R, Bai K, et al. Stronger associations of body Mass index and waist circumference with diabetes than waist-height ratio and triglyceride glucose index in the middle-aged and elderly population: a retrospective cohort study. *J Diabetes Res*. (2022) 2022:9982390. doi: 10.1155/2022/9982390

26. Marioni RE, Proust-Lima C, Amieva H, Brayne C, Matthews FE, Dartigues JF, et al. Cognitive lifestyle jointly predicts longitudinal cognitive decline and mortality risk. *Eur J Epidemiol*. (2014) 29:211–9. doi: 10.1007/s10654-014-9881-8

27. Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, Ballard-Barbash R, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med*. (2006) 355:763–78. doi: 10.1056/NEJMoa055643

28. Aune D, Sen A, Prasad M, Norat T, Janszky I, Tonstad S, et al. Bmi and all cause mortality: systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. *BMJ*. (2016) 353:i2156. doi: 10.1136/bmj.i2156

29. Lee HJ, Kim HK, Han KD, Lee KN, Park JB, Lee H, et al. Age-dependent associations of body Mass index with myocardial infarction, heart failure, and mortality in over 9 million Koreans. *Eur J Prev Cardiol*. (2022) 29:1479–88. doi: 10.1093/eurjpc/zwac094

30. Jung MH, Yi SW, An SJ, Balkau B, Yi JJ, Kim H. Complex interaction of fasting glucose, body Mass index, age and sex on all-cause mortality: a cohort study in 15 million Korean adults. *Diabetologia*. (2020) 63:1616–25. doi: 10.1007/s00125-020-05160-1

31. Lee DH, Keum N, Hu FB, Orav EJ, Rimm EB, Willett WC, et al. All cause and cause specific mortality in men: prospective us cohort study. *BMJ*. (2018) 362:k2575. doi: 10.1136/bmj.k2575

32. Maessen MF, Eijsvogels TM, Verheggen RJ, Hopman MT, Verbeek AL, de Vegt F. Entering a new era of body indices: the feasibility of a body shape index and body roundness index to identify cardiovascular health status. *PLoS One*. (2014) 9:e107212. doi: 10.1371/journal.pone.0107212

33. Nkwana MR, Monyeki KD, Lebelo SL. Body roundness index, a body shape index, Conicity index, and their association with nutritional status and cardiovascular risk factors in south African rural young adults. *Int J Environ Res Public Health*. (2021) 18:281. doi: 10.3390/ijerph18010281

34. Zhou D, Liu X, Huang Y, Feng Y. A nonlinear association between body roundness index and all-cause mortality and cardiovascular mortality in general population. *Public Health Nutr*. (2022) 25:3008–15. doi: 10.1017/S1368980022001768

35. Oates EH, Antoniewicz MR. Coordinated reprogramming of metabolism and cell function in adipocytes from proliferation to differentiation. *Metab Eng*. (2022) 69:221–30. doi: 10.1016/j.ymben.2021.12.005

36. Koliaki C, Liatis S, Kokkinos A. Obesity and cardiovascular disease: revisiting an old relationship. *Metabolism*. (2019) 92:98–107. doi: 10.1016/j.metabol.2018.10.011

37. Gancheva S, Jelenik T, Alvarez-Hernandez E, Roden M. Interorgan metabolic crosstalk in human insulin resistance. *Physiol Rev*. (2018) 98:1371–415. doi: 10.1152/physrev.00015.2017

38. Henegar C, Tordjman J, Achard V, Lacasa D, Cremer I, Guerre-Millo M, et al. Adipose tissue Transcriptomic signature highlights the pathological relevance of extracellular matrix in human obesity. *Genome Biol*. (2008) 9:R14. doi: 10.1186/gb-2008-9-1-r14

39. Jiang C, Qu A, Matsubara T, Chanturiya T, Jou W, Gavrilova O, et al. Disruption of hypoxia-inducible factor 1 in adipocytes improves insulin sensitivity and decreases adiposity in high-fat diet-fed mice. *Diabetes*. (2011) 60:2484–95. doi: 10.2337/db11-0174

40. Apovian CM, Bigornia S, Mott M, Meyers MR, Ulloor J, Gagua M, et al. Adipose macrophage infiltration is associated with insulin resistance and vascular endothelial dysfunction in obese subjects. *Arterioscler Thromb Vasc Biol*. (2008) 28:1654–9. doi: 10.1161/ATVBAHA.108.170316

41. Skurk T, Alberti-Huber C, Herder C, Hauner H. Relationship between adipocyte size and Adipokine expression and secretion. *J Clin Endocrinol Metab*. (2007) 92:1023–33. doi: 10.1210/jc.2006-1055

42. Costa RM, Neves KB, Tostes RC, Lobato NS. Perivascular adipose tissue as a relevant fat depot for cardiovascular risk in obesity. *Front Physiol*. (2018) 9:253. doi: 10.3389/fphys.2018.00253

43. Tang J, Zhao S, Yu S, Chi C, Ji H, Xiong J, et al. Association between hypertension-mediated organ damage and obesity defined by novel anthropometric indices in community-dwelling elderly individuals. *Clin Nutr*. (2021) 40:4473–80. doi: 10.1016/j.clnu.2020.12.035

44. Başıbüyük GÖ, Ayremlou P, Saeidlou SN, Ay F, Dalkıran A, Simzari W, et al. A comparison of the different anthropometric indices for assessing malnutrition among older people in Turkey: a large population-based screening. *J Health Popul Nutr*. (2021) 40:13. doi: 10.1186/s41043-021-00228-z

45. Blond K, Aarestrup J, Vistisen D, Bjerregaard LG, Jensen GB, Petersen J, et al. Associations between body Mass index trajectories in childhood and cardiovascular risk factors in adulthood. *Atherosclerosis*. (2020) 314:10–7. doi: 10.1016/j.atherosclerosis.2020.10.011

46. Tanamas SK, Wong E, Backholer K, Abdullah A, Wolfe R, Barendregt J, et al. Duration of obesity and incident hypertension in adults from the Framingham heart study. *J Hypertens*. (2015) 33:542–5. doi: 10.1097/HJH.0000000000000441

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Changes in body weight and cardiovascular risk factors in a Chinese population with type 2 diabetes mellitus: a longitudinal study

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Introduction: The primary care management of blood glucose, blood pressure, lipid profiles, and body weight is important among patients with type 2 diabetes mellitus (T2DM) to prevent disease progression. Information on how weight changes would improve or deteriorate cardiovascular (CV) risk factors is warranted for making primary care recommendations. We aimed to investigate the changes in body weight and CV risk factors and to analyse their association in a Chinese population with T2DM.

Methods: We retrieved longitudinal data between 2020 and 2021 from 1,758 adult primary care patients enrolled in a diabetic retinopathy (DR) screening programme. Linear associations of changes in body weight with CV risk factors were explored. Multivariable logistic regression analysis was performed to examine associations between different weight change categories and the worsening of CV risk factors.

Results: The mean age of all the participants was 63.71 years, and over half of participants were females. During a one-year follow-up period, 24.7% of patients had a weight loss of ≥3%, while 22.2% of patients had a weight gain of ≥3%. Patients who had a weight loss of ≥3% were more likely to prevent the worsening of haemoglobin A1c (HbA1c) and triglycerides, while those who had a weight gain of ≥3% tended to have worsened HbA1c, lipid profiles, and blood pressure.

Conclusion: Results from this real-world investigation suggested the concurrent need for weight loss intervention among patients who are overweight or obese and weight gain prevention among patients whose body weight falls within the normal range in the context of community-based diabetes management.

KEYWORDS

weight changes, cardiovascular risk factors, type 2 diabetes mellitus, primary care, general practice, community medicine

1 Introduction

The global prevalence of diabetes was estimated at 9.3% in 2019, and it is predicted that this number will rise to 10.2% (578 million people) by 2030, and 10.9% (700 million people) by 2045 (1). Adults with type 2 diabetes mellitus (T2DM) are at high risk of cardiovascular (CV) disease, which represents the most common complication and the leading cause of mortality in people with T2DM (2, 3). This has contributed substantially to treatment costs for T2DM at both individual and population levels globally (4). Elevated blood pressure (BP), blood glucose, and lipid levels are all important physiological and biochemical risk factors closely associated with the onset of CV disease (5). Obesity is a pathological condition that plays a central role in the pathophysiology of T2DM while aggregating several CV risk factors (6–8). Weight gain has been shown to be associated with the worsening of CV risk factors and increased risk of metabolic syndrome (9, 10), yet obesity management is still challenging particularly in low- and middle-income countries (11).

Current estimates suggest that nearly 130 million people are living with diabetes in China (12), which account for nearly one-fourth of patients with diabetes worldwide. Compared to western countries where the majority of patients with diagnosed diabetes are overweight or obese (5, 13), a large proportion (43%) of patients with T2DM in China are of normal weight with a body mass index (BMI) falling within the range of 18.5 kg/m^2 to 23.9 kg/m^2 (14). However, previous studies on the relationship between changes in weight and a set of CV risk factors including BP, blood glucose and lipid levels were mainly conducted in the overweight or obese population, with less attention paid to people with normal weight (15–18). Further investigations are warranted to understand how weight changes may impact CV risk factors in the Chinese population with T2DM.

Much evidence from randomised controlled trials indicates that lifestyle interventions on weight management could significantly improve CV risk factors in T2DM patients (16, 19, 20). However, trials conducted in clinical settings are often difficult to reflect the exposure-outcome relationships in real-world settings (21). The significant effect achieved in clinical trials may not necessarily translate into sustainable lifestyle modification in daily practice and community settings (22, 23). Given the widespread difficulties in weight loss in diabetes management, information on how weight changes would improve or deteriorate CV risk factors is essential for making tailored primary care recommendations to successfully prevent the progression of T2DM (24).

The main objective of this study was to assess the longitudinal changes in body weight and CV risk factors in a primary care population with T2DM. The study also aimed to address the research question of whether there is a significant association between different weight change categories and changes in haemoglobin A1c (HbA1c), BP, and lipid profiles in the study population.

2 Materials and methods

2.1 Study design

This was a longitudinal, observational study conducted in Guangdong province, southern China between September 2020 and December 2021. The study was part of a larger project on screening for diabetic retinopathy (DR) in collaboration with the Guangzhou Diabetic Eye Study Group at the Zhongshan Ophthalmic Center, Sun Yat-Sen University. The anthropometric and clinical parameters including weight, height, BP, HbA1c, and lipid profiles were measured annually from September 2020 to January 2021, and from September 2021 to December 2021, respectively. The study period did not cover the Chinese New Year to minimise the possibility of acute diet change.

2.2 Setting and data source

The study participants were patients with diabetes who were drawn from community and township health centres. These community-based primary care facilities offer a comprehensive package of diabetes management care that is integrated as part of the free-of-charge, national basic public health service delivery (25, 26). Routine diabetic care includes periodic blood glucose tests, regular follow-up exams, and tailored advice on medicine use, diet modification, and physical exercise. An interviewer-administered questionnaire was used to collect information on socio-demographics (i.e., age, sex, education level, place of residence, marital status, living relationships, and household income), lifestyle behaviours, medical history, and drug use. The anthropometrics (i.e., height and weight) and BP parameters were measured by clinical staff. The HbA1c and lipid panel testing was performed in centralised clinical laboratory. The check-up data were retrieved electronically from the computerised records.

2.3 Participants

The target subjects in the study were primary care patients with clinically-diagnosed T2DM. Diabetes was diagnosed as a fasting plasma glucose level ≥7.0 mmol/L or HbA1c ≥6.5% (27). The presence of T2DM was assessed by the attending primary care physician according to the Chinese Diabetes Society guideline and the World Health Organization (WHO) recommendation (27, 28). A total of 1,795 patients with T2DM participated in both the 2020 and 2021 waves of DR screening. We excluded patients who did not have body weight measured in either wave (n=22). Patients with weight change below $P_{0.5}$ or above $P_{99.5}$(n=15) were also excluded to take into account the possible measurement error while minimising the impact of excess weight loss or weight gain on the change of CV risk factors. This yielded a total of 1,758 patients with T2DM included in the final analysis.

2.4 Study variables and measurements

Self-reported information on age, sex, residence place, education level, living relationships, marital status, household income, smoking status, drinking status, duration of diabetes, medical history (e.g., hypertension, heart disease, and stroke), and current use of antihypertensive drugs and glucose-lowering agents was collected. The anthropometric parameters were measured by medical staff following a standardised protocol. Weight was measured with light clothing and without shoes by a calibrated weighing scale. Height was measured using a wall-mounted stadiometer with the position of the body being straight against the wall. The BMI was calculated as weight in kilograms divided by squared height in meters (kg/m^2). BP was measured by routinely validated automatic sphygmomanometers at a seated position after at least 5 minutes of rest, and the arm with the higher BP values was used. The average of two BP readings, 1-2 min apart, was recorded. A fasting venous blood sample was collected. Plasma cholesterol, triglycerides, and HbA1c were measured using an automated, clinical chemistry analyzer (TBA-120FR, Toshiba, Japan) with coefficients of variation in compliance with the laboratory measurement standard.

2.5 Definitions

Weight gain was defined as an increase of 3% and above in body weight during 2020-2021, while weight loss was defined as a decrease of 3% and more in body weight during the same study period. A change in body weight of at least 3% has been considered clinically meaningful given that it is unlikely caused by measurement error or normal weight fluctuations (29–31). Worsening of HbA1c, triglycerides, total cholesterol, low-density lipoprotein (LDL) cholesterol, systolic BP, and diastolic BP were defined as increased values in 2021 compared with that in 2020, except for high-density lipoprotein (HDL) cholesterol which was defined as decrease values in 2021 compared with that in 2020.

2.6 Statistical analysis

Data entry was performed by two trained research assistants with double verification using EpiData 3.1 (Denmark). Descriptive statistics were used to describe the demographics, lifestyle behaviours, medical history, and clinical parameters of patients according to different weight change categories. Between-group differences were assessed by independent *t*-tests or chi-square tests, where appropriate. Pearson correlation between weight change and CV risk factor change was determined. The proportion of patients with worsening CV risk factors were plotted against different weight change categories, and tests for trend were conducted. Multivariable logistic regression analysis was performed to explore the association with a 95% confidence interval (95%CI) between different weight change categories and worsening of CV risk factors after adjusting for age, sex, baseline BMI, education level, residence place, marital status, living relationships, household income, smoking status, alcohol drinking, duration of diabetes, antihypertensive medication use, oral hypoglycaemic drugs use, insulin use, and presence of CV comorbidities. Data analysis was conducted using Stata 14 (StataCorp, TX). A p-value <0.05 was considered statistically significant.

2.7 Ethics consideration

All participants provided written informed consent. Data anonymisation was performed by removing all patient identifiers from the dataset prior to data analysis. Ethics approval was granted by the Zhongshan Ophthalmic Center Medical Ethics Committee (Ref: 2017KYPJ094) at Sun Yat-Sen University following the Declaration of Helsinki 2013.

3 Results

3.1 Characteristics of study participants

A total of 1,758 patients with T2DM who met the eligibility criteria were included in the study. The mean age and baseline BMI of all participants was 63.71 years (standard deviation [SD]: 9.39) and 24.36 kg/m^2 (SD: 3.36), respectively. More than half of the participants (56.3%) were females. Almost one-fourth (24.7%) of patients had a weight loss of ≥3%, and their mean baseline BMI was 24.63 kg/m^2. Slightly above one-fifth (22.2%) of patients had a weight gain of ≥3%, and their mean baseline BMI was 23.39 kg/m^2. The weight gain group had the highest proportion of patients with formal education and those who were rural residents (Table 1). A higher proportion of patients who had concurrent hypertension and antihypertensive drug use was observed in the weight loss group (Table 2). There were no significant differences in the distribution of age, sex, marital status, living relationships, smoking status, alcohol drinking, household income, duration of diabetes, presence of CV comorbidities, and glucose-lowering medication use across the three groups.

3.2 Changes in body weight and CV risk factors

Haemoglobin A1c, HDL cholesterol, and triglycerides decreased significantly between 2020 and 2021, while LDL cholesterol increased during the study period. We did not observe significant changes in body weight, total cholesterol, systolic BP, and diastolic BP over time. In addition, we observed significant correlations of weight change with a set of changes in HbA1c (Pearson correlation [r]=0.096, p<0.001), LDL cholesterol (r=0.070, p=0.007), triglycerides (r=0.133, p<0.001), total cholesterol (r=0.070, p=0.007), systolic BP (r=0.136, p<0.001), and diastolic BP (r=0.083, p<0.001). There was also no

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TABLE 1 Baseline characteristics of study participants by different weight change categories.

Variables	All patients (N =1,758)	Weight loss (n=434)	Weight stability (n=933)	Weight gain (n=391)	*p*-value
Age, years	63.71 (9.39)	63.69 (9.52)	64.05 (9.32)	62.90 (9.40)	0.123
Sex					
Male	768 (43.7%)	183 (42.2%)	415 (44.5%)	170 (43.5%)	0.721
Female	990 (56.3%)	251 (57.8%)	518 (55.5%)	221 (56.5%)	
Education level					
No formal education	575 (32.7%)	171 (39.4%)	288 (30.9%)	116 (29.7%)	0.003
Primary school and above	1,183 (67.3%)	263 (60.6%)	645 (69.1%)	275 (70.3%)	
Place of residence					
Rural	1,142 (65.0%)	294 (67.7%)	574 (61.5%)	274 (70.1%)	0.004
Urban	616 (35.0%)	140 (32.3%)	359 (38.5%)	117 (29.9%)	
Marital status					
Married	1,441 (82.0%)	357 (82.3%)	764 (81.9%)	320 (81.8%)	0.984
Others	317 (18.0%)	77 (17.7%)	169 (18.1%)	71 (18.2%)	
Living relationships					
Living alone	220 (12.5%)	41 (9.4%)	127 (13.6%)	52 (13.3%)	0.083
Living with a partner	1,538 (87.5%)	393 (90.6%)	806 (86.4%)	339 (86.7%)	
Smoking status					
Current smoking	300 (17.1%)	78 (18.0%)	152 (16.3%)	70 (17.9%)	0.657
Others	1,458 (82.9%)	356 (82.0%)	781 (83.7%)	321 (82.1%)	
Alcohol drinking					
Regular drinking	193 (11.0%)	37 (8.5%)	115 (12.3%)	41 (10.5%)	0.105
Others	1,565 (89.0%)	397 (91.5%)	818 (87.7%)	350 (89.5%)	
Household income, CNY					
<3,000 per month	1,293 (73.8%)	332 (76.9%)	672 (72.1%)	289 (74.3%)	0.173
≥3,000 per month	460 (26.2%)	100 (23.1%)	260 (27.9%)	100 (25.7%)	
Baseline BMI, kg/m^2	24.36 (3.36)	24.63 (3.29)	24.64 (3.41)	23.39 (3.16)	<0.001

BMI, body mass index. Weight gain was defined as an increase of ≥3% in body weight, and weight loss was defined as a decrease of ≥3% in body weight. Weight stability was defined as having a weight change of <3% in body weight during the study period.

significant correlation between weight change and change in HDL cholesterol (Table 3).

3.3 Worsening of CV risk factors across different weight change categories

The highest proportion of patients with worsening CV risk factors was found in the weight gain group, where 37.4% of patients had increased HbA1c, 66.0% had increased LDL cholesterol, 64.2% had decreased HDL cholesterol, 55.8% had increased triglycerides, 59.1% had increased total cholesterol, 57.8% had increased systolic BP, and 52.3% had increased diastolic BP. An increasing trend in the proportion of patients with the worsening of HbA1c (p<0.001), triglycerides (p<0.001), total cholesterol (p<0.001), systolic BP (p<0.001), and diastolic BP (p=0.027) was observed across the three groups from weight loss to weight gain (Figure 1).

3.4 Associations between different weight categories and worsening of CV risk factors

The multivariable logistic regression analysis showed that having a weight loss of ≥3% was negatively associated with increased HbA1c (adjusted odds ratio [aOR]=0.698, 95%CI: 0.522-0.933, p=0.015) and increased triglycerides (aOR=0.675, 0.520-0.876, p=0.003) after adjusting for age, sex, baseline BMI, education level, residence

TABLE 2 Medical history and use of medications by different weight change categories.

Variables	All patients (N =1,758)	Weight loss (n=434)	Weight stability (n=933)	Weight gain (n=391)	*p*-value
Duration of T2DM					
<10 years	1,288 (73.3%)	319 (73.5%)	680 (72.9%)	289 (74.1%)	0.896
≥10 years	469 (26.7%)	115 (26.5%)	253 (27.1%)	101 (25.9%)	
Presence of hypertension					
Yes	725 (41.2%)	192 (44.2%)	397 (42.6%)	136 (34.8%)	0.011
No	1,033 (58.8%)	242 (55.8%)	536 (57.4%)	255 (65.2%)	
Presence of CV disease					
Yes	244 (13.9%)	61 (14.1%)	125 (13.4%)	58 (14.8%)	0.783
No	1,514 (86.1%)	373 (85.9%)	808 (86.6%)	333 (85.2%)	
Use of antihypertensive drugs					
Yes	618 (35.2%)	163 (37.6%)	339 (36.3%)	116 (29.7%)	0.033
No	1,140 (64.8%)	271 (62.4%)	594 (63.7%)	275 (70.3%)	
Use of oral hypoglycaemic drugs					
Yes	1,304 (74.2%)	329 (75.8%)	692 (74.2%)	283 (72.4%)	0.532
No	454 (25.8%)	105 (24.2%)	241 (25.8%)	108 (27.6%)	
Use of insulin					
Yes	179 (10.2%)	34 (7.8%)	107 (11.5%)	38 (9.7%)	0.111
No	1,579 (89.8%)	400 (92.2%)	826 (88.5%)	353 (90.3%)	

T2DM, type 2 diabetes mellitus; CV, cardiovascular. Weight gain was defined as an increase of ≥3% in body weight, and weight loss was defined as a decrease of ≥3% in body weight. Weight stability was defined as having a weight change of <3% in body weight during the study period.

place, marital status, living relationships, household income, smoking status, alcohol drinking, duration of diabetes, antihypertensive medication use, oral hypoglycaemic drugs use, insulin use, and presence of CV comorbidities. Meanwhile, having a weight gain of ≥3% was positively associated with increased HbA1c (aOR=1.347, 1.024-1.772, p=0.033), increased triglycerides (aOR=1.491, 1.147-1.938, p=0.003), increased total cholesterol (aOR=1.466, 1.127-1.908, p=0.004), increased systolic BP (aOR=1.445, 1.129-1.850, p=0.003), and increased diastolic BP (aOR=1.345, 1.053-1.718, p=0.018) (Figure 2).

TABLE 3 Changes in CV risk factors and their correlations with weight change.

	Baseline		Changes during 2020-2021		Correlation with weight change
	N	Mean ± SD	N	Mean (95%CI)	
Weight, kg	1,758	59.79 ± 10.44	1,758	-0.02 (-0.15, 0.11)	
HbA1c, %	1,658	7.98 ± 2.39	1,503	-0.95 (-1.07, -0.84)†	0.096†
LDL cholesterol, mmol/L	1,659	2.24 ± 0.78	1,505	0.26 (0.22, 0.30)†	0.070*
HDL cholesterol, mmol/L	1,662	1.41 ± 0.65	1,508	-0.07 (-0.11, -0.03)†	-0.023
Triglycerides, mmol/L	1,662	2.19 ± 1.78	1,507	-0.09 (-0.17, -0.004)*	0.133†
Total cholesterol, mmol/L	1,662	5.28 ± 1.39	1,505	0.04 (-0.02, 0.11)	0.070*
Systolic BP, mmHg	1,752	141.46 ± 19.24	1,745	0.76 (-0.14, 1.66)	0.136†
Diastolic BP, mmHg	1,752	84.14 ± 11.18	1,743	-0.12 (-0.69, 0.45)	0.083†

* p<0.05, † p<0.001.
HbA1c, haemoglobin A1c; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BP, blood pressure.

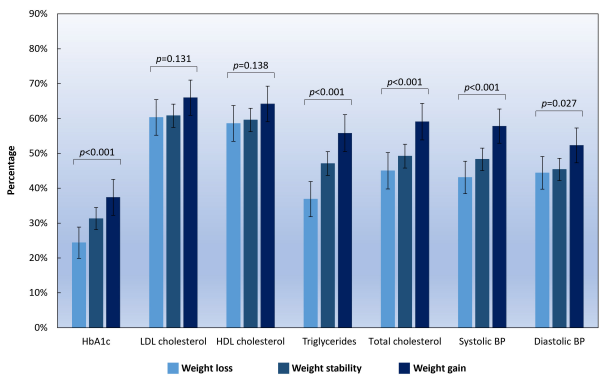

FIGURE 1
Percentage of patients who had worsening CV risk factors according to different weight change categories. Note: HbA1c, haemoglobin A1c; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BP, blood pressure. Weight gain was defined as an increase of ≥3% in body weight, and weight loss was defined as a decrease of ≥3% in body weight. Weight stability was defined as having a weight change of <3% in body weight during the study period. Error bars indicate 95% confidence intervals.

4 Discussion

4.1 Main findings

We examined changes in body weight and CV risk factors during a one-year follow-up period in a Chinese primary care population with T2DM. Nearly one in four patients had a weight loss of ≥3%, while slightly above one-fifth of patients had a weight gain of ≥3%. Significant linear correlations were found between weight change and a set of changes in HbA1c, LDL cholesterol, triglycerides, total cholesterol, and BP. The multivariable logistic regression analysis demonstrated that patients who had a weight loss of ≥3% were more likely to prevent the worsening of HbA1c and triglycerides while having a weight gain of ≥3% was found to be associated with the worsening of HbA1c, triglycerides, total cholesterol, and BP.

4.2 Relationship with other studies

Data from the United States described a growing toll of diabetes and obesity-related CV disease despite a decline in CV mortality over the past four decades (32). Global estimates of disease burden showed that CV disease attributable to elevated BMI was the main cause of death and disability-adjusted life years, accounting for 2.7 million deaths and 66.3 million disability-adjusted life years (33). Weight gain has been shown to induce early onset and accumulation of vascular risk factors, which are closely linked to cardiometabolic abnormalities such as atherosclerosis (34). Earlier findings from a large population-based cohort study in China suggested that the CV risk started to increase with mildly elevated body weight (23-25 kg/m^2) (35) – a level that is considered normal weight according to the WHO criteria (36). A cohort study conducted in the American population reported that people with weight-gain patterns were more prone to have above-goal HbA1c and BP than their counterparts with weight loss (15). This was similarly observed in our study in which having a weight gain of 3% and above was significantly associated with worsening of CV risk factors including HbA1c, triglycerides, total cholesterol, and both systolic and diastolic BP. The results were in line with our expectations and the existing literature which suggested that a progression from non-obese to becoming obese was accompanied by an increment in predicted risk for CV disease in the Japanese community residents (9). It is possible that low-grade inflammation and dysregulation of the endocrine and immune milieu in the adipose tissue could lead to abnormal production of adipokines and inflammatory molecules (37). Previous evidence also suggested a link between weight gain and increased risk of vascular dysfunction in patients with T2DM (38), which implies that physicians should move beyond a simple focus on glycaemic control and takes into account the importance of weight management in diabetes care.

Previous epidemiological studies have established that the rising prevalence of overweight and obesity contributes to the increased incidence of diabetes and CV disease (39–41). Weight loss has been incorporated as one of the major goals of interventions in T2DM patients who are overweight or obese to prevent the development of CV disease. An observational analysis of obese patients with T2DM in the Look AHEAD study showed that weight losses of 5 to <10% were associated with significant improvements in HbA1c, BP, triglycerides, and HDL cholesterol (17). Our data showed that weight loss of ≥3% was strongly associated with improved HbA1c and triglycerides. The benefits of weight loss on other CV risk factors such as total cholesterol and BP were also observed in our study albeit not statistically significant. This may be due to the use of a more conservative threshold level of 3% instead of 5% for determining the meaningful magnitude of weight change in our study given that achieving a greater level of weight loss requires intense interventions (16), which, however, was absent in the present study. It might also be explained by the increased fitness as a result of the long-term lifestyle intervention in the Look AHEAD study, which may improve CV risk factors beyond weight loss alone and further enhance the beneficial effect (42, 43). Nevertheless, we did observe significant associations of weight change with improved HbA1c, triglycerides, total cholesterol, systolic BP, and diastolic BP among patients who had a weight gain of ≥3% in our study. This implies the consistency of evidence that relates weight change to CV risk factors.

4.3 Implications for research and practice

Regular monitoring of BP, lipid profiles, and body weight has been emphasised in diabetes management (44, 45). A modest weight loss has been considered beneficial to improving glycaemic control, BP, lipid profiles, and metabolic parameters in T2DM patients (16, 17). Nevertheless, there remain multiple barriers to effective and sustainable weight management. First, it tends to be more difficult to lose weight for people with diabetes compared to those free of diabetes (46). Second, adherence to long-term lifestyle advice such as diet modification and aerobic exercise appears to be

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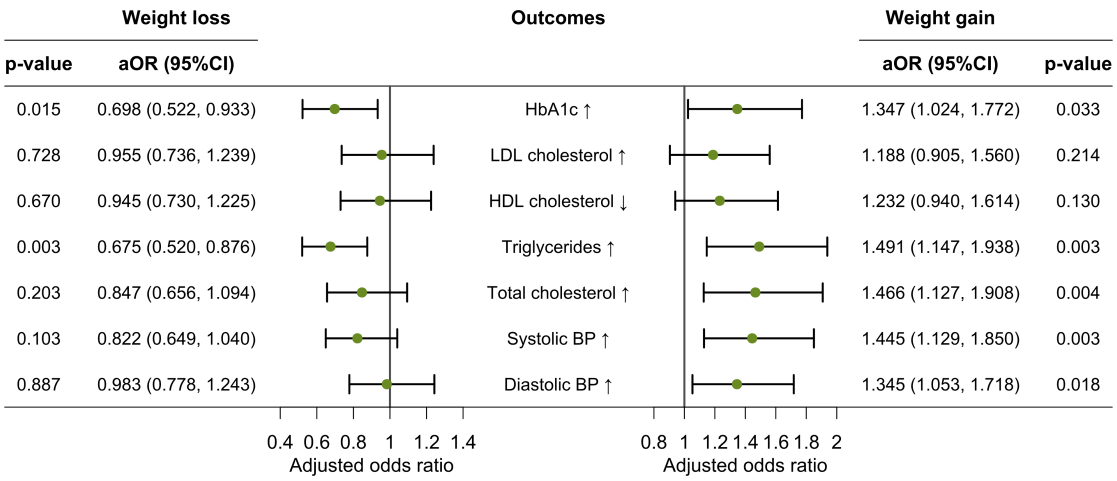

FIGURE 2
Multivariable logistic regression analysis of associations between weight loss/gain and worsening of CV risk factors. Note: aOR, adjusted odds ratio; HbA1c, haemoglobin A1c; LDL, low-density lipoprotein; HDL, high-density lipoprotein; BP, blood pressure. Weight gain was defined as an increase of ≥3% in body weight, and weight loss was defined as a decrease of ≥3% in body weight during the study period. Error bars indicate 95% confidence intervals.

complex and challenging (47, 48). A meta-analysis has revealed the difficulties in achieving a weight loss of more than 5% in most lifestyle weight-loss interventions (16). Third, certain antidiabetic agents may cause weight gain and thereby exacerbate other CV risk factors associated with T2DM (49). Our study suggested a beneficial impact of weight loss of ≥3% on CV risk factors. In the Chinese guideline on prevention and treatment of T2DM, achieving a weight loss of 3% to 5% has been considered fundamental to weight management for overweight or obese adults with T2DM (45). Previous real-world studies exhibited that in patients who were newly treated for T2DM, those with weight loss of ≥3% were more likely to achieve better glycaemic control (50). It is worth noting that the main purpose of our study was not to explore the threshold level *per se* for weight change. Instead, we are interested in understanding whether having a weight loss at a modest level that is culturally feasible in real-world settings could be associated with beneficial outcomes. Given the worsening of CV risk factors due to weight gain, regular monitoring of body weight should not be neglected in people whose BMI falls within the normal range. Maintaining optimal weight control shall necessitate appropriately designed health communication efforts (51), which could be made *via* interpersonal or mass media channels to reinforce diet, physical activity, and behavioural changes (52). Existing approaches for weight management advocate a cohesive engagement of primary care practitioners and multidisciplinary teams to overcome a variety of obstacles that hinder effective nonpharmacologic and pharmacologic treatment (53–55).

4.4 Strengths and weaknesses of the study

We presented primary care longitudinal data that reinforced the primacy of weight management as integral to diabetes care, while extending the existing evidence to a Chinese population with a particular focus on the changes in body weight and its association with changes in CV risk factors in the real-world setting. Unlike many other studies conducted in the west, nearly half of participants in our study had their BMI falling within the normal range at baseline. Both urban and rural participants were included to take into account the socioeconomic disparities. A broad range of information on patients' demographics, lifestyle behaviours, medical history, current use of antihypertensive drugs and glucose-lowering agents, presence of CV comorbidities, and clinical parameters was collected. All clinical measurements including physical examination and laboratory tests were performed under routine check-up procedures with quality control. However, our study had several limitations. First, lifestyle behaviours were considered confounding factors and were measured in a simplified dichotomous manner, which precluded the evaluation of the frequency and intensity of physical exercise, and intake of dietary compositions (56, 57). It is also possible that smoking cessation could be accompanied by weight gain, and may impact the association between weight gain and changes in CV outcomes (58, 59). Second, we did not have information on how weight loss was achieved, nor whether an individual's weight loss was intentional or secondary to disease. As indicated by earlier evidence, it is reasonable to assume a greater benefit of weight loss in patients who had the intention to lose weight (60). Third, we did not gather information on the fluctuation of weight during the period before baseline, and thus we cannot rule out the possibility that an individual was gaining or losing weight at study entry. Fourth, although the use of antihypertensive drugs, oral hypoglycaemic drugs and insulin was taken into account in the regression analysis, we were not able to determine whether there were changes either in diabetes medication (e.g., initiation of SGLT2i or GLP-1 receptor agonists) or in concomitant medications that might have affected weight or CV risk factors (e.g., initiation of or change in the dose of statin) during the course of this study. Last but not least, associations between the magnitude of weight change and subsequent CV outcomes may vary after the one-year follow-up period, which may warrant evidence from further long-term investigations with the assistance of wearable devices, digital eHealth platforms, and remote

patient monitoring tools to guide clinical decisions in primary care (61).

5 Conclusion

Our data from a primary care population of T2DM patients demonstrated the longitudinal changes in body weight along with a set of concurrent changes in CV risk factors in the real-world setting. Patients who had a weight loss of ≥3% were more likely to prevent the worsening of HbA1c and triglycerides, while those who had a weight gain of ≥3% tended to have worsened HbA1c, lipid profiles, and blood pressure. Our results suggested the concurrent need for weight loss intervention among patients who are overweight or obese and weight gain prevention among patients whose body weight falls within the normal range in the context of community-based diabetes management.

Data availability statement

The raw data supporting the conclusions of this article are available on reasonable request from the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee at Zhongshan Ophthalmic Center, Sun Yat-Sen University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Conceptualisation: Y-YL, HHXW, and YTL; data curation: WH and YTL; formal analysis: Y-YL; validation: Y-MY; methodology: Y-YL and HHXW; project administration: YTL; supervision: WH and HHXW; writing—original draft preparation: Y-YL, HHXW, and YTL; writing—review and editing: SZ, HC, and JH. All authors contributed to the article and approved the submitted version.

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Conflict of interest

Author JH was employed by Digital Education Holdings Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the international diabetes federation diabetes atlas, 9th edition. *Diabetes Res Clin Pract* (2019) 157:107843. doi: 10.1016/j.diabres.2019.107843

2. Einarson TR, Acs A, Ludwig C, Panton UH. Prevalence of cardiovascular disease in type 2 diabetes: A systematic literature review of scientific evidence from across the world in 2007-2017. *Cardiovasc Diabetol* (2018) 17(1):83. doi: 10.1186/s12933-018-0728-6

3. Zhang Y, Hu G, Yuan Z, Chen L. Glycosylated hemoglobin in relationship to cardiovascular outcomes and death in patients with type 2 diabetes: A systematic review and meta-analysis. *PloS One* (2012) 7:e42551. doi: 10.1371/journal.pone.0042551

4. Einarson TR, Acs A, Ludwig C, Panton UH. Economic burden of cardiovascular disease in type 2 diabetes: A systematic review. *Value Health* (2018) 21(7):881–90. doi: 10.1016/j.jval.2017.12.019

5. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. *Lancet.* (2017) 389:2239–51. doi: 10.1016/S0140-6736(17)30058-2

6. Vázquez LA, Rodríguez Á, Salvador J, Ascaso JF, Petto H, Reviriego J. Relationships between obesity, glycemic control, and cardiovascular risk factors: A pooled analysis of cross-sectional data from Spanish patients with type 2 diabetes in the preinsulin stage. *BMC Cardiovasc Disord* (2014) 14:153. doi: 10.1186/1471-2261-14-153

7. Tzotzas T, Evangelou P, Kiortsis DN. Obesity, weight loss and conditional cardiovascular risk factors. *Obes Rev* (2011) 12(5):e282–9. doi: 10.1111/j.1467-789X.2010.00807.x

8. Kim SH. Cardiovascular risk factors and obesity in adolescents. *Korean Circ J* (2020) 50(8):733–5. doi: 10.4070/kcj.2020.0247

9. Honda T, Ishida Y, Oda M, Noguchi K, Chen S, Sakata S, et al. Changes in body weight and concurrent changes in cardiovascular risk profiles in community residents in Japan: the hisayama study. *J Atheroscler Thromb* (2022) 29(2):252–67. doi: 10.5551/jat.59394

10. Sun J, Xi B, Yang L, Zhao M, Juonala M, Magnussen CG. Weight change from childhood to adulthood and cardiovascular risk factors and outcomes in adulthood: A systematic review of the literature. *Obes Rev* (2021) 22(3):e13138. doi: 10.1111/obr.13138

11. Ford ND, Patel SA, Narayan KM. Obesity in low- and middle-income countries: Burden, drivers, and emerging challenges. *Annu Rev Public Health* (2017) 38:145–64. doi: 10.1146/annurev-publhealth-031816-044604

12. Li Y, Teng D, Shi X, Qin G, Qin Y, Quan H, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American diabetes association: National cross sectional study. *BMJ* (2020) 369:m997. doi: 10.1136/bmj.m997

13. Centers for Disease Control and Prevention (CDC). Prevalence of overweight and obesity among adults with diagnosed diabetes–united states, 1988-1994 and 1999-2002. *MMWR Morb Mortal Wkly Rep* (2004) 53:1066–8.

14. Lv F, Cai X, Lin C, Hong T, Zhang X, Wang Z, et al. Sex differences in the prevalence of obesity in 800,000 Chinese adults with type 2 diabetes. *Endocr Connect.* (2021) 10:139–45. doi: 10.1530/EC-20-0547

15. Feldstein AC, Nichols GA, Smith DH, Stevens VJ, Bachman K, Rosales AG, et al. Weight change in diabetes and glycemic and blood pressure control. *Diabetes Care* (2008) 31(10):1960–5. doi: 10.2337/dc08-0426

16. Franz MJ, Boucher JL, Rutten-Ramos S, VanWormer JJ. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: A systematic review and meta-analysis of randomized clinical trials. *J Acad Nutr Diet.* (2015) 115(9):1447–63. doi: 10.1016/j.jand.2015.02.031

17. Wing RR, Lang W, Wadden TA, Safford M, Knowler WC, Bertoni AG, et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care* (2011) 34:1481–6. doi: 10.2337/dc10-2415

18. Blonde L, Pencek R, MacConell L. Association among weight change, glycemic control, and markers of cardiovascular risk with exenatide once weekly: A pooled analysis of patients with type 2 diabetes. *Cardiovasc Diabetol* (2015) 14:12. doi: 10.1186/s12933-014-0171-2

19. Lean ME, Leslie WS, Barnes AC, Brosnahan N, Thom G, McCombie L, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *Lancet.* (2018) 391(10120):541–51. doi: 10.1016/S0140-6736(17)33102-1

20. Zomer E, Gurusamy K, Leach R, Trimmer C, Lobstein T, Morris S, et al. Interventions that cause weight loss and the impact on cardiovascular risk factors: a systematic review and meta-analysis. *Obes Rev* (2016) 17(10):1001–11. doi: 10.1111/obr.12433

21. Heneghan C, Goldacre B, Mahtani KR. Why clinical trial outcomes fail to translate into benefits for patients. *Trials.* (2017) 18(1):122. doi: 10.1186/s13063-017-1870-2

22. Dunbar JA, Hernan AL, Janus ED, Vartiainen E, Laatikainen T, Versace VL, et al. Challenges of diabetes prevention in the real world: results and lessons from the Melbourne diabetes prevention study. *BMJ Open Diabetes Res Care* (2015) 3(1):e000131. doi: 10.1136/bmjdrc-2015-000131

23. Pomeroy J, Palacios C. Translating findings from lifestyle intervention trials of cardiovascular disease and diabetes to the primary care setting. *Curr Nutr Rep* (2012) 1(4):215–21. doi: 10.1007/s13668-012-0024-0

24. Li Y, Zhong Q, Zhu S, Cheng H, Huang W, Wang HHX, et al. Frequency of follow-up attendance and blood glucose monitoring in type 2 diabetic patients at moderate to high cardiovascular risk: A cross-sectional study in primary care. *Int J Environ Res Public Health* (2022) 19(21):14175. doi: 10.3390/ijerph192114175

25. Department of Primary Health Care and National Health Commission. *PRC. standards for national basic public health services* (2017). Available at: http://www.nhc.gov.cn/jws/s3578/201703/d20c37e23e1f4c7db7b8e25f34473e1b.shtml (Accessed 31 January 2023).

26. Yao J, Wang H, Yin J, Shao D, Guo X, Sun Q, et al. Factors associated with the utilization of community-based diabetes management care: A cross-sectional study in Shandong province, China. *BMC Health Serv Res* (2020) 20(1):407. doi: 10.1186/s12913-020-05292-5

27. Weng J, Ji L, Jia W, Lu J, Zhou Z, Zou D, et al. Chinese Diabetes society. standards of care for type 2 diabetes in China. *Diabetes Metab Res Rev* (2016) 32:442–58. doi: 10.1002/dmrr.2827

28. World Health Organization & International Diabetes Federation. *Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation*. (Geneva, Switzerland: World Health Organization) (2006).

29. Stevens J, Truesdale KP, McClain JE, Cai J. The definition of weight maintenance. *Int J Obes (Lond).* (2006) 30:391–9. doi: 10.1038/sj.ijo.0803175

30. Jakicic JM, Otto AD, Lang W, Semler L, Winters C, Polzien K, et al. The effect of physical activity on 18-month weight change in overweight adults. *Obes (Silver Spring)* (2011) 19:100–9. doi: 10.1038/oby.2010.122

31. McAdam-Marx C, Bellows BK, Unni S, Wygant G, Mukherjee J, Ye X, et al. Impact of adherence and weight loss on glycemic control in patients with type 2 diabetes: cohort analyses of integrated medical record, pharmacy claims, and patient-reported data. *J Manag Care Spec Pharm* (2014) 20:691–700. doi: 10.18553/jmcp.2014.20.7.691

32. Mensah GA, Wei GS, Sorlie PD, Fine LJ, Rosenberg Y, Kaufmann PG, et al. Decline in cardiovascular mortality: Possible causes and implications. *Circ Res* (2017) 120(2):366–80. doi: 10.1161/CIRCRESAHA.116.309115

33. GBD 2015 Obesity Collaborators, Afshin A, MH F, MB R, Sur P, Estep K, et al. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med* (2017) 377(1):13–27. doi: 10.1056/NEJMoa1614362

34. Ryder JR, Xu P, Inge TH, Xie C, Jenkins TM, Hur C, et al. Thirty-year risk of cardiovascular disease events in adolescents with severe obesity. *Obes (Silver Spring)* (2020) 28(3):616–23. doi: 10.1002/oby.22725

35. Zhu Y, Zheng R, Hu C, Qin G, Wang B, Wang T, et al. Association of early adulthood weight and subsequent weight change with cardiovascular diseases: Findings from REACTION study. *Int J Cardiol* (2021) 332:209–15. doi: 10.1016/j.ijcard.2021.02.086

36. WHO Global InfoBase team. The SuRF report 2. In: *Surveillance of chronic disease risk factors: Country-level data and comparable estimates*. (Geneva, Switzerland: World Health Organization) (2005).

37. Kahn CR, Wang G, Lee KY. Altered adipose tissue and adipocyte function in the pathogenesis of metabolic syndrome. *J Clin Invest.* (2019) 129(10):3990–4000. doi: 10.1172/JCI129187

38. Jiang L, Shi K, Guo YK, Ren Y, Li ZL, Xia CC, et al. The additive effects of obesity on myocardial microcirculation in diabetic individuals: A cardiac magnetic resonance first-pass perfusion study. *Cardiovasc Diabetol* (2020) 19(1):52. doi: 10.1186/s12933-020-01028-1

39. de Mutsert R, Sun Q, Willett WC, Hu FB, van Dam RM. Overweight in early adulthood, adult weight change, and risk of type 2 diabetes, cardiovascular diseases, and certain cancers in men: A cohort study. *Am J Epidemiol.* (2014) 179(11):1353–65. doi: 10.1093/aje/kwu052

40. Jung HS, Chang Y, Eun Yun K, Kim CW, Choi ES, Kwon MJ, et al. Impact of body mass index, metabolic health and weight change on incident diabetes in a Korean population. *Obes (Silver Spring).* (2014) 22(8):1880–7. doi: 10.1002/oby.20751

41. Messerli FH, Hofstetter L, Rimoldi SF, Rexhaj E, Bangalore S. Risk factor variability and cardiovascular outcome: JACC review topic of the week. *J Am Coll Cardiol* (2019) 73(20):2596–603. doi: 10.1016/j.jacc.2019.02.063

42. Johnston CA, Moreno JP, Foreyt JP. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *Curr Atheroscler Rep* (2014) 16(12):457. doi: 10.1007/s11883-014-0457-6

43. Gibbs BB, Brancati FL, Chen H, Coday M, Jakicic JM, Lewis CE, et al. Effect of improved fitness beyond weight loss on cardiovascular risk factors in individuals with type 2 diabetes in the look AHEAD study. *Eur J Prev Cardiol* (2014) 21(5):608–17. doi: 10.1177/2047487312462823

44. Handelsman Y, Bloomgarden ZT, Grunberger G, Umpierrez G, Zimmerman RS, Bailey TS, et al. American Association of clinical endocrinologists and American college of endocrinology - clinical practice guidelines for developing a diabetes mellitus comprehensive care plan - 2015. *Endocr Pract* (2015) 21 Suppl 1(Suppl 1):1–87. doi: 10.4158/EP15672.GL

45. Chinese Diabetes Society. Guidelines for the prevention and treatment of T2DM in China. *Chin J Diabetes Mellitus* (2021) 13(4):315–409. doi: 10.3760/cma.j.cn115791-20210221-00095

46. Lau DC. Diabetes and weight management. *Prim Care Diabetes.* (2010) 4 Suppl 1:S24–30. doi: 10.1016/S1751-9918(10)60006-X

47. Wong MCS, Wang HHX, Kwan MWM, Fong BCY, Chan WM, Zhang DX, et al. Dietary counselling has no effect on cardiovascular risk factors among Chinese grade 1 hypertensive patients: A randomized controlled trial. *Eur Heart J* (2015) 36(38):2598–607. doi: 10.1093/eurheartj/ehv329

48. Hu XJ, Wu HF, Li YT, Wang Y, Cheng H, Wang JJ, et al. Influence of health education on clinical parameters in type 2 diabetic subjects with and without hypertension: A longitudinal, comparative analysis in routine primary care settings. *Diabetes Res Clin Pract* (2020) 170:108539. doi: 10.1016/j.diabres.2020.108539

49. Niswender K. Diabetes and obesity: Therapeutic targeting and risk reduction - a complex interplay. *Diabetes Obes Metab* (2010) 12:267–87. doi: 10.1111/j.1463-1326.2009.01175.x

50. McAdam-Marx C, Mukherjee J, Bellows BK, Unni S, Ye X, Iloeje U, et al. Evaluation of the relationship between weight change and glycemic control after initiation of antidiabetic therapy in patients with type 2 diabetes using electronic medical record data. *Diabetes Res Clin Pract* (2014) 103:402–11. doi: 10.1016/j.diabres.2013.12.038

51. Wang HHX, Li YT, Wong MCS. Leveraging the power of health communication: Messaging matters not only in clinical practice but also in public health. *Hong Kong Med J* (2022) 28(2):103–5. doi: 10.12809/hkmj215128

52. Soleymani T, Daniel S, Garvey WT. Weight maintenance: Challenges, tools and strategies for primary care physicians. *Obes Rev* (2016) 17(1):81–93. doi: 10.1111/obr.12322

53. Wang HHX, Li YT, Wong MCS. Strengthening attributes of primary care to improve patients' experiences and population health: From rural village clinics to urban health centres. *Hong Kong Med J* (2022) 28(4):282–4. doi: 10.12809/hkmj215133

54. Semlitsch T, Stigler FL, Jeitler K, Horvath K, Siebenhofer A. Management of overweight and obesity in primary care-a systematic overview of international evidence-based guidelines. *Obes Rev* (2019) 20(9):1218–30. doi: 10.1111/obr.12889

55. Anderson J, Kushner R, Miller E, Nadglowski J, Still C. Overweight and obesity management for primary care clinicians: Executive summary. *Clin Diabetes.* (2022) 41(1):85–9. doi: 10.2337/cd22-0082

56. Swift DL, McGee JE, Earnest CP, Carlisle E, Nygard M, Johannsen NM. The effects of exercise and physical activity on weight loss and maintenance. *Prog Cardiovasc Dis* (2018) 61:206–13. doi: 10.1016/j.pcad.2018.07.014

57. Kim JY. Optimal diet strategies for weight loss and weight loss maintenance. *J Obes Metab Syndr* (2021) 30:20–31. doi: 10.7570/jomes20065

58. Tamura U, Tanaka T, Okamura T, Kadowaki T, Yamato H, Tanaka H, et al. Changes in weight, cardiovascular risk factors and estimated risk of coronary heart disease following smoking cessation in Japanese male workers: HIPOP-OHP study. *J Atheroscler Thromb* (2010) 17(1):12–20. doi: 10.5551/jat.1800

59. Takayama S, Takase H, Tanaka T, Sugiura T, Ohte N, Dohi Y. Smoking cessation without educational instruction could promote the development of metabolic syndrome. *J Atheroscler Thromb* (2018) 25(1):90–7. doi: 10.5551/jat.40063

60. Wannamethee SG, Shaper AG, Lennon L. Reasons for intentional weight loss, unintentional weight loss, and mortality in older men. *Arch Intern Med* (2005) 165 (9):1035–40. doi: 10.1001/archinte.165.9.1035

61. Wang HHX, Li YT, Zhang Y, Wong MCS. Revisiting primary healthcare and looking ahead. *Hong Kong Med J* (2023). doi: 10.12809/hkmj235139. Epub ahead of print

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The association between adherence to diet quality index and cardiometabolic risk factors in overweight and obese women: a cross-sectional study

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Background: Obesity and overweight status increase the risk of cardiovascular disease. Diet quality can also predict the risk of cardiovascular diseases in obese and overweight patients. Therefore, in this study, we sought to examine the relationship between diet quality index (DQI) and cardiometabolic risk factors in obese and overweight women.

Method: A cross-sectional study was conducted on 197 Iranian women with a Body Mass Index (BMI) > 25, 18–48 years, and recruited from 20 Tehran Health Centers. Nutrition intake and DQI were assessed using a 147-item semi-quantitative food frequency questionnaire (FFQ). Additionally, anthropometric measurements, body composition, biochemical evaluations, and cardiometabolic risk factors were evaluated.

Results: There was an association between DQI and waist-to-hip ratio (WHR), atherogenic index of plasma (AIP), and CHOLINDEX in obese women, after adjusting for potential confounders. Whereas, there were no significant associations of the tertiles of DQI compared with the first tertile in other cardiometabolic risk factors, before and after adjustment.

Conclusion: This study provides evidence that dietary intake and DQI are associated with cardiometabolic risk factors and that dietary modification may be a predictor for reducing WHR, AIP, and CHOLINDEX. However, more research is needed to develop a DQI that reflects changes in cardiometabolic risk factors by considering women's eating habits and patterns.

KEYWORDS

ABSI, cardiometabolic risk factors, DQI, dietary intake, obesity

Introduction

Cardiovascular disease (CVD) has been reported as being responsible for 46% of all deaths and 20–23% of the burden of disease in Iran in 2019 (1). The term cardiometabolic risk refers to clinical abnormalities, including obesity, diabetes, and high blood pressure, that should be diagnosed and treated early (2). Furthermore, young women have increasingly

prevalent risk factors for CVD (3). However, it is evident that women are less likely to receive preventive treatment, relative to men, and is influenced by behaviors, environment, lifestyle, and nutrition (3).

There are several important cardiometabolic risk factors, including lipid accumulation product (LAP), which is associated with glucose intolerance, CVD, and MetS (4), while the hypertriglyceridemic waist (HW) phenotype (5) is a clinical indicator of visceral obesity diagnosis that may be related to coronary risk factors among women (6). AIP and atherogenic coefficient (AC) are early biomarkers of CVD in developing countries (7), and Castelli Risk Index 1 (CRI-I) and CRI-II are additional, independent, and more precise, risk factors in comparison with traditional lipid parameters (8). Furthermore, an additional simple index, namely CHOLINDEX, considering three main cholesterol parameters, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG) levels, has been developed to evaluate cardiometabolic risk (9).

Another relevant predictor of health status is ABSI, an alternative anthropometric measurement that considers height, weight, and waist circumference (WC) and thus more representative of abdominal adipose tissue, and a significant risk factor in predicting premature mortality (10). In line with this, cohort studies have indicated that diabetes and mortality could be predicted by ABSI (11, 12). However, Maessen et al. showed that ABSI was not significantly associated with CVD risks, as compared to BMI and WC in adults (13), and among Iranian adults, it was concluded that ABSI was a weak predictor for CVD risks and MetS (14). In a cohort study conducted on 8,248 participants (4,471 women), the authors aimed to examine whether ABSI could improve the predictive performances for CVD of Framingham's general CVD algorithm. The results showed that ABSI was associated with an increased risk of incident CVD among both men and women but could not improve the predictability of the Framingham algorithm (15). In addition, the triglyceride glucose index (TyG) is one of the methods by which insulin resistance can be estimated (16). Furthermore, it has been indicated that TyG may be associated with high blood pressure, vascular stiffness, and coronary artery calcification (17–19).

Modifiable factors, including physical inactivity and nutrition, may contribute to accelerating cardiometabolic risk (20, 21). Earlier research has largely been concerned with the role of single nutrients and foods in chronic diseases; however, contemporary research has tended to assess the total diet (22, 23). To have a better understanding of overall eating patterns and behaviors in a population, the diet quality index (DQI) has been developed and evaluated (24). In postmenopausal women, it has been demonstrated that a low-quality diet, including the low intake of vegetables and fruits and excessive consumption of sodium, has detrimental impacts on cardiometabolic risk factors, such as abdominal obesity (25). A cross-sectional study based on the Australian Diabetes, Obesity, and Lifestyle study indicated that higher diet quality was significantly associated with cardiometabolic risk factors, including lower blood pressure, lower fasting plasma glucose, and greater insulin sensitivity among men and women (26). Moreover, it was reported that a higher DQI score at baseline was inversely associated with WC, TG, TG to HDL ratio, and the total cholesterol to HDL ratio after 9 years in Spanish adults (27). To our knowledge, the association of DQI with cardiometabolic risk factors and ABSI has scarcely been investigated. Therefore, in this study, we sought to examine the relationship between diet quality index (DQI) and cardiometabolic risk factors in obese and overweight women.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; WHR, waist-hip ratio; CI, confidence interval; OR, odds ratio; WC, waist circumference; DASH, Dietary Approaches to Stop Hypertension; WHO, World Health Organization; FFQ, food frequency questionnaire; FCT, food composition table; USDA, United States Department of Agriculture; IPAQ, physical activity questionnaire; MetS, metabolic syndrome; CVD, cardiovascular disease; BFM, body fat mass; TG, triglyceride; ABSI, a body shape index; CRI- I, CRI- II, Castelli Risk Index; TyG, triglyceride glucose index; LAP, Lipid accumulation product; AC, atherogenic coefficient; AIP, Atherogenic index of plasma; TyG-BMI, triglyceride glucose index- body mass index; TyG-WC, triglyceride glucose index- waist circumference; HW, hypertriglyceridemic waist.

Subjects and methods

This cross-sectional study was conducted using 197 women recruited from 20 Tehran Health Centers, using simple random sampling. The inclusion criteria were as follows: aged from 18 to 48 years, BMI $\geq$25 kg/m^2, without a history of hypertension, no intake of alcohol and opiate drugs, not being pregnant, and not having an acute or chronic infection; and the exclusion criteria were having a history of CVDs, thyroid, cancer, diabetes, liver disease, kidney disease, and smoking. In addition, participants who had been following any arbitrary special dietary regimen, those with chronic disease(s) affecting their diet, or if their daily energy intake was <800 or >4,200 kcal (28) were excluded. All participants were asked to sign the written consent before the study commencement, and the study was approved by the ethics committee of Tehran University of Medical Sciences (R.TUMS.VCR.REC.1395.1234).

Anthropometric measurements

The body compositions, including weight, fat and lean mass, and WHR, of the female participants were assessed by the bioelectric impedance analyzer (In Body 770 scanner, Korea) (29). In addition, height was measured to the nearest 0.5 cm to evaluate BMI as weight (kg) divided by height (m^2). WC measurement was performed at the point of the umbilicus after exhalation. According to the World Health Organization (WHO) criteria for the classification of weight, a BMI of $\geq$ 25 kg/m^2 was considered overweight, and a BMI of $\geq$ 30 kg/m^2 was considered obesity (30).

Biochemistry measurements

Blood samples were drawn after 12 h of overnight fasting to assess LDL, HDL-C, TG, fasting blood sugar (FBS), and total cholesterol by Pars Azmoon laboratory kits (test Pars Inc, Tehran,

Iran). The serum was separated and stored at a temperature of −70°C until the analyses were carried out after centrifugation. Levels of TG, total cholesterol, HDL-C, LDL-C, and fasting blood sugar (FBS) were measured using glycerol-3-phosphate oxidase phenol 4-amino antipyrine peroxidase (GPO-PAP), enzymatic endpoint, direct enzymatic clearance, and glucose oxidase phenol 4-amino, respectively.

Cardiometabolic risk factors calculation

ABSI = $\frac{WC}{BMI^{2/3}\ height^{1/2}}$ (10);
LAP index =(WC (cm)-58) × TG(mmol) (31);
AIP: $\log_{10}^{TG/HDL-C}$ (32);
AC: (TC– HDL)/HDL (8);
CRI-I = $\frac{\text{Total Cholesterol}}{HDLc}$, respectively (33);
CRI-II = $\frac{LDLc}{HDLc}$, respectively (33);
TyG =Ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2] (16);
CHOLINDEX =LDL-C-HDL-C (TG<400mg/dL), LDL-C-HDL-C +1/5 of TG (TG ≥ 400 mg/dL) (9);
TyG-BMI (triglyceride glucose index- body mass index) =Ln [fasting plasma glucose (mg/dL) × fasting triglycerides (mg/dL)/2] × BMI (34);
TyG-WC (triglyceride glucose index- waist circumference) =Ln [fasting plasma glucose (mg/dL) × fasting triglycerides (mg/dL)/2] × WC (35).
The HW phenotype was defined by the presence of increased WC (>88percentile by age and sex of the sample itself) and increased serum triglycerides (>100 mg/DL) (36).

Dietary intake measurement and DQI calculation

The dietary intake of the women was collected by an instructing nutritionist via a face-to-face interview with a 147-item semi-quantitative food frequency questionnaire (FFQ), where its validity and reliability were previously avowed in the Iranian population (37). The average consumption frequency was considered over the past year on a daily, weekly, and monthly basis. Household measures were taken into account for portion sizes and then converted to grams (38). The food composition table (FCT) of the United States Department of Agriculture (USDA) was used to evaluate energy and nutrients. The Iranian FCT was considered for local foods that were not present in the USDA FCT. There are seven food groups considered in the DQI, which are as follows: fast food (four items); vegetables and fruit (seven items); legumes, chicken, soy protein or fish (four items); sweets (six items); butter, hydrogenated oil, animal fats, or ghee (four items); egg, whole dairy products, or meat (four items); and olive and non-hydrogenated oil (two items). The calculation of this index is based on adequacy, variety, moderation, and balance (39). Variety was assessed by two components: "between-food groups" (0–15 points) and "within-protein source group" (0–5 points). Adequacy evaluates fruits, vegetables, grains, protein, fiber, calcium, iron, and vitamin C intakes (40 points). Moderation assesses total fat, saturated fat, cholesterol, sodium, and empty-calorie foods (30 points). The balance of the micronutrient distribution in the diet and the fatty acid ratio are also examined (10 points). Details about the scoring method of DQI were published previously (40). The whole DQI score is 100, such that a higher score indicates a better quality of the diet. Ultimately, the DQI score of participants was categorized based on tertiles.

Physical activity (PA) measurement

A valid and reliable international PA questionnaire (IPAQ), designed by the WHO and validated in Iranian women adults, was used to assess PA levels (41). The participants were asked to answer questions such as the time they spent on walking, moderate, and vigorous PA during the last week. Then, the time of each PA was converted to minutes per week and calculated as the metabolic equivalent of the task (MET/minutes/week).

Other covariates assessments

Demographic characteristics, including age, marital status, supplement consumption (multivitamins and minerals), socioeconomic status, education, and occupation status were collected.

Blood pressure measurements

Systolic and diastolic blood pressure (SBP and DBP) were evaluated after 15-min rest, using a mercury sphygmomanometer.

Statistical analysis

In this study, SPSS software version 26 (Chicago, USA) was used for all data analysis, and a p-value of < 0.05 was considered statistically significant. Participants were categorized according to tertiles of DQI. Kolmograph–Smirnov test and histogram inspection were used to determine the normal distribution of the data. All variables with normal distribution were analyzed by parametric tests, where one-way analysis of variance (ANOVA) for continuous variables and chi-square analysis for categorical variables were used to compare subject characteristics and dietary intake across tertiles of DQI score, reported as mean (SD). Analysis of covariance (ANCOVA) was used to examine demographic characteristics, anthropometric measurements, clinical assessments, and dietary intake across tertiles of DQI score via adjusting for age, BMI, physical activity, and energy intake in model 1 and education, economic status, and supplement consumption in model 2. Notably, BMI, as a colinear variable, was not adjusted for outcomes including BMI, BFM, WHR, WC, TyG-BMI, ti, LAP, and ABSI in model 1. To examine the association between DQI score and cardiometabolic risk factors, a binary logistic regression model was applied and reported as β and 95% confidence interval (CI).

TABLE 1 Baseline characteristics of participants.

Variables	Mean	SD
ABSI	0.078	0.002
AIP	0.348	0.235
TyG	8.376	0.498
CHOLINDEX	50.240	22.166

ABSI, a body shape index; AIP, Atherogenic index of plasma; TyG, triglyceride glucose index. All data are presented as mean and SD.

Results

Study population characteristics

In total, 197 women with a mean age and BMI of 35.5 years and 30.5 kg/m^2, respectively, participated in this study. The baseline characteristics of participants were presented in Table 1.

Baseline characteristics of participants across the tertiles of DQI scores

The characteristics of participants across the tertiles of DQI scores in overweight and obese women are shown in Table 2. Participants with a higher score of DQI were more physically active (*P*: 0.002), before and after adjusting for age, energy intake, BMI, and physical activity. Interestingly, there was a statistically significant age difference among women across the tertiles of DQI scores after controlling for confounders (*P*: 0.011), but not in the crude model (*P*: 0.118). However, there were no significant differences between tertiles in other characteristics.

Dietary intake of participants across the tertiles of DQI scores

The dietary intake of participants across the tertiles of DQI scores in overweight and obese women is presented in Table 3. Before adjusting for confounding factors, the consumptions of energy (*P*: 0.041), protein (*P*: 0.028), and carbohydrate ($P < 0.001$) increased from the first to the third tertiles of DQI. Women who adhered highly to DQI had a lower intake of total fat (*P*: 0.006), saturated fatty acids (*P*: 0.006), and mono-unsaturated fatty acids (*P*: 0.003); while, in contrast, results indicated a higher intake of iron ($P < 0.001$), calcium (*P*: 0.006), magnesium ($P < 0.001$), zinc (*P*: 0.006), selenium (*P*: 0.001), β carotene (*P*: 0.048), vitamin D (*P*: 0.049), vitamin B_1 (*P*: 0.001), vitamin B_6 (*P*: 0.009), folate ($P < 0.001$), and total fiber ($P < 0.001$). Regarding food groups, it should be mentioned that refined (*P*: 0.015) and whole (*P*: 0.002) grains, fruits ($P < 0.001$), vegetables (*P*: 0.001), and legumes (*P*: 0.001) were also consumed in higher quantities by women with a higher score of DQI. After controlling for energy intake, some nutrients remained statistically significant as follows: carbohydrate ($P < 0.001$), total fat ($P < 0.001$), saturated fatty acids ($P < 0.001$), mono-unsaturated fatty acids ($P < 0.001$), iron ($P < 0.001$), calcium (*P*: 0.039), magnesium ($P < 0.001$), zinc (*P*: 0.025), selenium (*P*: 0.029), thiamin (*P*: 0.001), folate ($P < 0.001$), and total fiber ($P < 0.001$). Also, whole grains (*P*: 0.009), fruits (*P*: 0.009), vegetables (*P*: 0.011), and legumes (*P*: 0.002) were the same as before adjustments. However, other nutrients showed no significant results across tertiles of DQI, before or after adjustment.

Association of DQI with cardiometabolic risk factors and ABSI

The associations of DQI with cardiometabolic risk factors in overweight and obese women are shown in Table 4. There were significant associations between DQI and WHR (β: −0.014, 95% CI: −0.039, 0.011, *P*-trend: 0.047), AIP (β: −0.086, 95% CI: −0.207, −0.006, *P*-trend: 0.027), and CHOLINDEX (β: −4.998, 95% CI: −15.597, 0.000, *P*-trend: 0.031) with the third tertile of DQI scores, as compared to people in the first tertile, in obese women after adjusting for age, BMI, PA, energy intake, education, socioeconomic status, and supplement use. However, in other cardiometabolic risk factors, no significant relationship was seen after adjusting for potential confounders. In the crude model, women who were in the second tertile of DQI had a lower score of TyG-BMI (β: −5.245, 95% CI: −22.555, −1.065, *P*: 0.043) and TyG-WC (β: −31.464, 95% CI: −91.980, −9.052, *P*: 0.038) than women in the first tertile, which was statistically significant. Although, this significant relationship disappeared after adjusting for potential confounders. Despite the level of other cardiometabolic risk factors, including BMI, BFM, WC, FBS, cholesterol, TG, HDL, LDL, SBP, DBP, ABSI, CRI-I and II, TyG, LAP, and AC, before and after adjustments, was lower in the third tertile of DQI compared to the first tertile, this relationship was not significant (*P*-value > 0.05).

Discussion

This cross-sectional study was conducted to evaluate the association between DQI and cardiometabolic risk factors and ABSI in Iranian women. Accordingly, our findings showed that a high-quality diet in women, assessed by adherence to the DQI, was inversely associated with cardiometabolic risk factors, including WHR, AIP, CHOLINDEX, TyG-BMI, and TyG-WC. There were no significant associations between DQI and other cardiometabolic risk factors and anthropometric indices, including ABSI in women.

Previous studies have shown that a high-quality diet can contribute to the maintenance of cardiovascular health in young and middle-aged adults (42–44). For instance, following a modified Mediterranean diet in the Coronary Artery Risk Development in Young Adults (CARDIA) study led to a reduction of metabolic disorders in middle-aged participants (43). Moreover, higher Alternate Healthy Eating Index scores in the China Health and Nutrition Survey (CHNS) study were related to lower odds of disorders, such as diabetes, and low LDL levels in male participants (45). In a cross-sectional study, it was demonstrated that a higher DASH score was associated with lower insulin resistance and lower serum levels of LDL, HDL, and VLDL, while subjects in the highest DASH quartile had lower odds of metabolic syndrome (46). In the cross-sectional Australian Health Survey, higher scores on the Dietary Guideline Index (DGI) were associated with lower

TABLE 2 General characteristics of participants across tertiles of DQI among overweight and obese women ($n = 197$).

	T1 ($n = 66$)	T2 ($n = 65$)	T3 ($n = 66$)	*P*-value	*P*-value*
Age (year)	35.2 ± 9.5	33.9 ± 7.6	37.8 ± 7.4	0.118	**0.011**
Physical activity (MET/h/w)	733.2 ± 620.4	808.2 ± 676.4	1,551.6 ± 1,618.7	**0.002**	**<0.001**
Anthropometric measurements					
Weight (kg)	77.5 ± 10.7	80.0 ± 11.5	78.8 ± 11.1	0.587	0.503
Height (cm)	159.4 ± 4.9	161.8 ± 6.0	160.2 ± 6.3	0.166	0.245
WC (cm)	110.8 ± 7.2	111.4 ± 7.0	112.5 ± 7.8	0.707	0.650
Socioeconomic status				0.556	0.692
Poor	14 (21.2)	11 (16.9)	13 (19.6)		
Moderate	21 (31.8)	32 (49.2)	28 (42.4)		
Good	31 (46.9)	22 (33.8)	25 (37.8)		
Occupation status				0.415	0.560
Unemployed	3 (4.5)	0 (0.0)	0 (0.0)		
Employed	63 (95.4)	65 (100.0)	66 (100.0)		
Marital status				0.583	0.176
Single	17 (25.7)	11 (16.9)	14 (21.2)		
Married	49 (74.2)	54 (83.0)	52 (78.7)		
Education status				0.793	0.710
Under diploma	6 (9.0)	5 (7.6)	3 (4.5)		
Diploma	19 (28.7)	22 (33.8)	18 (27.2)		
Bachelor and higher	41 (62.1)	38 (58.4)	45 (68.1)		
Supplement use[$]				0.870	0.670
Yes	45 (68.1)	47 (72.3)	43 (65.1)		
No	21 (31.8)	19 (29.2)	23 (34.8)		

DQI, diet quality index; WC, waist circumference.
Values are mean ± standard deviation (SD) for continuous variables and number and percentage for dichotomous variables. Using one-way ANOVA for continuous variables and Chi-square test for categorical variables.
*P-value: adjusted for age, energy intake, BMI, and physical activity.
The categorical variables were reported in n (%).
[$]Multivitamins and minerals supplements were considered.
Bold values indicate *P*-value < 0.05 significant.

glucose, body mass index, and waist circumference (47). On the other hand, a systematic review and meta-analysis demonstrated that there was no considerable relation between dietary diversity score and most CMRs (48). However, little is known regarding the association between DQI and cardiometabolic risk factors and anthropometric indices.

In a cohort study, a 13-year follow-up among 4,390 adult participants indicated that lower scores of DQI were associated with higher scores of impaired HDL, FBG, LDL, and WC (49). In a cross-sectional study, which was carried out in 2021, it was observed that DQI score was inversely associated with serum level of TC, but positively associated with HDL (50). Alkerwi et al., in the Observation of Cardiovascular Risk Factors in Luxembourg (ORISCAV-LUX) study, found an inverse association between DQI score and total cholesterol, LDL, and HDL levels (51). In a cohort study among 451 participants, after 6.7 years of follow-up, a positive association was found between DQI score and HDL, although only in male participants (52). In a study by Kim et al., DQI had a significant association with fasting plasma glucose in diabetic patients (53). Moreover, results of a 10-year follow-up cohort study, across 10 European countries with over 450,000 participants, indicated that DQI scores were inversely associated with cardiovascular disease mortality and its risk factors, including blood lipids and glucose (54).

Based on our results, the DQI score was not related to the serum glycemic and lipid profile markers; however, the DQI score was inversely associated with CHOLINDEX, TyG-BMI, and TyG-WC, which are related indices to insulin resistance and lipid parameters. In a cross-sectional study conducted on patients with type 2 diabetes, there was no significant relationship between DQI scores and glycemic status and lipid profile parameters in diabetic patients (55). In addition, Daneshzad et al. did not observe any significant association between DQI and CVD risk factors in a cross-sectional study on diabetic women (56). However, in the Korea National Health and Nutritional Examination Survey, higher scores of DQI in middle-aged and older women were associated with a lower risk

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TABLE 3 Dietary intake of participants across tertiles of DQI among overweight and obese women ($n = 197$).

	Mean ± SD			*P*-value	*P*-value*
	T1 ($n = 66$)	T2 ($n = 65$)	T3 ($n = 66$)		
Energy intake (kcal/d)	2,406.0 ± 753.3	2,785.5 ± 731.8	2,715.5 ± 658.3	**0.041**	–
Macronutrients					
Protein (g/d)	80.6 ± 34.8	92.8 ± 27.2	97.8 ± 22.6	**0.028**	0.189
Carbohydrate (g/d)	309.9 ± 93.6	393.0 ± 107.6	422.4 ± 122.0	**<0.001**	**<0.001**
Total fat (g/d)	100.0 ± 35.6	103.1 ± 35.4	80.8 ± 20.4	**0.006**	**<0.001**
Micronutrients					
Cholesterol (mg/d)	258.3 ± 144.8	261.0 ± 104.9	220.9 ± 64.9	0.233	**0.006**
SFA (g/d)	31.5 ± 15.1	28.0 ± 9.7	23.1 ± 5.6	**0.006**	**<0.001**
MUFA (g/d)	35.0 ± 13.3	33.2 ± 11.5	26.4 ± 7.0	**0.003**	**<0.001**
Linoleic acid (g/d)	18.5 ± 8.6	19.0 ± 8.9	15.1 ± 5.4	0.079	**0.007**
Linolenic acid (g/d)	1.2 ± 0.5	1.2 ± 0.6	1.1 ± 0.6	0.684	0.170
Fe (mg/d)	15.6 ± 4.9	20.0 ± 5.7	21.5 ± 5.8	**<0.001**	**<0.001**
Calcium (mg/d)	1,011.7 ± 399.8	1,192.1 ± 398.2	1,295.8 ± 365.4	**0.006**	**0.039**
Mg (mg/d)	386.5 ± 134.4	479.5 ± 126.0	531.7 ± 141.6	**<0.001**	**<0.001**
Zn (mg/d)	11.4 ± 4.3	13.6 ± 4.2	14.4 ± 4.0	**0.006**	**0.025**
Selenium (mg/d)	102.2 ± 31.4	129.7 ± 42.2	135.0 ± 53.9	**0.001**	**0.029**
Vitamin A (RAE/d)	713.0 ± 460.7	837.2 ± 365.9	838.6 ± 343.7	0.262	0.889
β carotene	4,591.3 ± 3,540.6	5,416.5 ± 2,478.6	6,361.9 ± 3,234.0	**0.048**	0.195
Vitamin D (μg)	1.5 ± 1.2	2.3 ± 1.6	2.2 ± 1.7	**0.049**	0.226
Vitamin E (mg)	18.2 ± 107	19.1 ± 9.6	15.6 ± 6.0	0.248	0.126
Thiamin (mg)	1.8 ± 0.5	2.1 ± 0.5	2.3 ± 0.7	**0.001**	**<0.001**
Vitamin B_6 (mg)	1.9 ± 0.7	2.2 ± 0.6	2.3 ± 0.5	**0.009**	0.074
Folate (μg/d)	522.3 ± 147.7	614.4 ± 168.4	713.2 ± 183.7	**<0.001**	**<0.001**
Vitamin B_{12} (μg/d)	4.2 ± 1.9	4.8 ± 2.9	4.1 ± 1.5	0.294	0.302
Total fiber (g/d)	34.7 ± 15.0	46.5 ± 15.9	55.1 ± 17.4	**<0.001**	**<0.001**
Food groups					
Refined grain (g/d)	352.8 ± 148.9	456.9 ± 234.7	494.0 ± 276.3	**0.015**	0.068
Whole grain (g/d)	4.2 ± 4.8	6.1 ± 9.1	12.4 ± 15.1	**0.002**	**0.009**
Fruits (g/d)	359.5 ± 215.2	585.7 ± 312.9	590.1 ± 337.9	**<0.001**	**0.009**
Vegetables (g/d)	343.2 ± 230.3	486.7 ± 234.2	549.8 ± 267.2	**0.001**	**0.011**
Nuts (g/d)	13.7 ± 17.6	15.4 ± 17.1	17.3 ± 18.7	0.677	0.621
Dairy (g/d)	319.0 ± 205.7	404.3 ± 225.5	432.3 ± 227.6	0.059	0.213
Legumes (g/d)	46.1 ± 27.1	45.6 ± 35.3	77.4 ± 56.6	**0.001**	**0.002**

MUFA, monounsaturated fatty acid; SFA, saturated fatty acid.

Values are mean ± standard deviation (SD) for continuous variables. Using one-way ANOVA for continuous variables and Chi-square test for categorical variables.

*Adjusted for energy intake.

Bold values indicate *P*-value < 0.05 significant.

of body composition abnormalities (57), while Gregory et al.'s DQI was positively associated with BMI and WC (58). Nevertheless, in a cross-sectional study from the results of the Tehran Lipid and Glucose Study, no significant association was observed between DQI and BMI and WC (59). In this study, our results suggested that DQI was inversely associated with WHR, but there was no association between DQI and BMI, BFM, and WC. According to the extant literature, possible reasons for the inconsistency of the published results could be related to the differences in the sample size, different designs of the studies, and differences in the health status of participants.

The present results of the study showed that women with the highest score of DQI had a higher intake of whole grains, fruits, vegetables, legumes, and total fiber, in addition to a

TABLE 4 Association of DQI with cardiometabolic risk factors among overweight and obese women ($n = 197$).

	T1 ($n = 66$)	T2 ($n = 65$)		*P*-value	T3 ($n = 66$)		*P*-value	*P*-trend
		β	95% CI		β	95% CI		
BMI (kg/m^2)								
Crude model	Ref	−0.059	(−1.621,1.504)	0.941	0.137	(−1.492, 1.766)	0.869	0.876
Model 1		0.127	(−1.504, 1.758)	0.879	0.543	(−1.303, 2.389)	0.564	0.575
Model 2		0.297	(−1.305, 1.898)	0.716	0.140	(−1.684, 1.964)	0.880	0.854
BFM								
Crude model	Ref	0.346	(−2.854, 3.546)	0.832	0.036	(−3.300, 3.372)	0.983	0.973
Model 1		0.760	(−2.582, 4.102)	0.656	1.290	(−2.494, 5.073)	0.504	0.498
Model 2		1.049	(−2.209, 4.306)	0.528	0.510	(−3.201, 4.220)	0.788	0.744
WHR								
Crude model	Ref	−0.001	(−0.022, 0.021)	0.956	−0.008	(−0.031, 0.014)	0.476	0.488
Model 1		0.001	(−0.021, 0.023)	0.955	−0.007	(−0.032, 0.018)	0.580	0.605
Model 2		0.000	(−0.022, 0.022)	0.982	−0.014	(−0.039, 0.011)	**0.073**	**0.047**
WC (cm)								
Crude model	Ref	0.407	(−3.446, 4.259)	0.836	−0.233	(−4.250, 3.783)	0.909	0.922
Model 1		0.546	(−3.452, 4.544)	0.789	0.873	(−3.653, 5.399)	0.705	0.700
Model 2		0.585	(−3.381, 4.550)	0.773	−0.424	(−4.940, 4.093)	0.854	0.890
FBS (mmol/L)								
Crude model	Ref	−2.532	(−6.753, 1.689)	0.240	−2.673	(−6.968, 1.623)	0.223	0.206
Model 1		−2.536	(−7.001, 1.929)	0.266	−1.793	(−6.674, 3.088)	0.471	0.421
Model 2		−3.024	(−7.688, −1.641)	0.034	−1.358	(−6.517, 3.802)	0.606	0.508
Cholesterol (mmol/L)								
Crude model	Ref	−3.721	(−17.970,0.528)	0.609	0.852	(−13.647, 15.350)	0.908	0.945
Model 1		4.974	(−9.151, 19.098)	0.490	6.303	(−9.138, 21.743)	0.424	0.405
Model 2		1.375	(−12.885, 15.635)	0.850	2.802	(−12.972, 18.576)	0.728	0.726
TG (mmol/L)								
Crude model	Ref	−10.899	(−38.885, 17.086)	0.445	0.792	(−27.950, 29.533)	0.957	0.986

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TABLE 4 (Continued)

	T1 ($n = 66$)	T2 ($n = 65$)		*P*-value	T3 ($n = 66$)		*P*-value	*P*-trend
		β	95% CI		β	95% CI		
Model 1		−1.810	(−30.306, 26.687)	0.901	−1.063	(−32.386, 30.261)	0.947	0.938
Model 2		−2.012	(−31.141, 27.117)	0.892	−6.222	(−38.58,9 26.144)	0.706	0.712
HDL (mmol/L)								
Crude model	Ref	1.294	(−2.967, 5.555)	0.552	−0.326	(−4.662, 4.010)	0.883	0.925
Model 1		2.453	(−1.995, 6.901)	0.180	2.429	(−2.433, 7.292)	0.328	0.196
Model 2		3.306	(0.004, 7.707)	0.161	3.513	(−0.354, 8.381)	0.157	0.147
LDL (mmol/L)								
Crude model	Ref	−4.381	(−14.187, 5.425)	0.381	−2.452	(−12.431, 7.526)	0.630	0.595
Model 1		1.039	(−8.633, 10.711)	0.833	2.247	(−8.326, 12.820)	0.677	0.677
Model 2		0.809	(−8.462, 10.080)	0.864	−1.485	(−11.739, 1.770)	0.077	0.812
SBP								
Crude model	Ref	−0.387	(−6.131, 5.357)	0.895	0.902	(−5.089, 6.892)	0.768	0.783
Model 1		0.036	(−6.050, 6.123)	0.991	0.237	(−6.664, 7.137)	0.946	0.948
Model 2		0.941	(−5.321, 7.208)	0.768	−0.080	(−7.208, 7.048)	0.982	0.989
DBP								
Crude model	Ref	−2.138	(−6.123, 1.847)	0.293	−1.103	(−5.259, 3.053)	0.603	0.567
Model 1		−1.277	(−5.453, 2.898)	0.549	−0.983	(−5.717, 3.751)	0.684	0.655
Model 2		−0.634	(−5.009, 3.742)	0.777	−1.036	(−6.016, 3.944)	0.684	0.677
ABSI								
Crude model	Ref	−3.237	(−0.001, 0.001)	0.960	−0.001	(−0.002, 0.001)	0.370	0.383
Model 1		−8.239	(−0.001, 0.001)	0.901	−0.001	(−0.002, 0.001)	0.487	0.503
Model 2		0.000	(−0.002, 0.001)	0.731	−0.001	(−0.002, 0.001)	0.325	0.335
AIP								
Crude model	Ref	−0.063	(−0.170, 0.000)	0.050	−0.005	(−0.115, 0.105)	0.933	0.855
Model 1		−0.045	(−0.156, 0.065)	0.423	−0.051	(−0.172, 0.071)	0.414	0.388
Model 2		−0.049	(−0.158, 0.060)	0.378	−0.086	(−0.207, −0.006)	0.126	**0.027**

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TABLE 4 (Continued)

	T1 ($n = 66$)	T2 ($n = 65$)		*P*-value	T3 ($n = 66$)		*P*-value	*P*-trend
		β	95% CI		β	95% CI		
CRI_I								
Crude model	Ref	−0.169	(−0.583, 0.244)	0.422	0.113	(−0.308, 0.533)	0.599	0.661
Model 1		−0.063	(−0.496, 0.370)	0.175	0.026	(−0.447, 0.499)	0.714	0.945
Model 2		−0.197	(−0.609, 0.015)	0.119	0.122	(−0.578, 0.334)	0.600	0.533
CRI_II								
Crude model	Ref	−0.150	(−0.432, 0.131)	0.296	−0.007	(−0.293, 0.280)	0.964	0.900
Model 1		−0.073	(−0.363, 0.217)	0.120	−0.008	(−0.325, 0.309)	0.961	0.918
Model 2		−0.104	(−0.378, 0.101)	0.059	−0.123	(−0.427, 0.180)	0.426	0.397
CHOLIndex								
Crude model	Ref	−5.675	(−15.784, 0.034)	0.091	−2.127	(−12.412, 8.159)	0.685	0.634
Model 1		−1.414	(−11.637, 0.809)	0.066	−0.182	(−11.358, 10.994)	0.975	0.951
Model 2		−2.497	(−12.080, 7.085)	0.610	−4.998	(−15.597, 0.000)	0.055	**0.031**
TyG								
Crude model	Ref	−0.140	(−0.367, 0.007)	0.066	−0.048	(−0.281, 0.185)	0.684	0.620
Model 1		−0.079	(−0.307, 0.048)	0.074	−0.086	(−0.336, 0.164)	0.501	0.475
Model 2		−0.077	(−0.306, 0.152)	0.510	−0.144	(−0.398, 0.110)	0.077	0.260
TyG–BMI								
Crude model	Ref	−5.245	(−22.555, −1.065)	**0.043**	−1.668	(−19.441, 16.104)	0.854	0.821
Model 1		1.739	(−15.546, 19.024)	0.844	2.032	(−16.963, 21.026)	0.834	0.825
Model 2		3.617	(−13.388, 20.622)	0.677	−4.186	(−23.128, 1.757)	0.085	0.736
TyG–WC								
Crude model	Ref	−31.464	(−91.980, −9.052)	**0.038**	−13.835	(−68.512, 40.842)	0.620	0.564
Model 1		−10.284	(−71.397, 0.030)	0.052	−1.135	(−62.779, 60.510)	0.971	0.136
Model 2		−25.579	(−80.893, 29.735)	0.365	−54.768	(−110.920, 1.384)	0.056	0.054
LAP								
Crude model	Ref	−8.149	(−25.671, 9.374)	0.362	4.717	(−12.962, 22.396)	0.601	0.669
Model 1		0.915	(−15.986, 17.816)	0.916	8.107	(−10.333, 26.547)	0.389	0.413
Model 2		1.724	(−15.822, 19.269)	0.847	2.747	(−16.554, 22.048)	0.780	0.773

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TABLE 4 (Continued)

	T1 ($n = 66$)	T2 ($n = 65$)		*P*-value	T3 ($n = 66$)		*P*-value	*P*-trend
		β	95% CI		β	95% CI		
AC								
Crude model	Ref	−0.169	(−0.583, 0.244)	0.422	0.113	(−0.308, 0.533)	0.599	0.66
Model 1		−0.063	(−0.496, 0.370)	0.775	0.026	(−0.447, 0.499)	0.914	0.945
Model 2		−0.197	(−0.609, 0.215)	0.349	−0.122	(−0.578, 0.334)	0.600	0.533

ABSI, a body shape index; AC, atherogenic coefficient; AIP, atherogenic index of plasma; BFM, body fat mass; BMI, body mass index; CI, confidence interval; CRI-I, Castelli risk index 1; FBS, fasting blood sugar; HDL, high-density lipoprotein; LAP, lipid accumulation product; LDL; low-density lipoprotein; TG, triglyceride; TyG, Triglyceride-glucose index; WC, waist circumference; WHR, waist-hip ratio.

Binary logistic regression was used.

Model 1: adjusted for age, physical activity, energy intake, and BMI. Note: BMI as a colinear variable was not adjusted for BMI, BFM, WHR, WC, TyG-BMI, Tyg-WC, LAP, and ABSI.

Model 2: adjusted for model 1 further with education, socioeconomic status, and supplement use.

Bold values indicate *P*-value < 0.05 significant.

lower intake of total fat and saturated fatty acids. It has been reported that a high-quality diet is related to a decreased risk of mortality caused by cardiovascular diseases (60). Dietary combinations can have considerable efficacy on insulin sensitivity (61). The types of fat consumption have been investigated and discussed as a factor in cardiovascular (62), as part of nutritional planning, and for the increase of insulin sensitivity (63). The quality of dietary fats can affect the composition of cell membranes and their functions and also cause to alter in insulin signaling pathways in tissues (64). For example, saturated fatty acids can induce insulin resistance by reducing the release of adiponectin and disrupting insulin signaling pathways associated with glucose uptake in adipose tissue. In addition, fatty acids lead to insulin resistance by causing chronic and mild inflammation through inflammatory cytokines, lipids and their metabolites, and reactive oxygen species (65–67). The saturated fatty acid could cause activates serine kinase proteins, leading to inflammatory pathways, and through reduction tyrosine phosphorylation of insulin receptor substrate 1, adverse affect insulin transportation (57). In addition, other negative results of its consumption include formation of antagonists against insulin activity, such as sphingolipids (68), and the expression of nuclear factor kappa B (NF-kB) and cyclooxygenase-2 (COX-2) (69). Intake of complex carbohydrates, such as fiber, and sources rich in polyphenols and antioxidants, including vegetables, fruits, and legumes, can contribute to an ameliorated cardiovascular status, due to their anti-inflammatory properties (70–72). Dietary fiber intake can, through its fermentation by intestinal bacteria and the production of short-chain fatty acids, lead to a reduction in the synthesis of cholesterol in the body (73, 74). The short-chain fatty acids lead to a decrease in the levels of C-reactive protein and interleukin-6 (75, 76). The benefits of polyphenols are related to their anti-inflammatory and antioxidant properties (77) because they can reduce the release of NO and PGE2 by suppressing the expression of iNOS and PGE2, and also reduce the release of IL-1b and TNF-a, an effect that has been related to suppressing activation of the NF-kB pathway (78, 79). Consumption of these products leads to ameliorate regulation of fat and carbohydrate metabolism, improvement of hyperglycemia, a decrease of dyslipidemia, increased sensitivity to insulin, amendment of adipose tissue metabolism, and decrease in oxidative stress (80). One of the most well-known effects of polyphenols on carbohydrate metabolism is the suppression of the function of the key enzymes (including alpha-glucosidase and alpha-amylase) responsible for its digestion in the gastrointestinal tract (81, 82). Some types of polyphenols can interfere with the absorption of glucose from the small intestine by inhibiting sodium-dependent glucose transporters, such as SGLT1 (83, 84). Polyphenolic ingredients regulated at blood sugar level after meals and improved glucose intolerance by facilitating insulin response and reducing the secretion of hormones such as glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like polypeptide-1 (GLP-1) (85, 86). Some polyphenols can regulate the lipolysis mechanism through the induction of adipose tissue lipase, hormone sensitive lipase, enhances gene expression of mitochondrial uncoupling protein 2 (UCP-2) and carnitin palmitoyl transferase-1 (CPT-1) (87, 88). Most polyphenolic compounds, because of their particular structure, have been known as antioxidant phytochemicals (89).

They improve the oxidant-antioxidant equilibrium through the endogenous antioxidant system. These bioactive factors diminish lipid peroxidation and increase the total antioxidant capacity of plasma. In addition, they induce enzymes including superoxide dismutase, catalase, and glutathione peroxidase (90).

This study represents a novel addition to the literature, where we elucidate the relationship between DQI and cardiometabolic risk factors in obese and overweight women. Indeed, among the strengths of our study, unlike most of the studies conducted on the relationship between DQI and cardiometabolic risk factors, which only used BMI, WC, and usual glycemic and lipid serum parameters, our study also investigated the relationship of other atherogenic indices, lipid ratios, and anthropometric indices. Nevertheless, despite the strength and novelty of this study, some limitations should be noted. First, the sample included only women; although this was a purposeful decision, based on the dearth of data in the literature. In addition, since this study was performed only in one province, the results cannot be attributed to the total population. Furthermore, using FFQ makes measurement errors inevitable; these largely emanant from recall and other subjective biases. Finally, because of the cross-sectional design of the study, causal inferences cannot be made.

Conclusion

In this study, we showed that the higher DQI score was associated with lower WHR, AIP, CHOLINDEX, TyG-BMI, and TyG-WC in overweight and obese women. However, more studies are needed to confirm these findings and elucidate their mechanistic etiology in the future.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethics approval and consent to participate was presented in article. Each participant was informed completely regarding the study protocol and provided a written and informed consent form before taking part in the study. The study protocol was approved by the ethics committee of Tehran University of Medical Sciences (TUMS) with the following identification (R.TUMS.VCR.REC.1395.1234.).

Author contributions

AMo, AMi, and KM designed the search. AMi and MG conducted the sampling. FS performed statistical analysis. AMo, AA, and CC wrote the manuscript. CC and YA revised the article. KM and AMi have responsibility for the final content. All authors have read and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. Sarrafzadegan N, Mohammmadifard N. Cardiovascular disease in Iran in the last 40 years: prevalence, mortality, morbidity, challenges and strategies for cardiovascular prevention. *Arch Iran Med.* (2019) 22:204–10.

2. Cannon CP. Cardiovascular disease and modifiable cardiometabolic risk factors. *Clin Cornerstone.* (2007) 8:11–28. doi: 10.1016/S1098-3597(07)80025-1

3. Garcia M, Mulvagh SL, Bairey Merz CN, Buring JE, Manson JE. Cardiovascular disease in women: clinical perspectives. *Circ Res.* (2016) 118:1273–93. doi: 10.1161/CIRCRESAHA.116.307547

4. Kahn HS. The "lipid accumulation product" performs better than the body mass index for recognizing cardiovascular risk: a population-based comparison. *BMC Cardiovasc Disord.* (2005) 5:1–10. doi: 10.1186/1471-2261-5-26

5. Brisson D, Perron P, Guay SP, Gaudet D, Bouchard L. The "hypertriglyceridemic waist" phenotype and glucose intolerance in pregnancy. *CMAJ.* (2010) 182:E722–5. doi: 10.1503/cmaj.100378

6. LaMonte MJ, Ainsworth BE, DuBose KD, Grandjean PW, Davis PG, Yanowitz FG, et al. The hypertriglyceridemic waist phenotype among women. *Atherosclerosis.* (2003) 171:123–30. doi: 10.1016/j.atherosclerosis.2003.07.008

7. Fernández-Macías JC, Ochoa-Martínez AC, Varela-Silva JA, Pérez-Maldonado IN. Atherogenic index of plasma: novel predictive biomarker for cardiovascular illnesses. *Arch Med Res.* (2019) 50:285–94. doi: 10.1016/j.arcmed.2019.08.009

8. Bhardwaj S, Bhattacharjee J, Bhatnagar M, Tyagi S, Delhi N. Atherogenic index of plasma, castelli risk index and atherogenic coefficient-new parameters in assessing cardiovascular risk. *Int J Pharm Biol Sci.* (2013) 3:359–64.

9. Akpinar O, Bozkurt A, Acarturk E, Seydaoglu G. A new index (CHOLINDEX) in detecting coronary artery disease risk. *Anatol J Cardiol.* (2013) 13:98. doi: 10.5152/akd.2013.098

10. Krakauer NY, Krakauer JC. A new body shape index predicts mortality hazard independently of body mass index. *PLoS ONE.* (2012) 7:e39504. doi: 10.1371/journal.pone.0039504

11. He S, Chen X. Could the new body shape index predict the new onset of diabetes mellitus in the Chinese population? *PLoS ONE.* (2013) 8:e50573. doi: 10.1371/journal.pone.0050573

12. Krakauer NY, Krakauer JC. Dynamic association of mortality hazard with body shape. *PLoS ONE.* (2014) 9:e88793. doi: 10.1371/journal.pone.0088793

13. Maessen MF, Eijsvogels TM, Verheggen RJ, Hopman MT, Verbeek AL, Vegt FD. Entering a new era of body indices: the feasibility of a body shape index and body roundness index to identify cardiovascular health status. *PLoS ONE.* (2014) 9:e107212. doi: 10.1371/journal.pone.0107212

14. Haghighatdoost F, Sarrafzadegan N, Mohammadifard N, Asgary S, Boshtam M, Azadbakht L. Assessing body shape index as a risk predictor for cardiovascular diseases and metabolic syndrome among Iranian adults. *Nutrition.* (2014) 30:636–44. doi: 10.1016/j.nut.2013.10.021

15. Bozorgmanesh M, Sardarinia M, Hajsheikholeslami F, Azizi F, Hadaegh F. CVD-predictive performances of "a body shape index" versus simple anthropometric measures: Tehran lipid and glucose study. *Eur J Nutr.* (2016) 55:147–57. doi: 10.1007/s00394-015-0833-1

16. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord.* (2008) 6:299–304. doi: 10.1089/met.2008.0034

17. Lee SB, Ahn CW, Lee BK, Kang S, Nam JS, You JH, et al. Association between triglyceride glucose index and arterial stiffness in Korean adults. *Cardiovasc Diabetol.* (2018) 17:1–6. doi: 10.1186/s12933-018-0692-1

18. Kim MK, Ahn CW, Kang S, Nam JS, Kim KR, Park JS. Relationship between the triglyceride glucose index and coronary artery calcification in Korean adults. *Cardiovasc Diabetol.* (2017) 16:1–7. doi: 10.1186/s12933-017-0589-4

19. Lambrinoudaki I, Kazani MV, Armeni E, Georgiopoulos G, Tampakis K, Rizos D, et al. The TyG index as a marker of subclinical atherosclerosis and arterial stiffness in lean and overweight postmenopausal women. *Heart Lung Circul.* (2018) 27:716–24. doi: 10.1016/j.hlc.2017.05.142

20. Laslett LJ, Alagona P, Clark BA, Drozda JP, Saldivar F, Wilson SR, et al. The worldwide environment of cardiovascular disease: prevalence, diagnosis, therapy, and policy issues: a report from the American College of Cardiology. *J Am Coll Cardiol.* (2012) 60:S1–S49. doi: 10.1016/j.jacc.2012.11.002

21. Jardim TV, Mozaffarian D, Abrahams-Gessel S, Sy S, Lee Y, Liu J, et al. Cardiometabolic disease costs associated with suboptimal diet in the United States: a cost analysis based on a microsimulation model. *PLoS Med.* (2019) 16:e1002981. doi: 10.1371/journal.pmed.1002981

22. Newby P, Tucker KL. Empirically derived eating patterns using factor or cluster analysis: a review. *Nutr Rev.* (2004) 62:177–203. doi: 10.1111/j.1753-4887.2004.tb00040.x

23. Waijers PM, Feskens EJ, Ocké MC. A critical review of predefined diet quality scores. *Br J Nutr.* (2007) 97:219–31. doi: 10.1017/S0007114507250421

24. Gil Á, de Victoria EM, Olza J. Indicators for the evaluation of diet quality. *Nutricion Hospitalaria.* (2015) 31:128–44.

25. de Almeida Ventura D, de Matos Fonseca V, Ramos EG, Marinheiro LPF, de Souza RAG, de Miranda Chaves CRM, et al. Association between quality of the diet and cardiometabolic risk factors in postmenopausal women. *Nutr J.* (2014) 13:1–10. doi: 10.1186/1475-2891-13-121

26. McNaughton SA, Dunstan DW, Ball K, Shaw J, Crawford D. Dietary quality is associated with diabetes and cardio-metabolic risk factors. *J Nutr.* (2009) 139:734–42. doi: 10.3945/jn.108.096784

27. Funtikova A, Baena-Díez J, Koebnick C, Gomez S, Covas M, Goday A, et al. Validity of a short diet-quality index to predict changes in anthropometric and cardiovascular risk factors: a simulation study. *Eur J Clin Nutr.* (2012) 66:1369–71. doi: 10.1038/ejcn.2012.131

28. Willett W. Issues in analysis and presentation of dietary data. *Nutrition Epidemiol.* (1998) 13:321–46. doi: 10.1093/acprof:oso/9780195122978.003.13

29. Mirzababaei A, Shiraseb F, Abaj F, Khosroshahi RA, Tavakoli A, Koohdani F, et al. The effect of dietary total antioxidant capacity (DTAC) and Caveolin-1 gene variant interaction on cardiovascular risk factors among overweight and obese women: a cross-sectional investigation. *Clin Nutr.* (2021) 40:4893–903. doi: 10.1016/j.clnu.2021.07.013

30. WHO. *Nutrition*. (2023). Available online at: https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi (accessed 2023).

31. Vieira BA, Sauer P, Marcadenti A, Piovesan CH. Association between LAP Index (Lipid Accumulation Product) and metabolic profile in hospitalized patients. *Nutr Hosp.* (2015) 31:2771–4.

32. Shen S, Lu Y, Qi H, Li F, Shen Z, Wu L, et al. Association between ideal cardiovascular health and the atherogenic index of plasma. *Medicine.* (2016) 95:3866. doi: 10.1097/MD.0000000000003866

33. Bhardwaj S, Bhattacharjee J, Bhatnagar M, Tyagi S. Atherogenic index of plasma, castelli risk index and atherogenic coefficient-new parameters in assessing cardiovascular risk. *Int J Pharm Biol Sci.* (2013) 3:359–64.

34. Wang X, Liu J, Cheng Z, Zhong Y, Chen X, Song W. Triglyceride glucose-body mass index and the risk of diabetes: a general population-based cohort study. *Lipids Health Dis.* (2021) 20:1–10. doi: 10.1186/s12944-021-01532-7

35. Hameed EK. TyG index a promising biomarker for glycemic control in type 2 Diabetes Mellitus. *Diabetes Metab Syndr.* (2019) 13:560–3. doi: 10.1016/j.dsx.2018.11.030

36. Costa PRF, Assis AMO, Cunha CM, Pereira EM, Jesus GDS, Silva L, et al. Hypertriglyceridemic waist phenotype and changes in the fasting glycemia and blood pressure in children and adolescents over one-year follow-up period. *Arq Bras Cardiol.* (2017) 109:47–53. doi: 10.5935/abc.20170067

37. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran lipid and glucose study. *Public Health Nutr.* (2010) 13:654–62. doi: 10.1017/S1368980009991698

38. Ghaffarpour M, Houshiar-Rad A, Kianfar H. The manual for household measures, cooking yields factors and edible portion of foods. *Tehran.* (1999) 7:42–58.

39. Kim S, Haines PS, Siega-Riz AM, Popkin BM. The Diet Quality Index-International (DQI-I) provides an effective tool for cross-national comparison of diet quality as illustrated by China and the United States. *J Nutr.* (2003) 133:3476–84. doi: 10.1093/jn/133.11.3476

40. Mohammadifard N, Kelishadi R, Safavi M, Sarrafzadegan N, Sajadi F, Sadri GH, et al. Effect of a community-based intervention on nutritional behaviour in a developing country setting: the Isfahan Healthy Heart Programme. *Public Health Nutr.* (2009) 12:1422–30. doi: 10.1017/S1368980008004230

41. Bassett Jr DR. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exer.* (2003) 35:1396. doi: 10.1249/01.MSS.0000078923.96621.1D

42. Chomistek AK, Chiuve SE, Eliassen AH, Mukamal KJ, Willett WC, Rimm EB. Healthy lifestyle in the primordial prevention of cardiovascular disease among young women. *J Am Coll Cardiol.* (2015) 65:43–51. doi: 10.1016/j.jacc.2014.10.024

43. Steffen LM, Van Horn L, Daviglus ML, Zhou X, Reis JP, Loria CM, et al. A modified Mediterranean diet score is associated with a lower risk of incident metabolic syndrome over 25 years among young adults: the CARDIA (Coronary Artery Risk Development in Young Adults) study. *Br J Nutr.* (2014) 112:1654–61. doi: 10.1017/S0007114514002633

44. Liu K, Daviglus ML, Loria CM, Colangelo LA, Spring B, Moller AC, et al. Healthy lifestyle through young adulthood and the presence of low cardiovascular disease risk profile in middle age: the Coronary Artery Risk Development in (Young) Adults (CARDIA) study. *Circulation.* (2012) 125:996–1004. doi: 10.1161/CIRCULATIONAHA.111.060681

45. Wang Z, Siega-Riz AM, Gordon-Larsen P, Cai J, Adair LS, Zhang B, et al. Diet quality and its association with type 2 diabetes and major cardiometabolic risk factors among adults in China. *Nutr Metabol Cardiovasc Dis.* (2018) 28:987–1001. doi: 10.1016/j.numecd.2018.06.012

46. Phillips CM, Harrington JM, Perry IJ. Relationship between dietary quality, determined by DASH score, and cardiometabolic health biomarkers: a cross-sectional analysis in adults. *Clin Nutr.* (2019) 38:1620–8. doi: 10.1016/j.clnu.2018.08.028

47. Livingstone KM, McNaughton SA. Association between diet quality, dietary patterns and cardiometabolic health in Australian adults: a cross-sectional study. *Nutr J.* (2018) 17:1–13. doi: 10.1186/s12937-018-0326-1

48. Qorbani M, Mahdavi-Gorabi A, Khatibi N, Ejtahed H-S, Khazdouz M, Djalalinia S, et al. Dietary diversity score and cardio-metabolic risk factors: an updated systematic review and meta-analysis. *Eating Weight Disord Stud Anorexia Bulimia Obesity.* (2022) 27:85–100. doi: 10.1007/s40519-020-01090-4

49. Nouri F, Sadeghi M, Mohammadifard N, Roohafza H, Feizi A, Sarrafzadegan N. Longitudinal association between an overall diet quality index and latent profiles of cardiovascular risk factors: results from a population based 13-year follow up cohort study. *Nutr Metab.* (2021) 18:1–13. doi: 10.1186/s12986-021-00560-5

50. Zamani B, Daneshzad E, Mofrad MD, Namazi N, Larijani B, Bellissimo N, et al. Dietary quality index and cardiometabolic risk factors among adult women. *Iran J Public Health.* (2021) 50:1713. doi: 10.18502/ijph.v50i8.6819

51. Alkerwi AA, Vernier C, Crichton GE, Sauvageot N, Shivappa N, Hébert JR. Cross-comparison of diet quality indices for predicting chronic disease risk: findings from the Observation of Cardiovascular Risk Factors in Luxembourg (ORISCAV-LUX) study. *Br J Nutr.* (2015) 113:259–69. doi: 10.1017/S0007114514003456

52. Asghari G, Mirmiran P, Hosseni-Esfahani F, Nazeri P, Mehran M, Azizi F. Dietary quality among Tehranian adults in relation to lipid profile: findings from the Tehran Lipid and Glucose Study. *J Health Popul Nutr.* (2013) 31:37. doi: 10.3329/jhpn.v31i1.14747

53. Kim J, Cho Y, Park Y, Sohn C, Rha M, Lee M-K, et al. Association of dietary quality indices with glycemic status in Korean patients with type 2 diabetes. *Clin Nutr Res.* (2013) 2:100–6. doi: 10.7762/cnr.2013.2.2.100

54. Lassale C, Gunter MJ, Romaguera D, Peelen LM, Van der Schouw YT, Beulens JW, et al. Diet quality scores and prediction of all-cause, cardiovascular and cancer mortality in a pan-European cohort study. *PLoS ONE.* (2016) 11:e0159025. doi: 10.1371/journal.pone.0159025

55. Ziaee RS, Keshani P, Salehi M, Ghaem H. Diet quality indices and their correlation with glycemic status and lipid profile in patients with type 2 diabetes. *Adv Prev Med*. (2021) 2021:2934082. doi: 10.1155/2021/2934082

56. Daneshzad E, Larijani B, Azadbakht L. Diet quality indices and cardiovascular diseases risk factors among diabetic women. *J Sci Food Agric*. (2019) 99:5926–33. doi: 10.1002/jsfa.9867

57. Kim J, Lee Y, Kye S, Chung Y-S, Kim J-H, Chon D, et al. Diet quality and osteosarcopenic obesity in community-dwelling adults 50 years and older. *Maturitas*. (2017) 104:73–9. doi: 10.1016/j.maturitas.2017.08.007

58. Gregory CO, McCullough ML, Ramirez-Zea M, Stein AD. Diet scores and cardio-metabolic risk factors among Guatemalan young adults. *Br J Nutr*. (2008) 101:1805–11. doi: 10.1017/S000711450813584X

59. Asghari G, Mirmiran P, Rashidkhani B, Asghari-Jafarabadi M, Mehran M, Azizi F. The association between diet quality indices and obesity: Tehran Lipid and Glucose Study. *Archiv Iran Med*. (2012) 15.

60. Fox CS, Golden SH, Anderson C, Bray GA, Burke LE, De Boer IH, et al. Update on prevention of cardiovascular disease in adults with type 2 diabetes mellitus in light of recent evidence: a scientific statement from the American Heart Association and the American Diabetes Association. *Circulation*. (2015) 132:691–718. doi: 10.1161/CIR.0000000000000230

61. Mann JI. Nutrition recommendations for the treatment and prevention of type 2 diabetes and the metabolic syndrome: an evidenced-based review. *Nutr Rev*. (2006) 64:422–7. doi: 10.1111/j.1753-4887.2006.tb00227.x

62. Zong G, Li Y, Wanders AJ, Alssema M, Zock PL, Willett WC, et al. Intake of individual saturated fatty acids and risk of coronary heart disease in US men and women: two prospective longitudinal cohort studies. *Br Med J*. (2016) 355:i5796. doi: 10.1136/bmj.i5796

63. Vickers NJ. Animal communication: when i'm calling you, will you answer too? *Curr Biol*. (2017) 27:R713–5. doi: 10.1016/j.cub.2017.05.064

64. Ginsberg BH, Brown TJ, Simon I, Spector AA. Effect of the membrane lipid environment on the properties of insulin receptors. *Diabetes*. (1981) 30:773–80. doi: 10.2337/diab.30.9.773

65. Dali-Youcef N, Mecili M, Ricci R, Andrès E. Metabolic inflammation: connecting obesity and insulin resistance. *Ann Med*. (2013) 45:242–53. doi: 10.3109/07853890.2012.705015

66. Zhang P, Chen L, Zhao Q, Du X, Bi M, Li Y, et al. Ferroptosis was more initial in cell death caused by iron overload and its underlying mechanism in Parkinson's disease. *Free Rad Biol Med*. (2020) 152:227–34. doi: 10.1016/j.freeradbiomed.2020.03.015

67. Khodabandehloo H, Gorgani-Firuzjaee S, Panahi G, Meshkani R. Molecular and cellular mechanisms linking inflammation to insulin resistance and β-cell dysfunction. *Transl Res*. (2016) 167:228–56. doi: 10.1016/j.trsl.2015.08.011

68. Holland WL, Brozinick JT, Wang L-P, Hawkins ED, Sargent KM, Liu Y, et al. Inhibition of ceramide synthesis ameliorates glucocorticoid-, saturated-fat-, and obesity-induced insulin resistance. *Cell Metab*. (2007) 5:167–79. doi: 10.1016/j.cmet.2007.01.002

69. Lee SFA. Saturated fatty acids, But not unsaturated fatty acids, induce the expression of cyclooxygenase-2 mediated through toll-like receptor 4. *J Biol Chem*. 276:16683–9. doi: 10.1074/jbc.M011695200

70. Zhu F, Du B, Xu B. Anti-inflammatory effects of phytochemicals from fruits, vegetables, and food legumes: a review. *Crit Rev Food Sci Nutr*. (2018) 58:1260–70. doi: 10.1080/10408398.2016.1251390

71. Nielsen SJJ, Trak-Fellermeier MA, Joshipura K. The association between dietary fiber intake and CRP levels, US adults, 2007–2010. *FASEB J*. (2017) 31:648.8-8. doi: 10.1096/fasebj.31.1_supplement.648.8

72. Serafini M, Peluso I. Functional foods for health: the interrelated antioxidant and anti-inflammatory role of fruits, vegetables, herbs, spices and cocoa in humans. *Curr Pharm Des*. (2016) 22:6701–15. doi: 10.2174/1381612823666161123094235

73. Liu S, Buring JE, Sesso HD, Rimm EB, Willett WC, Manson JE, et al. prospective study of dietary fiber intake and risk of cardiovascular disease among women. *J Am Coll Cardiol*. (2002) 39:49–56. doi: 10.1016/S0735-1097(01)01695-3

74. Xu X, Zhang J, Zhang Y, Qi H, Wang P. Associations between dietary fiber intake and mortality from all causes, cardiovascular disease and cancer: a prospective study. *J Transl Med*. (2022) 20:1–8. doi: 10.1186/s12967-022-03558-6

75. Krishnamurthy VMR, Wei G, Baird BC, Murtaugh M, Chonchol MB, Raphael KL, et al. High dietary fiber intake is associated with decreased inflammation and all-cause mortality in patients with chronic kidney disease. *Kidney Int*. (2012) 81:300–6. doi: 10.1038/ki.2011.355

76. Jiao J, Xu J-Y, Zhang W, Han S, Qin L-Q. Effect of dietary fiber on circulating C-reactive protein in overweight and obese adults: a meta-analysis of randomized controlled trials. *Int J Food Sci Nutr*. (2015) 66:114–9. doi: 10.3109/09637486.2014.959898

77. Rice-Evans C, Miller N. Antioxidant activities of flavonoids as bioactive components of food. *Biochem Soc Trans*. (1996) 24:790–5. doi: 10.1042/bst0240790

78. Ha SK, Park H-Y, Eom H, Kim Y, Choi I. Narirutin fraction from citrus peels attenuates LPS-stimulated inflammatory response through inhibition of NF-κB and MAPKs activation. *Food Chem Toxicol*. (2012) 50:3498–504. doi: 10.1016/j.fct.2012.07.007

79. Comalada M, Ballester I, Bailon E, Sierra S, Xaus J, Gálvez J, et al. Inhibition of pro-inflammatory markers in primary bone marrow-derived mouse macrophages by naturally occurring flavonoids: analysis of the structure–activity relationship. *Biochem Pharmacol*. (2006) 72:1010–21. doi: 10.1016/j.bcp.2006.07.016

80. Bahadoran Z, Mirmiran P, Azizi F. Dietary polyphenols as potential nutraceuticals in management of diabetes: a review. *J Diabet Metabol Disord*. (2013) 12:1–9. doi: 10.1186/2251-6581-12-43

81. Iwai K. Antidiabetic and antioxidant effects of polyphenols in brown alga Ecklonia stolonifera in genetically diabetic KK-Ay mice. *Plant Foods Hum Nutr*. (2008) 63:163–9. doi: 10.1007/s11130-008-0098-4

82. Tadera K, Minami Y, Takamatsu K, Matsuoka T. Inhibition of α-glucosidase and α-amylase by flavonoids. *J Nutr Sci Vitaminol*. (2006) 52:149–53. doi: 10.3177/jnsv.52.149

83. Kobayashi Y, Suzuki M, Satsu H, Arai S, Hara Y, Suzuki K, et al. Green tea polyphenols inhibit the sodium-dependent glucose transporter of intestinal epithelial cells by a competitive mechanism. *J Agric Food Chem*. (2000) 48:5618–23. doi: 10.1021/jf0006832

84. Johnston K, Sharp P, Clifford M, Morgan L. Dietary polyphenols decrease glucose uptake by human intestinal Caco-2 cells. *FEBS Lett*. (2005) 579:1653–7. doi: 10.1016/j.febslet.2004.12.099

85. Johnston KL, Clifford MN, Morgan LM. Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine. *Am J Clin Nutr*. (2003) 78:728–33. doi: 10.1093/ajcn/78.4.728

86. Dao T-MA, Waget A, Klopp P, Serino M, Vachoux C, Pechere L, et al. Resveratrol increases glucose induced GLP-1 secretion in mice: a mechanism which contributes to the glycemic control. *PLoS ONE*. (2011) 6:e20700. doi: 10.1371/journal.pone.0020700

87. Nakazato K, Song H, Waga T. Effects of dietary apple polyphenol on adipose tissues weights in Wistar rats. *Exp Anim*. (2006) 55:383–9. doi: 10.1538/expanim.55.383

88. Osada K, Suzuki T, Kawakami Y, Senda M, Kasai A, Sami M, et al. Dose-dependent hypocholesterolemic actions of dietary apple polyphenol in rats fed cholesterol. *Lipids*. (2006) 41:133–9. doi: 10.1007/s11745-006-5081-y

89. Dembinska-Kiec A, Mykkänen O, Kiec-Wilk B, Mykkänen H. Antioxidant phytochemicals against type 2 diabetes. *Br J Nutr*. (2008) 99:ES109–7. doi: 10.1017/S000711450896579X

90. Crespy V, Williamson G. A review of the health effects of green tea catechins in in vivo animal models. *J Nutr*. (2004) 134:3431S–40S. doi: 10.1093/jn/134.12.3431S

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Association of predicted body composition with occurrence of atrial fibrillation

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Background: Body mass index (BMI) is insufficient evidence as a risk factor for numerous health disorders. Body composition may be more appropriate for confirming the association with cardiovascular diseases, including atrial fibrillation (AF). This study aimed to examine the association between body composition and the occurrence of AF.
Methods: A total of 2,673,108 participants (48.6% women) without AF at baseline from the Korean national health insurance data were included. Body composition including appendicular skeletal muscle mass, body fat mass, and lean body mass were indirectly measured through validated anthropometric prediction equations. The diagnosis of AF and comorbidities were defined.
Results: With a median of 9.5 (interquartile range 9.2–10.1) years' follow-up, 25,841 (0.96%) cases of incident AF were included. In multivariable analysis, higher appendicular skeletal muscle was related to low risk of AF [hazard ratio (HR) 0.829, 95% confidence interval (CI) 0.753–0.912 for men (fifth quintile) and HR 0.888, 95% CI 0.792–0.995 for women (fifth quintile)]. In contrast, a higher body fat mass [HR 1.345, 95% CI 1.221–1.483 for men (fifth quintile) and HR 1.420, 95% CI 1.274–1.591 for women (fifth quintile)] and lean body mass [HR 2.241, 95% CI 2.182–2.303 for men (fifth quintile) and HR 1.516, 95% CI 1.368–1.667 for women (fifth quintile)] were associated with the occurrence of AF.
Conclusions: In this study, body composition parameters were associated with the occurrence of AF. It should be noted that when appendicular skeletal muscle mass decreases and body fat mass and lean body mass increase, the risk of AF may be increased in general population except underweighted BMI group.

KEYWORDS

body composition, body mass index, atrial fibrillation, big data, analysis

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia that increases the possibility of mortality, stroke, and systemic embolism (1). Globally, the present age has entered the age of aging, and the incidence of vascular risk factors has also increased. These changes have caused the incidence of AF to increase in Asian and Western populations continuously (2, 3). Therefore, it is important to control and recognize the association or risk factors for the occurrence of AF. To date, risk factors for AF, including hypertension, diabetes mellitus, coronary artery occlusive disease, aortic atheroma, poor oral hygiene, smoking, and cardiomyopathy, have been suggested. However, information regarding further modifiable associative or risk factors for AF is still lacking (4–6).

Obesity is explained as an excess of health-impairing fat mass and is commonly defined as a body mass index (BMI) $\geq$30 kg/m^2 (7). The worldwide prevalence of obesity has

increased over the past few decades, and the global burden of obesity is still increasing (8). It is well known that obesity, especially high levels of fat mass, worsens cardiovascular risk factors, including hypertension, lipoprotein metabolism, insulin resistance, and inflammation (9, 10). Considering the association of obesity with AF, obesity is associated with an increase in AF (11, 12). Therefore, it is important to develop an accurate method that measures obesity. Although BMI is frequently used to define obesity, the results of studies using BMI to determine the relationship between obesity and AF are inconsistent. Previous studies that defined obesity as an increased BMI showed a positive correlation between obesity and the risk of AF (13). On the other hand, other studies have showed the obesity paradox, where obese and overweight patients with AF, have a better prognosis than their leaner counterparts (14, 15). Therefore, body composition parameters, not simply BMI, may be more appropriate to confirm the association with disease (16).

To date, studies regarding the relationship between body composition and AF have been limited. In a previous study, increased body fat indices, independent of BMI, were related to the incidence of AF (17). Moreover, another study showed that high lean body mass was a determinant of AF incidence in postmenopausal women (18). Nevertheless, there have been few studies of longitudinal design targeting a general population of large sample sizes on the relationship of body composition with the occurrence of AF. Therefore, we aimed to investigate the association of predicted appendicular skeletal muscle mass index (pASMMI), predicted body fat mass index (pBFMI), and predicted lean body mass index (pLBMI), which were derived from an equation previously validated in the Korean population (16), with the occurrence of AF in a longitudinal setting.

2. Methods

2.1. Participants

This study was performed using the National Health Insurance Service Health Screening dataset (NHIS-HEALS) provided by the Korean government. In South Korea, adults over the age of 20 are supported to undergo free health screening every other year. The Korean government combined the results of national health screening with age, sex, and sociodemographic data as well as the national health claim data, which 97% of the South Korean population are enrolled, including household income and medical history, which includes diagnostic codes, medication prescriptions, treatment or procedure information, hospitalization, and date of mortality (19). Of these data, 2,815,596 participants who underwent a national health examination between 2010 and 2011 and aged between 20 and 79 years were used to construct a dataset (NHIS-2021-1-715) and used it through a predetermined identification and validation process (6, 20). Among 2,815,596 participants, those ($n = 130,044$) with at least one missing value regarding demographic data, lifestyle, and laboratory findings were excluded. Patients with a previous history of AF ($n = 12,444$) were excluded. Finally, 2,673,108 participants were included in this study (**Figure 1**). Our study was permitted by the Institutional Review Board of Ewha Womans University Seoul Hospital (Institutional Review Board approval number: SEUMC 2022-02-018).

2.2. Predicted body composition and covariates

pASMMI, pBFMI, and pLBMI were investigated using validated anthropometric prediction equations from the Korean National Health and Nutrition Examination Survey cohort (16). In a previous study, body fat mass, lean body mass, and appendicular skeletal muscle mass were identified using dual-energy x-ray absorptiometry, and a prediction equation was constructed using different combinations of age, height, weight, level of serum creatinine, waist circumference, and lifestyle factors (physical activity, alcohol use, and smoking habit) as predictor variables (16). The combination of age, height, weight, waist circumference, serum creatinine level, and lifestyle factors were chosen in this study to create equations for the body composition. This predictive model was validated as having high predictive power, a moderate agreement rate, and low bias in the Korean general population. Appendicular skeletal muscle mass, lean body mass, and body fat mass were presented as an index (weight [kg] divided by height squared [m^2]) for pASMMI, pBFMI, and pLBMI, respectively (**Supplementary Methods 1**). Predicted body composition including pASMMI, pBFMI, and pLBMI divided into quintiles (**Supplementary Methods 2**).

Detailed definitions of covariates are provided in **Supplementary Methods 3** and previous studies (21). Variables including age, sex, BMI, household income (quartiles), smoking status (never, former, or current), alcohol consumption (none, moderate, or heavy), physical activity (low or moderate), comorbidities (hypertension, diabetes mellitus, dyslipidemia,

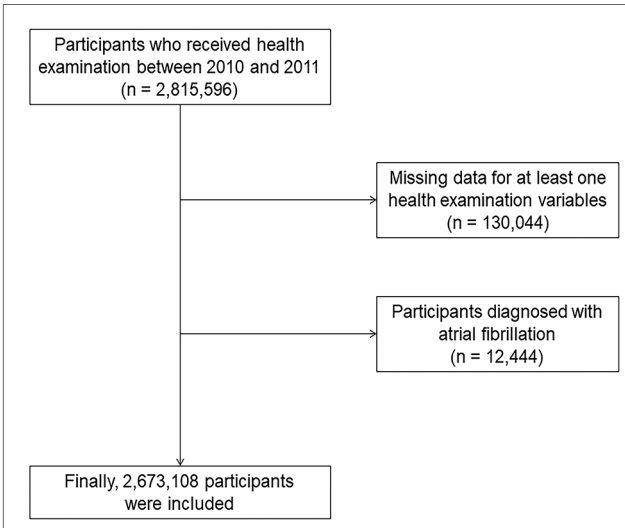

FIGURE 1
Flowchart of participant selection.

cancer, renal disease, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, peripheral arterial disease, heart failure, and liver disease) were collected (6, 22, 23). Comorbidities were defined considering the International Classification of Diseases, Tenth Revision (ICD-10) codes, medication history, and laboratory findings from health examinations (6, 22).

2.3. Outcomes

The primary outcome was an occurrence. The index date was considered the date of the national health examination. If more than one check-up was performed between 2010 and 2011, the most recent health examination results were used for statistical analysis. The diagnostic accuracy of the ICD-10 code (I48) for AF in the NHIS has been validated (94%) (6). Follow-up was carried out until 31 December 2020 or until the first occurrence of death or AF.

2.4. Statistical analysis

Chi-squared tests and independent t-tests were performed to compare and categorical and continuous variables, respectively. For categorical variables, we tested the proportional hazard assumption using the Schoenfeld residuals. No departure from the proportional hazard assumption was detected (**Supplementary Methods 4**). The Cox proportional hazards model presented with hazard ratios (HR) with 95% confidence intervals (CI) was used to estimate the effect of body composition, pASMMI, pBFMI, and pLBMI, on the incidence of AF. In multivariable analysis, the following potential confounders were adjusted: BMI, household income, hypertension, diabetes mellitus, dyslipidemia, cancer, renal disease, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, peripheral arterial disease, heart failure, and liver disease. Generally standardized criteria of muscle and fat masses are not available currently. Sarcopenia is defined by authorized working groups such as the European Working Group on Sarcopenia in Older Persons and the Asian Working Group for

TABLE 1 Baseline characteristics of the study participants.

Variable	Total	Men	Women	*P*-value
Number of participants	2,673,108	1,375,179	1,297,929	
Age, years	48.58 ± 14.05	47.47 ± 13.74	49.76 ± 14.28	<.001
Body mass index (kg/m^2)	23.74 ± 3.27	24.24 ± 3.09	23.22 ± 3.36	<.001
Household income				<.001
First quartile, lowest	502,975 (18.82)	203,592 (14.80)	299,383 (23.07)	
Second quartile	575,250 (21.52)	281,507 (20.47)	293,743 (22.63)	
Third quartile	722,093 (27.01)	399,920 (29.08)	322,173 (24.82)	
Fourth quartile, highest	872,790 (32.65)	490,160 (35.64)	382,630 (29.48)	
Smoking status				<.001
Never	1,646,321 (61.59)	418,419 (30.43)	1,227,902 (94.60)	
Former	392,042 (14.67)	368,402 (26.79)	23,640 (1.82)	
Current	634,745 (23.75)	588,358 (42.78)	46,387 (3.57)	
Alcohol consumption (drinks/week)				<.001
None	1,426,626 (53.37)	453,292 (32.96)	973,334 (74.99)	
Moderate	711,582 (26.62)	490,812 (35.69)	220,770 (17.01)	
Heavy	534,900 (20.01)	431,075 (31.35)	103,825 (8.00)	
Physical activity (min/week)				<.001
Low	1,606,512 (60.10)	779,725 (56.70)	826,787 (63.70)	
Moderate	1,066,596 (39.90)	595,454 (43.30)	471,142 (36.30)	
Comorbidities				
Hypertension	723,813 (27.08)	380,805 (27.69)	343,008 (26.43)	<.001
Diabetes mellitus	356,894 (13.35)	199,744 (14.52)	157,150 (12.11)	<.001
Dyslipidemia	739,038 (27.65)	355,543 (25.85)	383,495 (29.55)	<.001
Cancer	68,694 (2.57)	31,074 (2.26)	37,620 (2.90)	<.001
Renal disease	240,220 (8.99)	107,009 (7.78)	133,211 (10.26)	<.001
COPD	45,053 (1.69)	27,048 (1.97)	18,005 (1.39)	<.001
OSAS	909 (0.03)	763 (0.06)	146 (0.01)	<.001
Peripheral arterial disease	58,460 (2.19)	26,592 (1.93)	31,868 (2.46)	<.001
Heart Failure	27,679 (1.04)	12,049 (0.88)	15,630 (1.20)	<.001
Liver disease	405,972 (15.19)	216,630 (15.75)	189,342 (14.59)	<.001
Predicted body composition index				
pASMMI (kg/m^2)	7.30 ± 1.22	8.28 ± 0.78	6.26 ± 0.57	<.001
pBFMI (kg/m^2)	6.49 ± 2.04	5.39 ± 1.43	7.64 ± 1.94	<.001
pLBMI (kg/m^2)	17.07 ± 2.24	18.64 ± 1.68	15.40 ± 1.39	<.001

P-values are obtained using Student's *t*-test and Chi-square test. Data are expressed as the mean ± standard deviation or *n* (%). COPD, chronic obstructive pulmonary disease; OSAS, obstructive sleep apnea syndrome; pASMMI, predicted appendicular skeletal muscle mass index; pBFMI, predicted body fat mass index; pLBMI, predicted lean body mass index.

Sarcopenia as the lowest quintile of study population (24, 25). According to these previous studies, we defined the lowest (first) quintile of pASMMI, pBFMI, and pLBMI from the study population as the reference group. For the sensitivity analysis, regression methods of Fine and Gray for competing risk data (death was a competing event for AF) were utilized according to sex. Subgroup analyses were performed with pASMMI, pBFMI, and pLBMI on the incidence of AF according to BMI categories; underweight (<18.5 kg/m^2), normal weight (18.5–24.99 kg/m^2), overweight (25–29.99 kg/m^2), and obesity (≥30 kg/m^2). Statistical analyses were performed using the SAS 9.4 version (SAS Inc., Cary, NC, USA) and R software, version 3.3.3 (R Foundation for Statistical Computing, Vienna, Austria). Two-sided *P*-values less than 0.05 were considered significant.

3. Results

Table 1 shows the results of comparing the baseline characteristics of 2,673,108 participants according to sex (n = 1,375,179 for men, n = 1,297,929 for women). The mean age of men was 47.47 ± 13.74 years and of women was 49.76 ± 14.28 years. Significant differences in BMI, smoking status, alcohol consumption, household income, physical activity, and comorbidities were observed between men and women (Table 1). According to BMI categories, the proportion of underweight, normal, overweight and obesity were as follows 3.7% (2.1% for men and 5.3% for women), 63.2% (59.3% for men and 67.3% for women), 29.3% (34.6% for men and 23.8% for women), and 3.8% (4.0% for men and 3.6% for women), respectively. The pASMMI (8.28 ± 0.78 kg/m^2 for men vs. 6.26 ± 0.57 kg/m^2 for women), pBFMI (5.39 ± 1.43 kg/m^2 for men vs. 7.64 ± 1.94 kg/m^2 for women), and pLBMI (18.64 ± 1.68 kg/m^2 for men vs. 15.40 ± 1.39 kg/m^2 for women) were significantly different according to sex (P < 0.001).

In multivariable analysis, higher pASMMI was related to low risk of AF regardless of sex [HR 0.829, 95% CI 0.753–0.912, P = 0.001 for men (fifth quintile) and HR 0.888, 95% CI 0.792–0.995, P = 0.041 for women (fifth quintile)] (Table 2). In contrast, higher pBFMI [HR 1.345, 95% CI 1.221–1.483, P < 0.001 for men (fifth quintile) and HR 1.420, 95% CI 1.274–1.591, P < 0.001 for women (fifth quintile)] and pLBMI [HR 2.241, 95% CI 2.182–2.303, P < 0.001 for men (fifth quintile) and HR 1.516, 95% CI 1.368–1.667, P < 0.001 for women (fifth quintile)] were positively related to an increased possibility of AF regardless of sex (Table 2). Similar associations were also observed after considering the competing risk of mortality (Table 3).

The results for the association of body composition with incident AF according to BMI subgroups are shown in Table 4 and Figures 2A,B. A higher pASMMI was related to a decreased possibility of AF in both sexes. In contrast, a higher pLBMI was also related to an increased risk of AF, except the underweight group in both sexes. Moreover, increased pBFMI was related to the incidence of AF, except the underweight group in men.

4. Discussion

The main finding of our study was that pASMMI was negatively associated with the risk of AF, and pBFMI and pLBMI were positively associated with the incidence of AF.

TABLE 2 Hazard ratios with 95% confidence interval for atrial fibrillation in multivariable Cox proportional hazards model.

Variable	Men		Variable	Women	
Predicted body composition index (kg/m^2)	Adjusted HR (95% CI)	*P*-value	Predicted body composition index (kg/m^2)	Adjusted HR (95% CI)	*P*-value
pASMMI			pASMMI		
First quintile (3.97–7.64)	1 (Reference)		First quintile (3.56–5.78)	1 (Reference)	
Second quintile (7.64–8.05)	0.939 (0.895–0.985)	0.009	Second quintile (5.78–6.06)	0.906 (0.846–0.971)	0.005
Third quintile (8.05–8.42)	0.914 (0.863–0.968)	0.002	Third quintile (6.06–6.33)	0.904 (0.840–0.973)	0.007
Fourth quintile (8.42–8.71)	0.878 (0.819–0.941)	0.003	Fourth quintile (6.33–6.69)	0.928 (0.854–0.098)	0.003
Fifth quintile (8.71–21.86)	0.829 (0.753–0.912)	0.001	Fifth quintile (6.69–14.85)	0.888 (0.792–0.995)	0.041
pBFMI			pBFMI		
First quintile (≥4.21)	1 (Reference)		First quintile (≥5.99)	1 (Reference)	
Second quintile (4.21–5.00)	1.035 (0.979–1.093)	0.223	Second quintile (5.99–6.98)	1.151 (1.076–1.231)	<.001
Third quintile (5.00–5.68)	1.086 (1.020–1.156)	0.009	Third quintile (6.98–7.93)	1.253 (1.131–1.397)	<.001
Fourth quintile (5.68–6.50)	1.187 (1.103–1.266)	<.001	Fourth quintile (7.93–9.15)	1.384 (1.267–1.503)	<.001
Fifth quintile (6.50≤)	1.345 (1.221–1.483)	<.001	Fifth quintile (9.15≤)	1.420 (1.274–1.591)	<.001
pLBMI			pLBMI		
First quintile (9.07–17.26)	1 (Reference)		First quintile (9.48–14.22)	1 (Reference)	
Second quintile (17.26–18.16)	1.247 (1.124–1.371)	<.001	Second quintile (14.22–14.93)	1.156 (1.081–1.227)	<.001
Third quintile (18.16–18.95)	1.452 (1.381–1.521)	<.001	Third quintile (14.93–15.60)	1.253 (1.167–1.305)	<.001
Fourth quintile (18.95–19.93)	1.697 (1.277–2.106)	<.001	Fourth quintile (15.60–16.47)	1.335 (1.234–1.433)	<.001
Fifth quintile (19.93–48.50)	2.241 (2.182–2.303)	<.001	Fifth quintile (16.47–35.91)	1.516 (1.368–1.667)	<.001

A multivariable model is used to determine the association of predicted body composition index with the development of atrial fibrillation adjusted for body mass index, household income, hypertension, diabetes mellitus, dyslipidemia, cancer, renal disease, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, peripheral arterial disease, heart failure, and liver disease. HR, hazard ratio; CI, confidence interval; pASMMI, predicted appendicular skeletal muscle mass index; pBFMI, predicted body fat mass index; pLBMI, predicted lean body mass index.

TABLE 3 Hazard ratios with 95% confidence interval for atrial fibrillation in competing risk analysis with fine - gray model.

Variable	Men		Variable	Women	
Predicted body composition index (kg/m^2)	Adjusted HR (95% CI)	*P*-value	Predicted body composition index (kg/m^2)	Adjusted HR (95% CI)	*P*-value
pASMMI			pASMMI		
First quintile (3.97–7.64)	1 (Reference)		First quintile (3.56–5.78)	1 (Reference)	
Second quintile (7.64–8.05)	0.968 (0.924–1.014)	0.172	Second quintile (5.78–6.06)	0.973 (0.919–1.032)	0.289
Third quintile (8.05–8.42)	0.936 (0.886–0.989)	0.019	Third quintile (6.06–6.33)	0.930 (0.902–0.962)	0.007
Fourth quintile (8.42–8.71)	0.884 (0.827–0.944)	0.003	Fourth quintile (6.33–6.69)	0.889 (0.831–0.943)	0.006
Fifth quintile (8.71–21.86)	0.801 (0.731–0.877)	<.001	Fifth quintile (6.69–14.85)	0.894 (0.842–0.946)	0.003
pBFMI			pBFMI		
First quintile (≥4.21)	1 (Reference)		First quintile (≥5.99)	1 (Reference)	
Second quintile (4.21–5.00)	1.067 (1.009–1.127)	0.022	Second quintile (5.99–6.98)	1.019 (0.918–1.123)	0.624
Third quintile (5.00–5.68)	1.125 (1.056–1.199)	0.003	Third quintile (6.98–7.93)	1.049 (0.969–1.136)	0.237
Fourth quintile (5.68–6.50)	1.226 (1.138–1.320)	<.001	Fourth quintile (7.93–9.15)	1.106 (1.012–1.208)	0.026
Fifth quintile (6.50≤)	1.362 (1.234–1.503)	<.001	Fifth quintile (9.15 ≤)	1.114 (1.001–1.223)	0.021
pLBMI			pLBMI		
First quintile (9.07–17.26)	1 (Reference)		First quintile (9.48–14.22)	1 (Reference)	
Second quintile (17.26–18.16)	1.206 (1.082–1.323)	<.001	Second quintile (14.22–14.93)	1.122 (1.097–1.149)	<.001
Third quintile (18.16–18.95)	1.322 (1.252–1.393)	<.001	Third quintile (14.93–15.60)	1.241 (1.193–1.293)	<.001
Fourth quintile (18.95–19.93)	1.594 (1.174–2.013)	<.001	Fourth quintile (15.60–16.47)	1.258 (1.234–1.284)	<.001
Fifth quintile (19.93–48.50)	2.121 (1.723–2.523)	<.001	Fifth quintile (16.47–35.91)	1.306 (1.288–1.327)	<.001

A multivariable model is used to determine the association of predicted body composition index with the development of atrial fibrillation adjusted for body mass index, household income, hypertension, diabetes mellitus, dyslipidemia, cancer, renal disease, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, peripheral arterial disease, heart failure, and liver disease. HR, hazard ratio; CI, confidence interval; pASMMI, predicted appendicular skeletal muscle mass index; pBFMI, predicted body fat mass index; pLBMI, predicted lean body mass index.

Generally, skeletal muscle mass is considered beneficial to health. However, it is rarely known how skeletal muscle mass affects for risk of AF. A previous study showed that patients with AF have a lower percentage of skeletal muscle mass (26).

TABLE 4 Subgroup analysis according to body mass index categories regarding predicted body composition indices and atrial fibrillation.

Variable	Men		Women	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Body mass index (kg/m^2)				
<18.50				
pASMMI	0.804 (0.577–1.121)	0.198	0.880 (0.465–1.662)	0.692
pBFMI	0.899 (0.743–1.088)	0.273	1.002 (0.811–1.239)	0.982
pLBMI	0.897 (0.767–1.050)	0.176	0.944 (0.726–1.226)	0.663
18.50–24.99				
pASMMI	0.863 (0.760–0.965)	0.014	0.915 (0.816–1.015)	0.095
pBFMI	1.118 (1.092–1.145)	<.001	1.084 (1.058–1.111)	<.001
pLBMI	1.034 (1.013–1.056)	0.002	1.097 (1.060–1.135)	<.001
25–29.99				
pASMMI	0.955 (0.914–0.993)	0.030	0.915 (0.849–0.986)	0.019
pBFMI	1.166 (1.128–1.205)	<.001	1.087 (1.050–1.126)	<.001
pLBMI	1.015 (1.005–1.025)	0.018	1.085 (1.034–1.138)	0.001
≥30				
pASMMI	0.857 (0.756–0.954)	0.034	0.894 (0.814–0.976)	<.001
pBFMI	1.215 (1.145–1.289)	<.001	1.083 (1.036–1.132)	0.004
pLBMI	1.034 (1.022–1.046)	0.025	1.075 (1.012–1.141)	0.019

A multivariable model is used to determine the association of predicted body composition index with the development of atrial fibrillation adjusted for body mass index, household income, hypertension, diabetes mellitus, dyslipidemia, cancer, renal disease, chronic obstructive pulmonary disease, obstructive sleep apnea syndrome, peripheral arterial disease, heart failure, and liver disease. HR, hazard ratio; CI, confidence interval; pASMMI, predicted appendicular skeletal muscle mass index; pBFMI, predicted body fat mass index; pLBMI, predicted lean body mass index.

In addition, both sarcopenia and the ratio of muscle components are associated with electrocardiogram abnormalities, including AF (27). In line with previous report that sarcopenic overweight/obese was associated with risk of AF (28) and sarcopenia was associated with cardiovascular disease including AF in older patients (27), our report that pASMMI showed a negative association with risk of AF regardless BMI. Because skeletal muscle generates considerable metabolic and oxygen demand in the body, it affects cardiac muscle, cardiac output, and heart rate (29).

Many previous epidemiologic studies have shown that obesity increases the risk of AF; however, confusion, including unexpected J- or U-shaped associations, has often been observed (30). Some studies in relation to obesity showed that greater lean body mass was a strong independent risk factor for AF, and fat mass was also related to a higher risk of AF (17, 18, 31, 32). Although previous studies showed that body fat composition/distribution, which may be linked to non-alcoholic fatty liver disease (NAFLD), has been associated with a higher occurrence of AF (33, 34), our study showed that body fat composition was associated with occurrence of AF after adjusting liver disease including NAFLD. Furthermore, though several controversies exist, regardless of BMI, our study showed a positive relationship between higher pBFMI and the incidence of AF, in line with the findings of previous studies (27, 32). Body fat mass is related to an increased risk of hypertension, insulin resistance, diabetes, coronary heart disease, and heart failure, which contribute to AF (34). Furthermore, increased left atrial size, volume overload, left ventricular diastolic dysfunction, and left atrial dysfunction due to body fat mass further contribute to electrophysiological remodeling and conduction abnormalities resulting in AF (35, 36).

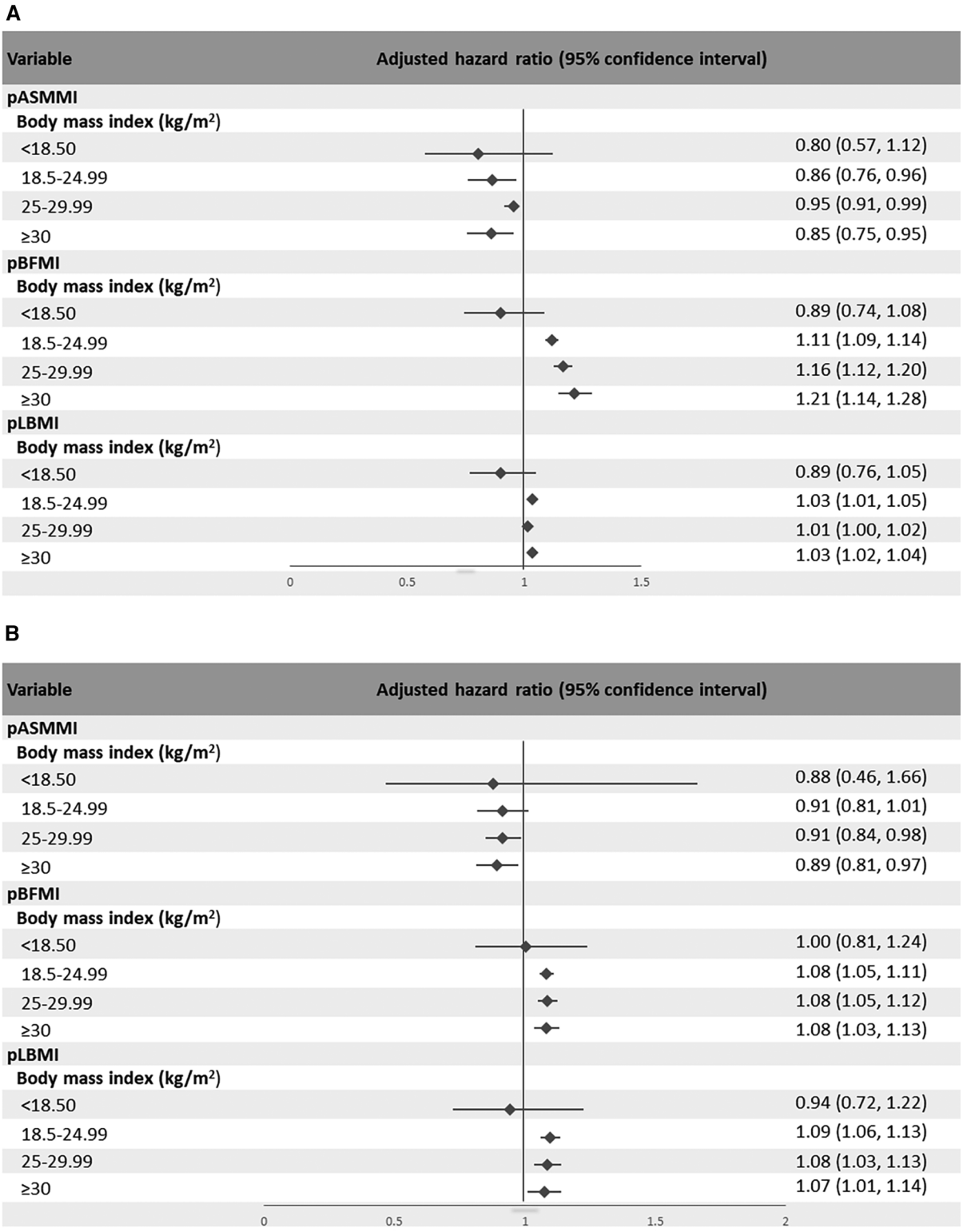

FIGURE 2
Forest plot showing the hazard ratio and 95% confidence intervals of the association between body composition indices according to subcategories of body mass index and atrial fibrillation for (A) men and (B) women.

Furthermore, our study showed a positive relationship between pLBMI and the risk of AF, in line with the findings of previous studies (31, 32, 37). But, because participants with low lean body mass were a relatively unhealthy group (38), effect lowering the risk of AF might be offset in participants with underweighted BMI. Also, in present study, the absolute

number of underweighted BMI groups is small. For those factors, the significant association between high lean body mass and AF risk might not be observed in underweighted BMI group. In addition, because most overweight and obese people have high predicted lean body mass and fat mass, a higher pLBMI was related to an increased risk of AF in overweight and obese participants (38).

In participants with underweight BMI, we observed a negative relationship between pLBMI and pASMMI and the risk of AF. A previous study suggested that being underweight was significantly related to an increased risk of AF (39). There are several potential mechanisms underlying this obesity paradox. An animal study suggested that the loss of myostatin, a well-known negative regulator of skeletal muscle growth that causes sarcopenia, can lead to AF (40). Studies have linked AF to a deficiency of trace elements (41). However, all of the predicted body composition indices were not significantly related to the occurrence of AF in underweight participants due to the small number of underweight participants.

The strength of our study is that it showed an association between body composition indices and AF in a large sample of the general Korean population in a longitudinal setting. Furthermore, our study could potentially serve as evidence for future randomized clinical trials investigating whether the risk of AF changes with the regulation of body composition and also facilitate future comparative research with direct measurements of body composition using dual energy x-ray absorptiometry or computed tomography scan. In addition, our findings could be practically utilized as evidence for the importance of maintaining a healthy body composition. In other words, our results could be used as educational materials for the general population, highlighting that the potential benefits of maintaining or increasing skeletal muscle mass and decreasing body fat mass cause reducing the risk of AF. However, our study has some limitations. First, although it was conducted with a longitudinal design, this is a retrospective study; therefore, we could not confirm the causal relationship or exclude confounders. Second, we used the equation for predicted body composition validated in the Korean population for large-scale analysis rather than directly conducting dual-energy x-ray absorptiometry. In addition, because the equation was estimated for the Korean population, these findings may not be generalizable to other ethnicities. Third, the predicted body composition indices were measured once or twice during the study period; thus, possible serial changes in body composition were not considered. Finally, this is an epidemiological study that cannot explain the basic mechanism of the association between body composition and AF.

In conclusion, our results demonstrated that a lower muscle mass, higher lean body mass, and higher fat mass were related to an increased risk of AF in general population except underweighted BMI group. These associations between AF and body composition differed according to the BMI categories. For studies with longitudinal settings and large sample sizes, body composition, including body fat mass, lean body mass, and skeletal muscle mass, may be more accurate in confirming the association with AF than BMI.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Institutional Review Board of Ewha Womans University Seoul Hospital (Institutional Review Board approval number: SEUMC 2022-02-018) The studies were conducted in accordance with the local legislation and institutional requirements. Informed consent was waived because retrospective anonymized data were used.

Author contributions

HGW, MKK, and T-JS contributed to the conception or design of the work; HGW and T-JS contributed to the acquisition, analysis, or interpretation of data for the work; HGW, MKK, and T-JS drafted the manuscript; HGW, MKK, and T-JS critically revised the manuscript. All gave final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2023.1159087/full#supplementary-material

References

1. Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, et al. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. *Circulation*. (2014) 129(8):837–47. doi: 10.1161/CIRCULATIONAHA.113.005119

2. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and risk factors in atrial fibrillation (ATRIA) study. *JAMA*. (2001) 285(18):2370–5. doi: 10.1001/jama.285.18.2370

3. Guo Y, Tian Y, Wang H, Si Q, Wang Y, Lip GYH. Prevalence, incidence, and lifetime risk of atrial fibrillation in China: new insights into the global burden of atrial fibrillation. *Chest*. (2015) 147(1):109–19. doi: 10.1378/chest.14-0321

4. Lau DH, Nattel S, Kalman JM, Sanders P. Modifiable risk factors and atrial fibrillation. *Circulation*. (2017) 136(6):583–96. doi: 10.1161/CIRCULATIONAHA.116.023163

5. Song TJ, Kim YD, Yoo J, Kim J, Chang HJ, Hong GR, et al. Association between aortic atheroma and cerebral small vessel disease in patients with ischemic stroke. *J Stroke*. (2016) 18(3):312–20. doi: 10.5853/jos.2016.00171

6. Chang Y, Woo HG, Park J, Lee JS, Song TJ. Improved oral hygiene care is associated with decreased risk of occurrence for atrial fibrillation and heart failure: a nationwide population-based cohort study. *Eur J Prev Cardiol*. (2020) 27(17):1835–45. doi: 10.1177/2047487319886018

7. WHO. Obesity: preventing and managing the global epidemic. In: *Report of a WHO consultation. World health organ tech rep ser*. Geneva: World Health Organization (2000). p. 1–253.

8. Dai H, Alsalhe TA, Chalghaf N, Riccò M, Bragazzi NL, Wu J. The global burden of disease attributable to high body mass index in 195 countries and territories, 1990-2017: an analysis of the global burden of disease study. *PLoS Med*. 2020;17(7):e1003198. doi: 10.1371/journal.pmed.1003198

9. Ortega FB, Lavie CJ, Blair SN. Obesity and cardiovascular disease. *Circ Res*. (2016) 118(11):1752–70. doi: 10.1161/CIRCRESAHA.115.306883

10. Krauss RM, Winston M, Fletcher RN, Grundy SM. Obesity: impact of cardiovascular disease. *Circulation*. (1998) 98(14):1472–6. doi: 10.1161/01.CIR.98.14.1472

11. Ueno K, Kaneko H, Kamiya K, Itoh H, Okada A, Suzuki Y, et al. Relationship of normal-weight central obesity with the risk for heart failure and atrial fibrillation: analysis of a nationwide health check-up and claims database. *Eur Heart J Open*. (2022) 2(3):oeac026. doi: 10.1093/ehjopen/oeac026

12. Pouwels S, Topal B, Knook MT, Celik A, Sundbom M, Ribeiro R, et al. Interaction of obesity and atrial fibrillation: an overview of pathophysiology and clinical management. *Expert Rev Cardiovasc Ther*. (2019) 17(3):209–23. doi: 10.1080/14779072.2019.1581064

13. Lee H, Choi EK, Lee SH, Han KD, Rhee TM, Park CS, et al. Atrial fibrillation risk in metabolically healthy obesity: a nationwide population-based study. *Int J Cardiol*. (2017) 240:221–7. doi: 10.1016/j.ijcard.2017.03.103

14. Sandhu RK, Ezekowitz J, Andersson U, Alexander JH, Granger CB, Halvorsen S, et al. The 'obesity paradox' in atrial fibrillation: observations from the ARISTOTLE (apixaban for reduction in stroke and other thromboembolic events in atrial fibrillation) trial. *Eur Heart J*. (2016) 37(38):2869–78. doi: 10.1093/eurheartj/ehw124

15. Wang J, Yang YM, Zhu J, Zhang H, Shao XH, Tian L, et al. Overweight is associated with improved survival and outcomes in patients with atrial fibrillation. *Clin Res Cardiol*. (2014) 103(7):533–42. doi: 10.1007/s00392-014-0681-7

16. Lee G, Chang J, Hwang S-S, Son JS, Park SM. Development and validation of prediction equations for the assessment of muscle or fat mass using anthropometric measurements, serum creatinine level, and lifestyle factors among Korean adults. *NRP*. (2020) 15(1):95–105. doi: 10.4162/nrp.2021.15.1.95

17. Tikkanen E, Gustafsson S, Knowles JW, Perez M, Burgess S, Ingelsson E. Body composition and atrial fibrillation: a Mendelian randomization study. *Eur Heart J*. (2019) 40(16):1277–82. doi: 10.1093/eurheartj/ehz003

18. Worm MS, Bager CL, Blair JPM, Secher NH, Riis BJ, Christiansen C, et al. Atrial fibrillation is associated with lean body mass in postmenopausal women. *Sci Rep*. (2020) 10(1):573. doi: 10.1038/s41598-019-57167-3

19. Chang Y, Lee JS, Woo HG, Ryu DR, Kim JW, Song TJ. Improved oral hygiene care and chronic kidney disease occurrence: a nationwide population-based retrospective cohort study. *Medicine (Baltimore)*. (2021) 100(47):e27845. doi: 10.1097/MD.0000000000027845

20. Kim J, Kim HJ, Jeon J, Song TJ. Association between oral health and cardiovascular outcomes in patients with hypertension: a nationwide cohort study. *J Hypertens*. (2022) 40(2):374–81. doi: 10.1097/HJH.0000000000003022

21. Lee K, Lee JS, Kim J, Lee H, Chang Y, Woo HG, et al. Oral health and gastrointestinal cancer: a nationwide cohort study. *J Clin Periodontol*. (2020) 47(7):796–808. doi: 10.1111/jcpe.13304

22. Kim HJ, Park MS, Shin JI, Park J, Kim DH, Jeon J, et al. Associations of heart failure with susceptibility and severe complications of COVID-19: a nationwide cohort study. *J Med Virol*. (2022) 94(3):1138–45. doi: 10.4162/nrp.2021.15.1.95

23. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, Ghali WA. New ICD-10 version of the charlson comorbidity index predicted in-hospital mortality. *J Clin Epidemiol*. (2004) 57(12):1288–94. doi: 10.1016/j.jclinepi.2004.03.012

24. Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian working group for sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *J Am Med Dir Assoc*. (2020) 21(3):300–7.e2. doi: 10.1016/j.jamda.2019.12.012

25. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: european consensus on definition and diagnosis: report of the European working group on sarcopenia in older people. *Age Ageing*. (2010) 39(4):412–23. doi: 10.1093/ageing/afq034

26. Anaszewicz M, Banas W, Wawrzenczyk A, Budzynski J. Body composition in patients with atrial fibrillation. *Acta Cardiol Sin*. (2019) 35(5):484–92. doi: 10.6515/ACS.201909_35(5).20190323A

27. Heshmat R, Shafiee G, Ostovar A, Fahimfar N, Maleki Birjandi S, Jabbari M, et al. Relationship between sarcopenia and electrocardiographic abnormalities in older people: the bushehr elderly health program. *Front Med (Lausanne*. (2021) 8:656181. doi: 10.3389/fmed.2021.656181

28. Xia MF, Chen LY, Wu L, Ma H, Li XM, Li Q, et al. Sarcopenia, sarcopenic overweight/obesity and risk of cardiovascular disease and cardiac arrhythmia: a cross-sectional study. *Clin Nutr*. (2021) 40(2):571–80. doi: 10.1016/j.clnu.2020.06.003

29. Bella JN, Devereux RB, Roman MJ, O'Grady MJ, Welty TK, Lee ET, et al. Relations of left ventricular mass to fat-free and adipose body mass: the strong heart study. The strong heart study investigators. *Circulation*. (1998) 98(23):2538–44. doi: 10.1161/01.CIR.98.23.2538

30. Wang TJ, Parise H, Levy D, D'Agostino RB, Wolf PA, Vasan RS, et al. Obesity and the risk of new-onset atrial fibrillation. *JAMA*. (2004) 292(20):2471–7. doi: 10.1001/jama.292.20.2471

31. Fenger-Grøn M, Overvad K, Tjønneland A, Frost L. Lean body mass is the predominant anthropometric risk factor for atrial fibrillation. *J Am Coll Cardiol*. (2017) 69(20):2488–97. doi: 10.1016/j.jacc.2017.03.558

32. Frost L, Benjamin EJ, Fenger-Gron M, Pedersen A, Tjonneland A, Overvad K. Body fat, body fat distribution, lean body mass and atrial fibrillation and flutter. A

danish cohort study. *Obesity (Silver Spring, Md)*. (2014) 22(6):1546–52. doi: 10.1002/oby.20706

33. Lee S-R, Han K-D, Choi E-K, Oh S, Lip GYH. Nonalcoholic fatty liver disease and the risk of atrial fibrillation stratified by body mass index: a nationwide population-based study. *Sci Rep*. (2021) 11(1):3737. doi: 10.1038/s41598-021-83367-x

34. Alon L, Corica B, Raparelli V, Cangemi R, Basili S, Proietti M, et al. Risk of cardiovascular events in patients with non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Eur J Prev Cardiol*. (2022) 29(6):938–46. doi: 10.1093/eurjpc/zwab212

35. Goudis CA, Korantzopoulos P, Ntalas IV, Kallergis EM, Ketikoglou DG. Obesity and atrial fibrillation: a comprehensive review of the pathophysiological mechanisms and links. *J Cardiol*. (2015) 66(5):361–9. doi: 10.1016/j.jjcc.2015.04.002

36. Aune D, Sen A, Norat T, Janszky I, Romundstad P, Tonstad S, et al. Body mass index, abdominal fatness, and heart failure incidence and mortality: a systematic review and dose-response meta-analysis of prospective studies. *Circulation*. (2016) 133(7):639–49. doi: 10.1161/CIRCULATIONAHA.115.016801

37. Fenger-Grøn M, Vinter N, Frost L. Body mass and atrial fibrillation risk: status of the epidemiology concerning the influence of fat versus lean body mass. *Trends Cardiovasc Med*. (2020) 30(4):205–11. doi: 10.1016/j.tcm.2019.05.009

38. Lee DH, Keum N, Hu FB, Orav EJ, Rimm EB, Willett WC, et al. Predicted lean body mass, fat mass, and all cause and cause specific mortality in men: prospective US cohort study. *BMJ (Clinical Research ed)*. (2018) 362:k2575. doi: 10.1136/bmj.k2575

39. Kang SH, Choi EK, Han KD, Lee SR, Lim WH, Cha MJ, et al. Underweight is a risk factor for atrial fibrillation: a nationwide population-based study. *Int J Cardiol*. (2016) 215:449–56. doi: 10.1016/j.ijcard.2016.04.036

40. Rosenberg MA, Das S, Quintero Pinzon P, Knight AC, Sosnovik DE, Ellinor PT, et al. A novel transgenic mouse model of cardiac hypertrophy and atrial fibrillation. *J Atr Fibrillation*. (2012) 4(5):415. doi: 10.4022/jafib.415

41. Demir M, Uyan U, Melek M. The effects of vitamin D deficiency on atrial fibrillation. *Clin Appl Thromb Hemost*. (2012) 20(1):98–103. doi: 10.1177/1076029612453762

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Significance of fatty liver index to detect prevalent ischemic heart disease: evidence from national health and nutrition examination survey 1999–2016

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Background: Non-alcoholic fatty liver disease (NAFLD) contributes to the development of ischemic heart disease via multiple mechanisms. Fatty liver index (FLI) has been proposed as an accurate, convenient, and economic surrogate of the severity of NAFLD. Our present study aims to assess the association between FLI and the prevalent IHD and to evaluate the potential value of FLI to refine the detection of prevalent IHD in the general population.
Methods: Our work recruited 32,938 subjects from the National Health and Nutrition Examination Survey 1999–2016. IHD was diagnosed according to the subjects' self-report. FLI was determined based on triglycerides, BMI, γ-glutamyltransferase, and waist circumference.
Results: 2,370 (7.20%) subjects were diagnosed with IHD. After adjustment of age, sex, race, current smoking, current drinking, PIR, BMI, WC, TC, TG, GGT, Scr, FPG, SBP, anti-hypertensive therapy, anti-diabetic therapy, and lipid-lowering therapy, one standard deviation increase of FLI resulted in a 27.0% increment of the risk of prevalent IHD. In the quartile analysis, we observed a 1.684 times risk of prevalent IHD when comparing the fourth quartile with the first quartile, and there was a trend towards higher risk across the quartiles. The smooth curve fitting displayed a linear relationship between FLI and the presence of IHD without any threshold or saturation effect. Subgroup analysis revealed a robust association in conventional cardiovascular subpopulations, and the association could be more prominent in female subjects and diabetes patients. ROC analysis demonstrated an incremental value of FLI for detecting prevalent IHD after introducing it to conventional cardiovascular risk factors (AUC: 0.823 vs. 0.859, P for comparison <0.001). Also, results from reclassification analysis implicated that more IHD patients could be correctly identified by introducing FLI into conventional cardiovascular risk factors (continuous net reclassification index: 0.633, $P < 0.001$; integrated discrimination index: 0.034, $P < 0.001$).
Conclusion: The current analysis revealed a positive and linear relationship between FLI and the prevalent IHD. Furthermore, our findings suggest the incremental value of FLI to refine the detection of prevalent IHD in the general population.

KEYWORDS

epidemiology, NHANES, fatty liver index, ischemic heart disease, general population

Introduction

Ischemic heart disease (IHD) has been one of the prominent causes of death globally for decades. The mortality caused by IHD reached 116.9 per 10,000 early in 2017 (1). Under this grim situation, an approach to improve and simplify the detection of subclinical IHD is essential to alleviate the burden of the secondary prevention of IHD.

The presence of non-alcoholic fatty liver disease (NAFLD) is closely associated with an increased risk of IHD (2, 3). From an epidemiological point of view, NAFLD and cardiovascular diseases share several risk factors, including metabolic dysfunction and lifestyle habits (4). Previous studies suggested an association between NAFLD and the risk of several cardiovascular diseases, particularly with IHD (5, 6). Published data have demonstrated that NAFLD is associated with subclinical atherosclerosis and an elevated ten-year IHD risk score independent of diabetes and hypertension (7–10). Furthermore, a recent systemic review, which included 20 studies, has demonstrated that NAFLD patients showed a significantly increased risk of myocardial infarction (11). The pathophysiological mechanism underlying this association is only partially discovered, but it is likely complex and resulting from the interplay of different, bidirectional pathways, including endothelial dysfunction, vascular inflammation, and impaired glucose and lipid metabolism (4). Due to the strong association between NAFLD and IHD, estimating the severity of NAFLD could be a possible approach to benefit the early detection of IHD in the general population. However, the current diagnosis of NAFLD relies on liver ultrasonography, computed tomography, magnetic resonance spectroscopy, and liver biopsy (12); all these methods are costly, inconvenient, and unsuitable for frequent monitoring in primary care conditions. Accordingly, an economical, convenient, and non-invasive method to achieve routine monitoring of NAFLD severity is needed to advance the early identification of IHD in the general population.

Fatty liver index (FLI) was proposed to assess the severity of NAFLD (13). Previous studies have identified its value in predicting several atherosclerotic cardiovascular diseases (14–16). However, evidence regarding the usefulness of FLI in improving the detection of IHD in the general population is still limited. Thus, the present work aims to assess the association between FLI and the prevalent IHD and investigate the potential of FLI to refine the detection of prevalent IHD in a general American population.

Methods

Study participants

Our population was derived from the National Health and Nutrition Examination Survey (NHANES) 1999–2016. A detailed description of the NHANES study's protocol and methods is available at its official website (https://wwwn.cdc.gov/nchs/nhanes/ContinuousNhanes/Default.aspx?BeginYear=2013). Briefly, the NHANES survey is conducted by the National Center for Health Statistics (NCHS), a department of the Centers for Disease Control and Prevention (CDC). The NHANES is a continuous cross-sectional survey conducted in America every two years. The survey adopts a multistage, stratified, and clustered probability sampled pattern to maintain its representativity. The primary objective of NHANES is to assess the number and percentage of people with selected diseases and risk factors in the American population. From 1999 to 2016, a total number of 92,062 subjects completed the data collection process. In the current analysis, we included subjects with completed data about the IHD questionnaire, FLI value, and related covariates, and finally included 32,938 subjects. The NCHS institutional Ethics Review Board approved the study protocol. All participants provided written informed consent. All data in the present analysis is accessible to the public at NHANES's official website.

Measurements

During the data collection process, interviews were performed at the subjects' homes, while physical and laboratory examinations were conducted in the Mobile Examination Center (MEC). Trained interviewers collected the demographic data with a computer-assisted personal interviewing method. If the subjects could not answer the questions alone, a family member would answer them. Current drinking was determined as having at least 12 drinks in the past year. Current smoking was defined as answering "every day" or "some days" for the question "Do you now smoke cigarettes?"

Anthropometric parameters were measured under the standard protocol. Height and waist circumference (WC) were quantified to the nearest 0.1 cm; weight was quantified to the nearest 0.1 kg. Blood pressure measurement was also performed according to standard operating procedure. After sitting and resting quietly for 5 min, the blood pressure was measured by a calibrated sphygmomanometer. We employed the mean of 3 blood pressure recordings in our analysis. Detailed information about the blood pressure measurement was documented in the "Physician Examination Procedures Manual" on the NHANES official website (https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/manuals.aspx?BeginYear=2013).

Laboratory tests were conducted at the laboratories certified by NCHS. Detailed information about the laboratory tests was summarized in the official "Laboratory procedures manual" (https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/manuals.aspx?BeginYear=2013). Briefly, the whole blood count differential used VCS technology, and the Beckman Coulter DXH 800 was used as the hematology analyzer. Blood lipids were quantified by enzymatic assay on the Roche Modular *P* and Roche Cobas 6,000 chemistry analyzers. Fasting plasma glucose was determined by the oxygen rate method on the Modular Chemistry side of the Beckman DxC800. The DxC800 modular chemistry side tested serum creatinine (Scr) through using the Jaffe rate method.

Definitions

The following standard formula calculated FLI: FLI = $[e^{0.953 \times \ln(TG) + 0.139 \times BMI + 0.718 \times \ln(GGT) + 0.053 \times WC - 15.745}]/[1 + e^{0.953 \times \ln(TG) + 0.139 \times BMI + 0.718 \times \ln(GGT) + 0.053 \times WC - 15.745}] \times 100$ (13), TG means triglycerides, BMI stands for body mass index, GGT indicates γ-glutamyltransferase, WC refers to waist circumference. Anti-diabetic therapy was defined as using any anti-diabetic medicine in the past two weeks. Diabetes was diagnosed as fasting plasma glucose (FPG) ≥7 mmol/L and / or self-reported anti-diabetic therapy according to the published guideline (17). Anti-hypertensive therapy referred to any blood pressure-lowering medicine intake in the past two weeks. Hypertension was diagnosed as mean systolic blood pressure (SBP) ≥140 mmHg and/or mean diastolic blood pressure ≥90 mmHg; Additionally, subjects with self-reported anti-hypertensive therapy were also recognized as hypertensive patients (18). Lipid-lowering therapy was determined as input of lipid-lowering medicine in the past two weeks. Diagnosis of IHD was identified if the subjects answered "yes" to the question "Ever told you had coronary heart disease? (Questionnaire code: MCQ160c)", "Ever told you had angina/angina pectoris? (Questionnaire code: MCQ160d)", or "Ever told you had a heart attack? (Questionnaire code: MCQ160e)".

Statistical analysis

Statistical analysis was performed using Stata Statistical Software (version 15.0; StataCorp. LLC. 4905 Lakeway Drive, College Station, Texas 77845 USA) and statistical software packages R (http://www.R-project.org, The R Foundation), EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA). Statistical significance was noted as a two-tailed P value < 0.05. Statistical data were weighted according to the survey design of NHANES (https://wwwn.cdc.gov/nchs/nhanes/tutorials/module3.aspx). Continuous variates were expressed as the mean value with 95% confidence intervals (CI). Categorical variates were also summarized as frequency and 95% CI. T-test and Chi-square test were performed to compare continuous and categorical variates, respectively. Multivariate logistic regression analysis was conducted to investigate the independent association between FLI and the prevalent IHD. Normalized FLI was generated by a z-score change [(FLI-mean of FLI)/SD]. The results of regression analysis were listed as odds ratios (ORs) and 95% confidence intervals (95% CI). To confirm whether the association between FLI and the prevalent IHD was linear in the full range of FLI, we employed a generalized additive model (GAM) with a spline smoothing function, and we also conducted a logarithmic likelihood ratio test to compare one pairwise and two pairwise logistic regression model. Finally, the current study also engaged receiver operating characteristic (ROC) curve and reclassification analysis, including continuous net reclassification index (NRI) and integrated discrimination index (IDI), to assess the potential value of FLI to improve the detection of prevalent IHD.

Results

Characteristics of the enrolled participants were summarized in **Table 1**. Among the enrolled 32,938 subjects, 2,370 (7.20%) subjects were detected as IHD patients. Regarding the demographic data, IHD patients were older than non-IHD subjects. Male distribution was significantly higher in the IHD group than in the non-IHD group. IHD patients had a relatively higher percentage of non-Hispanic white than non-IHD subjects. Non-IHD had substantially higher income level (displayed as higher PIR). The non-IHD group had a relatively higher percentage of current drinking status and a relatively lower percentage of current smoking than the IHD group. As for the anthropometric parameters, weight, BMI, WC, and SBP levels were significantly higher in the IHD group. Laboratory indexes like FPG, TG, GGT, and serum creatine (Scr) were substantially higher in the IHD group, and the TC was significantly lower in the IHD group than in the non-IHD group. About medical history characteristics, the IHD group had higher percentages of anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy, diagnosed hypertension, and diagnosed diabetes than the non-IHD group. Finally, the FLI level was significantly higher in the IHD group than in the non-IHD group.

Our study employed logistic regression analysis to evaluate the relationship between FLI and the prevalent IHD in our population (**Table 2**). In the crude model, each SD increase of the normalized FLI was associated with an additional 54.2% risk of the presence of IHD. After adjustment of age, sex, and race, the risk for each SD increase changed to 45.5%. Further adjustment of covariates, including current smoking, current drinking, PIR, BMI, WC, TC, TG, GGT, Scr, FPG, SBP, anti-hypertensive therapy, anti-diabetic therapy, and lipid-lowering therapy, diminished the risk for each SD increase of the normalized FLI to 27.0%. When dividing FLI into quartiles, the top quartile had a 1.684 times risk for the prevalent IHD than the bottom quartile, and the risk for prevalent IHD showed a trend towards a more significant risk across the quartiles (P for trend = 0.002).

To validate the trend towards a greater risk of prevalent IHD that was observed in the logistic regression analysis, we further conducted a smooth curve fitting. As displayed in **Figure 1**, the risk of IHD increased proportionally with the increment of Normalized FLI, and we did not observe any threshold or saturation phenomenon in the association between normalized FLI and the prevalent IHD. Consistently, P for non-linearity test was insignificant (0.276).

To determine the consistency of our main result among common cardiovascular subpopulations, we further employed subgroup analysis (**Figure 2**). The logistic models were adjusted for all covariates used in Model 2 of **Table 2**, except those used to define the subgroups. As displayed in **Figure 2**, the positive association between FLI and the prevalent IHD was also observed in age (<50 or ≥50 years old), sex (male or female), race (black, white, or others), obesity (BMI < 30 kg/m^2), hypertension (yes or no), and diabetes (yes or no) subgroups, and the interaction effect was insignificant in all these subgroups.

TABLE 1 Data characteristics of enrolled subjects grouped by the presence of IHD.

Variables	Total ($n = 32,938$)	IHD ($n = 2,370$)	non-IHD ($n = 30,568$)	*P* value
Age (years)	46.48 (46.07, 46.89)	64.57 (63.87, 65.27)	45.37 (44.97, 45.76)	<0.001
Male (%)	48.79 (48.31, 49.28)	59.87 (57.02, 62.66)	48.11 (47.58, 48.65)	<0.001
Race (%)				<0.001
Mexican American	8.95 (7.91, 10.12)	5.95 (4.95, 7.14)	9.14 (8.08, 10.32)	
Other Hispanic	6.74 (5.57, 8.12)	3.59 (2.54, 5.04)	6.93 (5.75, 8.33)	
Non-Hispanic White	37.46 (34.92, 40.07)	42.72 (38.55, 46.99)	37.13 (34.63, 39.71)	
Non-Hispanic Black	8.73 (7.85, 9.70)	7.09 (5.87, 8.55)	8.83 (7.93, 9.83)	
Others	38.12 (35.28, 41.05)	40.65 (36.73, 44.70)	37.97 (35.10, 40.92)	
PIR	3.02 (2.95, 3.08)	2.68 (2.57, 2.78)	3.04 (2.97, 3.10)	<0.001
Current smoking (%)	18.07 (17.26, 18.92)	19.83 (17.74, 22.10)	17.97 (17.13, 18.83)	0.094
Current drinking (%)	56.64 (55.00, 58.27)	53.90 (50.70, 57.06)	56.81 (55.15, 58.45)	0.052
Height (cm)	168.99 (168.82, 169.16)	168.35 (167.77, 168.92)	169.03 (168.86, 169.20)	0.982
Weight (kg)	81.83 (81.44, 82.23)	85.15 (84.03, 86.27)	81.63 (81.23, 82.03)	<0.001
BMI (kg/m^2)	28.57 (28.43, 28.71)	29.91 (29.57, 30.25)	28.49 (28.35, 28.63)	<0.001
WC (cm)	98.08 (97.71, 98.44)	105.12 (104.30, 105.95)	97.64 (97.28, 98.01)	<0.001
SBP (mmHg)	122.19 (121.82, 122.56)	129.82 (128.68, 130.96)	121.72 (121.37, 122.08)	<0.001
DBP (mmHg)	70.85 (70.50, 71.21)	67.23 (66.50, 67.96)	71.08 (70.73, 71.43)	<0.001
FPG (mmol/L)	5.42 (5.39, 5.45)	6.24 (6.11, 6.36)	5.36 (5.34, 5.39)	<0.001
TC (mmol/L)	5.11 (5.09, 5.13)	4.83 (4.76, 4.91)	5.12 (5.10, 5.15)	<0.001
TG (mmol/L)	1.70 (1.67, 1.72)	1.95 (1.87, 2.03)	1.68 (1.65, 1.71)	<0.001
GGT (U/L)	28.08 (27.54, 28.63)	32.25 (30.72, 33.77)	27.83 (27.25, 28.41)	<0.001
Scr (μmol/L)	77.60 (77.14, 78.06)	92.55 (90.24, 94.87)	76.69 (76.23, 77.15)	<0.001
Anti-hypertensive therapy (%)	24.20 (23.35, 25.07)	64.57 (61.96, 67.09)	21.72 (20.95, 22.52)	<0.001
Anti-diabetic therapy (%)	6.46 (6.12, 6.81)	21.38 (19.32, 23.60)	5.54 (5.23, 5.87)	<0.001
Lipid-lowering therapy (%)	14.40 (13.78, 15.04)	54.02 (51.10, 56.92)	11.97 (11.42, 12.54)	<0.001
Hypertension (%)	31.94 (30.98, 32.91)	70.56 (67.97, 73.03)	29.57 (28.65, 30.59)	<0.001
Diabetes (%)	9.96 (9.53, 10.40)	28.15 (25.99, 30.42)	8.84 (8.44, 9.27)	<0.001
FLI	51.35 (50.64, 52.06)	64.36 (62.84, 65.88)	50.55 (49.82, 51.27)	<0.001

Data were summarized as mean (95% confidence intervals) or numbers (95% confidence intervals) according to their data type. IHD, ischemic heart disease; PIR, poverty-income ratio; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; TC, total cholesterol; TG, triglycerides; GGT, γ-glutamyltransferase; Scr, serum creatine; FLI, fatty liver index.

TABLE 2 Independent association between FLI and the prevalent IHD.

Variables	Odds Ratio (95% CI)					
	Crude	*P* value	Model 1	*P* value	Model 2	*P* value
FLI (Per 1 SD increase)	1.542 (1.463, 1.627)	<0.001	1.455 (1.369, 1.546)	<0.001	1.270 (1.106, 1.458)	0.001
Quartiles of FLI						
Quartile 1	Reference		Reference		Reference	
Quartile 2	2.225 (1.809, 2.735)	<0.001	1.387 (1.124, 1.711)	0.003	1.232 (0.988, 1.538)	0.064
Quartile 3	2.865 (2.399, 3.421)	<0.001	1.727 (1.448, 2.059)	<0.001	1.370 (1.094, 1.716)	0.007
Quartile 4	3.555 (2.955, 4.278)	<0.001	2.611 (2.174, 3.135)	<0.001	1.684 (1.228, 2.310)	0.001
P for trend		<0.001		<0.001		0.002

Model 1: age, sex, race. Model 2: Model 1 + current smoking, current drinking, PIR, BMI, WC, TC, TG, GGT, Scr, FPG, SBP, anti-hypertensive therapy, anti-diabetic therapy, and lipid-lowering therapy. FLI, fatty liver index; IHD, ischemic heart disease; CI, confidence interval; SD, standard deviation; PIR, poverty-income ratio; BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, triglycerides; GGT, γ-glutamyltransferase; Scr, serum creatine; FPG, fasting plasma glucose; SBP, systolic blood pressure.

However, although the difference was insignificant, the effect size of the association was larger in female subjects and diabetes patients than in male subjects and non-diabetes subjects, respectively.

ROC and reclassification analysis were utilized to investigate the potential usefulness of FLI to improve the detection of prevalent IHD in our population (Table 3). Regarding the results of ROC analysis, although the AUC of FLI itself was limited, we still observed a significant improvement of the AUC (0.823 vs. 0.859, *P* for comparison <0.001) when introducing FLI into clinical risk factors (including age, sex, race, current smoking, current drinking, PIR, BMI, WC, TC, TG, GGT, Scr, FPG, SBP, anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy). Moreover, continuous NRI (0.633, $P < 0.001$) and IDI (0.034, $P < 0.001$) in the reclassification analysis also supported the usefulness of FLI in improving the detection of prevalent IHD.

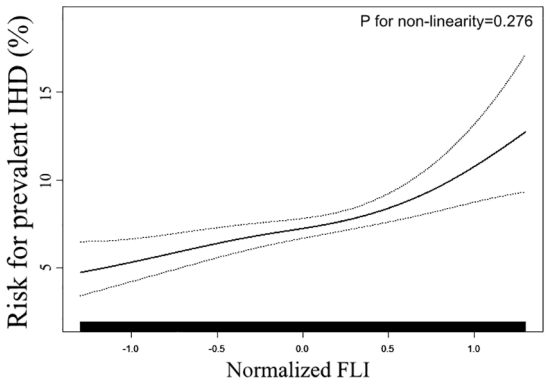

FIGURE 1
Smooth curve fitting evaluating the association between FLI and the prevent IHD. Smooth curve fitting was conducted through a generalized additive model with the adjustment of all covariates used in Model 2 of Table 2. In the plot, the ratio of prevalent IHD increased linearly with the increment of FLI, suggesting the association between FLI and prevalent LVH was linear in the full range of FLI. FLI: fatty liver index; IHD: ischemic heart disease.

Discussion

The current analysis discovered a positive association between FLI and the prevalent IHD in a representative American population. Furthermore, the association was nearly linear in the whole range of the FLI, indicating the ratio of prevalent IHD increases proportionally with the elevation of FLI. Moreover, the association was consistent in several conventional cardiovascular subpopulations, and the effect size was potentially larger in female subjects and diabetes patients. Additionally, both ROC and reclassification analysis supported the potential usefulness of FLI to improve the detection of prevalent IHD in the general population. In general, FLI may serve as a linear indicator with economic, convenient, and non-invasive characteristics to refine the detection of prevalent IHD in the general population. By applying FLI into clinical practice, general practitioners could improve the detection of IHD.

The findings from our present study supported our assumption that the FLI level is associated with the prevalent IHD in the general population. The first step of our analysis focused on the association between FLI level and the prevalent IHD via the logistic regression analysis. In the multivariate-adjusted model, our results demonstrated a significant and positive association between FLI level and the prevalent IHD. The Model 2 of **Table 2** was adjusted for demographic, anthropometric, laboratory, and medical history covariates. Therefore, the association between FLI and prevalent IHD was independent of the conventional cardiovascular risk factors. However, the logistic regression model was conducted under the hypothesis that the association between FLI and prevalent IHD was linear in the whole range of FLI. If the actual relationship is non-linear, the logistic regression results will deviate from the actual relationship, thereby giving us the wrong information. To address this question, we employed a smooth curve fitting (conducted by

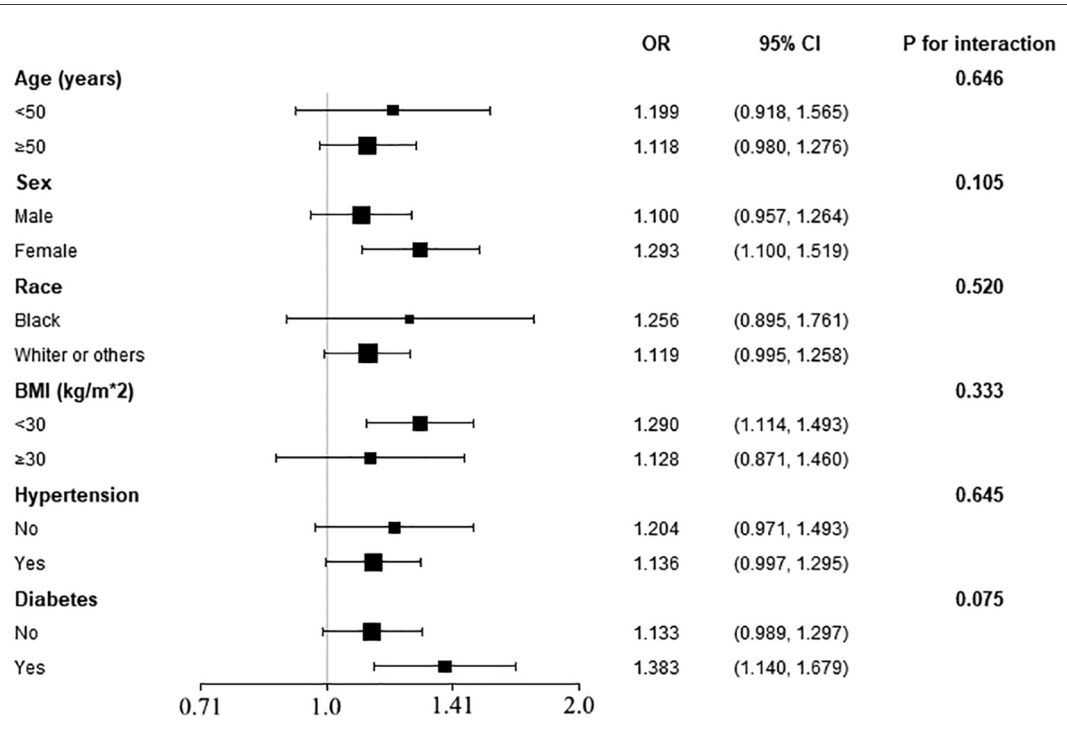

FIGURE 2
Subgroup analysis of the association between FLI and the prevalent IHD. The models were adjusted for all covariates used in Model 2 of Table 2, except for the variates used to define the stratum. *P* for interaction in all subgroups was insignificant, implicating the association between FLI and IHD was robust in these subpopulations.

TABLE 3 Assessment of the value of FLI for detecting prevalent IHD.

Model	AUC (95% CI)	*P* value	*P* for comparison	NRI (continuous)	*P* value	IDI	*P* value
FLI	0.603 (0.598, 0.609)	<0.001		–	–	–	–
Clinical risk factors[a]	0.823 (0.818, 0.827)	<0.001	<0.001	–	–	–	–
Clinical risk factors + FLI	0.859 (0.855, 0.862)	<0.001		0.633 (0.593, 0.673)	<0.001	0.034 (0.031, 0.038)	<0.001

[a]Clinical risk factors: age, sex, race, current smoking, current drinking, PIR, BMI, WC, TC, TG, GGT, Scr, FPG, SBP, anti-hypertensive therapy, anti-diabetic therapy, and lipid-lowering therapy. FLI, fatty liver index; IHD, ischemic heart disease; AUC, area under the curve; NRI, net reclassification index; IDI, integrated discrimination index; PIR, poverty-income ratio; BMI, body mass index; WC, waist circumference; TC, total cholesterol; TG, triglycerides; GGT, γ-glutamyltransferase; Scr, serum creatine; FPG, fasting plasma glucose; SBP, systolic blood pressure.

GAM) and a logarithmic likelihood ratio test in step two of our statistical analysis. The results displayed that the association between normalized FLI level and the prevalent IHD was positively linear in the full range of FLI. Therefore, the ratio of prevalent IHD may increase proportionally with the increment of FLI level in the full range of FLI, and there may be no threshold or saturation effect in their association.

To evaluate whether our main finding was consistent in conventional cardiovascular subgroups, we conducted a subgroup analysis. The results demonstrated no significant interaction between the grouping variates (including age, sex, race, BMI, hypertension, and diabetes) and the association between FLI and IHD. However, we also observed a trend towards a larger effect size (OR value) in female subjects and diabetes patients. The association of FLI and prevalent IHD could be more prominent in female and diabetes populations. And the insignificance of the interaction effect among sex and diabetes subgroups could be due to a lack of statistical power. Therefore, more studies with larger sample sizes are needed to confirm our observation. In general, our main result is still effective in these subpopulations; applying the relationship between FLI and the prevalent IHD in these subpopulations is reasonable, and in female subjects and diabetes patients, the association could be more prominent.

With a clear depiction of the association between FLI and the prevalent IHD, the fourth step of our analysis shifted the focus to the potential value of FLI to improve the detection of prevalent IHD in the general population. We used ROC and reclassification analysis to evaluate the novel index in this step. In ROC analysis, the AUC of FLI alone for recognizing prevalent IHD was limited. Therefore, using FLI alone in clinical practice will achieve a satisfying result. However, when introducing FLI into conventional cardiovascular risk factors, the entire model significantly improved the detecting ability of prevalent IHD. These findings suggest the potential value of FLI to optimize the detection of the prevalent IHD in the general population. Although the ROC analysis is the most popular approach to evaluate the value of a novel marker, we noticed that it concentrated on the integral ability of the entire model to detect prevalent conditions or diseases. Specifically, ROC analysis actually assesses the capability of the entire model (conventional cardiovascular risk factors + FLI) to identify the prevalent IHD rather than investigate the value of FLI itself to optimize the detection of prevalent IHD. ROC analysis could overestimate or underestimate the potential of FLI (19). Therefore, the results merely from ROC analysis could not provide accurate information about whether introducing FLI into conventional cardiovascular risk factors would make the detection of the prevalent IHD more accurate (20). To evaluate the value of FLI at an angle different from ROC analysis, statisticians have put forward the reclassification analysis, including NRI and IDI (21–23). In the present study, after adding FLI into conventional cardiovascular risk factors, both continuous NRI and IDI revealed a significant improvement in detecting the prevalent IHD. Therefore, combining FLI with conventional cardiovascular risk factors will reclassify more subjects into the actual categories (IHD or non-IHD). In general, the results from both ROC and reclassification analysis suggest that applying FLI could help optimize the detection of prevalent IHD in the general population.

Our findings were consistent with the results from two previous articles. Olubamwo et al. recruited 501 subjects without cardiometabolic disease (type 2 diabetes or cardiovascular disease) to assess the association between FLI and the risk of developing cardiometabolic diseases during a mean follow-up of 15 years. Their results demonstrated that persons with significant FLI increase will likely have an increasing cardiometabolic disease risk (24). Kim et al. employed the data from 3011,588 Korean to evaluate the usefulness of FLI in predicting major adverse cardiac events (MACEs, including IHD events) during a median follow-up of 6 years (14). Their results demonstrated a linear association between higher FLI values and higher incidence of the MACEs. Our study showed some differences with their work. Firstly, their studies focused on the value of FLI in predicting the development of cardiometabolic diseases or MACEs, and neither study conducted a specified subgroup regarding IHD. Meanwhile, our work was intended to investigate the potential of FLI to detect the presence of IHD in the general population. Therefore, the findings from our work and their studies supported the usefulness of FLI in different application conditions, our work suggested the value of FLI as a detection marker of IHD, and their studies implicated the value of FLI as a prediction index for the risk of developing cardiometabolic diseases or MACEs. Secondly, Olubamwo et al.'s study did not assess whether the association between FLI and outcomes was linear; Kim et al.'s study only evaluated the linearity by dividing FLI into deciles without any statistical test, which is relatively rough. On the contrary, our study employed a smooth curve fitting analysis and a logarithmic likelihood ratio test to investigate the linearity of the association between FLI and the prevalent IHD. Thirdly, both studies only provided the effect size of the associations between FLI and outcomes, but did not give information about the performance of FLI in ROC analysis. Our current study presented the ROC results and conducted the

reclassification analysis to assess the value of FLI to detect prevalent IHD from a different angle from ROC. Lastly, our study population also showed differences from their populations. Different lifestyles, diet habits, geographic and socioeconomic conditions could impact the association between FLI and outcomes.

Although similar, the current study differed from our previously published article (25). The current study discovered that FLI, and the underlying severity of NAFLD, are associated with the prevalent IHD. FLI could improve the detection of IHD in the general population. While in the previous study, we focused on the value of the weight-adjusted waist index in identifying prevalent HF in the general population. The current study focused on IHD, while the previous research focused on HF, the target disease differs between the two studies. As for the additional contribution of the current study, we identified a potential biomarker to improve the detection of IHD, which could improve cardiovascular health in the general population. Furthermore, the previous research focused on the impact of excessive fat accumulation on cardiovascular health, while the current study pays attention to the value of monitoring the severity of NAFLD.

There are multiple mechanisms behind the association between NAFLD and increased risk of IHD (26). Firstly, endothelial dysfunction was observed in NAFLD (27). NAFLD patients exhibit an elevated level of circulating ADMA, which is an endogenous antagonist of nitric oxide synthase and is positively associated with several cardiovascular diseases (28). Besides, other markers of endothelial dysfunction are also increased in NAFLD patients (29, 30). Disruption and dysfunction of the endothelial layer play a role in atherogenesis and subsequent cardiovascular diseases. Secondly, serum homocysteine is reported to be increased in NAFLD (31). Alteration of homocysteine metabolism results in increased burden of oxidative stress, which is generally increased in NAFLD (32). Oxidative stress is essential in cardiovascular pathophysiology (33). Additionally, cytokines released by the diseased liver drain into the systemic circulation, resulting in consequential cardiovascular effects. Systemic inflammation and circulating cytokines, such as interleukin 1, interleukin 6 and tumor necrosis factor α, are associated with cardiovascular diseases (34, 35). Thirdly, the lipid profile is significantly changed in NAFLD. Increased TG and LDL-c levels, decreased HDL-c level, and other changes in lipid components synergistically lead to more atherogenic lipid profiles (36, 37). Lastly, other mechanisms like arterial structural alterations, hepatokines, adipokines, Gut-liver axis, angiogenic factors, and genetic factors also play their roles in the mechanism underlying the association between NAFLD and IHD (26).

It is necessary to mention the limitations when interpreting our results. Firstly, due to the nature of the cross-sectional design of NHANES, our results could only provide a clue for the association between FLI and the prevalent IHD, as well as the potential value of FLI to improve the detection of prevalent IHD in the general population. Secondly, the detection of IHD in our analysis was based on the subjects' self-report. Therefore, the accuracy of the detection was limited. Nevertheless, the NHANES study was conducted according to standard operating procedures. The result from the questionnaire is still reliable. Thirdly, the findings of the current analysis were based on a general population in America. Therefore, whether these findings possess external applicability to the population with a different lifestyle, diet habit, geographic and socioeconomic conditions remain unclear. Fourthly, Although the P for non-linearity showed insignificance, **Figure 1** showed that the risk for prevalent IHD increased more rapidly with the elevation of FLI in the region of normalized FLI > 1 than in the region of normalized FLI < 1. We speculate that this phenomenon could be due to a lack of statistical power in this region. Therefore, more studies with larger sample sizes are needed to confirm this phenomenon. Fifthly, we observed a larger OR for the association between FLI and prevalent IHD in female subjects than in male subjects, and a larger OR for the association in diabetes patients than in non-diabetes subjects. However, due to the limited statistical power, the interaction effects of sex and diabetes did not achieve significance. Therefore, the association between FLI and prevalent IHD could be more prominent in females and diabetes patients, and more studies with larger sample sizes are needed to confirm our observation. Lastly, the same as other observational research, residual confounding caused by some unincluded covariables could lead to bias in our results. For example, as we mentioned before, homocysteine and cytokines like interleukin 1, interleukin 6, and tumor necrosis factor i play their roles in the association between NAFLD and IHD, but these variates were not collected in our current survey. Based on the above points, a long-term and prospective study with a more reliable IHD definition and more detailed information collection is warranted to confirm our findings in the future.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?BeginYear=1999.

Ethics statement

The studies involving humans were approved by The NCHS institutional Ethics Review Board. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

YN, GW, and WS designed the current study. YN and GW integrated and analyzed the data. YN, XF, and HN drafted the

manuscript. WS revised the manuscript and proofed it for publication. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

1. GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the global burden of disease study 2017. *Lancet*. (2018) 392 (10159):1736–88. doi: 10.1016/s0140-6736(18)32203-7

2. Kotronen A, Juurinen L, Tiikkainen M, Vehkavaara S, Yki-Järvinen H. Increased liver fat, impaired insulin clearance, and hepatic and adipose tissue insulin resistance in type 2 diabetes. *Gastroenterology*. (2008) 135(1):122–30. doi: 10.1053/j.gastro.2008.03.021

3. Gaggini M, Morelli M, Buzzigoli E, DeFronzo RA, Bugianesi E, Gastaldelli A. Non-alcoholic fatty liver disease (nafld) and its connection with insulin resistance, dyslipidemia, atherosclerosis and coronary heart disease. *Nutrients*. (2013) 5 (5):1544–60. doi: 10.3390/nu5051544

4. Kasper P, Martin A, Lang S, Kütting F, Goeser T, Demir M, et al. Nafld and cardiovascular diseases: a clinical review. *Clin Res Cardiol*. (2021) 110(7):921–37. doi: 10.1007/s00392-020-01709-7

5. Lonardo A, Sookoian S, Pirola CJ, Targher G. Non-alcoholic fatty liver disease and risk of cardiovascular disease. *Metab Clin Exp*. (2016) 65(8):1136–50. doi: 10.1016/j.metabol.2015.09.017

6. Stahl EP, Dhindsa DS, Lee SK, Sandesara PB, Chalasani NP, Sperling LS. Non-alcoholic fatty liver disease and the heart: JACC state-of-the-art review. *J Am Coll Cardiol*. (2019) 73(8):948–63. doi: 10.1016/j.jacc.2018.11.050

7. Mellinger JL, Pencina KM, Massaro JM, Hoffmann U, Seshadri S, Fox CS, et al. Hepatic steatosis and cardiovascular disease outcomes: an analysis of the framingham heart study. *J Hepatol*. (2015) 63(2):470–6. doi: 10.1016/j.jhep.2015.02.045

8. Sinn DH, Kang D, Chang Y, Ryu S, Gu S, Kim H, et al. Non-alcoholic fatty liver disease and progression of coronary artery calcium score: a retrospective cohort study. *Gut*. (2017) 66(2):323–9. doi: 10.1136/gutjnl-2016-311854

9. Wu R, Hou F, Wang X, Zhou Y, Sun K, Wang Y, et al. Non-alcoholic fatty liver disease and coronary artery calcification in a northern Chinese population: a cross sectional study. *Sci Rep*. (2017) 7(1):9933. doi: 10.1038/s41598-017-09851-5

10. Kozakova M, Palombo C, Eng MP, Dekker J, Flyvbjerg A, Mitrakou A, et al. Fatty liver index, gamma-glutamyltransferase, and early carotid plaques. *Hepatology*. (2012) 55(5):1406–15. doi: 10.1002/hep.25555

11. Alon L, Corica B, Raparelli V, Cangemi R, Basili S, Proietti M, et al. Risk of cardiovascular events in patients with non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Eur J Prev Cardiol*. (2022) 29(6):938–46. doi: 10.1093/eurjpc/zwab212

12. Neuschwander-Tetri BA, Caldwell SH. Non-alcoholic steatohepatitis: summary of an AASLD single topic conference. *Hepatology*. (2003) 37(5):1202–19. doi: 10.1053/jhep.2003.50193

13. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, et al. The fatty liver index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol*. (2006) 6:33. doi: 10.1186/1471-230x-6-33

14. Kim J, Moon J, Byun S, Lee J, Kang D, Sung K, et al. Fatty liver index and development of cardiovascular disease in Koreans without pre-existing myocardial infarction and ischemic stroke: a large population-based study. *Cardiovasc Diabetol*. (2020) 19(1):51. doi: 10.1186/s12933-020-01025-4

15. Wang C, Cai Z, Deng X, Li H, Zhao Z, Guo C, et al. Association of hepatic steatosis index and fatty liver index with carotid atherosclerosis in type 2 diabetes. *Int J Med Sci*. (2021) 18(14):3280–9. doi: 10.7150/ijms.62010

16. Yang YJ, Jung MH, Jeong SH, Hong YP, Kim YI, An SJ. The association between non-alcoholic fatty liver disease and stroke: results from the Korean genome and epidemiology study (koges). *Int J Environ Res Public Health*. (2020) 17(24):9568–79. doi: 10.3390/ijerph17249568

17. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes Mellitus. *Diabetes Care*. (2003) 26(Suppl 1):S5–20. doi: 10.2337/diacare.26.2007.s5

18. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the eighth joint national committee (jnc 8). *JAMA*. (2014) 311(5):507–20. doi: 10.1001/jama.2013.284427

19. Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation*. (2007) 115(7):928–35. doi: 10.1161/circulationaha.106.672402

20. Pickering JW, Endre ZH. New metrics for assessing diagnostic potential of candidate biomarkers. *Clin J Am Soc Nephrol*. (2012) 7(8):1355–64. doi: 10.2215/cjn.09590911

21. Pencina MJ, D'Agostino RB Sr., D'Agostino RB Jr., Vasan RS. Evaluating the added predictive ability of a new marker: from area under the roc curve to reclassification and beyond. *Stat Med* (2008) 27(2):157–72; discussion 207-12. doi: 10.1002/sim.2929

22. Pencina MJ, D'Agostino RB Sr., Steyerberg EW Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. *Stat Med*. (2011) 30(1):11–21. doi: 10.1002/sim.4085.

23. Grunkemeier GL, Jin R. Net reclassification Index: measuring the incremental value of adding a new risk factor to an existing risk model. *Ann Thorac Surg*. (2015) 99(2):388–92. doi: 10.1016/j.athoracsur.2014.10.084

24. Olubamwo OO, Virtanen JK, Pihlajamaki J, Mantyselka P, Tuomainen TP. Fatty liver index as a predictor of increased risk of cardiometabolic disease: finding from the kuopio ischaemic heart disease risk factor study cohort. *BMJ Open*. (2019) 9(9): e031420. doi: 10.1136/bmjopen-2019-031420

25. Zhang D, Shi W, Ding Z, Park J, Wu S, Zhang J. Association between weight-adjusted-waist index and heart failure: results from national health and nutrition examination survey 1999-2018. *Front Cardiovasc Med*. (2022) 9:1069146. doi: 10.3389/fcvm.2022.1069146

26. Francque SM, van der Graaff D, Kwanten WJ. Non-alcoholic fatty liver disease and cardiovascular risk: pathophysiological mechanisms and implications. *J Hepatol*. (2016) 65(2):425–43. doi: 10.1016/j.jhep.2016.04.005

27. Villanova N, Moscatiello S, Ramilli S, Bugianesi E, Magalotti D, Vanni E, et al. Endothelial dysfunction and cardiovascular risk profile in non-alcoholic fatty liver disease. *Hepatology*. (2005) 42(2):473–80. doi: 10.1002/hep.20781

28. Kasumov T, Edmison JM, Dasarathy S, Bennett C, Lopez R, Kalhan SC. Plasma levels of asymmetric dimethylarginine in patients with biopsy-proven non-alcoholic fatty liver disease. *Metab Clin Exp*. (2011) 60(6):776–81. doi: 10.1016/j.metabol.2010.07.027

29. Dogru T, Genc H, Tapan S, Aslan F, Ercin CN, Ors F, et al. Plasma fetuin-a is associated with endothelial dysfunction and subclinical atherosclerosis in subjects with non-alcoholic fatty liver disease. *Clin Endocrinol (Oxf)*. (2013) 78(5):712–7. doi: 10.1111/j.1365-2265.2012.04460.x

30. Elsheikh E, Younoszai Z, Otgonsuren M, Hunt S, Raybuck B, Younossi ZM. Markers of endothelial dysfunction in patients with non-alcoholic fatty liver disease and coronary artery disease. *J Gastroenterol Hepatol*. (2014) 29(7):1528–34. doi: 10.1111/jgh.12549

31. Pastore A, Alisi A, di Giovamberardino G, Crudele A, Ceccarelli S, Panera N, et al. Plasma levels of homocysteine and cysteine increased in pediatric nafld and strongly correlated with severity of liver damage. *Int J Mol Sci*. (2014) 15 (11):21202–14. doi: 10.3390/ijms151121202

32. Madan K, Bhardwaj P, Thareja S, Gupta SD, Saraya A. Oxidant stress and antioxidant status among patients with non-alcoholic fatty liver disease (nafld). *J Clin Gastroenterol*. (2006) 40(10):930–5. doi: 10.1097/01.mcg.0000212608.59090.08

33. Kim YW, Byzova TV. Oxidative stress in angiogenesis and vascular disease. *Blood*. (2014) 123(5):625–31. doi: 10.1182/blood-2013-09-512749

34. Racanelli V, Rehermann B. The liver as an immunological organ. *Hepatology*. (2006) 43(2 Suppl 1):S54–62. doi: 10.1002/hep.21060

35. Stoner L, Lucero AA, Palmer BR, Jones LM, Young JM, Faulkner J. Inflammatory biomarkers for predicting cardiovascular disease. *Clin Biochem*. (2013) 46(15):1353–71. doi: 10.1016/j.clinbiochem.2013.05.070

36. Alkhouri N, Tamimi TA, Yerian L, Lopez R, Zein NN, Feldstein AE. The inflamed liver and atherosclerosis: a link between histologic severity of non-alcoholic fatty liver disease and increased cardiovascular risk. *Dig Dis Sci*. (2010) 55 (9):2644–50. doi: 10.1007/s10620-009-1075-y

37. Ouweneel AB, Van Eck M. Lipoproteins as modulators of atherothrombosis: from endothelial function to primary and secondary coagulation. *Vascul Pharmacol*. (2016) 82:1–10. doi: 10.1016/j.vph.2015.10.009

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Association between weight change and the predicted 10-year risk for atherosclerosis cardiovascular disease among U.S. older adults: data from National Health and Nutrition Examination Survey 1999–2018

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Background: It remains controversial regarding the association between weight change and cardiovascular disease risk in older adults (aged ≥60 years). This study aimed to evaluate the association between weight change and the predicted 10-year atherosclerotic cardiovascular disease (ASCVD) risks in older adults.

Methods: This study used data from the National Health and Nutrition Examination Survey (NHANES). Older adults aged 60–79 years who were free of self-reported ASCVD at the time of the NHANES interview were included. Data were collected from January 1999 to December 2018 and analyzed in March 2022. We focused on the associations between weight change and the 10-year ASCVD risks with the percentage change in weight during short-term (1 year) and long-term (10 years), which categorized as moderate to high weight loss (≥10%), small weight loss (5.1–9.9%), stable weight (±5%), small weight gain (5.1–9.9%), and moderate to high weight gain (≥10%).

Results: The number of participants was 1,867 (mean age 67.49 years; 42.10% female) for the long-term interval (10 years) in our analysis, and 1894 for the short-term interval (1 years). We only observed an inverse association between long-term weight loss and the 10-year ASCVD risk in fully adjusted model (loss ≥ 10%: β = 2.52, 95%CI = 0.98, 4.05; loss 5.1% ~ 9.9%: β = 2.99, 95% CI = 1.30, 4.68), but all intervals of weight gain ≥5% were not significant associated with higher risk than stable weight. However, in the subgroup analyses, the association between long-term weight loss and the 10-year ASCVD risk was not significant in old-old (aged 75–79), obesity (BMI ≥ 35 kg/m^2), intentional weight loss, moderate physical activity and diabetics.

Conclusion: Older adults (aged 60–79 years) with weight loss >5% over the past 10 years have excess predicted 10-year ASCVD risk. Our study supports the benefits of stable weight in promoting cardiovascular health in older adults.

KEYWORDS
weight change, cardiovascular disease, NHANES, 10-year ASCVD risk, older adults

1. Introduction

The increasing incidence of overweight and obesity among the aging population is a growing public health problem worldwide (1). Between 2007 and 2016, the proportion of obesity increased from 35.1 to 41.0% in older Americans, giving rise to a significant future burden on the U.S. healthcare systems (2). Substantial epidemiologic evidence indicates that excess body weight is associated with a higher risk of mortality, primarily due to atherosclerotic cardiovascular disease (ASCVD) (3, 4). It is not unexpected since obesity is clearly associated with most of the classical cardiovascular risk factors like hypertension, hyperlipidemia, and diabetes (5). However, whether losing weight could have a favor effect on decreasing cardiovascular events risk in older adults remains controversial.

Previous studies on the association between weight loss and long-term cardiovascular outcomes in older adults are limited. Although several studies have indicated that weight loss improved physical function and reduced frailty in obese older adults (6, 7). Increasing evidence suggested that weight loss was not uniformly associated with improved long-term survival (8). A meta-analysis reported that weight loss and weight gain were associated with a 59 and 10% increased risk of mortality respectively, suggesting an obesity paradox in older adults (9). In addition, the effect of weight loss among cardiovascular disease patients is also controversial (10). A meta-analysis of 35,335 patients (mean age 64 years) showed that, overall, weight loss was associated with a higher risk of cardiovascular events, but intentional weight loss was associated with improved outcomes (11). However, it remains unknown whether weight loss is associated with an increased risk of ASCVD events among older adults who are free of a prior heart attack or stroke. It is imperative to understand the health impact of long-term weight change on ASCVD risk in the general older population.

Therefore, the primary goal of this study was to examine the association between weight change and the 10-year predicted ASCVD risk in older U.S. adults (aged ≥60 years) using data from the 1999–2018 National Health and Nutrition Examination Survey (NHANES).

2. Methods

2.1. Database and study subjects

In this study, the data were obtained from the NHANES (1999–2018). This is an ongoing cross-sectional survey conducted by the National Center for Health Statistics (NCHS), designed to be representative of the U.S. non-institutionalized, civilian population. During a home interview, data are collected on demographic, socioeconomic, and health-related topics (including weight history). A separate examination collects standardized physical assessments and laboratory measurements. The survey obtained written informed consents from all participants prior to data collection. Methodological details about the NHANES are available at: www.cdc.gov/nchs/nhanes/.

Older adults were defined as those of age 60 years and over (12). To estimate the 10-year ASCVD risk, the analytic sample was limited to 2,429 participants aged 60–79 years who were free of self-reported ASCVD at the beginning of the survey and met with high-density lipoprotein cholesterol (HDL-C) 20–100 mg/dL, total cholesterol (TC) 130–320 mg/dL, diastolic BP 30–140 mmHg and systolic BP 90–200 mmHg. After the exclusion of the participants with missing data on 10-year weight change ($n = 96$), 1-year weight change ($n = 64$) and BMI ($n = 11$), and those with a previous cancer diagnosis ($n = 455$), the number of participants included in the analysis was 1,867 for the long-term interval (10 years) and 1,894 for the short-term interval (1 years) (Figure 1).

2.2. Assessment of the predicted 10-year ASCVD risk

The primary outcome of this study was the 10-year ASCVD risk, defined as a first non-fatal myocardial infarction (MI), coronary heart disease (CHD) death, or fatal or non-fatal stroke over a 10-year period (13). According to the new pooled cohort equations (PCEs) introduced by the American College of Cardiology (ACC) and the American Heart Association (AHA) in 2013, the predictors used in estimating the 10-year risk of a first ASCVD event included age, sex, race, TC, HDL-C, treatment for hypertension, diabetes and current smoking status (13).

Data on age, sex, and race/ethnicity was obtained from the demographic questionnaire. The amount of TC (mg/dL) and HDL (mg/dL) was obtained from the laboratory file. Blood pressure was each calculated as the average of three readings. Participants self-reported currently smoking (yes, no), taking any blood pressure medications (yes, no), and had ever been told they had diabetes by a medical doctor (yes, no). Histories of diseases including CHD, MI, stroke, diabetes and cancer were ascertained through the question "Has a doctor or other health professional told you that you had diseases?"

2.3. Assessment of weight change

We used long-term (10 years) and short-term (1 year) weight change indicators according to the interval over which the change was assessed. The percentage change in weight was calculated from the difference between the present weight and the past weight, the specific formula was shown as followed:

Abbreviations: ASCVD, Atherosclerotic cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; NCHS, National Center for Health Statistics; HDL-C, High-density lipoprotein cholesterol; TC, Total cholesterol; MI, Myocardial infarction; CHD, Coronary heart disease; PCEs, Pooled cohort equations; ACC, American College of Cardiology; AHA, American Heart Association; BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; CI, Confidence interval; RCT, Randomized controlled trial.

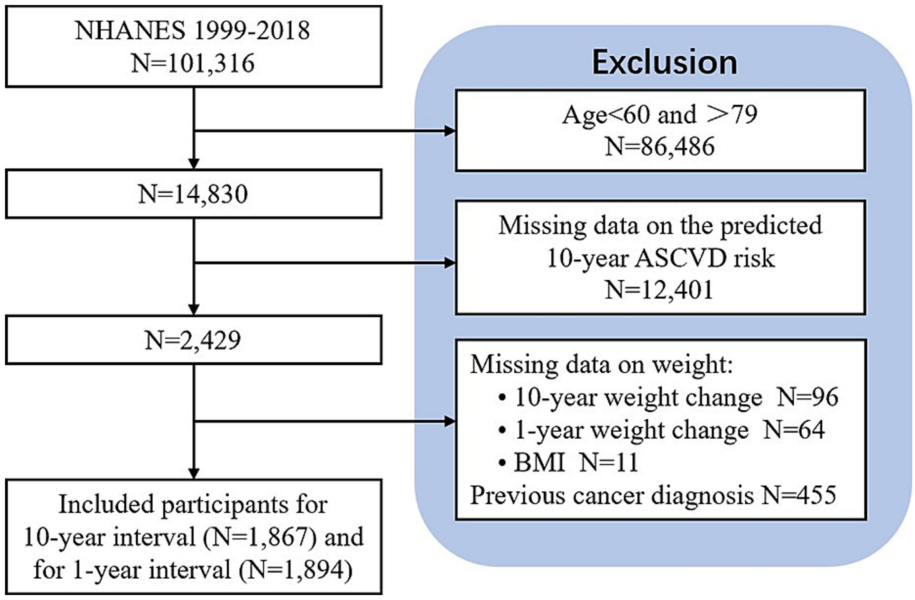


FIGURE 1
Flowchart of the study population.

$$\frac{W - W_0}{W_0} \times 100\%,$$

where W refers to the present weight and W_0 refers to their previous weight. All participants were asked to recall the weight 10 years ago or 1 year ago, and measured current weight in the NHANES examination. We classified the weight change into five categories: moderate-to-large weight loss (≥ 10%), small weight loss (5.1–9.9%), stable weight (± 5%), small weight gain (5.1–9.9%), and moderate-to-large weight gain (≥ 10%).

2.4. Assessment of covariates

The following covariates were included: age, sex, race, Body Mass Index (BMI), marital status, educational level, family income-to-poverty ratio, and physical activity. Marital status was categorized as married/partnered (married and living as married) and single/no partner (widowed, divorced, separated and never married). Educational level was classified as lower category (less than high school), intermediate category (high school graduate/GED, some college or AA degree) and higher category (college graduate or above). Physical activity was defined as sports, fitness and recreational activities, excluding work and transport activities. Physical activity was categorized as vigorous activity (cause large increases in breathing or heart rate), moderate activities (cause a small increase in breathing or heart rate) and none.

2.5. Statistical analysis

Categorical variables were expressed as frequency, and continuous variables were expressed as means ± standard deviations. Demographic and clinical data between the weight change groups were compared using the Kruskal-Wallis test and Fisher's exact test. Multiple linear regression analyses were used to estimate the independent relationship between weight change and the predicted 10-year risk of ASCVD events. When calculating the relative ASCVD risk of each weight change category, we used the "stable weight" category as the reference. In addition to the relative 10-year ASCVD risk of each weight change category, we fit a smoothing spline curve to examine the non-linearity of weight change and the 10-year ASCVD risks. Moreover, we performed stratified analyses by age, sex, race/ethnicity, current BMI, intention to lose weight, physical activity, treatment for hypertension, diabetes and current smoking status.

Three models were constructed: Model 1 was adjusted for none; Model 2 was adjusted for sex, age, and race/ethnicity; Model 3 was adjusted for sex, age, race/ethnicity, body mass index, income-poverty ratio, physical activity, education level, and marital status. In the subgroup analysis, the model is not adjusted for the stratification variable itself.

We used multiple imputations, based on 5 replications and a chained equation approach method in the RMI procedure, to account for missing data. All statistical analyses were performed by using R version 3.4.3 (The R Foundation)[1] and EmpowerStats software (X&Y solutions, Inc., Boston, MA)[2] and Graphpad Prisma 8.3.0, with statistically significant set at $p < 0.05$.

3. Results

3.1. Characteristics

The description of sociodemographic and medical characteristics of the participants with long-term (10 years) weight change was

1 http://www.R-project.org
2 www.empowerstats.com

TABLE 1 Characteristics of study participants according to 10-year weight change patterns in National Health and Nutrition Examination survey, 1999–2018.

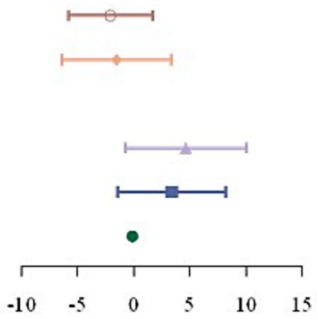
Weight change	All participants (*n* = 1,867)	Weight stable (*n* = 505)	Moderate-to-large weight loss (*n* = 259)	Small weight loss (*n* = 190)	Small weight gain (*n* = 260)	Moderate-to-large weight gain (*n* = 653)	*p*-value
Age (years), mean (SD)	67.47 ± 5.35	67.98 ± 5.38	68.22 ± 5.29	68.56 ± 5.52	66.72 ± 5.23	66.76 ± 5.24	**<0.001**
Sex, n (%)							**<0.001**
Male	1,081 (57.90%)	334 (66.14%)	150 (57.92%)	129 (67.89%)	169 (65.00%)	299 (45.79%)	
Female	786 (42.10%)	171 (33.86%)	109 (42.08%)	61 (32.11%)	91 (35.00%)	354 (54.21%)	
Race/ethnicity, n (%)							**0.002**
Mexican American	287 (15.37%)	73 (14.46%)	49 (18.92%)	38 (20.00%)	40 (15.38%)	87 (13.32%)	
Other Hispanic	153 (8.19%)	35 (6.93%)	23 (8.88%)	16 (8.42%)	16 (6.15%)	63 (9.65%)	
Non-Hispanic white	814 (43.60%)	242 (47.92%)	95 (36.68%)	63 (33.16%)	131 (50.38%)	283 (43.34%)	
Non-Hispanic Black	529 (28.33%)	125 (24.75%)	83 (32.05%)	61 (32.11%)	68 (26.15%)	192 (29.40%)	
Other race	84 (4.50%)	30 (5.94%)	9 (3.47%)	12 (6.32%)	5 (1.92%)	28 (4.29%)	
BMI (kg/m^2), mean ± SD	30.23 ± 6.21	28.42 ± 5.21	27.32 ± 5.60	27.60 ± 5.51	30.69 ± 4.85	33.37 ± 6.40	**<0.001**
Income poverty ratio, mean ± SD	2.52 ± 1.57	2.70 ± 1.61	1.98 ± 1.38	2.50 ± 1.54	2.89 ± 1.60	2.45 ± 1.56	**<0.001**
Educational level, n (%)							**<0.001**
Lower	624 (33.46%)	157 (31.09%)	129 (50.00%)	64 (33.68%)	63 (24.23%)	211 (32.36%)	
Intermediate	926 (49.65%)	251 (49.70%)	99 (38.37%)	99 (52.11%)	147 (56.54%)	330 (50.61%)	
Higher	315 (16.89%)	97 (19.21%)	30 (11.63%)	27 (14.21%)	50 (19.23%)	111 (17.02%)	
Marital status, n (%)							**0.006**
Married/partnered	1,143 (61.65%)	333 (66.60%)	144 (56.03%)	108 (57.14%)	173 (66.80%)	385 (59.32%)	
Single/no partner	711 (38.35%)	167 (33.40%)	113 (43.97%)	81 (42.86%)	86 (33.20%)	264 (40.68%)	
Physical activity, n (%)							**0.017**
Vigorous activity	204 (10.93%)	75 (14.85%)	25 (9.65%)	19 (10.00%)	27 (10.38%)	58 (8.88%)	
Moderate activity	553 (29.62%)	158 (31.29%)	64 (24.71%)	56 (29.47%)	84 (32.31%)	191 (29.25%)	
No	1,110 (59.45%)	272 (53.86%)	170 (65.64%)	115 (60.53%)	149 (57.31%)	404 (61.87%)	
Smoker, n (%)							**<0.001**
Yes	482 (25.82%)	104 (20.59%)	107 (41.31%)	59 (31.05%)	50 (19.23%)	162 (24.81%)	
No	1,385 (74.18%)	401 (79.41%)	152 (58.69%)	131 (68.95%)	210 (80.77%)	491 (75.19%)	
Diabetes, n (%)							**<0.001**
Yes	517 (27.69%)	118 (23.37%)	103 (39.77%)	65 (34.21%)	69 (26.54%)	162 (24.81%)	
No	1,350 (72.31%)	387 (76.63%)	156 (60.23%)	125 (65.79%)	191 (73.46%)	491 (75.19%)	
Treatment for hypertension, n (%)							0.051
Yes	1710 (91.59%)	457 (90.50%)	247 (95.37%)	173 (91.05%)	230 (88.46%)	603 (92.34%)	
No	157 (8.41%)	48 (9.50%)	12 (4.63%)	17 (8.95%)	30 (11.54%)	50 (7.66%)	
SBP (mmHg), mean ± SD	136.19 ± 19.55	135.66 ± 19.23	136.13 ± 21.90	139.06 ± 20.31	134.68 ± 18.19	136.38 ± 19.08	0.193
DBP (mmHg), mean ± SD	70.53 ± 12.28	70.38 ± 12.03	68.43 ± 12.05	71.75 ± 12.93	70.73 ± 11.83	71.05 ± 12.46	**0.029**
TC (mg/dL), mean ± SD	196.11 ± 36.68	196.99 ± 35.87	190.37 ± 36.16	195.02 ± 37.89	197.02 ± 36.21	197.67 ± 37.22	0.087
HDL (mg/dL), mean ± SD	67.47 ± 5.35	53.04 ± 15.72	55.15 ± 15.70	53.16 ± 15.81	51.15 ± 14.48	51.33 ± 14.36	**0.005**
The 10-year ASCVD risk, mean ± SD	23.21 ± 13.15	23.22 ± 13.16	26.59 ± 14.17	27.84 ± 13.44	21.69 ± 12.07	21.13 ± 12.46	**<0.001**

Boldface indicates statistical significance ($p < 0.05$). BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; ASCVD, atherosclerotic cardiovascular disease; SD, standard deviation.

presented in Table 1. A total of 1,867 older adults aged 60–79 years were enrolled in our analysis. Of all these participants, the mean age was 67.47 years (SD = 5.35), and 42.10% were female. For all participants, the mean predicted 10-year ASCVD risk was 23.21 (SD = 13.15). The mean BMI was 30.23 kg/m^2 (SD = 6.21). The distribution of 10-year weight change was 27.05% for weight stable (± 5.0%), 13.87% for moderate-to-large weight loss (> −10%), 10.18% for small weight loss (−5.1 to −9.9%), 13.93% for small weight gain (5.1~9.9%) and 34.98% for moderate-to-large weight gain (>10%). Among different groups of weight change, age, sex, race/ethnicity,

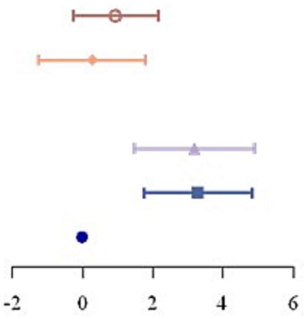
A

	N	β (95% CI)	P
Weight change pattern			
Gain ⩾10%	653 (34.98%)	-2.10 (-3.60, -0.59)	<0.01
Gain 5.1%~9.9%	260 (13.93%)	-1.53 (-3.47, 0.40)	0.12
Stable (±5.0%)	505 (27.05%)	Ref	
Loss -5.1%~-9.9%	190 (10.18%)	4.62 (2.46, 6.78)	<0.01
Loss ⩾10%	259 (13.87%)	3.37 (1.43, 5.31)	<0.01
Weight change	1867	**-0.12 (-0.14, -0.11)**	**<0.01**



B

	N	β (95% CI)	P
Weight change pattern			
Gain ⩾10%	653 (34.98%)	0.93 (-0.27, 2.14)	0.13
Gain 5.1%~9.9%	260 (13.93%)	0.27 (-1.26, 1.80)	0.73
Stable (±5.0%)	505 (27.05%)	Ref	
Loss -5.1%~-9.9%	190 (10.18%)	3.18 (1.47, 4.88)	<0.01
Loss ⩾10%	259 (13.87%)	3.27 (1.74, 4.81)	<0.01
Weight change	1867	**-0.02 (-0.03, -0.01)**	**<0.01**



C

	N	β (95% CI)	P
Weight change pattern			
Gain ⩾10%	653 (34.98%)	0.47 (-0.78, 1.72)	0.46
Gain 5.1%~9.9%	260 (13.93%)	0.26 (-1.27, 1.78)	0.74
Stable (±5.0%)	505 (27.05%)	Ref	
Loss -5.1%~-9.9%	190 (10.18%)	2.99 (1.30, 4.68)	<0.01
Loss ⩾10%	259 (13.87%)	2.52 (0.98, 4.05)	<0.01
Weight change	1867	**-0.02 (-0.04, -0.01)**	**<0.01**

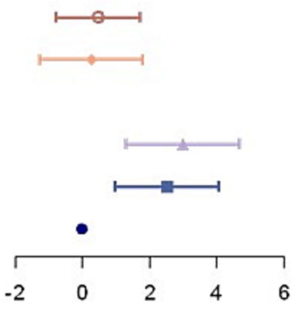


FIGURE 2
Association between 10-year weight change and the 10-year ASCVD risk. **(A)** Model 1, no covariates were adjusted. **(B)** Model 2, age, sex, and race/ethnicity were adjusted. **(C)** Model 3, age, sex, race/ethnicity, body mass index, income-poverty ratio, physical activity, education level, and marital status were adjusted. ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval.

BMI, income-poverty ratio, educational level, marital status, physical activity, smoker, diabetes, DBP, TC, and HDL were all significantly different ($p < 0.05$). Overall, older adults who had weight loss were more likely to be a racial/ethnic minority, single/no partner, and had lower income-to-poverty ratios and educational attainment, when compared to those with a stable weight. The descriptive statistics for the participants with short-term (1 year) weight change are shown in Supplementary material 1.

3.2. 10-year weight change and the predicted risk of ASCVD events

Results of multiple linear regression analyses of 10-year weight change and the 10-year risk of ASCVD events were displayed in Figure 2. Non-adjusted was displayed in Model 1 (Figure 2A), adjusted for age, sex, and race/ethnicity was displayed in Model 2 (Figure 2B), and adjusted for Model 2 plus BMI, income-poverty ratio, physical

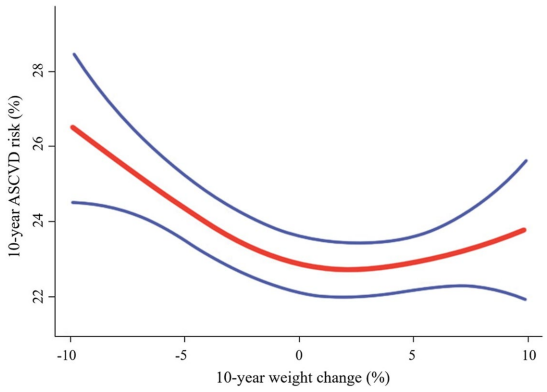


FIGURE 3
Correlation between 10-year weight change (−9.9 to 9.9%) and the 10-year ASCVD risk. Solid red line represents the smooth curve fit between variables. The area between two blue lined is expressed as a 95% CI. Age, sex, race/ethnicity, body mass index, income poverty ratio, physical activity, education level, and marital status were adjusted. ASCVD, atherosclerotic cardiovascular disease.

activity, education level, and marital status was displayed in Model 3 (Figure 2C). We observed a significant inverse association between weight change and the 10-year ASCVD risk.

Similar results were found when weight change was divided into five categories. Compared to weight stable (± 5.0%), both moderate-to-large (≥ 10%) and small (−5.1% ~ −9.9%) weight loss was associated with a higher risk in Model 1 and Model 2. In fully adjusted model (Model 3), the significant association remained unchanged (loss≥10%: $\beta = 2.52$, 95%CI = 0.98, 4.05; loss 5.1% ~ 9.9%: $\beta = 2.99$, 95% CI = 1.30, 4.68). While neither Model 2 nor Model 3 found no significant association between the weight gain categories and the 10-year ASCVD risk, weight gain ≥10% was associated with lower risk in non-adjusted model ($\beta = -2.10$, 95% CI = −3.60, −0.59).

To check the dose–response relationship between continuous 10-year weight change (−9.9 to 9.9%) and the predicted 10-year risk of ASCVD events, we plotted the spline curves, as seen in Figure 3. This result confirmed the dose–response relationship was most pronounced in the link between weight loss and the 10-year ASCVD risk: greater weight loss was associated with higher 10-year ASCVD risk.

However, this was not the case for short-term weight change. Each category had no significant association with 10-year ASCVD risk, as seen in Supplementary material 2.

Table 2 presents the results stratified according to age, sex, race/ethnicity, BMI, physical activity, Intention to lose weight, treatment for hypertension, diabetes, and current smoking status. Compared to people with stable weight, it can be observed that people who lose weight may associate with a higher 10-year risk, no matter with ages (except for people aged ≥75 years) and sexes in Model 3. However, in the subgroup analyses, the association between weight loss and the 10-year ASCVD risk was non-significant in older adults who were obese (≥ 35 kg/m^2), had intentional weight loss, and had moderate physical activity. In addition, moderate physical activity significantly decreases the 10-year ASCVD risk in older adults with moderate-to-large weight gain ($\beta = -2.70$, 95% CI = −4.97, −0.43). We also found that for diabetics, long-term weight change showed no significant association with the 10-year ASCVD risk. Subgroup analyses of short-term weight change and the 10-year ASCVD risk are presented in Supplementary material 3.

4. Discussion

The present study used a nationally representative sample of community-dwelling adults aged 60–79 years and assessed the risk of a first hard ASCVD event in the next 10 years according to the 2013 ACC/AHA equation. In this study, we found an inverse association between weight loss ≥5% and the predicted 10-year ASCVD risk in older adults, and no protective effect of weight gain.

Our results are generally in accordance with previous studies on the relationship between weight loss and cardiovascular and all-cause mortality in older adults. In a longitudinal observational cohort study conducted in the U.S. communities, weight loss of 5% or more in 3 years was associated with an increased risk of mortality in older adults (8). Likewise, community-dwelling older Japanese people with weight loss ≥5% in all terms was associated with a higher risk of all-cause mortality, not only in short-term (3 years), but also in medium-term (6–7 years) and long-term (12–13 years) (14). Moreover, a Tehran study of participants with type 2 diabetes aged ≥60 years without a history of cardiovascular disease and cancer at baseline has suggested that 3-year weight loss >5% was associated with an increased risk (marginally significant) of incident cardiovascular disease during more than 14 years of follow-up (15).

However, some previous studies reported conflicting results. For example, in a 12-month randomized controlled trial (RCT) of 164 obese older adults aged ≥65 years, there was a positive significant association between weight loss by exercise plus moderate caloric restriction and cardiometabolic risk (16). In addition, another RCT comprising 585 obese participants aged 60–80 years with hypertension found a favorable association between intentional weight loss (mean 4.4 kg) and reductions in the need for antihypertensive medication (17). This study also reported weight loss was not significantly associated with increased cardiovascular disease events during the first 2 years of follow-up (17), nor was all-cause mortality during over 12 years of follow-up (18).

In addition to the weight change calculated in different time intervals, the discrepancy between our study and previous ones may partly be related to current BMI and intention to lose weight. Indeed, our study indicated that the association between weight loss and the predicted 10-year risk was not significant in obesity (≥ 5 kg/m^2) and intentional weight loss. This may be due to the fact that unintentional weight loss in older adults is usually reflect disease severity (e.g., in patients with advanced heart disease, lung disease or malignant disease) or underlying disease, and is particularly relevant to worsened outcomes (19). Cancer or malignancy, which is characterized by substantial weight loss during 1 year or less, accounts for 16–36% of organic causes of unintentional weight loss in older adults (20). However, our study showed that, an increased risk of a first ASCVD event was associated with weight loss within 10 years rather than 1 year. In addition, another possibility for discrepancy is the difference in the level of physical activity. The loss of muscle mass (21) and bone strength (22) that occurs with age, which contributes to disability and frailty in older adults (23, 24). Physical activity alone,

TABLE 2 Stratified analyses of the association between 10-year weight change and the 10-year ASCVD risk.

	Weight stable	Moderate-to-large weight loss	Small weight loss	Small weight gain	Moderate-to-large weight gain
Age					
60–64	Ref	**2.55 (0.29, 4.80)**	1.61 (−0.95, 4.17)	−0.84 (−2.86, 1.17)	−0.69 (−2.40, 1.03)
65–69	Ref	**4.45 (1.70, 7.20)**	**4.12 (1.15, 7.10)**	−0.59 (−3.35, 2.17)	0.52 (−1.77, 2.81)
70–74	Ref	1.26 (−2.04, 4.55)	**5.50 (1.89, 9.11)**	0.40 (−2.99, 3.79)	2.07 (−0.70, 4.84)
75–79	Ref	0.57 (−4.86, 6.00)	−1.21 (−6.9, 4.47)	3.30 (−3.06, 9.66)	1.95 (−2.84, 6.73)
Sex					
Male	Ref	**2.43 (0.41, 4.44)**	1.76 (−0.35, 3.87)	0.29 (−1.65, 2.22)	−0.17 (−1.85, 1.51)
Female	Ref	**2.99 (0.58, 5.40)**	**5.81 (2.93, 8.68)**	−0.07 (−2.58, 2.44)	1.47 (−0.44, 3.38)
Race/Ethnicity					
Mexican American	Ref	2.51 (−0.72, 5.75)	2.40 (−1.06, 5.86)	1.31 (−2.1, 4.72)	−0.58 (−3.44, 2.28)
Other Hispanic	Ref	**6.24 (1.2, 11.29)**	**9.12 (3.61, 14.62)**	1.68 (−3.97, 7.33)	2.11 (−2.16, 6.39)
Non-Hispanic white	Ref	2.08 (−0.05, 4.21)	1.71 (−0.77, 4.18)	0.23 (−1.69, 2.14)	0.46 (−1.19, 2.11)
Non-Hispanic Black	Ref	2.82 (−0.57, 6.22)	3.31 (−0.37, 7.00)	0.00 (−3.58, 3.58)	1.65 (−1.23, 4.52)
Other race	Ref	2.42 (−5.61, 10.45)	−1.33 (−8.36, 5.70)	−3.68 (−14.19, 6.83)	−3.99 (−9.78, 1.80)
BMI					
<25.0	Ref	**3.53 (0.11, 6.95)**	1.23 (−2.48, 4.94)	1.86 (−3.71, 7.42)	−0.45 (−5.38, 4.47)
25.0–29.9	Ref	1.53 (−0.82, 3.88)	**3.56 (1.03, 6.09)**	0.67 (−1.66, 3.00)	−0.53 (−2.45, 1.40)
30.0–34.9	Ref	1.46 (−1.82, 4.75)	**4.36 (0.67, 8.05)**	−1.07 (−3.72, 1.58)	−0.13 (−2.47, 2.21)
≥35.0	Ref	2.43 (−2.47, 7.34)	1.54 (−4.07, 7.15)	1.72 (−2.3, 5.75)	2.54 (−0.49, 5.57)
Physical activity					
Vigorous activity	Ref	3.95 (−0.20, 8.10)	**5.22 (0.69, 9.75)**	0.77 (−3.23, 4.77)	−0.23 (−3.57, 3.12)
Moderate activity	Ref	0.46 (−2.37, 3.30)	1.60 (−1.34, 4.54)	−2.14 (−4.73, 0.45)	**−2.70 (−4.97,-0.43)**
No	Ref	**3.31 (1.25, 5.37)**	**3.46 (1.15, 5.78)**	1.49 (−0.64, 3.61)	**1.98 (0.28, 3.69)**
Intention to lose weight					
Yes	Ref	1.38 (−0.96, 3.72)	1.39 (−1.39, 4.18)	−0.34 (−2.45, 1.77)	0.29 (−1.43, 2.02)
No	Ref	**3.07 (1.03, 5.11)**	**3.51 (1.35, 5.67)**	0.69 (−1.5, 2.88)	0.58 (−1.24, 2.4)
Diabetes					
Yes	Ref	−1.34 (−4.29, 1.61)	1.25 (−2.06, 4.56)	−0.88 (−4.14, 2.39)	1.28 (−1.52, 4.09)
No	Ref	**1.57 (0.26, 2.87)**	**1.83 (0.44, 3.23)**	0.63 (−0.58, 1.83)	**1.57 (0.59, 2.55)**
Treatment for hypertension					
Yes	Ref	**2.27 (0.67, 3.88)**	**2.90 (1.11, 4.69)**	0.25 (−1.38, 1.88)	0.50 (−0.83, 1.82)
No	Ref	1.41 (−3.43, 6.24)	**5.01 (0.88, 9.13)**	0.48 (−2.93, 3.88)	0.46 (−2.62, 3.55)
Smoker					
Yes	Ref	1.20 (−1.76, 4.16)	**3.55 (0.07, 7.04)**	1.12 (−2.55, 4.78)	0.18 (−2.70, 3.06)
No	Ref	**1.73 (0.06, 3.40)**	**1.92 (0.18, 3.66)**	0.26 (−1.23, 1.74)	−0.11 (−1.35, 1.13)

Values are β (95% confidence interval). Adjusted for sex, race/ethnicity, BMI, income-poverty ratio, education level, marital status, and physical activity. The model is not adjusted for the stratification variable itself. Boldface indicates statistical significance ($p < 0.05$). BMI, body mass index; ASCVD, atherosclerotic cardiovascular disease.

without diet control, is not typically associated with significant weight loss and it can maintain lean body mass and muscle strength, improve cardiometabolic risk factors and physical function in older adults (7, 25, 26). However, because of the opposite effect observed in our study between vigorous and moderate intensity activity, further research is needed to clarify this issue.

A major strength of our study is the use of a nationally representative sample that represents the general U.S. adult population. Furthermore, with the comprehensive data collected in NHANES, a wide range of potential confounders including demographic, socioeconomic and lifestyle were able to be controlled.

As for the limitations. First, we used self-reported weight for the analysis, instead of measured weight, which may lead to the misclassification of weight change status. Secondly, we did not consider the fluctuation of body weight during the 10-year intervals. Third, weight lacks discriminatory power to differentiate between

body fat and lean mass. Therefore, future research should investigate the same question using indicators of body composition to more fully understand the mechanisms linking weight changes to ASCVD risk to mortality risk. Fourthly, we failed to consider specific modalities of losing weight, such as intermittent fasting, low-calorie diets, more exercise or bariatric surgery, which might cause bias. Finally, this study was cross-sectional research, and it cannot demonstrate the causation but only the association. Further and prospective studies should be completed in the future.

5. Conclusion

In this study of U.S. adults 60–79 years of age, we found that weight loss >5% over 10 years was significantly associated with an increased the predicted 10-year ASCVD risk. Our study supports the benefits of stable weight in promoting cardiovascular health in older adults. However, further prospective studies are required to elucidate the effect of weight management in later life on decreasing ASCVD risk.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/Supplementary material.

Ethics statement

The NHANES study was approved by the National Center for Health Statistics' Ethics Review Board. The study was conducted in accordance with the local legislation and institutional requirements. All participants provided written informed consent (parental consent was obtained for those < 18 years).

Author contributions

YP: full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. YP and HL: concept and design. JL, FL, and WY: acquisition, analysis, and interpretation of data. LT, AL, and YW: drafting of the manuscript. YP and HQ: statistical analysis. LL and HQ: administrative, technical, and material support. CF: supervision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2023.1183200/full#supplementary-material

References

1. Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, Lee A, et al. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med*. (2017) 377:13–27. doi: 10.1056/NEJMoa1614362

2. Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007-2008 to 2015-2016. *JAMA*. (2018) 319:1723–5. doi: 10.1001/jama.2018.3060

3. Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL. The effect of age on the association between body-mass index and mortality. *N Engl J Med*. (1998) 338:1–7. doi: 10.1056/NEJM199801013380101

4. Angelantonio E, Bhupathiraju S, Wormser D, Gao P, Kaptoge S, de Gonzalez AB, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet*. (2016) 388:776–86. doi: 10.1016/S0140-6736(16)30175-1

5. Jensen MD, Ryan DH, Apovian CM, Ard JD, Comuzzie AG, Donato KA, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association task force on practice guidelines and the Obesity Society. *Circulation*. (2014) 129:S102–38. doi: 10.1161/01.cir.0000437739.71477.ee

6. Villareal DT, Aguirre L, Gurney AB, Waters DL, Sinacore DR, Colombo E, et al. Aerobic or resistance exercise, or both, in dieting obese older adults. *N Engl J Med*. (2017) 376:1943–55. doi: 10.1056/NEJMoa1616338

7. Batsis JA, Gill LE, Masutani RK, Adachi-Mejia AM, Blunt HB, Bagley PJ, et al. Weight loss interventions in older adults with obesity: a systematic review of randomized controlled trials since 2005. *J Am Geriatr Soc*. (2017) 65:257–68. doi: 10.1111/jgs.14514

8. Newman AB, Yanez D, Harris T, Duxbury A, Enright PL, Fried LP, et al. Weight change in old age and its association with mortality. *J Am Geriatr Soc*. (2001) 49:1309–18. doi: 10.1046/j.1532-5415.2001.49258.x

9. Alharbi TA, Paudel S, Gasevic D, Ryan J, Freak-Poli R, Owen AJ. The association of weight change and all-cause mortality in older adults: a systematic review and meta-analysis. *Age Ageing*. (2021) 50:697–704. doi: 10.1093/ageing/afaa231

10. Romero-Corral A, Montori VM, Somers VK, Korinek J, Thomas RJ, Allison TG, et al. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet*. (2006) 368:666–78. doi: 10.1016/S0140-6736(06)69251-9

11. Pack QR, Rodriguez-Escudero JP, Thomas RJ, Ades PA, West CP, Somers VK, et al. The prognostic importance of weight loss in coronary artery disease: a systematic review and meta-analysis. *Mayo Clin Proc*. (2014) 89:1368–77. doi: 10.1016/j.mayocp.2014.04.033

12. World Health Organization. *Technical advisory group for measurement, monitoring and evaluation of the UN decade of healthy ageing*. Available at: https://www.who.int/groups/technical-advisory-group-for-measurement-monitoring-and-evaluation-of-the-un-decade-of-healthy-ageing (2022).

13. Goff DCJ, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation*. (2014) 129:S49–73. doi: 10.1161/01.cir.0000437741.48606.98

14. Murayama H, Liang J, Shaw BA, Botoseneanu A, Kobayashi E, Fukaya T, et al. Short-, medium-, and long-term weight changes and all-cause mortality in old age: findings from the National Survey of the Japanese elderly. *J Gerontol A Biol Sci Med Sci*. (2021) 76:2039–46. doi: 10.1093/gerona/glab052

15. Moazzeni SS, Hizomi Arani R, Deravi N, Hasheminia M, Khalili D, Azizi F, et al. Weight change and risk of cardiovascular disease among adults with type 2 diabetes: more than 14 years of follow-up in the Tehran lipid and glucose study. *Cardiovasc Diabetol*. (2021) 20:141. doi: 10.1186/s12933-021-01326-2

16. Ard JD, Gower B, Hunter G, Ritchie CS, Roth DL, Goss A, et al. Effects of calorie restriction in obese older adults: the CROSSROADS randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. (2017) 73:glw237–80. doi: 10.1093/gerona/glw237

17. Whelton PK, Appel LJ, Espeland MA, Applegate WB, Ettinger WHJ, Kostis JB, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. *JAMA*. (1998) 279:839–46. doi: 10.1001/jama.279.11.839

18. Brown RE, Kuk JL. Consequences of obesity and weight loss: a devil's advocate position. *Obes Rev*. (2015) 16:77–87. doi: 10.1111/obr.12232

19. Alibhai SM, Greenwood C, Payette H. An approach to the management of unintentional weight loss in elderly people. *CMAJ*. (2005) 172:773–80. doi: 10.1503/cmaj.1031527

20. McMinn J, Steel C, Bowman A. Investigation and management of unintentional weight loss in older adults. *BMJ*. (2011) 342:d1732. doi: 10.1136/bmj.d1732

21. Newman AB, Lee JS, Visser M, Goodpaster BH, Kritchevsky SB, Tylavsky FA, et al. Weight change and the conservation of lean mass in old age: the health, aging and body composition study. *Am J Clin Nutr*. (2005) 82:872–8. doi: 10.1093/ajcn/82.4.872

22. Ensrud KE, Vo TN, Burghardt AJ, Schousboe JT, Cauley JA, Taylor BC, et al. Weight loss in men in late life and bone strength and microarchitecture: a prospective study. *Osteoporos Int*. (2018) 29:1549–58. doi: 10.1007/s00198-018-4489-6

23. Gill LE, Bartels SJ, Batsis JA. Weight Management in Older Adults. *Curr Obes Rep*. (2015) 4:379–88. doi: 10.1007/s13679-015-0161-z

24. Grabowski DC, Ellis JE. High body mass index does not predict mortality in older people: analysis of the longitudinal study of aging. *J Am Geriatr Soc*. (2001) 49:968–79. doi: 10.1046/j.1532-5415.2001.49189.x

25. Brennan AM, Standley RA, Anthony SJ, Grench KE, Helbling NL, DeLany JP, et al. Weight loss and exercise differentially affect insulin sensitivity, body composition, cardiorespiratory fitness, and muscle strength in older adults with obesity: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. (2022) 77:1088–97. doi: 10.1093/gerona/glab240

26. Bouchonville M, Armamento-Villareal R, Shah K, Napoli N, Sinacore DR, Qualls C, et al. Weight loss, exercise or both and cardiometabolic risk factors in obese older adults: results of a randomized controlled trial. *Int J Obes*. (2014) 38:423–31. doi: 10.1038/ijo.2013.122

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Identification of risk factors for hypertension in overweight and obese people and analysis of risk factor interactions: an R-based analysis

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Objective: This study identified the independent risk factors for hypertension in overweight and obese people and also analyzed the interaction between the risk factors.

Methods: A total of 5,098 overweight and obese people were enrolled in this study. First, the clinical metabolic characteristics of hypertension and control groups were compared. The logistic regression (LR) and classification and regression trees (CRT)-based decision tree (DT) models were used to screen the independent risk factors for hypertension in overweight and obese people. The multiplicative and additive scale analyses were used to analyze the two risk factors with interaction from the perspective of statistics and biological interaction. Finally, the receiver operating characteristic (ROC) and calibration curves were used to analyze the accuracy and identification ability of the LR and DT models.

Results: Age, UA, FPG, SBP, Cr, AST, TG, and FPG were higher in the hypertension group than in the control group ($P < 0.05$). The results of LR revealed that NAFLD, FPG, age, TG, LDL-c, UA, and Cr were positively correlated with hypertension in overweight and obese people, and GFR was negatively correlated with hypertension in overweight and obese people ($P < 0.05$). The DT model suggested that the risk factors of age, FPG, and UA interacted with each other. The multiplicative single and multiple factor analysis for FPG + UA, age + UA, age + FPG revealed a positive multiplicative interaction ($P < 0.05$, $B \neq 0$, $OR > 1$). The additive single and multiple factor analysis for age + UA indicated a positive additive interaction. The ROC and calibration curve analysis indicated that the CRT decision tree, FPG + UA, age + UA, and age + FPG have certain accuracy and discrimination ability.

Conclusion: The independent risk factors for hypertension in overweight and obese people included NAFLD, FPG, age, TG, LDL-c, UA, and Cr. Among these, age + UA exhibited synergistic interaction, thereby providing a reference for the prevention and control of hypertension in overweight and obese people.

KEYWORDS

overweight and obese, hypertension, risk factor, interaction, models

Introduction

Hypertension is a common chronic disease worldwide that often leads to cardiovascular and brain complications. According to the Chinese guidelines for the prevention and treatment of hypertension (1), the number of patients with hypertension is increasing every year in China. The 2020 International Society of Hypertension guidelines (2) also mentioned that in spite of the measures adopted, the adverse effects of hypertension and cardiovascular disease persist in the world. Overweight and obesity are risk factors for hypertension (3), and a gradual increase in body mass index (BMI) is observed in such individuals. The risk of hypertension in overweight and obese people is 1.16–1.28 times higher than that of normal-weight people (4). Relevant studies have shown (5) that the risk of hypertension in overweight people is 3–4 times higher than that in normal-weight people, indicating that overweight and obese people are prone to hypertension.

According to research by Zhang et al. (6), the prevalence of obesity-related hypertension among Chinese adults aged 45 and above is 22.7%, affecting approximately 120 million people. Among individuals aged 45–54, 55–64, 65–74, and ≥75 years, the prevalence rates of obesity-related hypertension are 16.7%, 24.3%, 27%, and 26.7%, respectively. The obesity prevalence rates in these age groups are also 16.7%, 24.3%, 27%, and 26.7%, respectively. In comparison, for other populations such as the United States, the prevalence of obesity and hypertension is even more pronounced. The proportion of overweight or obese adults in the U.S. population is as high as 70.7%, with a hypertension prevalence rate of 1.21% among adults residing in medium to small metropolitan statistical areas (MSAs), and a prevalence rate of 1.06% for adults residing in non-MSAs. Furthermore, at least 75% of hypertension incidence is directly linked to obesity (7–9). Previous studies have focused on all aspects of hypertension in the general population. However, the metabolic characteristics of overweight and obese people differ from those of the general population. Therefore, the independent risk factors for hypertension and their interactions with each other will differ among such populations. This study screened the independent risk factors for hypertension in overweight and obese people and explored the influence of risk factor interaction on hypertension to provide a reference for the prevention and treatment of hypertension from the perspective of etiology.

Methods

Study participants

In this cross-sectional study, patients who were evaluated at the physical examination department of the Affiliated Hospital of Guilin Medical University from August 2019 to November 2019 were selected. The patients signed an informed consent form, and the study was approved by the ethics committee of Guilin Medical University (approval number: GLMU1A2019064). Inclusion criteria for study participants: BMI ≥ 24 kg/m^2; individuals willing to voluntarily participate in the study. Patients aged <18 years, pregnant women, and those with major diseases, such as malignant tumors, were excluded. A total of 5,098 patients with complete data were included in the study. The hospital had 84,000 discharges that year, and the sample size for this study is 5,098, accounting for 6.07% of the total. The age of the patients ranged from 18 to 85 years, with the average age being 44.92 ± 11.75 years. Of them, 3,609 were men aged 43.83 ± 11.72 years on average, accounting for 70.8% of the patients; moreover, 1,489 were women aged 47.54 ± 11.41 years on average, accounting for 29.2% of the patients. A total of 1,277 patients aged 50.55 ± 11.19 years on average were overweight and obese with hypertension; of these, 909 were men (71.1%), and 368 were women (28.9%). Moreover, 3,821 patients aged 43.03 ± 11.33 years on average were overweight and obese but without hypertension; of these, 2,700 were men (70.7%), and 1,121 were women (29.3%).

Data collection

This study is conducted by professional in-service medical examination physicians who have undergone standardized training in the physical examination center for testing and data collection. During the physical examination of the patients, trained physicians evaluated their characteristics, including age, nationality and marital status, disease history, hypertension, nonalcoholic fatty liver disease (NAFLD), malignant tumor, severe liver and kidney function injury, relevant medication history, personal history, and family history.

Physical measurement and measurement methods

The physical examination physicians used a SK-CK ultrasonic examination instrument (Shenzhen, China) to measure the height and weight of the patients. The height measurement was accurate to 0.1 cm, whereas the weight measurement was accurate to 0.1 kg. BMI was calculated using the following formula: BMI = weight (kg)/height (m^2). The patients were instructed to rest quietly for 5–10 min and to adopt a sitting position. Subsequently, the blood pressure of the right upper arm was measured with an accuracy of 1 mmHg (1 mmHg = 0.133 kPa).

Laboratory inspection and measurement methods

All the patients were instructed to have a light diet the day before the examination, and elbow venous blood (5 ml) was collected on an empty stomach on the morning of the examination day. The Roche's CobasC501 fully automatic biochemical analyzer (Roche Pharmaceutical Co. Ltd. matching reagent) was used to detect the biochemical indexes of fasting blood glucose (FPG), uric acid (UA), triglyceride (TG), total

cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), creatinine (Cr), blood urea nitrogen (BUN), alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Glomerular filtration rate (GFR) was calculated, and biochemical indicators are accurate to 2 decimal places. This study used the simplified Modification of Diet in Renal Disease (MDRD) formula that was improved by the Chinese: GFR (ml/[min × 1.73 m^2]) = 186 × (Cr [mg/dl])$^{-1.154}$ × (age)$^{-0.203}$ × (0.742 women). The diagnosis of NAFLD was confirmed by an ultrasound specialist used the Hitachi ARIETTA 70 high-end ultrasound.

Diagnostic criteria

The following diagnostic criteria of hypertension were defined in accordance with the global hypertension practice guide of the 2020 International Society of Hypertension (2): systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg. The patients who had a previous diagnosis of hypertension and were taking medicines were also considered to have hypertension, although their blood pressure was normal. The following diagnostic criteria of dyslipidemia were defined in accordance with the 2018 criteria of the American Association of Clinical Endocrinologists and American College of Endocrinology (AACE/ACE) for managing dyslipidemia (10): TC ≥ 6.2 mmol/L; TG ≥ 2.3 mmol/L; LDL-c ≥ 4.1 mmol/L; or HDL-c < 1.0 mmol/L. According to the diabetes prevention guideline (version 2, 2020 edition) in China (11), the diagnostic standard of diabetes is FPG ≥7.0 mmol/L. The diagnostic standard of abnormal glucose tolerance was 6.1 mmol/L ≤ FPG < 7.0 mmol/L. Both diabetes and glucose intolerance disorders were diagnosed on the basis of an FPG value of >6.1 mmol/L. According to the guidelines for the diagnosis and treatment of NAFLD (2018 update) (12), the working definition of the disease is as follows: the results of imaging examinations, such as color Doppler ultrasound and CT, are similar to alcoholic liver disease; however, the patient does not have excessive drinking history. According to the 2019 guidelines for primary diagnosis and treatment of obesity (13), patients with BMI ≥ 24 kg/m^2 are considered overweight and obese. According to the 2019 guidelines for the diagnosis and treatment of hyperuricemia and gout in China (14), hyperuricemia is defined as uric acid >420 μmol/L (both men and women). Fasting blood BUN ≥ 7.1 mmol/L was considered high BUN, while the fasting blood Cr level ≥110 μmol/L in men and ≥93 μmol/L in women was defined as hypercreatinine. Fasting blood ALT ≥ 40 U/L and fasting blood AST ≥ 40 U/L were considered high.

Statistical analysis

MedCalc19.0.4, SPSS 26.0, and Rx64 4.0.3 were used for statistical analysis. First, clinical data on relevant risk factors were analyzed in hypertension and control (nonhypertension) groups, and the logistic regression (LR) and classification and regression trees (CRT) models of hypertension in overweight and obese people were established. The relevant independent influencing factors and those with interaction were screened, and the influencing factors with interaction were substituted into the product term of LR for the single factor and multiple factors multiplicative interaction test. For an assumption of 0.05 as the test level, the product term coefficient B of the LR model $\neq 0$ [or the confidence interval of the odds ratio (OR) value does not include 1] and $P < 0.05$ indicated a multiplicative interaction between the two factors. $OR > 1$ indicated positive multiplicative interaction, whereas $OR < 1$ indicated negative multiplicative interaction. The receiver operating characteristic (ROC) and calibration curves of LR factors and CRT decision tree were used to analyze the accuracy and discrimination ability. The ggthemes program package was used for the visual analysis of additive interaction between relevant influencing factors. Three indicators, namely *RERI*, *AP*, and *SI*, were used to evaluate the meaningfulness of the additive interaction. No additive interaction between two factors was indicated by the confidence interval of 0 for *RERI* and *AP* and the confidence interval of 1 for *SI*. Contrasting results indicated an additive interaction.

Results

Clinical data analysis of hypertension and control groups

The overweight and obese patients with hypertension were defined as the hypertension group, and the overweight and obese patients without hypertension were defined as the control group. The analysis of clinical data revealed that age, UA, FPG, SBP, Cr, AST, TG, and FPG in the hypertension group were higher than those in the control group ($P < 0.05$; **Figure 1**).

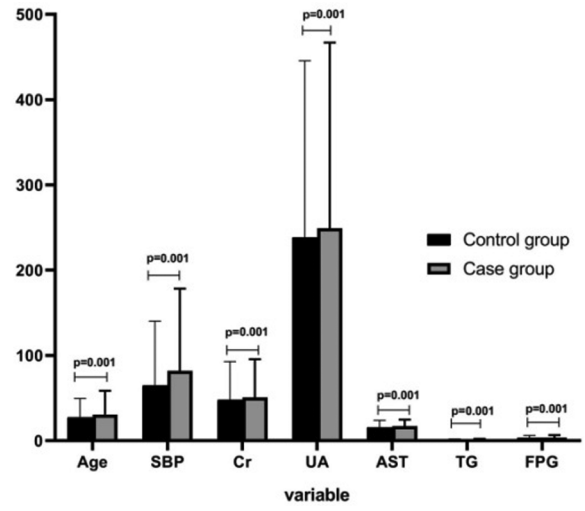

FIGURE 1
Comparison of influencing factors for hypertension in overweight and obese people between hypertension and control groups.

Logistic regression model construction

The risk factors were converted from continuous to classified variables. The risk factors were divided into two groups on the basis of their critical value. The value above the critical value was assigned as 1, and the value below the critical value was assigned as 0. The age boundary value was determined on the basis of the average age of overweight and obese patients with hypertension and without hypertension; 46 years was considered the average age, and the value ≥46 years was assigned as 1, whereas the value <46 years was assigned as 0 (Table 1).

Overweight and obese patients with hypertension were assigned as 1, and overweight and obese patients without hypertension were assigned as 0. A univariate LR model was constructed by considering the presence or absence of hypertension as the dependent variable, and sex, age, NAFLD, UA, FPG, GFR, TG, TC, LDL-c, HDL-c, Cr, BUN, ALT, and AST as the independent variables. The results revealed that NAFLD, FPG, age, TG, TC, LDL-c, UA, and Cr were positively correlated with hypertension in overweight and obese patients, and GFR was negatively correlated with hypertension in overweight and obese patients ($P < 0.05$). The significant factors in the univariate logistic analysis were used to perform the multivariate LR analysis. The results revealed that NAFLD, FPG, age, TG, LDL-c, UA, and Cr were negatively correlated with hypertension in overweight and obese patients, and GFR was positively correlated with hypertension in overweight and obese patients ($P < 0.05$).

Decision tree model construction

Hypertension was considered the dependent variable, and the screening of NAFLD, FPG, Age, TG, LDL-c, UA, Cr, and GFR as independent variables was performed by the LR model. The classification and regression trees (CRT) method was used to establish the decision tree (DT) model. The DT was set to three layers, and the tree was pruned to avoid overfitting. The results revealed that age, FPG, UA, TG, and LDL-c were the risk factors for hypertension in overweight and obese patients. The results suggested a possible interaction between age, FPG, and UA (Figure 2).

TABLE 1 Main variables and assignment of influencing factors for hypertension in overweight and obese people.

Variable	Assignment
Hypertension	NO = 0, YES = 1
MAFLD	NO = 0, YES = 1
UA (μmol/L)	<420 = 0; ≥420 = 1
Age (years)	<46 = 0, ≥46 = 1
Gender	Female = 0, Male = 1
FPG (mmol/L)	<6.1 = 0; ≥6.1 = 1
ALT (U/L)	<40 = 0; ≥40 = 1
AST (U/L)	<40 = 0; ≥40 = 1
TG (mmol/L)	<2.26 = 0; ≥2.26 = 1
TC (mmol/L)	<6.22 = 0; ≥6.22 = 1
LDL-c (mmol/L)	<4.14 = 0; ≥4.14 = 1
HDL-c (mmol/L)	<1.04 = 0; ≥1.04 = 1
BUN (mmol/L)	<7.1 = 0; ≥7.1 = 1
GFR (ml/(min × 1.73 m^2))	<90 = 0; ≥90 = 1
Cr (μmol/L)	Female: <93 = 0; ≥93 = 1
	Male: <110 = 0; ≥110 = 1

Multiplicative interaction analysis

The LR product term was used to analyze the multiplicative interaction of age, FPG, and UA screened by the DT model. The multivariate analysis included NAFLD, FPG, age, TG, LDL-c, UA, Cr, GFR, and other influencing factors screened by the LR model as confounding factors. The results indicated that FPG + UA, age + UA, and age + FPG had positive multiplicative interaction ($P < 0.05$, $B \neq 0$, and $OR > 1$; Table 2).

Model validation analysis

The ROC and calibration curves of the patients were constructed using the predictive variables obtained by the CRT DT and LR multivariate analysis of FPG + UA, age + UA, and age + FPG as variables, and the presence or absence of hypertension in overweight and obese patients as categorical variables. The results indicated the accuracy and discrimination ability of the CRT DT, FPG + UA, age + UA, and age + FPG models (Figures 3, 4).

Additive interaction analysis

The R was used to visually analyze the additive effect of single and multiple factors for FPG + UA, age + UA, and age + FPG. The multivariate analysis included NAFLD, FPG, age, TG, LDL-c, UA, Cr, GFR, and other influencing factors screened by the LR model as confounding factors. The results indicated that age + UA univariate and multivariate analyses (the confidence interval of *RERI* and *AP* does not include 0, and the confidence interval of *SI* does not include 1) and FPG + UA univariate analysis exhibited additive interaction; however, FPG + UA multivariate analysis and age + FPG univariate and multivariate analyses did not exhibit additive interaction (Tables 3, 4; Figures 5, 6).

Discussion

As the population of individuals with hypertension related to overweight and obesity continues to grow (6), corresponding research has also been increasing. This study aims to investigate the factors influencing hypertension in overweight and obese people and further explore the depth of their interactions using multiplicative and additive models. The goal is to provide valuable insights for clinical research. First, the clinical metabolic characteristics of hypertension and control groups were compared. The results indicated that age, UA,

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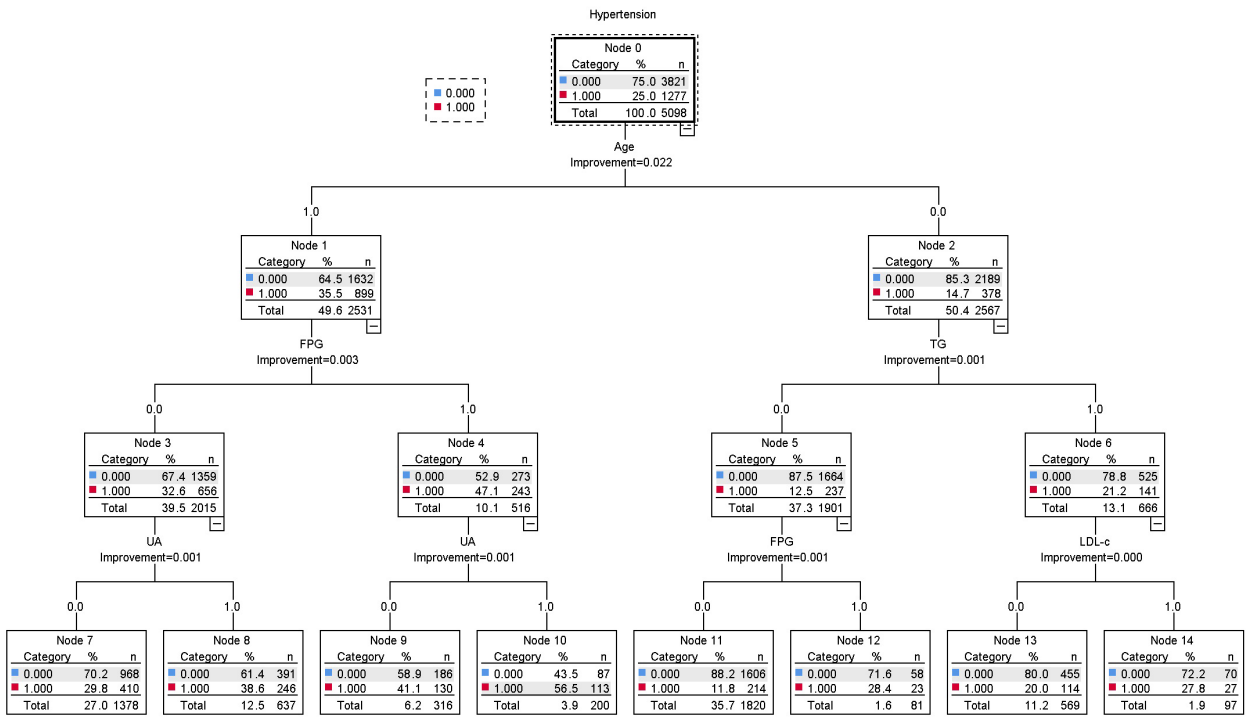

FIGURE 2
Decision tree model of influencing factors for hypertension in overweight and obese people.

FPG, SBP, Cr, AST, TG, and FPG of the hypertension group were higher than those of the control group. Second, the relevant risk factors for hypertension in overweight and obese people were screened. This study referred to the relevant program statements prepared by Xu et al. (15) and used dichotomous variables to explore the independent effects of risk factors and analyze the interaction. An LR model of hypertension in overweight and obese people was constructed, and a single factor and multiple factor analysis were performed to screen the independent influencing factors. The results indicated that NAFLD, FPG, age, TG, LDL-c, UA, and Cr were positively correlated with hypertension in overweight and obese patients, and GFR was negatively correlated with hypertension in overweight and obese patients. The DT analysis was performed using the CRT method, and the results revealed that the risk factors for hypertension in overweight and obese patients included age, FPG, UA, TG, and LDL-c; these results are similar to those of previous studies (16, 17). The CRT DT model also suggested that the prevalence rate of hypertension in overweight and obese patients aged ≥46 years and with FPG ≥ 6.1 mmol/L was 47.1%. However, the prevalence rate of hypertension in overweight and obese patients aged ≥46 years, with FPG ≥ 6.1 mmol/L, and with UA ≥ 420 μmol/L increased to 56.5%, suggesting that the interaction effect of age, FPG, and UA plays a crucial role in the prevalence of hypertension in overweight and obese people.

TABLE 2 Single and multiple factor multiplicative interaction analysis of risk factors for hypertension in overweight and obese people.

Multiplicative interaction		Number of people	Single factor analysis		*P* value	Multivariate analysis		*P* value
			B	*OR* value (95% CI)		*B*	*OR* value (95% CI)	
FPG	UA							
+	−	406	0.941	2.564 (2.166–3.035)	0.001	0.533	1.704 (1.422–2.042)	0.001
−	+	1,570	0.340	1.406 (1.234–1.600)	0.001	0.266	1.305 (1.129–1.509)	0.001
+	+	264	1.169	3.221 (2.508–4.137)	0.001	0.729	2.073 (1.591–2.702)	0.001
Age	UA							
+	−	1,694	1.160	3.190 (2.783–3.655)	0.001	1.049	2.856 (2.468–3.304)	0.001
−	+	997	0.340	1.406 (1.234–1.600)	0.001	0.266	1.305 (1.129–1.509)	0.001
+	+	837	1.006	2.735 (2.341–3.194)	0.001	0.732	2.080 (1.759–2.459)	0.001
Age	FPG							
+	−	2,015	1.160	3.190 (2.783–3.655)	0.001	1.049	2.856 (2.468–3.304)	0.001
−	+	154	0.941	2.564 (2.166–3.035)	0.001	0.533	1.704 (1.422–2.042)	0.001
+	+	516	1.116	3.054 (2.535–3.679)	0.001	0.958	2.606 (2.150–3.158)	0.001

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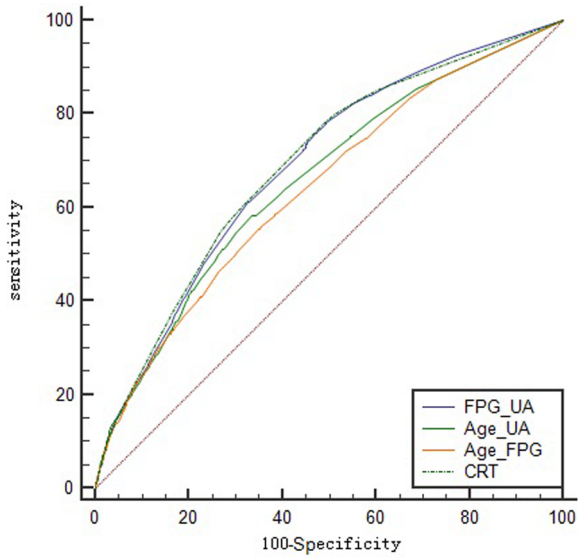

FIGURE 3
Logistic regression and classification tree ROC curve of hypertension in overweight and obese people.

TABLE 3 Evaluation indexes of additive interaction of risk factors for hypertension in overweight and obese people.

Additive interaction evaluation index	Single factor analysis	Multivariate analysis
FPG + UA		
RERI (95% CI)	1.188 (0.134–2.242)	0.794 (−0.036–1.625)
AP (95% CI)	0.307 (0.096–0.519)	0.273 (0.040–0.505)
SI (95% CI)	1.710 (1.095–2.671)	1.714 (0.991–2.961)
Age + UA		
RERI (95% CI)	1.458 (0.646–2.269)	0.758 (0.101–1.415)
AP (95% CI)	0.285 (0.156–0.414)	0.199 (0.046–0.352)
SI (95% CI)	1.548 (1.217–1.969)	1.371 (1.041–1.807)
Age + FPG		
RERI (95% CI)	1.200 (−0.087–2.488)	0.917 (−0.223–2.057)
AP (95% CI)	0.218 (0.009–0.426)	0.189 (−0.023–0.403)
SI (95% CI)	1.363 (0.970–1.915)	1.315 (0.930–1.859)

Interaction in the multivariate statistical analysis means that the effect of a certain factor varies with the level of other factors. When two factors coexist, the effect is not equal to the sum (additive interaction) or the product (multiplicative interaction) of the two factors acting alone. In this study, the multiplicative interaction was analyzed by constructing the LR product term by performing the single and multiple factor analysis of the relevant influencing factors. The multiple factor analysis included all the influencing factors for hypertension in overweight and obese people that were screened by the LR model as confounding factors. The results suggested that FPG + UA, age + UA, age + FPG, and other combinations have positive multiplicative interaction in the univariate and multivariate analyses ($P < 0.05$, $B \neq 0$, $OR > 1$). Compared with the independent existence of related factors, the combined existence will increase the prevalence rate of hypertension by 2–3 times.

Biological interaction is the combined effects, including synergism and antagonism, of two factors on biological mechanisms. Rothman (18) proposed that the evaluation of biological interaction should be based on the additive scale. In this study, we conducted a quantitative and visual analysis of the additive interaction between hypertension risk factors in

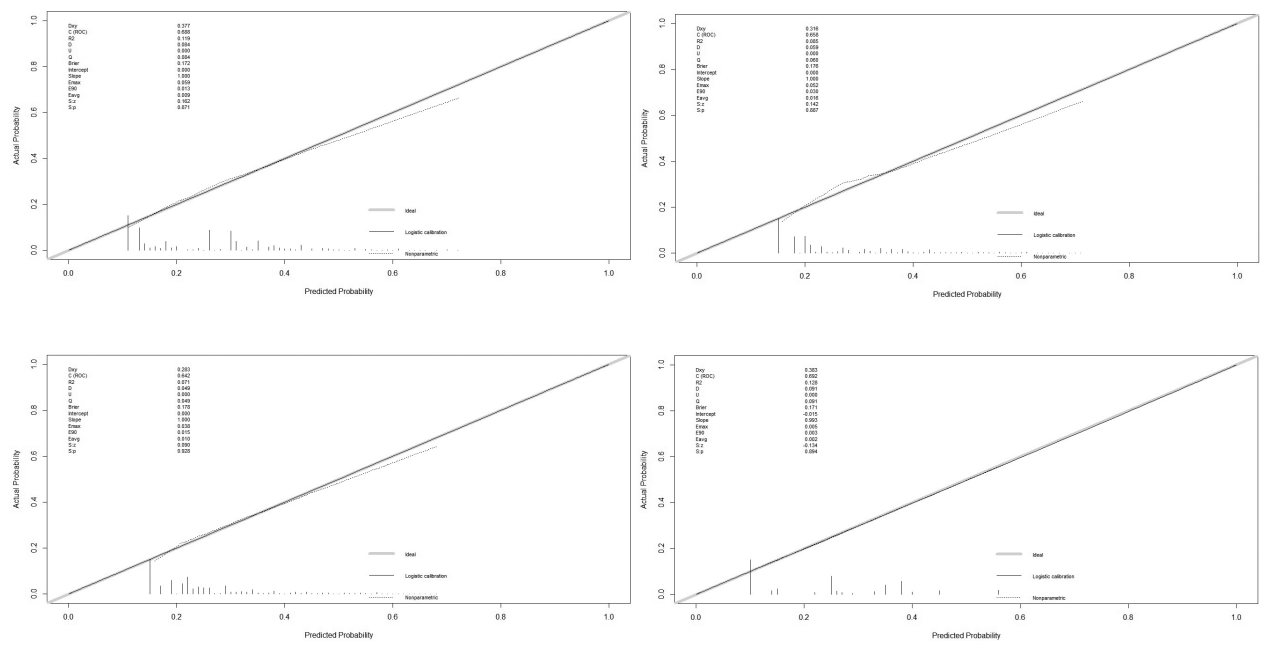

FIGURE 4
Logistic regression and classification tree calibration curve of hypertension in overweight and obese people (FPG + UA, Age + UA, Age + FPG, and CRT).

TABLE 4 Single and multiple factor additive interaction analysis of risk factors for hypertension in overweight and obese people.

Additive interaction		Number of people	Single factor analysis	Multivariate analysis
			OR value (95% CI)	*OR* value (95% CI)
FPG	UA			
+	−	406	2.334 (1.872–2.910)	1.996 (1.590–2.507)
−	+	1,570	1.337 (1.157–1.546)	1.115 (0.957–1.300)
+	+	264	3.860 (2.983–4.995)	2.907 (2.218–3.808)
Age	UA			
+	−	1,694	3.187 (2.662–3.815)	2.769 (2.300–3.334)
−	+	997	1.470 (1.180–1.831)	1.269 (1.012–1.592)
+	+	837	5.115 (4.181–6.258)	3.798 (3.055–4.722)
Age	FPG			
+	−	2,015	2.983 (2.572–3.460)	2.923 (2.503–3.414)
−	+	154	2.318 (1.596–3.365)	1.987 (1.359–2.907)
+	+	516	5.502 (4.469–6.773)	4.828(3.892–5.990)

overweight and obese people. The results indicated that the univariate and multivariate analyses of age + UA had additive interaction (the confidence interval of *RERI* and *AP* did not include 0, and the confidence interval of *SI* did not include 1). The quantitative analysis suggested that the prevalence of hypertension in overweight and obese patients increased 4 or 5 times when the two factors were combined.

The verification of the accuracy and discrimination ability of the LR and CRT DT models indicated that the four models, FPG + UA, age + UA, age + FPG, and CRT, have obvious discrimination ability ($P > 0.05$), and the ROC curve indicated that the four models have certain accuracy.

This study suggested that age is a crucial independent risk factor for hypertension in overweight and obese people. This finding is similar to those of previous studies. For example, Batte (19) and others suggested that overweight, obesity, and age >40 years are statistically significant predictors of hypertension. Ahammed (20) and others also reported that age has a significant impact on hypertension. The International Society of Hypertension 2020 guidelines (2) proposed that age >40 years can predict hypertension. Therefore, age is an independent risk factor for hypertension in overweight and obese people and may be related to impaired vascular endothelial function, oxidative stress, nitric oxide deficiency, and arterial remodeling (21, 22).

This study also suggested that hyperglycemia is a crucial risk factor for hypertension which is in agreement with the results of several studies. Insulin resistance (23) and chronic low-grade inflammation that may be partially mediated by insulin resistance (24) are the risk factors for hypertension in overweight and obese people. Hyperuricemia, as suggested by this study, is another important independent risk factor for hypertension in overweight and obese people (25), although the association mechanism between them remains unclear. Studies have demonstrated (26) that every 1% increase in serum UA level increases the risk of hypertension by 13%. Hyperuricemia, as an independent risk factor for hypertension in overweight and obese people, may be closely related to chronic kidney injury (27).

Big data statistical studies on hypertension in the Chinese population, such as the discussion on the prediction model and independent risk factors for hypertension in Central China by

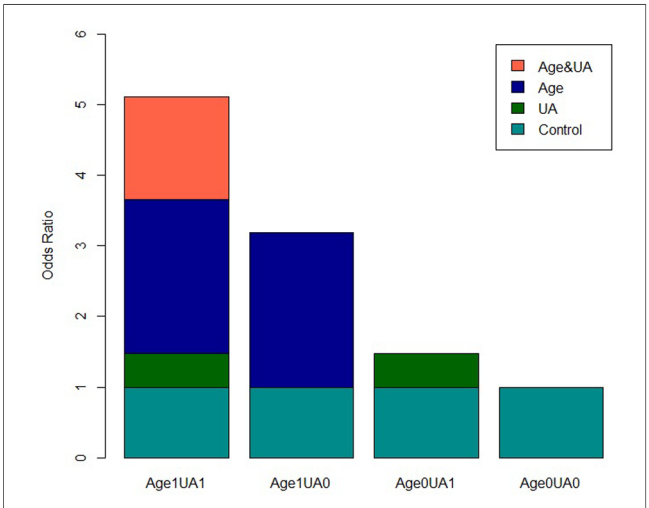

FIGURE 5
Visual analysis of single factor additive interaction of risk factors for hypertension in overweight and obese people.

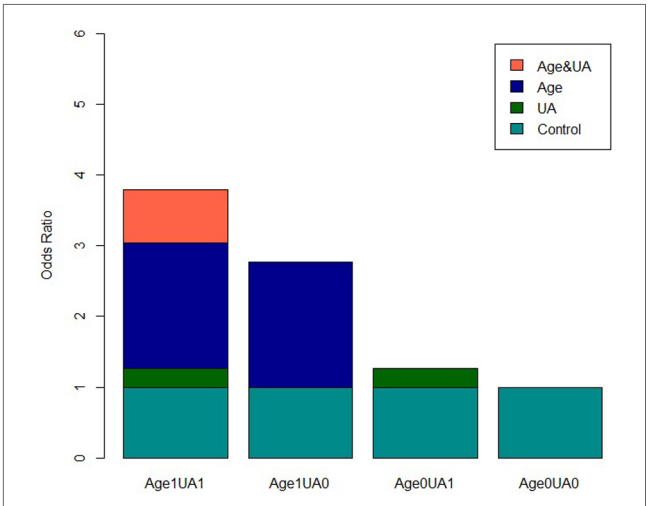

FIGURE 6
Visual analysis of multivariate additive interaction of risk factors for hypertension in overweight and obese people.

Ren et al. (28), Chen (29) and others, analyzed the population in northern China and constructed the corresponding prediction model of hypertension. These studies explored the independent risk factors but did not focus on the prevalence of hypertension in overweight and obese people and the interaction between relevant risk factors. Therefore, this study conducted multiplicative and additive interaction analyses of relevant risk factors. Both multiplicative and additive interactions were significant for patients aged ≥46 years with UA ≥ 420 μmol/L; the synergistic effect of the combination of the two risk factors has an important impact on the prevalence of hypertension in overweight and obese people. However, Kim (30) reported that the relationship between UA and hypertension often depends on age and sex. Therefore, for people aged above 46 years, it is crucial to control the level of UA for the prevention of hypertension.

Limitations

This study has limitations. Firstly, the study is a single-center research conducted on a specific group of individuals undergoing health check-ups at our institution. The sample size is not extensive, and due to the nature of health check-up participants, detailed inquiries about general aspects like sleep, diet, and mental well-being, akin to what would be done with hospitalized patients, were not included. As a result, lifestyle factors such as sleep patterns, dietary habits, and calorie intake were not considered in the study. Moreover, the study's focus on health check-up participants precluded the ability to precisely determine the duration of hypertension, overweight, and obesity. The timeframe during which these health issues were present and their duration could not be established, which is also a limitation of this research. Finally, the study is confined to a single center, lacking validation of the research findings and based solely on health check-up data from a specific region, potentially limiting its applicability to a broader population.

Future research should encompass multi-center collaborations to gather more diverse samples. Additionally, incorporating detailed inquiries about medical history and lifestyle factors, including sleep, diet, and calorie intake, alongside the examination variables like systolic and diastolic blood pressure, cholesterol, and triglycerides, would enhance the research's depth. Furthermore, validation measures are necessary to augment the study's credibility.

Conclusions

Independent risk factors for hypertension in overweight and obese people included NAFLD, FPG, age, TG, LDL-c, UA, and Cr. Among these, age + UA has a synergistic interaction, with the combined effect being four times higher than the single effect. The four models have obvious discrimination ability and certain accuracy. Therefore, older adults with hyperuricemia should monitor and control hypertension.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Ethics Committee of Guilin Medical University (approval number: GLMU1A2019064). The studies were conducted in accordance with the local legislation and institutional requirements. The human samples used in this study were acquired from primarily isolated as part of your previous study for which ethical approval was obtained. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

CSS Collected and XGQ count data and LLW writed papers. All authors contributed to the article and approved the submitted version.

Acknowledgment

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

1. Lisheng L, Zhaosu W, Jiguang W, Wen W, Yuqian B, Jun C, et al. Chinese guidelines for the prevention and treatment of hypertension, 2018 revision. *Prev Treat Cardiovasc Cerebrovasc Dis*. (2019) 19(1):1–44. doi: 10.3969/j.issn.1009-816X.2019.01.001

2. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, et al. 2020 International society of hypertension globalhypertension practice guidelines. *J Hypertens*. (2020) 38 (6):982–1004. doi: 10.1097/HJH.0000000000002453

3. Zengwu W, Guang H, Xin W, Zuo C, Linfeng Z, Min G, et al. Overweight/obesity and aggregation analysis of cardiovascular risk factors in middle-aged people in China. *Chin J Hypertens*. (2014) 22(10):1000. doi: 10.3760/cma.j.issn.0254-6450.2014.04.003

4. Baoyu F, Jichun C, Ying L, Jianfeng H, Jianxin L, Liancheng Z, et al. Follow up study on the relationship between over weight and obesity and hypertension in Chinese adults. *Chin J Epidemiol*. (2016) 37(5):606–11. doi: 10.3760/cma.j.issn.0254-6450.2016.05.004

5. Jun C, Luyuan C, Xiaoping C, Xiaoshu C, Yundai C, Wei C, et al. Chinese expert consensus on the management of obesity related hypertension. *Chin J Cardiovasc Dis*. (2016) 44(3):212–9. doi: 10.3760/cma.j.issn.0253-3758.2016.03.006

6. Zhang Y, Zhang WQ, Tang WW, Zhang WY, Liu JX, Xu RH, et al. The prevalence of obesity-related hypertension among middle-aged and older adults in China. *Front Public Health*. (2022) 10:865870. doi: 10.3389/fpubh.2022.865870

7. Wahab A, Dey AK, Bandyopadhyay D, Katikineni V, Chopra R, Vedantam KS, et al. And pulmonary hypertension: a tale of three diseases. *Curr Probl Cardiol*. (2021) 46(3):100599. doi: 10.1016/j.cpcardiol.2020.100599

8. Ostchega Y, Hughes JP, Zhang G, Nwankwo T, Graber J, Nguyen DT. Differences in hypertension prevalence and hypertension control by urbanization among adults in the United States, 2013–2018. *Am J Hypertens*. (2022) 35(1):31–41. doi: 10.1093/ajh/hpab067

9. Landsberg L, Aronne LJ, Beilin LJ, Burke V, Igel LI, Lloyd-Jones D, et al. Obesity-related hypertension: pathogenesis, cardiovascular risk, and treatment: a position paper of the obesity society and the American society of hypertension. *J Clin Hypertens (Greenwich)*. (2013) 15(1):14–33. doi: 10.1111/jch.12049

10. Jellinger PS, Handelsman Y, Rosenblit PD, Bloomgarden ZT, Fonseca VA, Garber AJ, et al. American Association of clinical endocrinologists and American college of endocrinology guidelines for management of dyslipidemia and prevention of cardiovascular disease. *Endocr Pract*. (2017) 23(Suppl 2):1–87. doi: 10.4158/EP171764.APPGL

11. Chinese Medical Association Diabetes Association. Guideline for prevention and treatment of type 2 diabetes in China (2020 edition). *Chin Diabetes J*. (2021) 13 (4):315–409. doi: 10.3760/cma.j.cn115791-20210221-00095

12. Fatty liver and alcoholic liver disease group of Hepatology branch of Chinese Medical Association, fatty liver disease expert committee of Chinese Medical Association. Guidelines for the prevention and treatment of nonalcoholic fatty liver disease (updated version in 2018). *J Pract Liver Dis*. (2018) 21(2):30–9. doi: 10.3760/cma.j.issn.1007-3418.2018.03.008

13. Chinese Medical Association, , Journal of Chinese Medical Association, General Medicine Branch of Chinese Medical Association, et al. Guidelines for primary diagnosis and treatmentof obesity (practical edition. 2019). *Chin J Gen Pract*. (2020) 19(2):102–7. doi: 10.3760/cma.j.issn.1671-7368.2020.02.003

14. Endocrinology branch of Chinese Medical Association. Chinese Guidelines for the diagnosis and treatment of hyperuricemia and gout (2019). *Chin J Endocrinol Metabolism*. (2020) 36(1):1–13. doi: 10.3760/cma.j.issn.1000-6699.2020.01.001

15. Xu M, Qiang D, Zhou Y, Shi S, Qin J, Tao Y, et al. Interaction analysis of logistic regression model using R software. *China Health Stat*. (2017) 34(4):670–5. doi: CNKI:SUN:ZGWT.0.2017-04-043

16. van Oort S, Beulens JWJ, van Ballegooijen AJ, Grobbee DE, Larsson SC. Association of cardiovascular risk factors and lifestyle behaviors with hypertension: a Mendelian randomization study. *Hypertension*. (2020) 76(6):1971–9. doi: 10.1161/HYPERTENSIONAHA.120.15761

17. Xiong XL, Ma YM, Zhou WH, Zhu DL, Xu R. Prevalence and associated risk factors of pre-hypertension and hypertension in young and middle-aged population in Nanjing. *Zhonghua Nei Ke Za Zhi*. (2021) 60(4):338–44. doi: 10.3760/cma.j.cn112138-20200817-00759

18. Rothman KJ. *Epidemiology: An introduction*. New York: Oxford University Press (2002). p. 168–80.

19. Batte A, Gyagenda JO, Otwombe K, Muhindo R, Bagasha P, Kiggundu D, et al. Prevalence and predictors of hypertension among adults in Mbarara city, Western Uganda. *Chronic Illn*. (2021) 19(1):132–45. doi: 10.1177/17423953211058408

20. Ahammed B, Maniruzzaman M, Talukder A, Ferdausi F. Prevalence and risk factors of hypertension among young adults in Albania. *High Blood Press Cardiovasc Prev*. (2021) 28(1):35–48. doi: 10.1007/s40292-020-00419-5

21. Lee JH, Kim KI, Cho MC. Current status and therapeutic considerations of hypertension in the elderly. *Korean J Intern Med*. (2019) 34(4):687–95. doi: 10.3904/kjim.2019.196

22. Xu X, Wang B, Ren C, Hu J, Greenberg DA, Chen T, et al. Age-related impairment of vascular structure and functions. *Aging Dis*. (2017) 8:590–610. doi: 10.14336/AD.2017.0430

23. Freeman AM, Acevedo LA, Pennings N. Insulin resistance. In: *Statpearls [internet]*. Treasure Island (FL): StatPearls Publishing (2021).

24. Mancusi C, Izzo R, di Gioia G, Losi MA, Barbato E, Morisco C, et al. Insulin resistance the hinge between hypertension and type 2 diabetes. *High Blood Press Cardiovasc Prev*. (2020) 27(6):515–26. doi: 10.1007/s40292-020-00408-8

25. Qian T, Sun H, Xu Q, Hou X, Hu W, Zhang G, et al. Hyperuricemia is independently associated with hypertension in men under 60 years in a general Chinese population. *J Hum Hypertens*. (2021) 35(11):1020–8. doi: 10.1038/s41371-020-00455-7

26. Borghi C, Domienik-Karłowicz J, Tykarski A, Widecka K, Filipiak KJ, Jaguszewski MJ, et al. Expert consensus for the diagnosis and treatment of patient with hyperuricemia and high cardiovascular risk: 2021 update. *Cardiol J*. (2021) 28 (1):1–14. doi: 10.5603/CJ.a2021.0001

27. Kawazoe M, Funakoshi S, Ishida S, Yoshimura C, Satoh A, Maeda T, et al. Effect of chronic kidney disease on the association between hyperuricemia and new-onset hypertension in the general Japanese population: ISSA-CKD study. *J Clin Hypertens (Greenwich)*. (2021) 23(12):2071–7. doi: 10.1111/jch.14390

28. Ren Z, Rao B, Xie S, Li A, Wang L, Cui G, et al. A novel predicted model for hypertension based on a large cross-sectional study. *Sci Rep*. (2020) 10(1):10615. doi: 10.1038/s41598-020-64980-8

29. Chen Y, Wang C, Liu Y, Yuan Z, Zhang W, Li X, et al. Incident hypertension and its prediction model in a prospective northern urban Han Chinese cohort study. *J Hum Hypertens*. (2016) 30(12):794–800. doi: 10.1038/jhh.2016.23

30. Kim W, Go TH, Kang DO, Lee J, Choi JY, Roh SY, et al. Age and sex dependent association of uric acid and incident hypertension. *Nutr Metab Cardiovasc Dis*. (2021) 31(4):1200–8. doi: 10.1016/j.numecd.2020.12.015

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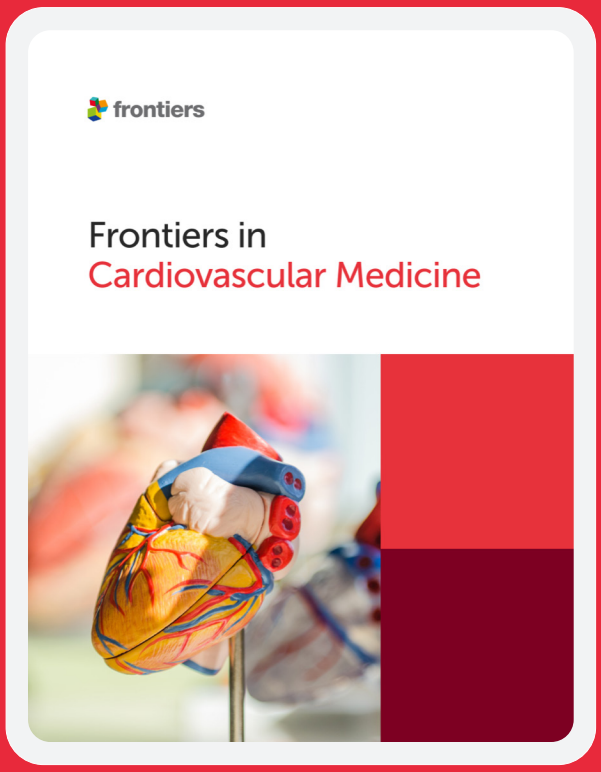

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