IJMS

Original Article

Associations between Chinese Visceral Adiposity Index and the Risk of Steatotic Liver Disease and Liver Fibrosis Related to Metabolic Dysfunction: A Large Cross-sectional Study

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Received: 18 November 2023
Revised: 11 January 2024
Accepted: 20 February 2024

Abstract

Background: The associations between Chinese visceral adiposity index (CVAI) and non-alcoholic fatty liver disease (NAFLD) or hepatic fibrosis in Westerners are not obvious. Furthermore, metabolic dysfunction-associated steatotic liver disease (MASLD) is the new nomenclature of NAFLD, with significantly different diagnostic criteria. The present study aimed to investigate the relationships between CVAI and MASLD or hepatic fibrosis in an American population, as well as to assess the diagnostic value of CVAI for MASLD and fibrosis.

Methods: After excluding missing data on calculations of indices, diagnosis of MASLD, and covariates, 3242 participants were selected from the National Health and Nutrition Examination Survey 2017-2020. Multivariate logistic regression analyses and restricted cubic spline (RCS) were used to determine the associations between CVAI and MASLD or fibrosis. The diagnostic capacity was evaluated by the area under the receiver operating characteristic (AUROC) curve. Data were analyzed using R software (version 4.2.2). $P<0.05$ was considered statistically significant.

Results: The risk of MASLD was increased at quartiles 2, 3, and 4 compared with quartile 1 of CVAI (OR [95% CI]=3.66 [2.44-5.63], 7.954 [5.31-12.23], and 14.84 [9.80-23.06], respectively), ($P<0.001$). The odds ratios (95% CI) of hepatic fibrosis risk were 1.23 [0.67, 2.30], 2.44 [1.39, 4.43], 7.46 [4.36, 13.30] for the quartiles 2, 3, and 4 compared to the lowest quartile ($P<0.001$). According to RCS, CVAI, MASLD, and fibrosis, all had positive relationships. CVAI had AUROCs of 0.759 and 0.771 for diagnosing MASLD and fibrosis, respectively.

Conclusion: The CVAI was positively related to the risk of MASLD or liver fibrosis and could be a novel biomarker for predicting MASLD and fibrosis in the American population.

Please cite this article as: Liu H, Deng M, Luo G, Chen J. Associations between Chinese Visceral Adiposity Index and the Risk of Steatotic Liver Disease and Liver Fibrosis Related to Metabolic Dysfunction: A Large Cross-sectional Study. Iran J Med Sci. doi: 10.30476/ijms.2024.100818.3335.

Keywords ● Adiposity ● Nutrition surveys ● Liver cirrhosis ● China ● Non-alcoholic fatty liver disease

What's Known

- The Chinese visceral adiposity index (CVAI), a novel biomarker of visceral obesity developed and validated principally among easterners, was found to be independently associated with non-alcoholic fatty liver disease (NAFLD) and liver fibrosis.

What's New

- It was found that CVAI was positively related to the risks of metabolic dysfunction-associated steatotic liver disease (MASLD), the new nomenclature of NAFLD, and liver fibrosis in western populations, suggesting that it could be a potential indicator for predicting MASLD and liver fibrosis in clinical practice.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the world, accounting for 25% of all cases of cirrhosis and

hepatocellular carcinoma.[1] NAFLD is expected to become the most prevalent cause of liver transplantation in Western countries by 2030.[2] Furthermore, NAFLD is significantly associated with liver-specific and overall mortality.[3] It is an increasing public health concern that poses a global challenge. However, there is presently no approved pharmacotherapy for NAFLD.[4] Hepatic fibrosis is the precursor of cirrhosis and a predictor of severe liver disease and liver-related mortality.[5] Therefore, it is essential to identify potential risk factors associated with NAFLD and liver fibrosis for the prediction, detection, and management of these diseases.

Obesity is a risk factor for a variety of metabolic diseases, such as metabolic syndrome and type 2 diabetes mellitus (T2DM), and is particularly associated with NAFLD.[2] It is worth noting that visceral fat is highly correlated with the severity of NAFLD and significantly increases risks of liver-specific and all-cause mortality in NAFLD patients.[6] Imaging examinations, including computed tomography and magnetic resonance imaging, are reliable methods for detecting abdominal adiposity, although they are expensive and involve radiation exposure. Hence, various anthropometric indicators such as waist circumference (WC), lipid accumulation product (LAP), visceral adiposity index (VAI), and Chinese visceral adiposity index (CVAI) have been used to assess abdominal obesity. Remarkably, CVAI appeared to have the strongest association with NAFLD among these abdominal adiposity indices,[7] indicating a prospective predictive value in metabolic disorders, T2DM, and NAFLD in the Chinese population.[7-9] In 2020, NAFLD was renamed metabolic dysfunction-associated fatty liver disease (MAFLD), and new diagnostic criteria were developed that are independent of alcohol intake or other concomitant liver diseases.[10] In one study, CVAI was found to be positively associated with MAFLD in Chinese adults with T2DM and may serve as an indicator for MAFLD.[11] Recently, metabolic dysfunction-associated steatotic liver disease (MASLD) has been proposed as the latest nomenclature for NAFLD in 2023.[12] Unlike MAFLD criteria, which require patients to meet two of seven metabolic disorders, MASLD is diagnosed based on one of five cardiovascular risk factors.[12] However, there is no convincing evidence of an independent relationship between CVAI and MASLD. Additionally, CVAI showed reliable screening value in the diagnosis of NALFD in Easterners, while it is indefinite whether it can be used as a predictor in Westerners. On the other hand, liver fibrosis is an important pathological manifestation of advanced chronic liver disease, particularly MASLD, and has a significant impact on the prognosis of patients with liver disease. However, there is little evidence on the relationship between CVAI and liver fibrosis.

In light of these facts, the present study attempted to determine the relationships between CVAI with MASLD and liver fibrosis in the American population and validate the effectiveness of CVAI in MASLD and fibrosis diagnoses.

Patients and Methods

Study Population

For conducting this cross-sectional study, the data were obtained from the National Health and Nutrition Examination Survey (NHANES) database between January 2017 and March 2020 (www.cdc.gov/nchs/nhanes/). The NHANES is an ongoing, national, and cross-sectional survey conducted in the United States, which collected demographic, clinical, dietary, and health-related questionnaires and examination data. The NHANES recruited a total of 15560 participants from January 2017 to March 2020. 5403 participants were excluded due to not having vibration-controlled transient elastography (VCTE) results, 386 with ineligible VCTE results due to being pregnant or having implantable electronic device, and 748 with incomplete VCTE exam (fasting time<3 hours, <10 valid liver stiffness measurements, or median (M/[IQR] interquartile range>30% stiffness), resulting in a population of 9023. Of them, 5325 participants were excluded due to unavailable information on the calculation of CVAI and diagnosis of MASLD. Participants with missing data on aspartate aminotransferase (AST), smoking, alcohol consumption, physical activity, or statin use were also excluded. Finally, 3242 American patients were included in our analysis (figure 1).

The Institutional Ethics Review Board of the National Center for Health Statistics (NCHS) approved the survey protocol (Protocol#2018-01). Moreover, each participant provided written informed consent before participating in the study.

Sociodemographic, Laboratory, and Clinical Data

In the NHANES database, demographic information including age, sex, race, smoking status, alcohol consumption, physical activity, and history of medication was gathered through household interviews using an interviewer-administered questionnaire. Participants underwent anthropometric and laboratory evaluations using a Mobile Examination Center (MEC).

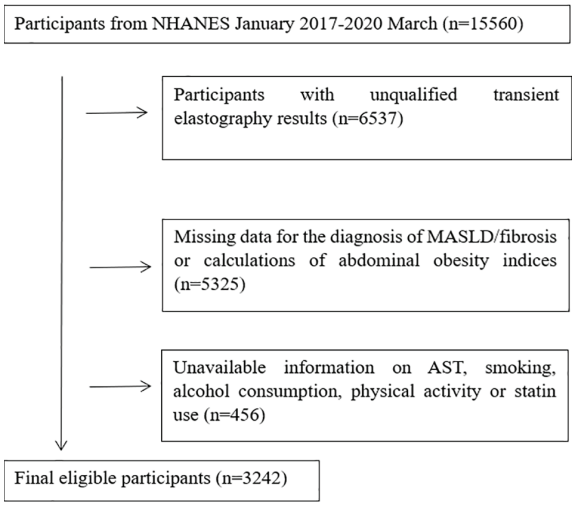

Figure 1: The flowchart indicates the participants of the study.

The website (https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Laboratory&Cycle=2017-2020) provided information about the measuring procedure. Anthropometric data, such as height (cm), weight (Kg), and WC (cm) were extracted. In addition, laboratory data including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transpeptidase (GGT), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), hemoglobin A1c (HbA1c), fasting plasma glucose (FPG) were extracted for this study.

Body mass index (BMI) was calculated by dividing the weight (Kg) by height in (m) squared. The smoking status was determined using the self-report questionnaire. Alcohol abuse was defined as consumption of ≥30 g/day in men and ≥20 g/day in women.[13] Participants who engaged in moderate/vigorous job or recreational activities were categorized as having had physical activity.[13] Hypertension was defined as a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg, as reported by a health practitioner, or current use of anti-hypertensive medications.[14] Diabetes mellitus can be diagnosed in the following conditions: 1) reported by a health professional, 2) utilizing anti-diabetic medications, 3) HbA1c (%)>6.5; 4) FPG (mmol/L) ≥7.0 mmol/L, 5) random blood glucose (mmol/L) ≥11.1 mmol/L.[15] Viral hepatitis was defined as the presence of hepatitis B virus surface antigen (HBsAg) and hepatitis C virus (HCV) RNA or antibodies.

The calculations of LAP, VAI, and CVAI were consistent with the previously reported formula.[7]

For men:

LAP=[WC (cm)-65]×TG (mmol/L)

VAI=WC (cm)÷[39.68+1.88×BMI (Kg/m^2)]×[TG (mmol/L)÷1.03]×[1.31÷HDL (mmol/L)]

CVAI=-267.93+0.68×age (year)+0.03×BMI (Kg/m^2)+4.00×WC (cm)+22.00×LgTG (mmol/L)-16.32×HDL (mmol/L)

For women:

LAP=[WC (cm)-58]×TG (mmol/L)

VAI=WC (cm)÷[36.58+1.89×BMI (Kg/m2)]×[TG (mmol/L)÷0.81]×[1.52÷HDL (mmol/L)]

CVAI=-187.32+1.71×age (year)+4.32×BMI (Kg/m^2)+1.12×WC (cm)+39.76×LgTG (mmol/L)-11.66×HDL (mmol/L)

Definition of MASLD and Significant Fibrosis

VCTE is a well-studied method with high diagnostic accuracy for evaluating steatosis and fibrosis in large populations.[16] The elastography measurements were obtained in the NHANES MEC, using the FibroScan® (model 502 V2 Touch) equipped with a medium or extra-large wand (probe). Examinations were considered reliable only when measures, taken after a fasting period of at least three hours, proved valid for 10 times, and each valid measure exhibited an interquartile IQR/M <30%. Previous studies defined liver steatosis as a median Controlled Attenuation Parameter (CAP) ≥274 dB/m and severe liver fibrosis as a median Liver Stiffness Measurement (LSM) ≥8.0 KPa.[17, 18] MASLD was defined as steatosis along with one of the five cardiovascular risk factors, and no other discernible reason, such as excessive drinking, viral hepatitis, or steatogenic pharmaceutical use (amiodarone, valproate, methotrexate, tamoxifen, and corticosteroid).[12]

Statistical Analysis

Continuous variables were expressed as median (interquartile range), and categorical variables were presented as frequency (percentages). To compare characteristics between groups, the Kruskal-Wallis test was used for continuous variables, and the Chi square test was used for categorical variables. Logistic regression analysis was used to investigate the associations between CVAI and MASLD or liver fibrosis. Model 1 was a crude model with no adjusted variable. Model 2 was adjusted for covariables including age, sex, race, HbA1c, FPG, ALT, AST, GGT, and TC. In Model 3, covariables were further adjusted for smoking status, alcohol abuse, physical activity, statin use, hypertension, and diabetes. Moreover, the restricted cubic spline (RCS) was used to investigate the relationships between CVAI, MASLD, and fibrosis on a continuous scale. We used the area under the receiver operating characteristic (AUROC) curve to evaluate the predictive performances of abdominal indices. The DeLong test was utilized

to compare AUROCs. The optimal cut-offs were selected according to the highest Youden index. All analyses were conducted using R software, version 4.2.2 (R Development Core Team, New Zealand). P≤0.05 indicated statistical significance.

Results

Characteristics of the Participants

A total of 3242 participants were enrolled in this study for final analysis (figure 1). In the US population, 825 participants were diagnosed

Table 1: Characteristics of enrolled participants according to CVAI in the US population

Characteristics	Q1 (<87.21) n=811	Q2 (87.21-135.681) n 810	Q3 (135.681-181.014) n=810	Q4 (>181.014) n=811	P value
Chinese visceral adiposity index					
Age (years)	31.00 [23.00, 44.00]	51.00 [37.00, 61.00]	56.00 [42.00, 66.00]	60.00 [45.00, 69.00]	<0.001
Sex, n (%)					<0.001
Male	315 (38.8%)	360 (44.4%)	420 (51.9%)	514 (63.4%)	
Female	496 (38.4%)	450 (55.6%)	390 (48.1%)	297 (36.6%)	
Race, n (%)					<0.001
Mexican American	85 (10.5%)	122 (15.1%)	120 (14.8%)	107 (13.2%)	
Other Hispanic	64 (7.9%)	96 (11.9%)	101 (12.5%)	72 (8.9%)	
Non-Hispanic White	248 (30.6%)	246 (30.4%)	287 (35.4%)	351 (43.3%)	
Non-Hispanic Black	222 (27.4%)	180 (22.2%)	189 (23.3%)	218 (26.9%)	
Other Race	192 (23.7%)	166 (20.5%)	113 (14.0%)	63 (7.8%)	
Smoking status, n (%)					<0.001
Never	541 (66.7%)	513 (63.3%)	464 (57.3%)	378 (46.6%)	
Former	117 (14.4%)	150 (18.5%)	212 (26.2%)	296 (36.5%)	
Current	153 (18.9%)	147 (18.1%)	134 (16.5%)	137 (16.9%)	
Alcohol abuse, n (%)	99 (12.2%)	117 (14.4%)	100 (12.3%)	72 (8.9%)	0.01
Physical activity, n (%)	636 (78.4%)	586 (72.3%)	568 (70.1%)	548 (67.6%)	<0.001
Diabetes, n (%)	30 (3.7%)	104 (12.8%)	195 (24.1%)	349 (43.0%)	<0.001
Hypertension, n (%)	89 (11.0%)	254 (31.4%)	376 (46.4%)	460 (56.7%)	<0.001
Viral hepatitis, n (%)	19 (2.3%)	33 (4.1%)	17 (2.1%)	20 (2.5%)	0.06
Statin use, n (%)	30 (3.7%)	147 (18.1%)	214 (26.4%)	297 (36.6%)	<0.001
BMI (Kg/m^2)	22.60 [20.70, 24.95]	26.80 [24.70, 29.30]	30.00 [27.60, 33.00]	35.90 [32.40, 41.30]	<0.001
WC (cm)	80.50 [75.25, 85.80]	93.65 [89.50, 97.50]	103.15 [99.00, 108.00]	118.30 [112.20, 127.00]	<0.001
ALT (IU/L)	14.00 [11.00, 19.00]	18.00 [13.00, 25.00]	19.00 [14.00, 27.00]	21.00 [15.00, 31.00]	<0.001
AST (IU/L)	18.00 [15.00, 22.00]	19.00 [16.00, 24.00]	19.00 [16.00, 24.00]	19.00 [16.00, 25.00]	<0.001
GGT (IU/L)	15.00 [11.00, 21.00]	20.00 [14.00, 30.00]	24.00 [17.00, 33.00]	25.00 [18.00, 40.00]	<0.001
TC (mmol/L)	4.42 [3.84, 5.07]	4.84 [4.19, 5.56]	4.84 [4.16, 5.59]	4.55 [3.93, 5.25]	<0.001
TG (mmol/L)	0.66 [0.48, 0.88]	0.98 [0.69, 1.42]	1.14 [0.82, 1.68]	1.34 [0.96, 1.86]	<0.001
HDL (mmol/L)	1.53 [1.32, 1.81]	1.37 [1.14, 1.66]	1.27 [1.06, 1.47]	1.11 [0.98, 1.32]	<0.001
HbA1c (%)	5.30 [5.10, 5.50]	5.50 [5.30, 5.80]	5.60 [5.40, 6.00]	5.90 [5.50, 6.70]	<0.001
FPG (mmol/L)	5.33 [5.05, 5.61]	5.61 [5.27, 6.10]	5.83 [5.44, 6.49]	6.27 [5.72, 7.33]	<0.001
VAI	0.67 [0.45, 0.99]	1.19 [0.74, 1.93]	1.50 [1.00, 2.51]	1.93 [1.25, 3.02]	<0.001
LAP	12.50 [7.79, 19.33]	32.27 [22.22, 45.16]	48.50 [34.64, 69.50]	77.66 [54.32, 108.29]	<0.001
MAFLD, n (%)	33 (4.1%)	138 (17.0%)	262 (32.3%)	392 (48.3%)	<0.001
Liver fibrosis, n (%)	23 (2.8%)	33 (4.1%)	64 (7.9%)	196 (24.2%)	<0.001

The Kruskal-Wallis test was used to compare continuous data between subject groups, and the Chi square test was used for categorical variables. A P value of less than 0.05 was considered statistically significant. BMI: Body mass index; WC: Waist circumference; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyltranspeptidase; TC: Total cholesterol; TG: Triglyceride; HDL: High-density lipoprotein; HbA1c: Hemoglobin A1c; FPG: Fasting plasma glucose; VAI: Visceral adiposity index; LAP: Lipid accumulation product; MASLD: Metabolic dysfunction-associated steatotic liver disease

with MASLD, and 316 participants had hepatic fibrosis. The baseline characteristics of participants according to the quartiles of CVAI are shown in table 1. Individuals with high CVAI values were older, had less frequent physical activity, higher prevalence of hypertension, and diabetes, as well as had higher BMI, WC, ALT, AST, GGT, TC, TG, HbA1c, FPG, LAP, VAI, and CVAI while lower HDL than the group of people having low values of CVAI. The proportions of MASLD and liver fibrosis were significantly higher in the groups with higher CVAI.

Association between CVAI and MASLD

Multivariate logistic regression models were performed to investigate the relationship between CVAI and MASLD diagnosed by VCTE (table 2). After adjusting for age, sex, race, HbA1c, FPG, ALT, AST, GGT, TC, smoking status, alcohol overuse, physical activity, statin use, hypertension, and diabetes in model 3, High CVAI values (Q2-Q4 groups) had a significant positive association with MASLD compared to the Q1 reference group (odds ratio (OR)=3.66, 95% Confidence interval (CI)=2.44-5.63 for Q2, OR=7.95, 95% CI=5.31-12.23 for Q3 and OR=14.84, 95% CI=9.80-23.06 for Q4, P<0.001). Furthermore, the multivariable-adjusted spline model revealed a monotonically increasing correlation between CVAI and the risk of MASLD (figure 2A).

Association between CVAI and Liver Fibrosis

Hepatic fibrosis represents the prognosis of chronic liver disease. Logistic regression analyses were also executed to investigate the association between CVAI and significant fibrosis diagnosed by VCTE in the NHANES group (table 2).

Table 2: The associations between CVAI with MASLD and liver fibrosis

CVAI	Model 1	Model 2	Model 3
	OR (95% CI)	OR (95% CI)	OR (95% CI)
The association between CVAI and MASLD			
Q1 (<87.21)	Reference	Reference	Reference
Q2 (87.21-135.68)	4.24 (2.86, 6.44)	3.62 (2.42, 5.55)	3.66 (2.44, 5.63)
Q3 (135.68-181.01)	10.08 (6.87, 15.22)	7.80 (5.25, 11.92)	7.95 (5.31, 12.23)
Q4 (>181.01)	20.69 (14.04, 31.40)	14.76 (9.85, 22.73)	14.84 (9.80, 23.06)
P value	<0.001	<0.001	<0.001
The association between CVAI and fibrosis			
Q1 (<87.21)	Reference	Reference	Reference
Q2 (87.21-135.68)	1.32 (0.76, 2.33)	1.25 (0.68, 2.31)	1.23 (0.67, 2.30)
Q3 (135.68-181.01)	2.60 (1.58, 4.42)	2.63 (1.51, 4.72)	2.44 (1.39, 4.43)
Q4 (>181.01)	9.52 (5.98, 15.80)	8.49 (5.02, 14.98)	7.46 (4.36, 13.30)
P value	<0.001	<0.001	<0.001

Logistic regression analysis was performed to explore the associations between CVAI and MASLD or liver fibrosis. P<0.05 was considered statistically significant. Model 1: No covariates were adjusted. Model 2: Age, sex, race, HbA1c, FPG, ALT, AST, GGT and TC were adjusted. Model 3: Age, sex, race, SBP, DBP, HbA1c, FPG, ALT, AST, GGT, TC, smoking status, excessive alcohol consumption, physical activity, statin use, hypertension, and diabetes were adjusted. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyl transpeptidase; TC: Total cholesterol; HbA1c: Hemoglobin A1c; FPG: Fasting plasma glucose; CVAI: Chinese visceral adiposity index; MASLD: Metabolic-associated fatty liver disease

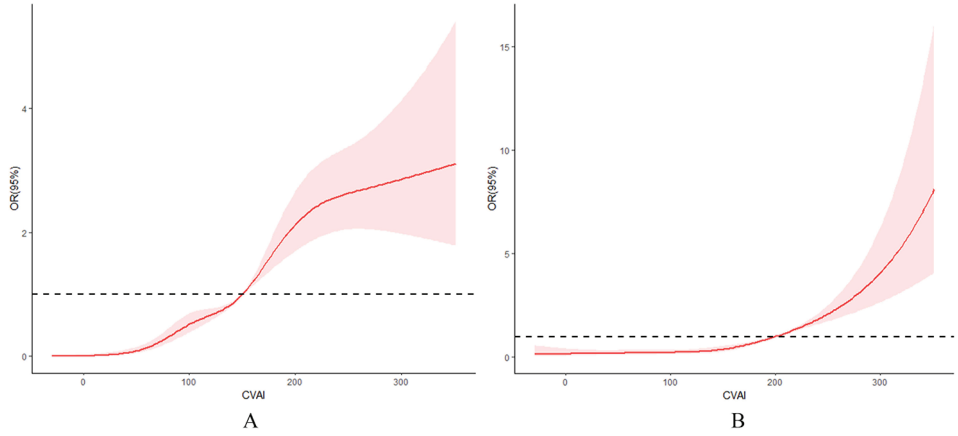

Figure 2: The associations between CVAI and (A) metabolic dysfunction-associated steatotic liver disease and (B) liver fibrosis on a continuous scale are shown. Solid lines represent odds ratios (OR), and the shade area represents 95% confidence intervals (CI). The model was adjusted for age, sex, race, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transpeptidase, total cholesterol, triglyceride, hemoglobin A1c, fasting plasma glucose, smoking status, alcohol overuse, physical activity, statin use, hypertension, and diabetes.

In all models, high CVAI had a significantly positive association with fibrosis. The association between high CVAI (Q3 and Q4 groups) and hepatic fibrosis was still significant (OR=2.44, 95% CI=1.39-4.43 for Q3 group and OR=7.46, 95% CI=4.36-13.30 for Q4 group, respectively, P<0.001) after further adjustment for age, sex, race, HbA1c, FPG, ALT, AST, GGT, TC, smoking status, excessive alcohol consumption, physical activity, statin use, hypertension, and diabetes in model 3. Moreover, a monotonically increasing association was found between CVAI and hepatic fibrosis (figure 2B).

Diagnostic Ability of CVAI for MASLD

The AUROC values together with the optimal cut-offs and ROC curves of abdominal obesity indices were displayed in table 3 and figure 3A. The CVAI showed a valuable diagnostic role for MASLD in the US general population, with the AUROCs of 0.759 (95% CI=0.742-0.777), which was significantly higher than WC (OR=0.729, 95% CI=0.711-0.748), LAP (OR=0.739, 95% CI=0.721-0.757), and VAI (OR=0.739, 95% CI=0.721-0.757). The optimal CVAI cut-off for diagnosing MASLD was 136.654, with a

Table 3: Diagnostic performances of CVAI for MASLD

Index	AUROC 95% CI	AUROC difference	Cut-off	SEN	SPC	Youden index
Diagnostic ability for MASLD in the general population						
CVAI	0.759 (0.742, 0.777)	Reference	136.654	0.790	0.608	0.398
WC	0.729 (0.711, 0.748)	<0.001	99.550	0.742	0.611	0.353
LAP	0.739 (0.721, 0.757)	0.01	37.263	0.785	0.585	0.370
VAI	0.739 (0.721, 0.757)	<0.001	1.549	0.625	0.689	0.314
Diagnostic ability for MASLD in non-obese population (BMI≤25)						
CVAI	0.840 (0.803, 0.876)	Reference	70.877	0.951	0.642	0.593
WC	0.764 (0.712, 0.815)	<0.001	82.650	0.869	0.587	0.456
LAP	0.823 (0.771, 0.875)	0.41	21.316	0.787	0.716	0.503
VAI	0.775 (0.705, 0.845)	0.03	1.441	0.656	0.822	0.478
Diagnostic ability for MASLD in the obese population (BMI>25)						
CVAI	0.688 (0.666, 0.711)	Reference	154.898	0.715	0.569	0.284
WC	0.649 (0.626, 0.672)	<0.001	103.550	0.685	0.545	0.249
LAP	0.660 (0.637, 0.683)	0.01	47.098	0.685	0.564	0.249
VAI	0.637 (0.614, 0.661)	<0.001	1.549	0.628	0.607	0.235
Diagnostic ability for MASLD in females						
CVAI	0.760 (0.736, 0.785)	Reference	133.828	0.734	0.664	0.398
WC	0.717 (0.690, 0.744)	<0.001	99.450	0.713	0.624	0.338
LAP	0.739 (0.712, 0.765)	0.03	37.250	0.804	0.576	0.380
VAI	0.704 (0.675, 0.733)	<0.001	1.550	0.674	0.662	0.336
The diagnostic ability for MASLD in males						
CVAI	0.758 (0.734, 0.783)	Reference	136.872	0.853	0.532	0.385
WC	0.741 (0.716, 0.767)	<0.001	102.950	0.697	0.676	0.373
LAP	0.741 (0.716, 0.766)	0.10	38.540	0.756	0.613	0.369
VAI	0.691 (0.663, 0.719)	<0.001	1.446	0.622	0.686	0.308

AUROC: Area under the receiver operating characteristic curve; SEN: Sensitivity; SPE: Specificity; WC: Waist circumference; LAP: Lipid accumulation product; VAI: Visceral adiposity index; CVAI: Chinese visceral adiposity index; MASLD: Metabolic dysfunction-associated steatotic liver disease

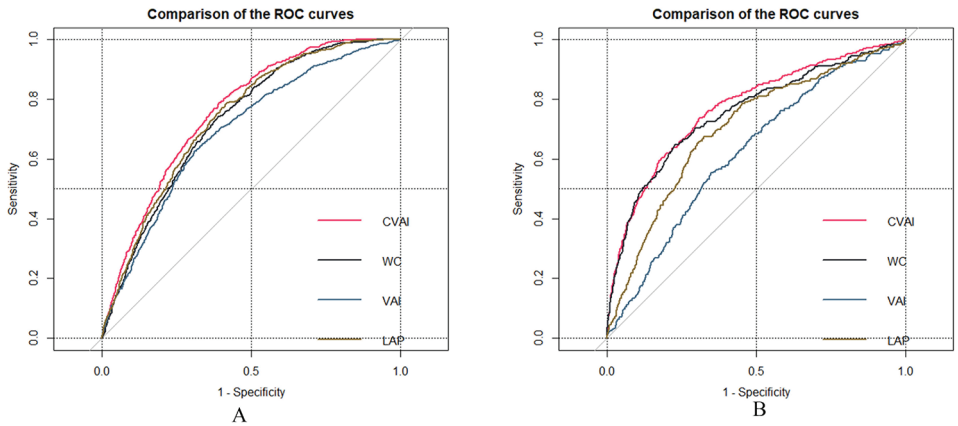

Figure 3: The receiver operating characteristic curves of abdominal obesity indices for (A) metabolic dysfunction-associated steatotic liver disease and (B) liver fibrosis are shown.

Table 4: Diagnostic performances of CVAI for fibrosis

Index	AUROC 95% CI	AUROC difference	Cut-off	SEN	SPC	Youden index
Diagnostic ability for liver fibrosis in the general population						
CVAI	0.771 (0.742, 0.800)	Reference	160.717	0.737	0.691	0.428
WC	0.754 (0.723, 0.785)	<0.001	109.650	0.649	0.773	0.422
LAP	0.701 (0.670, 0.731)	<0.001	53.062	0.658	0.693	0.351
VAI	0.621 (0.590, 0.652)	<0.001	1.613	0.554	0.651	0.205
Diagnostic ability for liver fibrosis in the non-obese population (BMI≤25)						
CVAI	0.625 (0.535, 0.715)	Reference	65.134	0.659	0.573	0.232
WC	0.585 (0.484, 0.686)	0.13	88.950	0.366	0.832	0.198
LAP	0.541 (0.439, 0.642)	<0.001	31.124	0.293	0.830	0.123
VAI	0.540 (0.446, 00.633)	0.01	0.881	0.561	0.580	0.141
Diagnostic ability for liver fibrosis in obese population (BMI>25)						
CVAI	0.787 (0.759, 0.815)	Reference	188.629	0.684	0.755	0.439
WC	0.771 (0.740, 0.801)	0.02	109.650	0.745	0.684	0.429
LAP	0.692 (0.660, 0.723)	<0.001	53.062	0.738	0.593	0.331
VAI	0.771 (0.740, 0.801)	<0.001	1.612	0.611	0.578	0.189
Diagnostic ability for liver fibrosis in females						
CVAI	0.826 (0.791, 0.860)	Reference	155.218	0.791	0.743	0.534
WC	0.799 (0.757, 0.840)	0.01	109.650	0.713	0.776	0.489
LAP	0.759 (0.721, 0.796)	<0.001	41.962	0.884	0.567	0.451
VAI	0.675 (0.632, 0.717)	<0.001	1.625	0.674	0.631	0.305
Diagnostic ability for liver fibrosis in males						
CVAI	0.727 (0.683, 0.771)	Reference	190.256	0.626	0.769	0.395
WC	0.719 (0.675, 0.764)	0.05	110.950	0.588	0.793	0.381
LAP	0.661 (0.617, 0.705)	<0.001	53.062	0.599	0.700	0.299
VAI	0.591 (0.548, 0.634)	<0.001	1.155	0.642	0.513	0.155

AUROC: Area under the receiver operating characteristic curve; SEN: Sensitivity; SPE: Specificity; WC: Waist circumference; LAP: Lipid accumulation product; VAI: Visceral adiposity index; CVAI: Chinese visceral adiposity index; MASLD: Metabolic dysfunction-associated steatotic liver disease

sensitivity of 0.608 and a specificity of 0.790. The diagnostic performance was further evaluated in several subgroups divided by BMI and sex. The CVAI had the highest AUROC value in all subgroups compared to WC, LAP, and VAI (table 3).

Diagnostic Ability of CVAI for Liver Fibrosis

The CVAI also showed significantly higher AUROC value (OR=0.771, 95% CI=0.742-0.800) in hepatic fibrosis detection than those of WC (OR=0.754, 95% CI=0.723-0.785), LAP (OR=0.701, 95% CI=0.670-0.731), and VAI (OR=0.621, 95% CI=0.590-0.652). The best cut-off values of CVAI, WC, LAP, and VAI were 160.717 (sensitivity 0.737, specificity 0.691), 109.650 (sensitivity 0.649, specificity 0.773), 53.062 (sensitivity 0.658, specificity 0.693), and 1.613 (sensitivity 0.554, specificity 0.651), respectively. In the subgroup analyses, the CVAI outperformed WC, LAP, and VAI in fibrosis diagnosis, with the highest values of AUROC (table 4 and figure 3B).

Discussion

In this large-scale cross-sectional study, the associations between CVAI and MASLD or hepatic fibrosis among Americans were investigated. There were significant positive correlations between CVAI and the probability of MASLD and hepatic fibrosis. The ROC curves indicated that CVAI had a satisfactory performance for screening MASLD and liver fibrosis. Therefore, CVAI might serve as a biomarker for both MASLD and liver fibrosis with diagnostic value in the American population.

The CVAI is a novel index based on age, BMI, WC, TG, and HDL, which reflects the amount of visceral fat. Previous investigations on NAFLD and chronic hepatitis C reported an association between visceral obesity and liver damage, including steatosis and disease progression.[19-21] Excessive accumulation of visceral adipose tissue was associated with chronic systemic inflammation and was related to increased hepatic inflammation and fibrosis.[22, 23] Visceral adipose tissue could lead to the release of free fatty acids, secretion of adipokines, and infiltration of immune cells, which in turn could trigger lipotoxicity, promote the production of proinflammatory mediators, and drive insulin resistance and metabolic disorders, and ultimately contribute to the

stimulation of inflammation, tissue regeneration, and fibrogenesis.[1, 6, 24] Furthermore, the positive associations between CVAI and obesity-related metabolic diseases were reported.[7, 9, 25, 26]

The findings of the present study were consistent with a recent study by Zhao and others, who enrolled 24191 Chinese participants and found that CVAI was independently associated with the risk of MASLD.[27] However, several differences existed between the findings of this study and those of the present study, including ethnicity and the diagnostic criteria of MASLD. The assessment of MASLD was based on the MAFLD standards proposed by Zhao and colleagues in 2020.[27] In fact, MASLD is the latest nomenclature of NAFLD, with significantly different diagnostic criteria compared to MAFLD. MAFLD might identify more patients because its definition is independent of excessive alcohol consumption and viral hepatitis.[28] A previous study also reported that CVAI was significantly related to NAFLD prevalence and had the highest diagnostic value for NAFLD compared to WC, VAI, and LAP.[7] Similar findings were found in this study when MASLD, the new term of NAFLD, was adopted. Moreover, an independent relationship between CVAI and NAFLD was revealed in specific populations, such as early postmenopausal women, lean adults, and T2DM patients.[11, 29, 30] On the other hand, hepatic fibrosis has been repeatedly shown to be the histological alteration with the highest prognostic significance in a range of chronic liver diseases, including NAFLD. Studies on the relationship between CVAI and liver fibrosis are inadequate. One recent research based on 147 biopsy-confirmed NAFLD patients provided evidence for an independent relationship between CVAI and liver fibrosis. However, the study group seemed insufficient and lacked a healthy control population.[31] All these studies were conducted in Asian populations. CVAI is a novel visceral obesity biomarker established based on Chinese data and validated primarily among Chinese. Furthermore, different ethnic groups had different body fat characteristics, and there were associations between strong ethnic heterogeneity in anthropometric measures and NAFLD.[32, 33] Therefore, the correlations between CVAI and MASLD or liver fibrosis are worth further exploring among various ethnic populations living in different regions. The consistency of the results in Caucasians strengthened the hypothesis of positive relationships between CVAI and MASLD or hepatic fibrosis. However, the findings of the present study were different from certain previous investigations.[29-31] Significant heterogeneity existed across different analyses because of the diagnostic criteria (NAFLD, MAFLD, or MASLD), subjects being investigated (T2DM patients, lean individuals, or general population), ethnicity (Asian or Caucasian), and the study design (prospective or cross-sectional). Further subgroup analyses were performed to test the robustness of the findings. It is worth mentioning that CVAI seemed to outperform other traditional obesity indices in predicting both MASLD and fibrosis among the different subgroups. The reason might be that traditional obesity indices such as WC were more strongly associated with subcutaneous fat than visceral adipose tissue. However, CVAI was a reliable surrogate biomarker of visceral obesity.[34] According to the results of the present study, the CVAI, a novel index established and validated primarily among eastern populations, indicated promising predictive value in western populations, ensuring the generalizability and inclusiveness of CVAI.

There are some limitations that need to be noted. First, fatty liver and hepatic fibrosis were diagnosed by VCTE in NHANES rather than a liver biopsy. However, VCTE was a well-validated method in diagnosing steatosis and fibrosis, with high sensitivity and specificity.[35, 36] Second, this cross-sectional design could not determine the causal relationships between CVAI and MASLD or fibrosis, which required further investigation in prospective studies.

Conclusion

This study was the first study that investigated the correlations between CVAI, MASLD, and fibrosis in the general US population with the largest sample size. CVAI was positively associated with MASLD and liver fibrosis. The CVAI had a satisfactory ability to distinguish MASLD and fibrosis and might be a novel indicator for identifying MASLD and liver fibrosis patients in clinical practice.

Authors' Contribution

H.L, M.D, G.L, and J.C conceived and designed the study; performed the analysis; and wrote and reviewed the manuscript. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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