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Weight-adjusted waist circumference index with hepatic steatosis and fibrosis in adult females: a cross-sectional, nationally representative study (NHANES 2017–2020)

Yu-E Lian[1†], Yixuan Wang[1†], Yinyin Yang[2] and Jiayu Chen[1*]

Abstract

Background Obesity is detrimental to liver health. Weight-adjusted waist circumference (WWI) is a new indicator of obesity that is superior to body mass index (BMI) and waist circumference (WC) in predicting obesity. There are limited studies on the relationship between Metabolic Associated Fatty Liver Disease (MASLD) and WWI. Therefore, this study aimed to investigate the association between WWI, Controlled Attenuation Parameters (CAP), and Liver Stiffness Measurement (LSM), with special attention to gender differences.

Methods This cross-sectional study included participants from the 2017 to 2020 National Health and Nutrition Examination Survey (NHANES). The study used multiple linear regression models, smoothed curves, and threshold effects analyses to describe the relationships between variables. Multiple regression analyses were used to examine the associations between the four obesity indicators and CAP and LSM. Subject work characteristics (ROC) curves were used to assess the predictive value of WWI and other traditional obesity indicators for hepatic steatosis and liver fibrosis, and predictive power was assessed by area under the curve (AUC).

Results The study involved 6713 participants, including 3072 men (46%) and 3641 women (54%). The results showed that among female participants, higher WWI was associated with hepatic steatosis (OR = 1.71, 95% CI: 1.43, 2.04; $P < 0.0001$) and hepatic fibrosis (OR = 2.11, 95% CI: 1.58, 2.84; $P < 0.0001$). Smoothed curve fitting of WWI versus CAP showed a statistically significant positive correlation between WWI in male and female participants There was a statistically significant positive correlation with CAP for both male and female participants. The same significant non-linear relationship was found between WWI and LSM, with no significant difference between males and females. WWI was also a good predictor of hepatic steatosis compared to other obesity indicators and was more pronounced in male participants (AUC = 0.8224). Whereas in the comparison of WWI with LSM, wBMI was a better predictor in female participants (AUC = 0.7751).

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Conclusions Based on this study, WWI was significantly associated with the risk of hepatic steatosis and hepatic fibrosis in women, suggesting the potential of WWI as a screening tool. Due to the cross-sectional design, causality cannot be inferred. Longitudinal studies are needed to validate our findings.

Keywords Weight-adjusted waist circumference, Metabolic associated fatty liver disease, Cross-sectional study, NHANES

Background

Non-alcoholic cirrhosis (NAFLD) is a chronic liver disease in which large amounts of fatty substances accumulate in hepatocytes due to abnormalities in the functioning of fat metabolism. It is the most common chronic liver disease in clinical practice [1]. It is strongly associated with an elevated risk of developing type 2 diabetes, hypertension, cardiovascular disease, and chronic kidney disease [2, 3]. In 2020, an international panel of experts proposed renaming NAFLD as In 2020, an international panel of experts proposed renaming NAFLD as Metabolic Associated Fatty Liver Disease (MASLD) [4] Statistically, MASLD has become a global health problem affecting approximately 30% of the world's population as the number of patients with obesity and metabolic syndrome continues to increase [5, 6]. Patients with MASLD are often associated with a variety of metabolic comorbidities including hyperglycaemia, hyperuricemia, and hyperlipidaemia, which are high-risk factors for type 2 diabetes mellitus and the development of cardiovascular and cerebrovascular diseases [7]. In conclusion, the management of MASLD remains suboptimal.

Body mass index (BMI) is the simplest and most commonly used measure of obesity in humans. A recent study found that BMI is mainly limited to assessing obesity (fat mass), whereas the degree of abdominal obesity is a better indicator of an individual's health and mortality risk [8]. Therefore, waist circumference (WC) has been proposed to indicate metabolic obesity [9]. In 2018 [10], researchers proposed and used WWI to measure central obesity in humans. In recent years, WWI has been found to be strongly associated with abdominal aortic calcification, development of hypertension, and cardiovascular mortality [11–13].

However, there is a paucity of research on the relationship between WWI and MASLD, and only a few researchers have examined the predictive value of waist circumference as well as other body measurements for hepatic steatosis [14, 15]; therefore, the present study utilised the National Health and Nutrition Examination Survey (NHANES) to explore the relationship between WWI and hepatic steatosis and hepatic fibrosis in the US adult population.

Materials and methods

Survey description

Health examination information from a countrywide representative sample of noninstitutionalised U.S. citizens and civilian populations was gathered from the National Health and Nutrition Examination Survey (NHANES) sample using a complicated, multistage sampling design [16].

The NCHS Research Ethics Review Board approved all NHANES study protocols and written informed consent was obtained from all survey participants. This investigation, was performed using the NHANES data, which covered the years 2017 to 2020 [17–20].

Study population

The study population was drawn from NHANES 2017 to 2020. Figure 1 illustrates the process of including and excluding participants. A total of 15,560 participants were enrolled in this study, while those younger than 18 years of age ($n = 5,867$), those with missing data on waist circumference and body weight ($n = 1,249$), those with alcoholism, hepatitis B or C virus infection ($n = 1,163$), those with missing data on vibration-controlled transient elastography (VCTE) ($n = 387$), and those with liver stiffness quartiles ≥ 30% ($n = 181$) were excluded. Ultimately, 6713 eligible participants were included in the final analysis.

Calculation of WWI

WC and body weight for obesity were predicted using WWI. WWI positively correlated with obesity [10]. In mobile examination centres, technically proficient health personnel gather anthropometric data on weight and waist circumference [21]. For subsequent analyses, participants were categorised according to WWI quartiles, considering WWI as a continuous variable. The exposure variable in our study was WWI: WWI (cm/√kg) is computed by dividing WC (cm) by the square root of body weight (kg).

Other indicators of obesity

The obesity indicators included in this study include waist-BMI ratio (wBMI) (Eq. 1), body mass index (BMI) (Eq. 2), and waist-to-height ratio (WHtR) (Eq. 3) These obesity indicators were determined based on the body measurements screening programme. The formulae for these indicators are as follows [22].

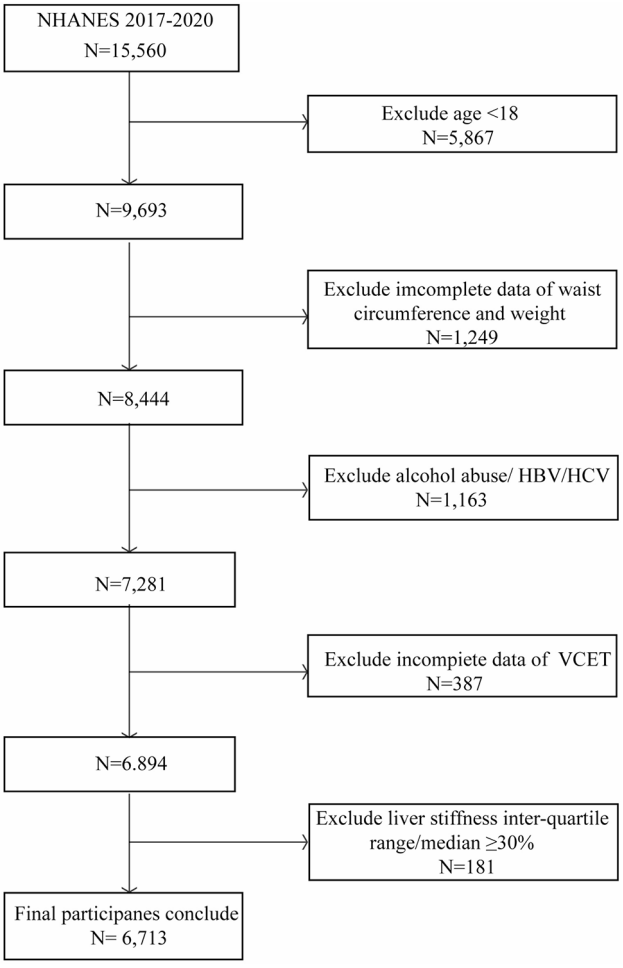

Fig. 1 Chart for the selection of NHANES samples from 2017 to 2020

$$wBMI = \mathrm{W}C\,(m) * BMI \tag{1}$$

$$BMI = \frac{\mathrm{W}eight\,(kg)}{\mathrm{H}eight(m)^2} \tag{2}$$

$$WHtR = \frac{WC\,(cm)}{Height\,(cm)} \tag{3}$$

Measurement of hepatic steatosis and hepatic fibrosis

The primary objective of NHANES Ultrasound Transient Elastography of the Liver is to provide objective measurements of liver disease manifestations, hepatic fibrosis, and steatosis. Liver ultrasound transient elastography is performed on a Fibro Scan instrument and reflects the degree of hepatic steatosis by measuring the Controlled Attenuation Parameter (CAP). The FibroScan® uses ultrasound and VCTETM to determine liver stiffness and to record the Controlled Attenuation Parameter (CAPTM) as an indicator of hepatic steatosis [23]. CAP ≥ 288 dB/m was considered to be a sign of steatosis. A recent meta-analysis showed that VCTE-derived liver stiffness measurements (LSM) have a low positive predictive value, LSM < 8 kPa can be used to exclude advanced fibrosis, VCTE LSM between 8 and 12 kPa may be associated with fibrotic NASH, and LSM > 12 kPa is associated with a high likelihood of advanced fibrosis [24, 25]. All participants were 18 years of age and older. Participants who were unable to lie on the examination table, were pregnant at the time of the examination (or were unsure if they were pregnant) were unable to obtain urine for a pregnancy test, had an implanted electronic medical device, had a bandage, or had an injury to the right side of the abdomen on the ribs (where measurements would be taken) were excluded.

Covariate

Demographic covariates included age, marriage, race, poverty-to-income ratio (PIR), and education level. Anthropometric and laboratory test covariates included body mass index (kg/m2), hip circumference (cm), triglycerides (TG, mmol/L), low-density lipoprotein cholesterol (LDL-C, mmol/L), total cholesterol (TC, mmol/L), high-density lipoprotein cholesterol (HDL-C, mmol/L), and urine creatinine (UCR, μmol/L). The remaining covariates were as follows: presence of smoking, presence of diabetes, hypertension, cardiovascular disease, hyperlipidaemia, sleep disorders, and sedentary time (hours/week). Hypertension was defined as taking anti-hypertensive medication, receiving a diagnosis of hypertension from a physician, or having three consecutive measurements of systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg [26]. Body mass index was categorised as normal weight, overweight and obese. Standard measurement procedures for variables in this study are available at www.cdc.gov/nchs/nhanes. Covariates are shown in Table 1 (end of text).

Data analysis

Data is analysed and displayed graphically using R (version 4.1.3) and Empower Stats (version 2.0). Data were analysed and displayed graphically using R (version 4.1.3) and Empower Stats (version 2.0). Continuous variables were expressed as mean and standard error (SE) and categorical variables were expressed as proportions. Both CAP and LSM were statistically analysed as categorical variables. The WWI was divided into tertiles according to their values, i.e., Q1, Q2, and Q3 representing the CAP different intervals. When categorised according to the WWI tertiles, the t-test or chi-square test was used to analyse the differences between the subjects. In this study, logistic regression analysis was used to analyse the association between WWI and the risk of hepatic steatosis and liver fibrosis (odds ratio (OR) and 95% confidence interval (CI)). Three different models were used to test the relationship between the variables. Model 1 is not

Table 1 Baseline characteristics of study participants

Characteristics[a,b]	Males (N = 3,072)			P-value	Females (N = 3,641)			P-value
	Weight-adjusted-waist index (WWI)				Weight-adjusted-waist index (WWI)			
	Q1 (N = 1,266)	Q2 (N = 1,093)	Q3 (N = 713)		Q1 (N = 969)	Q2 (N = 1,133)	Q3 (N = 1,539)	
Age, (years), (%)				< 0.001				< 0.001
18–39	800 (63.19%)	273 (24.98%)	81 (11.36%)		608 (62.75%)	386 (34.07%)	283 (18.39%)	
40–59	319 (25.20%)	429 (39.25%)	166 (23.28%)		267 (27.55%)	442 (39.01%)	490 (31.84%)	
≥ 60	147 (11.61%)	391 (35.77%)	466 (65.36%)		94 (9.70%)	305 (26.92%)	766 (49.77%)	
RACE, (%)				< 0.001				< 0.001
Mexican American	130 (10.27%)	150 (13.72%)	93 (13.04%)		75 (7.74%)	140 (12.36%)	222 (14.42%)	
Other Hispanic	112 (8.85%)	107 (9.79%)	87 (12.20%)		92 (9.49%)	134 (11.83%)	174 (11.31%)	
Non-Hispanic White	339 (26.78%)	374 (34.22%)	318 (44.60%)		316 (32.61%)	336 (29.66%)	560 (36.39%)	
Non-Hispanic Black	420 (33.18%)	244 (22.32%)	115 (16.13%)		277 (28.59%)	313 (27.63%)	366 (23.78%)	
Other Race - Including Multi-Racial	265 (20.93%)	218 (19.95%)	100 (14.03%)		209 (21.57%)	210 (18.53%)	217 (14.10%)	
Education level, (%)				< 0.001				< 0.001
Less than high school	137 (10.82%)	216 (19.76%)	160 (22.44%)		65 (6.71%)	167 (14.74%)	338 (21.96%)	
High school or above high school	953 (75.28%)	851 (77.86%)	541 (75.88%)		787 (81.22%)	933 (82.35%)	1178 (76.54%)	
Others	176 (13.90%)	26 (2.38%)	12 (1.68%)		117 (12.07%)	33 (2.91%)	23 (1.49%)	
PIR	2.76 ± 1.69	2.88 ± 1.64	2.63 ± 1.57	0.022	2.70 ± 1.72	2.72 ± 1.63	2.36 ± 1.55	< 0.001
Marry, (%)	680 (67.73%)		387 (59.08%)	< 0.001				< 0.001
Married/Living with Partner	737 (58.21%)	905 (82.80%)	627 (87.94%)		580 (59.86%)	904 (79.79%)	1316 (85.51%)	
Widowed/Divorced /Separated	353 (27.88%)	165 (15.10%)	76 (10.66%)		271 (27.97%)	194 (17.12%)	201 (13.06%)	
Never married	176 (13.90%)	23 (2.10%)	10 (1.40%)		118 (12.18%)	35 (3.09%)	22 (1.43%)	
BMI (kg/m^2), (%)				< 0.001				< 0.001
Normal weight	466 (36.81%)	124 (11.36%)	31 (4.37%)		477 (49.28%)	211 (18.66%)	116 (7.54%)	
Overweight	455 (35.94%)	317 (29.03%)	132 (18.62%)		248 (25.62%)	291 (25.73%)	269 (17.48%)	
Obese	345 (27.25%)	651 (59.62%)	546 (77.01%)		243 (25.10%)	629 (55.61%)	1154 (74.98%)	
Smoking, (%)				< 0.001				< 0.001
Yes	432 (34.12%)	507 (46.39%)	348 (48.81%)		213 (21.98%)	303 (26.74%)	501 (32.55%)	
No	834 (65.88%)	586 (53.61%)	365 (51.19%)		756 (78.02%)	830 (73.26%)	1038 (67.45%)	
Hypertension, (%)				< 0.001				< 0.001
Yes	222 (17.54%)	430 (39.34%)	379 (53.16%)		134 (13.83%)	353 (31.16%)	794 (51.59%)	
No	1044 (82.46%)	661 (60.48%)	333 (46.70%)		833 (85.96%)	780 (68.84%)	743 (48.28%)	
Unclear	0 (0.00%)	2 (0.18%)	1 (0.14%)		2 (0.21%)	0 (0.00%)	2 (0.13%)	
Diabetes, (%)				< 0.001				< 0.001
Yes	73 (5.77%)	216 (19.76%)	254 (35.62%)		33 (3.41%)	117 (10.33%)	392 (25.47%)	
No	1192 (94.15%)	877 (80.24%)	459 (64.38%)		936 (96.59%)	1015 (89.59%)	1146 (74.46%)	
Unclear	1 (0.08%)	0 (0.00%)	0 (0.00%)		0 (0.00%)	1 (0.09%)	1 (0.06%)	

Table 1 (continued)

Characteristics[a,b]	Males (N = 3,072)			P-value	Females (N = 3,641)			P-value
	Weight-adjusted-waist index (WWI)				Weight-adjusted-waist index (WWI)			
	Q1 (N = 1,266)	Q2 (N = 1,093)	Q3 (N = 713)		Q1 (N = 969)	Q2 (N = 1,133)	Q3 (N = 1,539)	
CVD, (%)				0.561				0.494
Yes	17 (17.35%)	40 (18.02%)	43 (21.61%)		19 (23.46%)	36 (18.95%)	91 (23.10%)	
No	81 (82.65%)	182 (81.98%)	156 (78.39%)		62 (76.54%)	154 (81.05%)	303 (76.90%)	
Dyslipidemia, (%)				< 0.001				< 0.001
Yes	232 (18.33%)	423 (38.70%)	363 (50.91%)		134 (13.83%)	353 (31.16%)	794 (51.59%)	
No	1030 (81.36%)	661 (60.48%)	346 (48.53%)		833 (85.96%)	780 (68.84%)	743 (48.28%)	
Unclear	4 (0.32%)	9 (0.82%)	4 (0.56%)		2 (0.21%)	0 (0.00%)	2 (0.13%)	
Sleep apnoea, (%)				< 0.001				< 0.001
Yes	204 (16.11%)	266 (24.34%)	217 (30.43%)		215 (22.19%)	332 (29.30%)	525 (34.11%)	
No	1062 (83.89%)	827 (75.57%)	496 (69.57%)		754 (77.71%)	801(70.52%)	1014 (65.89%)	
Hip measurement, (cm)	99.36 ± 9.18	105.11 ± 10.72	110.12 ± 13.63	< 0.001	101.23 ± 12.36	108.15 ± 14.37	114.88 ± 16.33	< 0.001
Minutes sedentary activity, (min/d), (%)				0.043				0.664
< 240	414 (32.75%)	348 (31.87%)	195 (27.35%)		292 (30.13%)	372 (32.95%)	498 (32.40%)	
240–330	332 (26.27%)	283 (25.92%)	178 (24.96%)		257 (26.52%)	283 (25.07%)	382 (24.85%)	
> 330	518 (40.98%)	461 (42.22%)	340 (47.69%)		420 (43.34%)	474 (41.98%)	657 (42.75%)	
Laboratory features								
Total cholesterol (mmol/L)	4.62 ± 1.02	4.83 ± 1.07	4.61 ± 1.10	< 0.001	4.62 ± 0.93	4.93 ± 1.01	4.96 ± 1.05	< 0.001
Triglyceride (mmol/L)	4.62 ± 1.02	4.83 ± 1.07	4.61 ± 1.10	< 0.001	0.78 ± 0.47	1.09 ± 0.64	1.37 ± 0.78	< 0.001
LDL-cholesterol (mmol/L)	2.77 ± 0.89	2.93 ± 0.96	2.64 ± 0.91	< 0.001	2.62 ± 0.81	2.92 ± 0.88	2.90 ± 0.94	< 0.001
HDL- cholesterol (mmol/L)	1.33 ± 0.34	1.22 ± 0.34	1.18 ± 0.32	< 0.001	1.62 ± 0.43	1.49 ± 0.41	1.41 ± 0.38	< 0.001
Urinary Albumin(mg/L)	22.78 ± 103.21	42.70 ± 235.51	91.94 ± 575.02	< 0.001	23.95 ± 97.74	36.20 ± 274.91	66.79 ± 412.15	< 0.001
UCR(μmol/L)	14307.38 ± 8660.28	12798.05 ± 7510.47	12018.38 ± 6650.64	< 0.001	11308.51 ± 7666.86	10457.33 ± 7533.17	9629.45 ± 6879.89	< 0.001
CAP (dB/m), (%)				< 0.001				< 0.001
< 288	893 (92.16%)	830 (73.26%)	828 (53.0%)		1964 (87.87%)	1400 (62.89%)	1083 (48.09%)	
>=288	76 (7.84%)	303 (26.74%)	711 (46.20%)		271 (12.13%)	826 (37.11%)	1169 (51.91%)	
LSM (Kpa)				< 0.001				< 0.001
< 8	1204 (95.10%)	977 (89.39%)	561 (78.68%)		946 (97.63%)	1087 (95.94%)	1325 (86.09%)	
>=8	63 (4.90%)	116 (10.61%)	152 (21.32%)		23 (2.37%)	46 (4.06%)	214 (13.91%)	

PIR: household income-to-poverty ratio; BMI, body mass index; CVD: cardiovascular disease; LDL-cholesterol, low-density lipoprotein cholesterol; HDL-cholesterol, high-density lipoprotein cholesterol; UCR, urinary creatinine; CAP: controlled attenuation parameter; LSM: liver stiffness measure; WWI: weight-adjusted waist circumference index

[a]Missing treatment: categorical variables (adding dummy variables), continuous variables (multipipe interpolations)

[b]Data are presented as mean ± standard deviation, media (interquartile range), or members (%) as appropriate

adjusted for covariates. Model 2 adjusted for age, race, education level and marital status. Model 3 adjusted for age, race, education level and marital status, household income to poverty ratio, body mass index, hip circumference, presence of hypertension, diabetes, hyperlipidaemia and sleep disorders. Smoothed curves were then fitted to determine whether there were linear or non-linear associations between WWI and CAP and LSM. If non-linear associations existed, threshold effects analyses were used to provide each interval and calculate thresholds. Multivariate regression analyses were used to test for associations between the 4 obesity indicators and CAP and LSM. Subject work characteristics (ROC) curves were used to assess the predictive value of the WWI and other traditional obesity indicators for sensory hepatic steatosis and hepatic fibrosis, and discriminatory power was assessed by area under the curve (AUC).

Results

Baseline characteristics

The study included 6713 participants, 3072 (46.0%) males and 3641 (54.0%) females, with an age (mean ± standard deviation) of 48.107 ± 18.425. The study found that among the male participants, those in the highest tertile group compared to the lowest tertile tended to be older, non-Hispanic white, married or divorced, and had a had higher BMI, hip circumference, sedentary time, CAP levels, smoked, and had hypertension, diabetes, hyperlipidaemia, and sleep disorders.

Female participants were the same as males, except that no significant differences were found in the number of sedentary hours among female participants. However, there was no significant difference in cardiovascular disease history between male and female participants.

Correlation between WWI and CAP and LSM

As shown in Table 1, logistic regression analyses indicated a statistically significant association between WWI and CAP and LSM in fully adjusted models for females but not for male participants. Each 1-unit increase in WWI in women was associated with a 1.71-fold increase in the risk of hepatic steatosis (OR = 1.71, 95% CI: 1.43, 2.04; $P < 0.0001$) and a 2.11-fold increase in the risk of liver fibrosis (OR = 2.11, 95% CI: 1.58, 2.84; $P < 0.0001$). In males, each 1-unit increase in WWI was associated with a 2.53-fold increase in the risk of hepatic steatosis (OR = 2.53, 95% CI: 1.98, 3.25; $P < 0.0001$). Subsequent sensitivity analyses using WWI as a categorical variable (tertiles) showed that in the highest tertile subgroup, WWI was statistically significantly associated with both CAP and LSM in female participants, whereas there was no statistically significant association between WWI and CAP and LSM in male participants.

Smoothed curve fitting showed that a non-linear relationship was found between WWI and CAP levels after adjusting for all variables (Fig. 2). There were differences in the relationship between WWI values and CAP by gender. In male participants, there was a very strong positive association between WWI and CAP when WWI < 10.7 (OR = 15.2, 95% CI: 10.2–22.5; $P < 0.001$), which gradually weakened after the inflection point (OR = 3.1, 95% CI: 2.5, 3.9; $P < 0.001$). In female participants, the upward trend of CAP with increasing WWI became slower when WWI exceeded a certain value (Table 2).

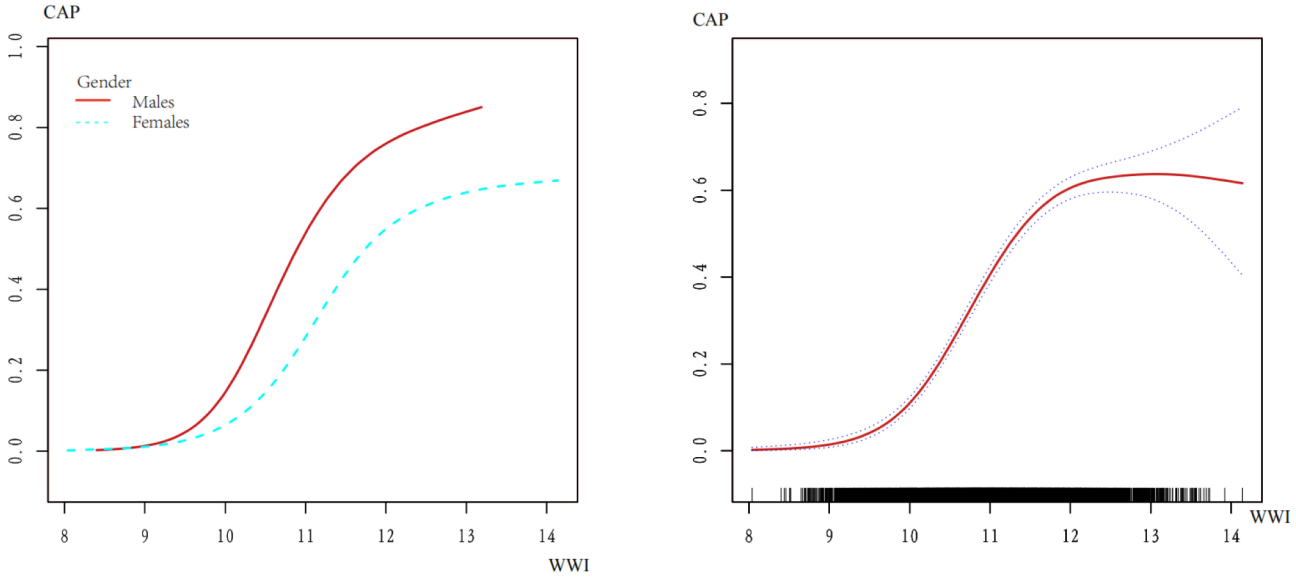

Fig. 2 Association between weight-adjusted waist circumference index and CAP. The solid red lines indicate smooth curves fitted between the variables. The blue bars indicate 95% confidence intervals of the fit. CAP, controlled attenuation parameters

Table 2 Correlation between WWI and CAP and LSM

Variable	Model 1				Model 2				Model 3			
	OR(95%CI)		*P*-value		OR(95%CI)		*P*-value		OR(95%CI)		*P*-value	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
CAP	3.76 (3.33,4.24)	2.65 (2.40,2.92)	< 0.0001	< 0.0001	5.25 (4.52,6.10)	2.66 (2.39, 2.97)	< 0.0001	< 0.0001	2.53 (1.98,3.25)	1.71 (1.43,2.04)	< 0.0001	< 0.0001
Quartiles of WWI												
Q1	1	1			1	1			1	1		
Q2	4.64 (3.87,5.55)	3.83 (3.05, 4.81)	< 0.0001	< 0.0001	5.20 (4.26, 6.35)	3.54 (2.80, 4.47)	< 0.0001	< 0.0001	1.66 (0.64, 4.31)	1.51 (0.61, 3.74)	0.2953	0.3780
Q3	8.91 (7.23, 11.00)	8.80 (7.09, 10.94)	< 0.0001	< 0.0001	12.85 (9.98, 16.56)	8.23 (6.52, 10.40)	< 0.0001	< 0.0001	2.23 (0.70, 7.11)	2.70 (1.10, 6.60)	0.1743	0.0297
LSM	2.32 (1.98,2.70)	2.53 (2.18, 2.95)	< 0.0001	< 0.0001	2.28 (1.90,2.73)	2.11 (1.58, 2.84)	< 0.0001	< 0.0001	1.19 (0.86, 1.65)	2.11 (1.58, 2.84)	=	< 0.0001
Quartiles of WWI												
Q1	1	1			1	1			1	1		
Q2	2.16 (1.54, 3.04)	1.56 (0.93, 2.63)	< 0.0001	0.0918	2.16 (1.54, 3.04)	1.56 (0.93, 2.63)	< 0.0001	0.0918	1.33 (0.76, 2.32)	0.94 (0.38, 2.31)	0.3137	0.8847
Q3	4.83 (3.38, 6.90)	5.71 (3.58, 9.09)	< 0.0001	< 0.0001	4.83 (3.38, 6.90)	5.71 (3.58, 9.09)	< 0.0001	< 0.0001	1.52 (0.80, 2.90)	2.84 (1.25, 6.43)	0.1990	0.0123

CAP, controlled attenuation parameters; LSM, liver stiffness measurement

Model 1: Unadjusted for covariates

Model 2: Adjusted for age,race, Education level and Marry

Model 3: Adjusted for age,race, Education level and Marry, household income to poverty ratio, BMI, Hypertension, Diabetes, Dyslipidemia, Sleep apnea, Hip measurement, Minutes sedentary activity and hip circumference

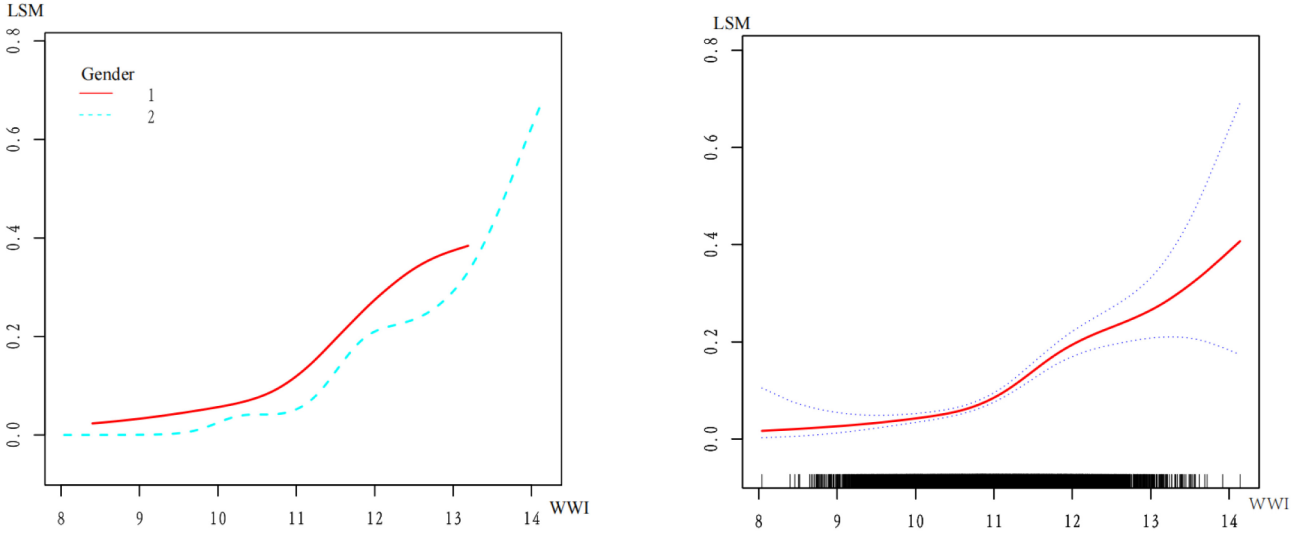

Fig. 3 Association between weigh t-adjusted waist circumference index and LSM. The solid red lines indicate smooth curves fitted between the variables. The blue bars indicate 95% confidence intervals of the fit. LSM, liver stiffness measurements

Table 3 Threshold effect analysis of WWI on CAP using a two-piecewise linear regression model

WWI	**CAP**		
	Males	**Females**	**Total**
Fitting by the standard linear model			
Adjust β(95%CI) *P*-value	5.2 (4.5, 6.1) < 0.001	2.7(2.4,3.0) < 0.001	2.7 (2.5, 2.9) < 0.001
Fitting by two-piecewise linear model			
Inflection point	10.7	11.7	11.4
<K segment effect	15.2(10.2,22.5) < 0.001	4.5 (3.7, 5.4) < 0.001	5.1 (4.4, 5.9) < 0.001
>K segment effect	3.1 (2.5, 3.9) < 0.001	1.3 (1.0, 1.6) 0.049	1.3 (1.1, 1.5) 0.003
Logarithmic likelihood ratio test *P*-value	< 0.001	< 0.001	< 0.001
WWI	**LSM**		
	Males	**Females**	**Total**
Fitting by the standard linear model			
Adjust β(95%CI) *P*-value	2.47 (2.02, 3.03) < 0.0001	2.70 (2.25, 3.24) < 0.0001	2.58 (2.26, 2.96) < 0.0001
Fitting by two-piecewise linear model			
Inflection point	10.55	12.09	12.1
<K segment effect	1.76 (1.03, 3.02) 0.0404	3.60 (2.69, 4.82) < 0.0001	2.93 (2.45, 3.49) < 0.0001
>K segment effect	2.74 (2.12, 3.55) < 0.0001	1.57 (1.00, 2.47) 0.0506	1.68 (1.12, 2.53) 0.0125
Logarithmic likelihood ratio test *P*-value	0.202	0.009	0.026

There was also a significant non-linear relationship between WWI and LSM. The effect of WWI on LSM was more pronounced at lower WWI values for females (OR = 3.60,95% CI: 2.69, 4.82; $P < 0.0001$) and more pronounced at higher WWI values for males (OR = 2.74,95% CI: (2.12, 3.55); $P < 0.0001$). (Fig. 3; Table 2).

Correlation of four obesity indicators with hepatic steatosis and hepatic fibrosis

As shown in Table 3, WWI was also a good predictor of hepatic steatosis compared to other obesity indicators and was a better predictor for male participants (AUC = 0.8224). analysis of the WWI versus LSM showed that wBMI was a better predictor for female participants (AUC = 0.7751) (Figs. 4 and 5).

Discussion

The study involved 6713 participants, including 3072 men (46%) and 3641 women (54%). The results showed that higher WWI was associated with hepatic steatosis and hepatic fibrosis in female participants. The same significant non-linear relationship was found between WWI and LSM, with no significant difference between males and females. WWI was also a good predictor of hepatic steatosis compared to other obesity indicators and was more pronounced in male participants. Whereas in the comparison of WWI with LSM, wBMI was a better predictor in female participants.

The association between obesity and the increasing prevalence of MASLD is well-documented [27]. MASLD is considered a multisystemic disease that is notably

4 WWI, BMI, wBMI and WHtR predicted the area under the ROC curve for hepatic steatosis.

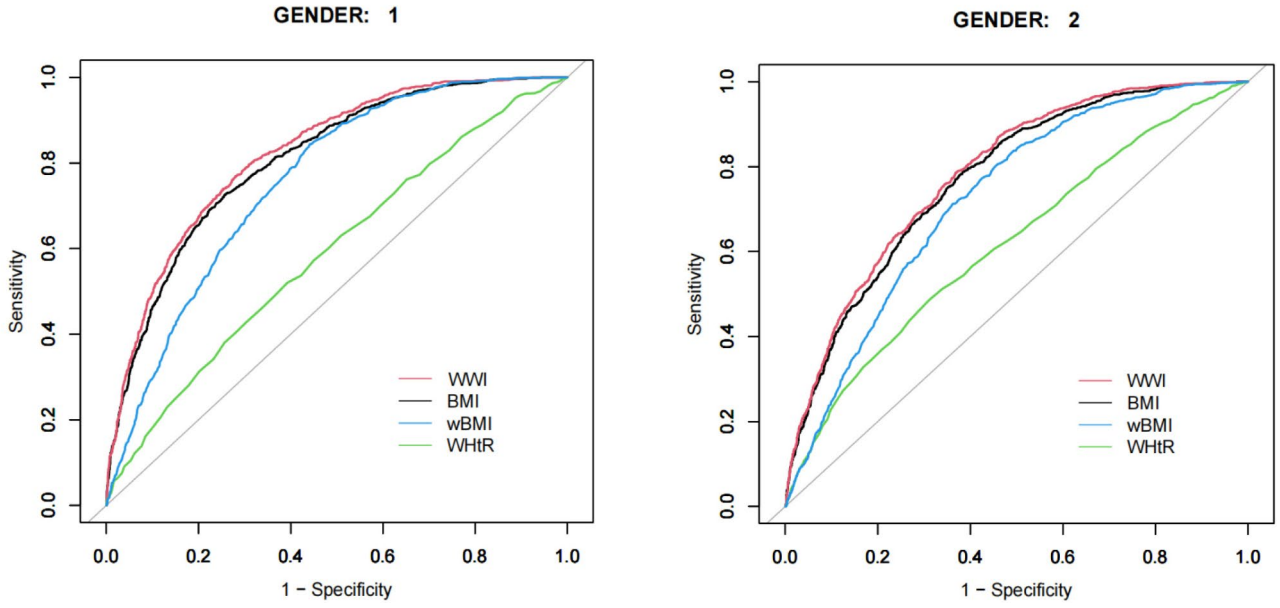

Fig. 4 WWI, BMI, wBMI and WHtR predicted the area under the ROC curve for hepatic steatosis. 1, males; 2, females; WWI, weight-adjusted waist circumference; wBMI, waist circumference-BMI ratio BMI, body mass index; WHtR, waist circumference-height ratio

5 WWI, BMI, wBMI and WHtR predicted the area under the ROC curve for liver fibrosis.

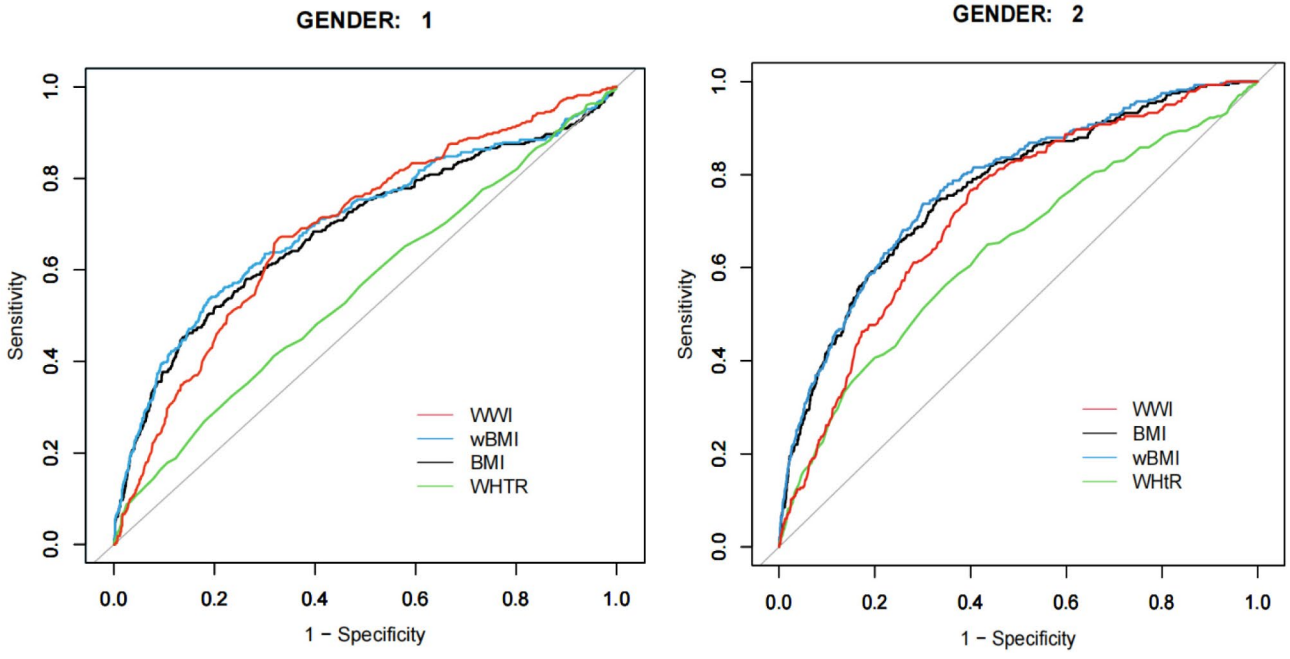

Fig. 5 WWI, BMI, wBMI and WHtR predicted the area under the ROC curve for liver fibrosis. 1, males; 2, females; WWI, weight-adjusted waist circumference; wBMI, waist circumference-BMI ratio BMI, body mass index; WHtR, waist circumference-height ratio

Table 4 Comparison of AUC values between WWI and other obesity indicators

Test	AUC	95%CL	Best threshold	Sensitivity	Specificity
	CAP				
	Males				
WWI	0.8224	0.8078–0.8371	28.5950	0.7207	0.7681
wBMI	0.7579	0.7412–0.7746	10.6350	0.5585	0.8444
BMI	0.8075	0.7922–0.8228	28.8350	0.7445	0.7246
WHtR	0.5907	0.5701–0.6113	1.1450	0.6071	0.5204
	Females				
WWI	0.7826	0.7672–0.7980	28.0050	0.6311	0.7862
wBMI	0.7239	0.7070–0.7408	11.3150	0.6378	0.7128
BMI	0.7706	0.7548–0.7865	28.7050	0.6162	0.7881
WHtR	0.6172	0.5972–0.6373	1.2450	0.6887	0.4862
	LSM				
	Males				
WWI	0.6901	0.6598–0.7203	11.1050	0.6718	0.6697
wBMI	0.7001	0.6660–0.7342	36.2600	0.8097	0.5380
BMI	0.6874	0.6528–0.7220	32.4050	0.7984	0.5198
WHtR	0.5565	0.5222–0.5908	1.1050	0.6813	0.4121
	Females				
WWI	0.7213	0.6923–0.7503	11.4050	0.600	0.7668
wBMI	0.7751	0.7466–0.8035	33.5100	0.699	0.7376
BMI	0.7649	0.7354–0.7944	31.6750	0.6710	0.7447
WHtR	0.6362	0.6001–0.6722	1.2450	0.6531	0.5618

AUC, area under the curve; 95%CI, confidence interval; WWI, weight-adjusted waist waist; wBMI, waist circumference-BMI ratio BMI, body mass index; WHtR, waist circumference-height ratio

associated with metabolic comorbidities [28]. The underlying cause may be an imbalance in lipid metabolism, which triggers inflammation, tissue regeneration, and fibroplasia [29, 30]. The hallmarks of centripetal obesity include an excessive build-up of abdominal fat and an enlarged waist circumference; married females are more prone to this type of obesity than single females [31, 32].

In this study, the correlation between WWI and CAP was found to be stronger in older adult women. This observation may be due to the effect of estrogen on lipid metabolism and fat distribution [33–35]. In women, hypogonadism and increased liver enzymes are associated with a higher prevalence of MASLD and advanced fibrosis. The prevalence of MASLD is higher in postmenopausal women compared with premenopausal women. Limited data suggest that higher free testosterone levels in premenopausal women are associated with an increased risk of MASLD after menopause [36]. In addition, there is an association between higher testosterone levels and lower serum estradiol levels and NASH [37]. Limited studies have demonstrated the benefits of hormone replacement therapy for MASLD [38]. The present study shows that WWI is positively associated with hepatic steatosis and hepatic fibrosis, and that an apparently relevant increase in abdominal obesity is strongly associated with the severity and progression of MASLD, although a direct causal relationship has not been established.

Prolonged sedentary behaviour can have a significant impact on the relationship between WWI and CAP. In the Nurses' Health Study (NHS) [38], sedentary female participants had a much higher risk of obesity, which was associated with levels of physical activity; even a slight increase in moderate physical activity significantly reduced their risk of obesity [39]. Thus, sedentary behaviour may be a risk factor for MASLD and an independent predictor.

Strengths and limitations

The present study has the following four strengths. Firstly, this study provides clinical evidence supporting the association of WWI with CAP and provides a rich and relevant literature for early prevention of hepatic steatosis and hepatic fibrosis in obesity. Second, the present study adjusted for many covariates and enhanced control for confounding variables. Third, this study enhances the current understanding of the WWI as a novel predictor for the early assessment of MASLD and provides a simple anthropometric measure for the early prevention of MASLD in obese men and women, which can help prevent hepatic steatosis associated with pseudo-obesity. Finally, the sample in this study was representative of the real world.

However, this study has several limitations. First, the cross-sectional design precluded causal inferences. Second, hepatic steatosis and hepatic fibrosis were assessed

by non-invasive indicators (e.g., CAP, FIB-4) rather than liver biopsy, which may introduce classification bias. Third, residual confounding by unmeasured variables (e.g., genetic factors, pharmacological factors) cannot be excluded.

Conclusion

Our study demonstrated that elevated WWI was strongly associated with the FibroScan® parameters used to support and monitor MASLD in adult women in the U.S. Based on our findings, WWI was significantly associated with the risk of hepatic steatosis and hepatic fibrosis in women, suggesting that WWI has the potential to be a screening tool. More advanced statistical techniques and study designs are needed to minimise the effects of confounding variables, and more data are needed for validation.

Abbreviations

BMI	Body mass index
CAP	Controlled attenuation parameters
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
LSM	Liver stiffness measurements
MASLD	Metabolic Associated Fatty Liver Disease
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
NHANES	National Health and Nutrition Examination Survey
PIR	Poverty-to-income ratio
TC	Total cholesterol
TG	Triglycerides
UA	Urinary albumin
UCR	Urinary creatinine
VCTE	Vibration-controlled transient elastography
WC	Waist circumference
WWI	Weight-adjusted waist circumference
wBMI	Waist-BMI ratio
WHtR	Waist-to-height ratio

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Author contributions

Yu-E Lian and Yixuan Wang contributed equally to this work.All authors made substantial intellectual contributions to the study and are eligible for authorship. Authors' responsibilities: study conception and design (Y.-E.L., Y.-X.W., C.-J.Y) data collection (Y.-E.L., Y.-X.W.), data analyses (Y.-E.L., Y.-X.W., C.-J.Y); interpretation of the results (all authors); drafting of the manuscript (Y.-E.L., Y.-X.W.); review of the manuscript (all authors).).

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Data availability

Publicly available datasets were analysed in this study. This data can be found at www.cdc.gov/nchs/nhanes/.

Declarations

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. The Ethics Committee of the National Centre for Health Statistics approved. The patients/participants provided written informed consent to participate in this study.

Competing interests

The authors declare no competing interests.

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