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Weight-adjusted-waist index: an innovative indicator of breast cancer hazard

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Abstract

Background Central obesity and breast cancer (BC) have been identified as relevant by empirical research. The weight-adjusted-waist index (WWI) is a novel methodology for quantifying central obesity. Inspection of the association between WWI and BC in American adult women was the primary goal of the current investigation.

Methods Cross-sectional assessments were conducted on information gathered from 10,193 National Health and Nutrition Examination Survey (NHANES) participants from 2011 to 2018. The waist circumference was divided by the square root of the body's mass to compute WWI. Data were assessed via descriptive statistics to present data distributions according to BC grouping and WWI grouping, receiver operating characteristic curves (ROCs) to evaluate the obesity indicators' applied value, logistic regression to reflect associations between WWI and BC prevalence, and restricted cubic splines (RCSs) and subgroup analysis forest plots to visualise and complement the relationships.

Results This study enrolled 10,193 participants whose WWI ranged from 8.38 to 14.41, 259 of whom were diagnosed with BC, and the results revealed significant differences in baseline characteristics between the groups. With an area under the curve (AUC) value (95% confidence interval) (CI)of 0.611 (0.577–0.644), WWI was a promising indicator of BC with good application value rather than waist circumference (WC), body mass index (BMI), or waist-height ratio (WHtR). WWI and BC laid out a substantial relationship, yielding an odds ratio (OR) of 1.54 and a 95% CI of (1.34, 1.79), which remained at 1.19 (1.00, 1.42) after considerable adjustments were made, according to the logistic regression analysis. Compared with the lowest quartile of WWI, the highest quartile had a 62% greater in the probability of suffering from BC. With the RCS's inverted U-shape highlighting the importance of considering the nonlinear nature of the relationship and subgroup analyses reflecting variations among populations, all the results demonstrated that WWI was a well-suggestive indicator of BC hazard.

Conclusion The current investigation revealed a meaningful association between the prevalence of BC and WWI, which was superior to other obesity indicators, albeit one that was more complex than the positive relationship initially derived. There existed a turning point for BC prevalence at WWI of approximately 12 cm/√kg. Nevertheless, maintaining WWI in the lower range is critical for preventing and administering BC and minimizing disease risk.

Keywords National Health and Nutrition Examination Survey, Breast cancer, Weight-adjusted-waist index, Obesity

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Introduction

The most frequently detected malignancy among women worldwide is breast cancer (BC), which is associated with major morbidity, death, and economic costs, and it is more prevalent in high-income nations [1]. BC prevention is an urgent public health priority across the globe [2]. Since the mid-2000s, female BC incidence rates have been gradually increasing at a rate of approximately 0.6% per year [3]. Estimates indicate that by 2040, there will be more than three million new diagnoses of BC and more than one million fatalities annually [4]. Given the high incidence rate, even minor percentage reductions obtained through preventative measures are noteworthy [5]. BC mostly affects middle-aged and older women. Early diagnosis and treatment are critical for achieving a favourable prognosis [6]. The investigation of fresh data on BC trends is critical for preventing and controlling disease onset and progression, as well as improving health [7]. Thus, determining variables associated with BC risk is critical.

The ingestion of high-sugar and high-fat foods, along with a sedentary lifestyle, causes disparities in energy intake and expenditure, ultimately contributing to obesity [8]. Over the past century, obesity has become a severe health concern as a consequence of the intricate interplay between genetic, metabolic, behavioral, and environmental variables [9]. Obesity affects approximately 1 billion individuals globally, with 41.9% of the US population falling into this category [10]. Causing pharmaceutical underdosing and metabolic abnormalities, it is an important trigger for an abundance of nontransmissible illnesses, such as diabetes, cardiovascular disorders, and cancer [11, 12]. The waist circumference (WC), body mass index (BMI), and waist-height ratio (WHtR), which are regularly utilized as obesity markers, have intrinsic constraints that have given rise to a variety of "obesity paradoxes" [13]. In 2018, researchers presented an innovative obesity indicator known as the weight-adjusted-waist index (WWI), which shows greater stability and delivers a more precise gauge of visceral fat and muscle mass than BMI and other variables do [14]. There is a strong association between increased WWI and a range of diseases.

The presence of extra adipocytes, as well as obesity-induced alterations in adipose tissue, might boost BC [12]. It increases the chance of being diagnosed with a larger, higher-grade tumor and is an independent predictor of distant metastases, which may result in shorter disease-free periods and lower overall survival rates, affecting the efficacy and toxicity of systemic cancer therapies [10, 15]. Strong epidemiologic and clinical evidence indicates the importance of central obesity in the occurrence and development of BC [16–18]. Overall obesity, particularly central obesity, causes systemic and localized low-grade chronic inflammation, which induces an increase in tumor-promoting oxidative stress and ultimately transforms normal cells' transcriptional profiles into oncogenic cells [19]. WWI explains weight-independent central obesity and separates fat from muscle mass [20].

It is worthwhile to investigate whether there is a possible association between body fat composition and cancer via easily measurable measures of obesity. Extensive studies have proposed an association between BMI and BC, whereas a prospective cohort study by Liu et al. demonstrated a weak positive association between a 5-unit increase in BMI and a 2% increase in BC risk, implying that BMI as a measurement fails to optimally capture the pathogenic mechanisms of obesity [21–23]. The dose-response meta-analysis by Chen et al. exhibited the strength of exploring central obesity metrics, whereas the relationships between central obesity and BC risk embodied by WC and WHtR remained weak [17]. As a newly proposed metric, the preponderance of WWI reflecting central obesity is apparent, but to date, no research has revealed a relationship between WWI and BC. The goal of this study was to perform a cross-sectional investigation via information collected from the National Health and Nutrition Examination Survey (NHANES) to gain insight into this association, in order to explore obesity indicators suggestive of BC risk, make horizontal comparisons with other obesity indicators, and visualize the applicability of the WWI.

Research methodology

Study design and screening of the population

NHANES, initiated by the National Center for Health Statistics, is a countrywide initiative that centers on the well-being and dietary conditions of American citizens every two years, aiming to gather thorough insight into current illness patterns and offer guidance for creating public health strategies. The NHANES webpage was visited at https://www.cdc.gov/nchs/nhanes/ to access all of the datasets. We examined data from the previous four periods (2011–2018), with an overall count of 39,156 participants participating in four consecutive NHANES survey cycles. The study eliminated 19,308 male subjects. Subsequently, individuals under the age of 20 and pregnant women were removed, along with those missing information at baseline, leaving a total research population of 10,193. The screening procedure is depicted in Fig. 1.

Diagnostic criteria for BC

The Medical Conditions Questionnaire was the source of BC's self-reported diagnosis. The subjects were asked

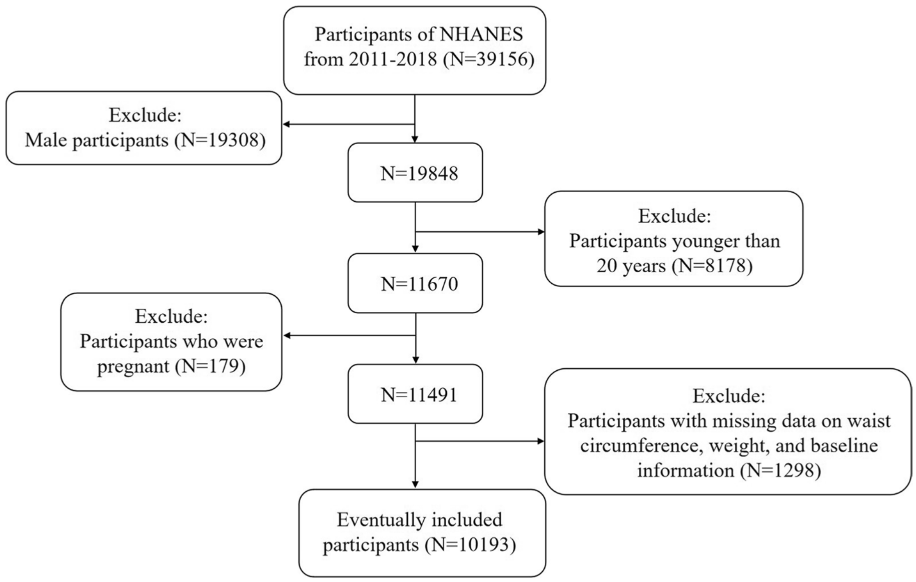


Fig. 1 Flowchart of participant selection from NHANES 2011–2018

if a medical professional or other health specialist had ever informed them of having cancer or another form of malignancy. The participants who responded "yes" were asked, "What type of cancer is this?" Those who exclusively indicated BC (main and isolated tumors) were classified as BC individuals. Subjects who responded negatively, had a prior diagnosis of another type of cancer, or had a previous bout of BC in conjunction with other cancers were classified as non-BC patients [24, 25]. This was the survey's outcome variable.

Definition of obesity indicators

WWI is an anthropometric measure based on body weight, and WC is the central obesity assessment. NHANES body measurements were carried out by trained health technicians in physical examination rooms with the same layout and equipment, and there was quality assurance such as observation and validation, which ensured consistency in data acquisition, and weight, WC, and BMI were adopted. Each participant's WWI score was calculated as WC (cm) divided by the square root of weight (kg). WHtR was computed from the ratio of waist circumference to height. This study employed WWI as an exposure variable.

Ascertaining covariables

Individuals were split into two categories by age: <70 years and ≥ 70 years. There were two categories according to marital status: married and unmarried (single, separated, widowed, or cohabiting partners). Non-Hispanic whites, non-Hispanic blacks, Mexican Americans, and other races were identified. Education levels were separated into four distinct groups: below high school, high school level or equivalent, some college or AA degree, and above college. Household income is divided by the poverty line for the period surveyed to obtain the poverty-to-income ratio (PIR). Total cholesterol (TC) was determined via standardized laboratory tests. A history of physician-diagnosed hypertension, a measured mean systolic blood pressure of at least 140 mmHg, or a mean diastolic blood pressure of at least 90 mmHg, or the use of antihypertensive medication were all considered indicators of hypertension. A diagnosis of diabetes, in addition to self-reporting, is accompanied by a fasting plasma glucose level over 7.0 mmol/L, a glycosylated haemoglobin (HbA1c) level over 6.5%, and/or the need for antidiabetic medication. A question about receiving a diagnosis of coronary heart disease (CHD) from a physician or other healthcare professional was posed to the participants. Those who replied "yes" to this question were diagnosed with CHD, whereas those who did not were classified as having no CHD. Self-reported physical activity was categorized on the basis of respiratory rate and heart rate as vigorous with large increases or moderate with small increases, and the rest were defined as no. Nonsmokers were individuals who had consumed fewer than 100 cigarettes throughout their entire lifespan or did not smoke at all. Individuals who smoked were either habitual smokers or had smoked more than 100 cigarettes. Abstainers consumed a maximum of 12 alcoholic beverages annually, whereas individuals who consumed more alcoholic beverages were classified as drinkers.

Statistical assessments

R (version 4.2.2) and EmpowerStats (http://www.empowerstats.com) were utilized for all of the analyses. Categorical variables were presented as percentages via Pearson's chi-square test, whereas continuous variables were expressed as medians (interquartile ranges) (IQRs) via the Wilcoxon rank sum test and the Kruskal-Wallis rank sum test, respectively. To assess the application value of each obesity indicator in BC, receiver operating characteristic (ROC) curves were plotted, the area under the curve (AUC) was computed to quantify the findings, and the optimal cut-off point of WWI, which was prominent, was determined. Odds ratio (OR) and 95% confidence interval (CI) were utilized to estimate the noteworthy relationship between BC and WWI after controlling for possible covariates or not, employing logistic regression models. One remained unadjusted, and the other was adjusted for age, race, education level, marital status, PIR, TC, alcohol consumption, smoking status, hypertension, diabetes mellitus, CHD, and physical activity. The restricted cubic spline (RCS) was utilized to depict the association between WWI and BC to visualize possible nonlinear relationships; it was conducted with 3 knots at the 10th, 50th, and 90th percentiles, and the inflection points were identified for segmented logistic regression allowing for a more nuanced understanding of the relationship. Subgroups were analysed by selecting confounding factors, mainly reflecting metabolic status, underlying diseases and lifestyle, which were representative of the population, and forest plots were constructed to display the differences. Values with $P<0.05$ were viewed as statistically noteworthy.

Results

Baseline traits of the investigated population

Table 1 demonstrates the demographic and clinical features of the participants classified by BC as a column-stratified variable. Significant differences in age, race, PIR, TC, hypertension, diabetes mellitus, CHD, and physical activity were observed when characteristics were compared between groups ($P<0.05$). BC patients were more likely to be older, be non-Hispanic white, have high levels of TC, suffer from underlying diseases, be less physically active, and have high obesity indicators. Among the four indicators, WWI and WC differed considerably in BC intergroup comparisons, yet BMI and WHtR did not, reflecting a strong relationship between central obesity indicators and BC. The aggregate data highlighted significant disparities in health and sociodemographic characteristics associated with BC status.

The participants were categorized into quartiles in Table 2 according to their WWI values. As WWI values increased, there were notable and continuous increases in the prevalence of BC (Q1: 1.41%, Q2: 2.12%, Q3: 2.71%, Q4: 3.92%, $P<0.001$). WWI quartile groups showed significant differences in all domains ($P<0.001$). Compared with those in quartile 1, participants in quartile 4 were older, less educated, poorer, had higher TC levels, had a higher prevalence of underlying diseases, were less active, and were addicted to smoking. The proportion of alcohol consumption fell as WWI increased, suggesting that lifestyle changes may have occurred. These factors emphasize demographic and health-related disparities among WWI groups, providing meaningful insights into the associations between WWI and a variety of characteristics and reflecting their potential impact on health outcomes.

Assessment of the application potential of obesity indicators

As shown in Fig. 2, ROC curves were plotted to assess the potential value of obesity metrics including WWI, WC, BMI, and WHtR for BC, with WWI dominance highlighted by an AUC value (95% CI) of 0.611 (0.577–0.644), along with WC of 0.547 (0.515–0.579). Using Youden's index as an assessment measure, the ideal cut-off point for WWI was determined to be 11.41, with a sensitivity of 61.4%, specificity of 56.3%, and accuracy of 56.4%. WWI, an indicator of central obesity, provides remarkable advantages and has promising applications in suggesting BC risk.

Associations between WWI and BC

Table 3 demonstrates the associations between WWI and BC through logistic regression analysis. A substantial positive relationship between WWI and BC was observed in the unadjusted model (OR = 1.54; 95% CI: 1.34–1.79; $P<0.0001$). After all confounders were corrected for, the positive association remained statistically significant (OR = 1.19; 95% CI: 1.00–1.42; $P=0.0448$). This association persisted even after WWI was quartetized (P for trend < 0.05). The BC prevalence increased incrementally with increasing WWI, with an obvious upwards trend. The top quartile of WWI displayed a 62% higher prevalence of BC than did the lowest quartile in the adjusted model.

RCS was utilized for flexible modelling to illustrate the possible nonlinear relationship between WWI and BC. The unadjusted and adjusted model RCS analyses revealed a statistically significant nonlinear relationship between WWI and BC ($P<0.05$), with the nonlinear component not dominating (P-nonlinear > 0.05). Figure 3A identified the inflection point at 11.28 cm/$\sqrt{\text{kg}}$ as the overall population median for WWI. Figure 3B exhibited an inverted U-shape in the adjusted relationship, implying an identifiable inflection point positioned

Table 1 Baseline characteristics of BC group versus non-BC group

Characteristic	Overall, N = 10,193	BC		P value
		Yes, N = 259	No, N = 9,934	
Age				< 0.001[1]
< 70	8,671 (85.07%)	153 (59.07%)	8,518 (85.75%)	
≥ 70	1,522 (14.93%)	106 (40.93%)	1,416 (14.25%)	
Race				0.003[1]
Mexican American	1,392 (13.66%)	30 (11.58%)	1,362 (13.71%)	
Non-Hispanic White	3,693 (36.23%)	122 (47.10%)	3,571 (35.95%)	
Non-Hispanic Black	2,321 (22.77%)	50 (19.31%)	2,271 (22.86%)	
Other Race	2,787 (27.34%)	57 (22.01%)	2,730 (27.48%)	
Educational level				0.362[1]
Below high school	2,093 (20.53%)	47 (18.15%)	2,046 (20.60%)	
High school level or equivalent	2,140 (20.99%)	52 (20.08%)	2,088 (21.02%)	
Some college or AA degree	3,397 (33.33%)	83 (32.05%)	3,314 (33.36%)	
Above college	2,563 (25.14%)	77 (29.73%)	2,486 (25.03%)	
Marital status				0.960[1]
Yes	4,707 (46.18%)	120 (46.33%)	4,587 (46.17%)	
No	5,486 (53.82%)	139 (53.67%)	5,347 (53.83%)	
PIR	2.02 (1.10, 3.72)	2.51 (1.47, 4.28)	2.01 (1.10, 3.70)	< 0.001[2]
TC (mg/dL)	190 (166, 216)	198 (176, 217)	190 (166, 216)	0.022[2]
Alcohol consumption				0.062[1]
Yes	5,070 (49.74%)	114 (44.02%)	4,956 (49.89%)	
No	5,123 (50.26%)	145 (55.98%)	4,978 (50.11%)	
Smoking status				0.196[1]
Yes	3,359 (32.95%)	95 (36.68%)	3,264 (32.86%)	
No	6,834 (67.05%)	164 (63.32%)	6,670 (67.14%)	
Hypertension				< 0.001[1]
Yes	4,306 (42.24%)	164 (63.32%)	4,142 (41.70%)	
No	5,887 (57.76%)	95 (36.68%)	5,792 (58.30%)	
Diabetes mellitus				< 0.001[1]
Yes	1,692 (16.60%)	75 (28.96%)	1,617 (16.28%)	
No	8,501 (83.40%)	184 (71.04%)	8,317 (83.72%)	
Coronary heart disease				0.028[1]
Yes	257 (2.52%)	12 (4.63%)	245 (2.47%)	
No	9,936 (97.48%)	247 (95.37%)	9,689 (97.53%)	
Physical activity				0.021[1]
Vigorous	1,302 (12.77%)	20 (7.72%)	1,282 (12.91%)	
Moderate	2,278 (22.35%)	53 (20.46%)	2,225 (22.40%)	
No	6,613 (64.88%)	186 (71.81%)	6,427 (64.70%)	
BMI (kg/m^2)	28.5 (24.1, 33.8)	28.6 (24.8, 33.8)	28.5 (24.0, 33.8)	0.484[2]
WC (cm)	96.5 (85.4, 108.3)	99.4 (89.7, 109.1)	96.4 (85.4, 108.3)	0.009[2]
WHtR	0.45 (0.38, 0.54)	0.46 (0.40, 0.53)	0.45 (0.38, 0.54)	0.695[2]
WWI (cm/$\sqrt{kg}$)	11.28 (10.69, 11.87)	11.61 (11.09, 12.17)	11.27 (10.68, 11.86)	< 0.001[2]

Median (IQR) for continuous variables; percentages for categorical variables

[1] Pearson's Chi-squared test

[2] Wilcoxon rank sum test

PIR poverty-to-income ratio, *TC* total cholesterol, *BC* breast cancer, *BMI* body mass index, *WC* waist circumference, *WHtR* waist-height ratio, *WWI* weight-adjusted-waist index

Table 2 Baseline characteristics of the study population according to WWI in NHANES 2011–2018

Characteristic	Weight-adjusted-waist index (cm/√kg)				*P* value
	[8.38,10.69), *N* = 2,548	[10.69,11.28), *N* = 2,548	[11.28,11.87), *N* = 2,548	[11.87,14.41], *N* = 2,549	
Age					< 0.001[2]
< 70	2,454 (96.31%)	2,291 (89.91%)	2,101 (82.46%)	1,825 (71.60%)	
≥ 70	94 (3.69%)	257 (10.09%)	447 (17.54%)	724 (28.40%)	
Race					< 0.001[2]
Mexican American	182 (7.14%)	300 (11.77%)	435 (17.07%)	475 (18.63%)	
Non-Hispanic White	988 (38.78%)	897 (35.20%)	812 (31.87%)	996 (39.07%)	
Non-Hispanic Black	652 (25.59%)	598 (23.47%)	592 (23.23%)	479 (18.79%)	
Other Race	726 (28.49%)	753 (29.55%)	709 (27.83%)	599 (23.50%)	
Educational level					< 0.001[2]
Below high school	258 (10.13%)	406 (15.93%)	619 (24.29%)	810 (31.78%)	
High school level or equivalent	415 (16.29%)	546 (21.43%)	571 (22.41%)	608 (23.85%)	
Some college or AA degree	902 (35.40%)	886 (34.77%)	834 (32.73%)	775 (30.40%)	
Above college	973 (38.19%)	710 (27.86%)	524 (20.57%)	356 (13.97%)	
Marital status					< 0.001[2]
Yes	1,115 (43.76%)	1,281 (50.27%)	1,229 (48.23%)	1,082 (42.45%)	
No	1,433 (56.24%)	1,267 (49.73%)	1,319 (51.77%)	1,467 (57.55%)	
PIR	2.53 (1.27, 4.44)	2.24 (1.18, 4.07)	1.91 (1.07, 3.56)	1.63 (0.96, 2.79)	< 0.001[1]
TC (mg/dL)	181 (160, 205)	192 (168, 217)	195 (173, 222)	193 (167, 219)	< 0.001[1]
Alcohol consumption					< 0.001[2]
Yes	1,539 (60.40%)	1,310 (51.41%)	1,189 (46.66%)	1,032 (40.49%)	
No	1,009 (39.60%)	1,238 (48.59%)	1,359 (53.34%)	1,517 (59.51%)	
Smoking status					< 0.001[2]
Yes	730 (28.65%)	816 (32.03%)	866 (33.99%)	947 (37.15%)	
No	1,818 (71.35%)	1,732 (67.97%)	1,682 (66.01%)	1,602 (62.85%)	
Hypertension					< 0.001[2]
Yes	482 (18.92%)	929 (36.46%)	1,296 (50.86%)	1,599 (62.73%)	
No	2,066 (81.08%)	1,619 (63.54%)	1,252 (49.14%)	950 (37.27%)	
Diabetes mellitus					< 0.001[2]
Yes	92 (3.61%)	254 (9.97%)	514 (20.17%)	832 (32.64%)	
No	2,456 (96.39%)	2,294 (90.03%)	2,034 (79.83%)	1,717 (67.36%)	
Coronary heart disease					< 0.001[2]
Yes	23 (0.90%)	36 (1.41%)	59 (2.32%)	139 (5.45%)	
No	2,525 (99.10%)	2,512 (98.59%)	2,489 (97.68%)	2,410 (94.55%)	
Physical activity					< 0.001[2]
Vigorous	358 (14.05%)	342 (13.42%)	329 (12.91%)	273 (10.71%)	
Moderate	615 (24.14%)	590 (23.16%)	539 (21.15%)	534 (20.95%)	
No	1,575 (61.81%)	1,616 (63.42%)	1,680 (65.93%)	1,742 (68.34%)	
BC					< 0.001[2]
Yes	36 (1.41%)	54 (2.12%)	69 (2.71%)	100 (3.92%)	
No	2,512 (98.59%)	2,494 (97.88%)	2,479 (97.29%)	2,449 (96.08%)	

Median (IQR) for continuous variables; percentages for categorical variables

[1] Kruskal-Wallis rank sum test

[2] Pearson's Chi-squared test

PIR poverty-to-income ratio, *TC* total cholesterol, *BC* breast cancer

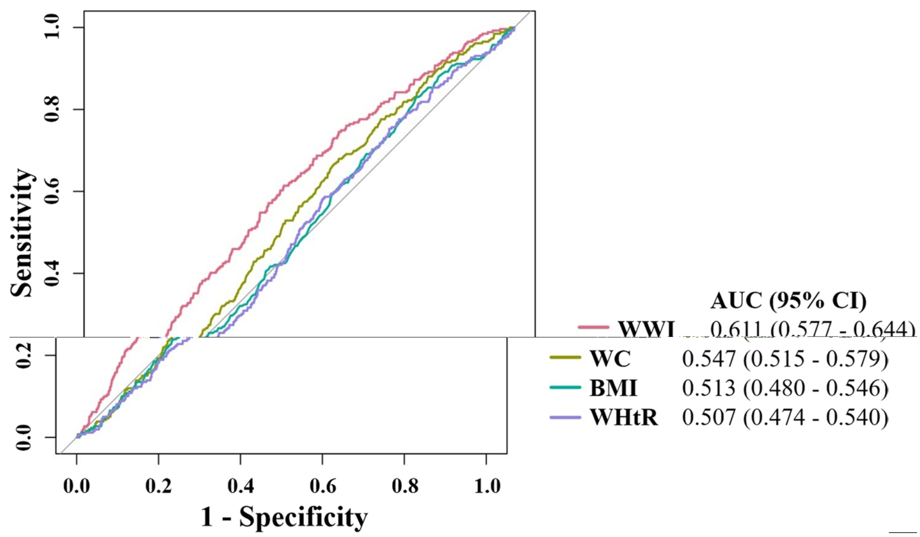


Fig. 2 ROC curve for BC

Table 3 Odds ratios and 95% confidence intervals for BC according to WWI

Exposure	OR (95%CI), *P* value	
	Unadjusted model	Adjusted model
WWI (continuous)	1.54 (1.34, 1.79) < 0.0001	1.19 (1.00, 1.42) 0.0448
WWI (quartile)		
Q1 [8.38, 10.69)	Reference	Reference
Q2 [10.69, 11.28)	1.51 (0.99, 2.31) 0.0572	1.24 (0.80, 1.92) 0.3348
Q3 [11.28, 11.87)	1.94 (1.29, 2.92) 0.0014	1.37 (0.88, 2.11) 0.1600
Q4 [11.87, 14,41]	2.85 (1.94, 4.19) < 0.0001	1.62 (1.05, 2.51) 0.0299
***P*for trend**	1.68 (1.41, 2.00) < 0.0001	1.26 (1.03, 1.55) 0.0247

WWI was transformed from a continuous variable into a categorical variable (quartiles)

WWI weight-adjusted-waist index, *OR* odds ratio, *95% CI* 95% confidence interval

Adjusted model: adjusted for age, race, education level, marital status, PIR, TC, alcohol consumption, smoking status, hypertension, diabetes mellitus, coronary heart disease, and physical activity

at the highest point of the curve, with a WWI of approximately 12.00 cm/√kg, illustrating the turning point of the relationship and splitting the data into two sections. Segmented logistic regressions were then performed on the two models and the effects of WWI on BC are displayed in Table 4. The prevalence of BC in the unadjusted model consistently tended to increase, rising dramatically by 104% with each unit rise in WWI before the inflection point of 11.28 cm/√kg and 31% thereafter. In the adjusted model, the prevalence of BC rose by 73% with each unit rise in WWI below 12.00 cm/√kg but fell by 12% beyond. The upwards trend in the association between WWI and BC shifted, while WWI was approximately 12.00 cm/√kg, followed by a negative trend.

Subgroup analyses revealing potential variations among populations

Subgroup analyses were carried out to uncover potential variations among populations as well as to examine the sturdiness of the relationship between WWI and BC; the findings are displayed in Fig. 4. Tests of

Table 4 Effect of WWI on BC: odds ratios from segmented logistic regression analysis

Model	Inflection point	Characteristic	OR	95% CI	*P* value
Unadjusted model	11.28	WWI < Inflection point	2.04	1.25, 3.34	0.004
		WWI ≥ Inflection point	1.31	0.99, 1.74	0.057
Adjusted model	12.00	WWI < Inflection point	1.73	1.34, 2.24	< 0.001
		WWI ≥ Inflection point	0.88	0.50, 1.55	0.65

WWI weight-adjusted-waist index, *OR* odds ratio, *95% CI* 95% confidence interval

Adjusted model: adjusted for age, race, education level, marital status, PIR, TC, alcohol consumption, smoking status, hypertension, diabetes mellitus, coronary heart disease, and physical activity

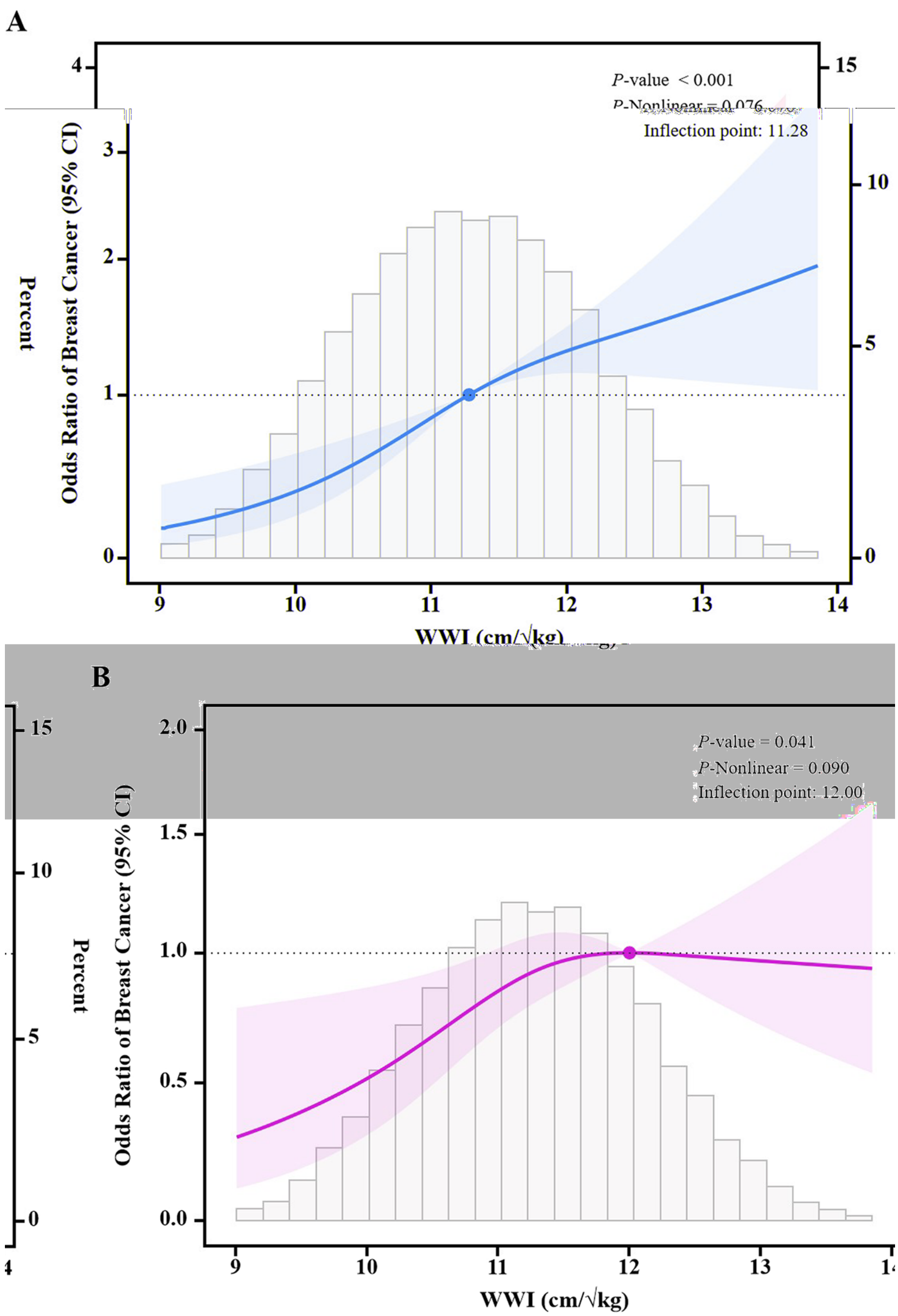
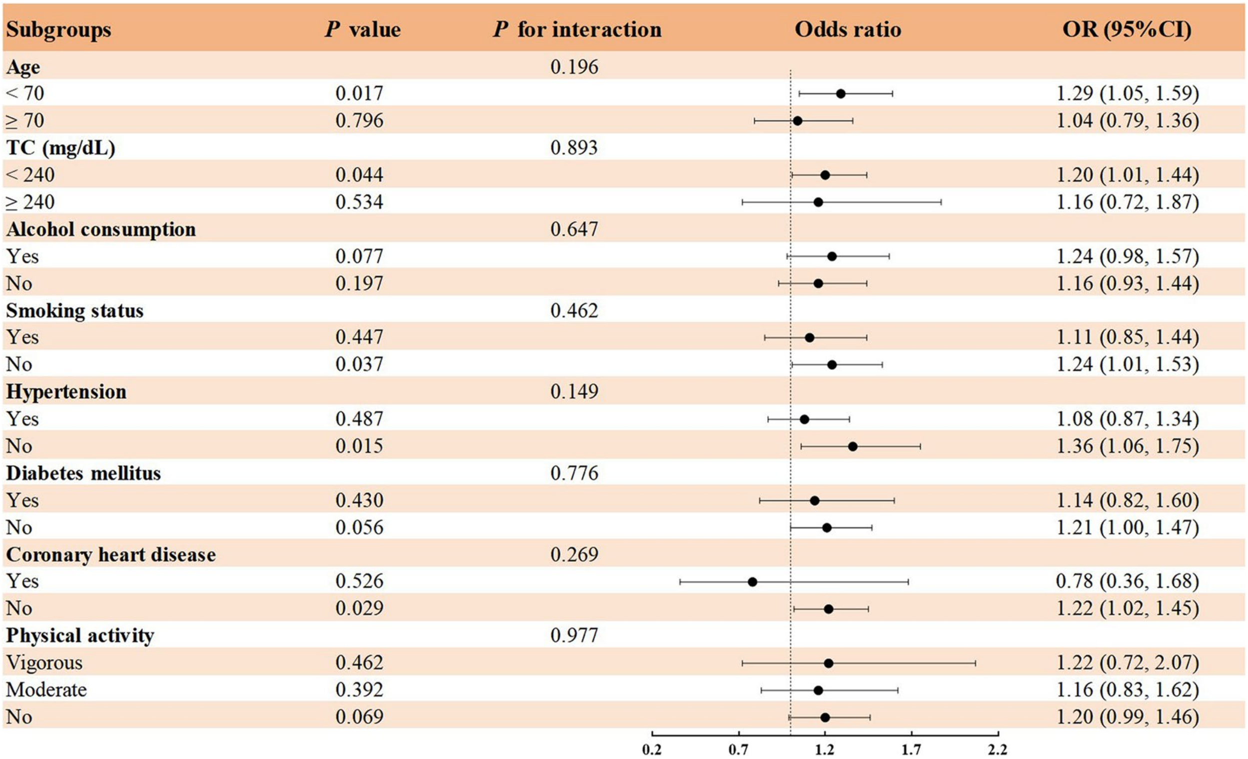


Fig. 3 **A** Restricted cubic splines for the relationship between WWI and BC (unadjusted model). **B** Restricted cubic splines for the relationship between WWI and BC (adjusted model)

interactions indicated that the association between WWI and BC did not vary significantly across groups, indicating that age, TC, diabetes, blood pressure, CHD, physical activity, smoking, and alcohol consumption did not have a notable effect on this meaningful relationship (P for interaction > 0.05). The associations between WWI and BC were significant in people under 70 years of age (OR = 1.29; 95% CI: 1.05–1.59; $P = 0.017$), those with TC < 240 mg/dL (OR = 1.20; 95% CI: 1.01–1.44; $P = 0.044$), those without smoking habits (OR = 1.24; 95% CI: 1.01–1.53; $P = 0.037$), hypertension (OR = 1.36; 95% CI: 1.06–1.75; $P = 0.015$), and CHD (OR = 1.22; 95% CI: 1.02–1.45; $P = 0.029$). In a state of healthy body metabolism and the absence of underlying



Subgroups	*P* value	*P* for interaction	Odds ratio	OR (95%CI)
Age		0.196		
< 70	0.017			1.29 (1.05, 1.59)
≥ 70	0.796			1.04 (0.79, 1.36)
TC (mg/dL)		0.893		
< 240	0.044			1.20 (1.01, 1.44)
≥ 240	0.534			1.16 (0.72, 1.87)
Alcohol consumption		0.647		
Yes	0.077			1.24 (0.98, 1.57)
No	0.197			1.16 (0.93, 1.44)
Smoking status		0.462		
Yes	0.447			1.11 (0.85, 1.44)
No	0.037			1.24 (1.01, 1.53)
Hypertension		0.149		
Yes	0.487			1.08 (0.87, 1.34)
No	0.015			1.36 (1.06, 1.75)
Diabetes mellitus		0.776		
Yes	0.430			1.14 (0.82, 1.60)
No	0.056			1.21 (1.00, 1.47)
Coronary heart disease		0.269		
Yes	0.526			0.78 (0.36, 1.68)
No	0.029			1.22 (1.02, 1.45)
Physical activity		0.977		
Vigorous	0.462			1.22 (0.72, 2.07)
Moderate	0.392			1.16 (0.83, 1.62)
No	0.069			1.20 (0.99, 1.46)

Fig. 4 Subgroup analysis of the association between WWI and BC

disease, the application of WWI for suggesting BC hazard was relatively appropriate.

Discussion

Owing to the meaningful association between WWI and the prevalence of BC, this cross-sectional study of 10,193 adults implied that WWI was a well-suggestive indicator of BC hazard. Maintaining WWI in the lower range was critical to preventing and administering BC and minimizing disease risk. The relationship between WWI and BC was intricate. The initial conclusion of a positive association was based on logistic regression and remained statistically significant even after accounting for confounders. However, the overall relationship between WWI and BC was not strictly linear, and the inverted U shape of the RCS emphasized the existence of a turning point in the relationship, implying that WWI above 12.00 cm/√kg was less suggestive of BC risk, which was inconsistent with the actual situation and required further exploration. Excessive central obesity may be theoretically protective against BC, which is not the case. A thorough review of the study data revealed that the inflection point occurred within the highest quartile of WWI, and the logistic regression's strong positive association prior to the inflection point may have hidden the nonlinear nature of the relationship, as shown in detail by the RCS, where segmented logistic regression took into account the pattern of associations in distinct parts of the curve. Thus, the positive relationship could be interpreted as a general trend in WWI over some specific range, such as a significant increase in the prevalence of BC with increasing WWI before the inflection point. Regarding the reason for the inflection point and the downwards trend, since people with excessive obesity and high WWI values constituted a minority of the population, there was a certain survivorship bias that was predisposed to such a deviation. Moreover, people with excessive obesity obtain medical therapies earlier, thus somewhat mitigating the risk factors for the development of BC, which might be one of the primary causes of this finding. Subgroup analysis and interaction tests verified the strength of the positive associations across a range of statistical scenarios, suggesting the promising value of applying WWI in a population with metabolically healthy bodies and no underlying disease. These data indicate that higher WWI may appear to be a separate risk indicator for BC, emphasizing the relationship between central obesity and BC and stressing the crucial role of WWI in both the evaluation and management of BC hazard. Mechanistic exploration of precisely how central obesity is associated with BC is urgently needed and could provide valuable insights into the development of targeted interventions.

There have been various studies that back up the relationship between obesity and BC. Picon-Ruiz et al. stated that obesity contributes to a high risk of BC and poor outcomes and that exercise and weight loss reduce the inflammatory microenvironment, improve antitumour immunity, and reduce estrogen levels in obese BC patients, all of which coincide with a lower likelihood of cancer and a favourable prognosis [26]. According to Dietze et al., non-Hispanic European American women were less likely than African American women to be obese and to be given the diagnosis of triple-negative breast cancer (TNBC), and obesity may contribute to the development, progression, and invasion of TNBC [27]. Mechanistic evidence shows that obesity-related variables cause metabolic modifications that promote tumor development [28]. A climbing tide of investigations have illustrated the intimate relationship between obesity and BC, with traditional markers of obesity including BMI, WHtR, and WC. With a higher BMI, the risk of advanced BC is elevated, according to a multicenter study conducted by Noureen et al. [29]. Chen et al. noted that among early-stage BC patients undergoing adjuvant chemotherapy, severe obesity (BMI $\geq$ 40.0 kg/m^2) at baseline was substantially related to shorter disease-free survival and overall survival and that BMI could impact the prognosis of patients receiving docetaxel treatment [30]. Central obesity, as defined by WHtR, is linked to an increased likelihood of metastasis in women diagnosed with stage I–III BC, as highlighted by Olsson and colleagues [31]. Chen et al. conducted a thorough meta-analysis and discovered a substantial link between pre- and postmenopausal BC and central obesity, using WC and WHtR as measurements [17]. Despite the apparent relationship between these standard measurements and BC, the conundrum of fat acting as a protective factor persists [32, 33]. The "obesity paradox," which claims that fat has a protective benefit, is deceptive. A recognized risk factor for poor cancer survival and a higher prevalence of several cancer types is obesity. To avoid deviation, investigating alternate body composition indices for measuring obesity is necessary [32, 34, 35]. BMI and abdominal obesity (WHtR of $\geq$ 0.85 or WC of $\geq$ 88 cm) differed significantly among races, as did muscle mass and fat distribution [27]. WWI, a novel measure of obesity, integrates the advantages of WC while minimizing its correlation with BMI to effectively indicate central obesity independent of weight. It may provide a further thorough and exact assessment of obesity, potentially revealing the relationship between obesity and BC more effectively [36, 37]. In recent studies, WWI has been found to be an excellent predictor of several diseases. Ye et al. focused on the relationship between higher WWI and a rise in the occurrence of strokes [38]. Yu et al. noted that every unit rise in WWI increased the likelihood of nonalcoholic fatty liver disease by 72% in the population at large, particularly among males [39]. Park et al.'s cohort study compared WWI's predictive ability to BMI, WC, and WHtR and discovered that WWI could be used as a composite predictor of cardiometabolic morbidity and mortality, with positive associations with all outcomes that BMI and WC may not capture, which had optimal performance [14]. Similarly, Zheng et al. reported a more robust relationship between WWI and albuminuria than between BMI and WC, with WWI performing better [40]. WWI offers the potential for additional studies in forecasting the likelihood of different illnesses and warrants the consideration of medical experts. With the paving of previous studies, we evaluated obesity markers horizontally and came to a similar conclusion that WWI was markedly superior to WC, BMI, and WHtR, both in terms of representing between-group variations and practical applicability. Given that obesity is a recognized risk factor for BC development, previous studies have been limited to exploring obsolete obesity indicators such as BMI and WC, which presented consistently weak relationships [17, 23, 41]. The existence of molecular links between central obesity and BC implies that WWI should be investigated as a novel marker that captures obesity characteristics.

There are several potential mechanisms to elucidate the positive association between WWI and BC pathogenesis. Initially, elevated WWI inextricably suggested a modified function of adipose tissue, the death of adipocytes, and persistent low-grade inflammation. Immune cells infiltrate inflammatory adipose tissue, which remodels and experiences a drastically changed local environment that encourages BC formation [42]. Additionally, fibroblasts in adipose tissue are crucial for aromatase expression, which converts androgens into estrogens, and high levels of estrogen in women increase the risk of BC [43]. Furthermore, the higher lipolytic activity of visceral adipose tissue results in unchecked elevated levels of free fatty acids, which have a variety of lipotoxic consequences. Thus, hyperinsulinemia occurs, and metabolic and endocrine factor dysregulation causes a tumorigenic inflammatory state. A key mechanism linking central obesity to BC is the systemic release of proinflammatory cytokines, which alter insulin-initiated signalling pathways and cause insulin resistance. Low levels of adiponectin, excessive levels of leptin, and abnormal signalling pathways can all be tied to more aggressive BC [19, 44, 45].

The investigation's credibility and representativeness are enhanced by its reliance on NHANES data, which are characteristic of the U.S. population, along with comprehensive, consistent, and reliable data collection. Relevant factors were adjusted via multifactorial regression to investigate the independent impacts of WWI on BC, and subgroup analysis was performed to explain the associations among diverse groups by employing rigorous statistical approaches for noncollinear variables. WWI, a novel obesity indicator, is generated via a reasonably simple formula that is suitable for practical use and could provide new insights into BC risk management.

However, this study has several drawbacks. The limitations of using a cross-sectional research methodology prevented the ability to definitively link WWI and BC causally and ignored the variation in survival durations between the baseline primary exposure and the uncensored participants with confirmation of the final clinical outcome. Moreover, the BC inclusion criteria depended on self-declaration without a registry-based confirmation, which may have hampered accuracy, led to bias, and did not allow for a more in-depth analysis of the relationships between different BC subtypes or stages and WWI. Despite adjusting for certain variables, the influence of others could not be fully eradicated, but the data showed that the current associations between WWI and BC were adequately stable and unlikely to be substantially influenced by uncontrolled variables. The presentation of the data was directly tied to the number of research participants, particularly the overly obese population, which affected the statistics to some extent. Regrettably, the details of the crowd could not be fully captured, and the study could only depend on the existing data. It is crucial to understand the causes of this nonlinear relationship, along with the variables affecting the inflection point in the future. Further expanding the sample size, improving the survey's accuracy and comprehensiveness, and additionally exploring the uneven distribution of survival time may aid in the presentation of reliable outcomes. The medicine and particular therapy of the researched group can be investigated thoroughly. Overall, this study contributes to the existing knowledge on the relationship between obesity indices and BC by filling a gap in the understanding of the association of the innovative central obesity indicator WWI. Retaining WWI at a low level was crucial for preventing and managing BC and minimizing disease risk.

Conclusion

This study revealed a meaningful but complicated association between WWI and BC prevalence, still implying that WWI is an innovative suggestive indicator of BC hazard and has more application value compared with other obesity indicators, which may provide new foundations for central obesity and public health strategies related to BC. Given the present constrained study size, higher-quality prospective investigations and survival analyses are needed to corroborate these findings.

Abbreviations

WWI	Weight-adjusted-waist index
BC	Breast cancer
NHANES	National Health and Nutrition Examination Survey
OR	Odds ratio
CI	Confidence interval
WC	Waist circumference
BMI	Body mass index
WHtR	Waist-height ratio
PIR	Poverty-to-income ratio
TC	Total cholesterol
HbA1c	Glycosylated haemoglobin
CHD	Coronary heart disease
IQR	Interquartile range
AUC	Area under the curve
ROC	Receiver operating characteristic
RCS	Restricted cubic splines
TNBC	Triple-negative breast cancer

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Authors' contributions

XYH, HZC, WYD: study design, drafting, and plotting. LFD, STW, and JXL: gathering, organizing, and analysis. AQ, CQC, WYD, XL: interpreting, reviewing. XYH: writing. All the authors checked out and approved the final paper.

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Data availability

The data used in this study are publicly available in the NHANES database (www.cdc.gov/nchs/nhanes). Raw data can be obtained from the corresponding author.

Declarations

Ethics approval and consent to participate

This research employed information gathered from publicly accessible databases; it needed no ethical approval.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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