Clinical Interventions in Aging

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ORIGINAL RESEARCH

Association Between Weight-Adjusted Waist Index and Cognitive Function in Older Adults Without Diabetes: A Cross-Sectional Study

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Background: This study investigates the correlation between the weight-adjusted waist index (WWI) and cognitive performance in the senior American population, focusing on those without diabetes from 2011 to 2014.

Methods: We analyzed data from the 2011–2012 and 2013–2014 National Health and Nutrition Examination Surveys (NHANES), focusing on non-diabetic participants aged 60 and older who completed cognitive tests: Establish a Registry for Alzheimer's disease (CERAD), the Animal Fluency test (AFT), and Digit Symbol Substitution test (DSST). WWI was calculated using waist circumference divided by the square root of body weight. We employed linear univariate and multivariate analyses, along with curve fitting, we conducted subgroup and interaction analyses to elucidate the relationships under investigation.

Results: The study incorporated a cohort of 1649 participants aged 60 years and older, each with a complete set of data, enabling a thorough analysis. After adjusting for confounding factors, significant negative correlations were found between WWI and both CERAD (β: −0.48; 95% CI: −0.92 to −0.05; P=0.03) and DSST (β: −1.15; 95% CI: −2.09 to −0.21; P=0.017) scores, suggesting a link to cognitive decline. No association was found with AFT scores. The relationship between WWI and DSST was found to be nonlinear (P for non-linearity=0.022). Additionally, the association between WWI and CERAD was also observed (P for non-linearity=0.042). However, linear relationships were observed between WWI and AFT (P for non-linearity=0.418). The subgroup analysis was overall stable.

Conclusion: Our cross-sectional study indicates a strong link between a high WWI and reduced cognitive function in non-diabetic older Americans, as shown by CERAD and DSST scores. Attaining an optimal WWI may be vital for cognitive decline, highlighting its role in a potential preventative approach.

Clinical Trial Registry Number and Website Where It Was Obtained: The study design and data are publicly accessible at www.cdc.gov/nchs/nhanes/.

Keywords: cognitive function, non-diabetic, NHANES, cross-sectional study, weight-adjusted-waist index, WWI

Introduction

As the global population continues to age, the issue of cognitive decline in the elderly has become a significant challenge in public health.[1] Cognitive disorders, which encompass a decline in areas such as memory, language, executive function, spatial vision, comprehension, judgment, and calculation, are early indicators of neurodegenerative diseases like Alzheimer's and vascular dementia. Projections suggest that the global number of individuals with dementia will increase from 58 million in 2022 to 82 million by 2050.[2] In the United States, the number of adults aged 65 and older with clinical Alzheimer's disease is expected to rise from 6.9 million in 2024 to 13.8 million by 2060.[3] This growing prevalence poses a threat to the quality of life for the elderly and places greater demands on socioeconomic systems and healthcare

Received: 4 October 2024
Accepted: 13 January 2025
Published: 25 January 2025

resources. Early identification of risk factors for cognitive disorders, along with appropriate preventive measures, is crucial in slowing disease progression and improving patient quality of life.

Obesity can exert adverse effects on the central nervous system,[4] particularly central obesity, has been linked to an increased risk of cognitive impairment in older adults,[5] and nearly doubles the risk of Alzheimer's disease (AD).[6] The weight-adjusted waist index (WWI)[7] is a novel measure of central obesity that outperforms body mass index (BMI). Existing research indicates a negative association between WWI and cognitive function, linking higher indices to poorer cognitive status.[8–10]

In these studies, a subset of participants had diabetes. However, diabetes confers a 1.25 to 1.91-fold increased risk for cognitive disorders, encompassing cognitive impairment and dementia.[11] Diabetes also can accelerate the progression of cognitive impairment to dementia.[12,13] In light of the significant non-diabetic population, this study is explore the relationship between Weight-Adjusted Waist Index (WWI) and cognitive function in this population using data from the National Health and Nutrition Examination Survey (NHANES).

Material and Methods

Data Sources

This study used data from two NHANES cycles (2011–2012 and 2013–2014). NHANES uses a complex, stratified, and multistage design with sample weight to exactly estimate the prevalence of various diseases. The NHANES protocol was approved by the NCHS Research Ethics Committee after thorough review. Written informed consent was obtained from all participants, confirming their voluntary participation. Detailed study design and NHANES data can be accessed on the website: www.cdc.gov/nchs/nhanes/.[14]

In light of the Ethical Review Methods for Life Science and Medical Research Involving Human Beings. We have found that Article 32 of this regulation specifically exempts research from requiring ethical approval under certain conditions. According to Article 32:

Ethical approval is not required for research that meets the criteria of (a) using legally obtained public data, or data generated by observation and not interfering with public behavior; and (b) using anonymized informational data to conduct the research. Our study complies with exemption criteria, utilizing legally obtained public data and ensuring no disruption to public conduct. The research was also conducted with anonymized data, ethical approval and consent were not required.

Measurement of WWI

The WWI is a new index for the evaluation of human obesity that is proportional to age and reflects physical alterations associated with age. WWI (cm/√kg) was calculated by dividing weight (kg) by the square root of waist (cm)(7). The body measures data were collected, in the Mobile Examination Center (MEC), by trained health technicians.

Cognitive Function Assessment

In the NHANES study, participants underwent various cognitive function tests to evaluate their memory and executive skills: 1) word learning and recall modules from the Consortium to Establish a Registry for Alzheimer's disease (CERAD); 2) the Animal Fluency test (AFT); and 3) the Digit Symbol Substitution test (DSST).

The CERAD Word Learning subtest (CERAD W-L) assesses immediate and delayed learning ability for new verbal information (memory sub-domain).[15] The test consists of three consecutive learning trials, and a delayed recall. Participants are instructed to read aloud 10 unrelated words, then recall as many words as possible. The delayed word recall occurred after the other two cognitive exercises (Animal Fluency and DSST) were completed (approximately 8–10 minutes from the start of the word learning trials). The final score for the CERAD test is the sum of the three learning trials and the delayed recall, each scored from 0 to 10.

Animal Fluency test (AFT) examines categorical verbal fluency, a component of executive function.[16] Participants are asked to name as many animals as possible in one minute. A point is given for each named animal.

The Digit Symbol Substitution test (DSST), a performance module from the Wechsler Adult Intelligence Scale (WAIS III), relies on processing speed, sustained attention, and working memory.[17] The exercise is conducted using a paper form that has a key at the top containing 9 numbers paired with symbols. Participants have 2 minutes to copy the corresponding symbols in the 133 boxes that adjoin the numbers. The score is the total number of correct matches.

Covariates

We included a range of covariates previously identified in the literature as related to obesity factors and cognitive function. These primarily included sociodemographic [age, gender, race and ethnicity, marital status and poverty-to-income ratios (PIR), education level], Lifestyle (BMI, Smoking status, drinking status), and comorbidities (history of hypertension, coronary heart disease, stroke, angina, heart attack and congestive heart failure).[8–10,18–20]

Statistical Analysis

The Kolmogorov–Smirnov test was used to determine the normality of continuous variables. Normally distributed variables were presented as mean (standard deviation), while skewed variables were presented as median (interquartile range, 25–75%). Categorical variables were represented by percentage (%). Statistical tests such as ANOVA, Kruskal–Wallis, and chi-squared tests were applied to compare differences across groups.

The multivariate linear regression explored WWI as a continuous variable. β and 95% confidence interval (CI) were calculated to assess the relationship between WWI and cognitive function. Model 1 represented the crude model without any adjustment for variables. Model 2 was adjusted for age, gender, race/ethnicity, marital status, poverty income ratio, and education level. Model 3 was further adjusted for health habits (smoking, drinking) and comorbidities (coronary heart disease, stroke, angina, heart attack, congestive heart failure and hypertension). We conducted a restricted cubic spline (RCS) to explore the dose–response relationship between WWI and global cognition, modified by adjusting the cofounders consistent with model 3. The subgroup analysis was conducted using the following variables: gender, age (<70 vs ≥ 70 years), BMI (<25 vs 25–30 or ≥ 30 kg/m^2), and history of relevant diseases.

Analysis was performed using R 4.2.1 (http://www.Rproject.org; The R Foundation, Vienna, Austria) and the Free Statistics software (version 1.9.2; Beijing Free Clinical Medical Technology Co., Ltd, Beijing, China). In all analyses, a two-sided p-value < 0.05 indicated statistical significance.

Results

Study Population

Of the 3632 participants aged ≥ 60 years, we excluded subjects with incomplete cognitive information (n=698) and participants with incomplete waist and weight measurements (n=172). Then this study excluded those participants who with diabetes (n=912), according to the American Diabetes Association (ADA)'s diabetes diagnostic criteria, diabetes is defined by self reported diagnosis, use of insulin or oral hypoglycemic medication, FBG ≥ 126 mg/dL, 2-hour post-load glucose after OGTT ≥ 200 mg/dL, random blood glucose (mmol/L) ≥ 11.1 or HbA1c level ≥ 6.5%.[21] Next, this study excluded participants who had unavailable data on covariates (n = 201). Therefore, 1649 participants were included in the final analyses (Figure 1).

Baseline Characteristics

A total number of 1649 non-diabetic participants aged ≥60 years were included in the analysis. Table 1 shows the general characteristics of the participants according to weight-adjusted-waist index quintile. According to the WWI, we conducted quintiles analysis, Q1 (<10.79 cm/√kg), Q2 (10.79–11.18 cm/√kg), Q3 (11.18–11.54 cm/√kg), Q4 (11.54–11.93 cm/√kg), Q5 (>11.93 cm/√kg). Among all participants, the mean age was 69.2 (6.8) years, and 868 (52.6%) individuals were female and 53.1% within Non-Hispanic White. The mean values of the cognitive function tests were as follows: CERAD 25.5 (6.6), AFT 17.2 (5.6), and DSST 49.0 (17.0). Compared with other groups, group 5 (WWI ≥ 11.93) tended to be older, female, non-Hispanic white, not living alone, low level in PIR, low education level, a higher BMI, never smokers and current drinkers. This group shows a significantly higher prevalence of coronary heart disease, stroke, angina, heart attack,

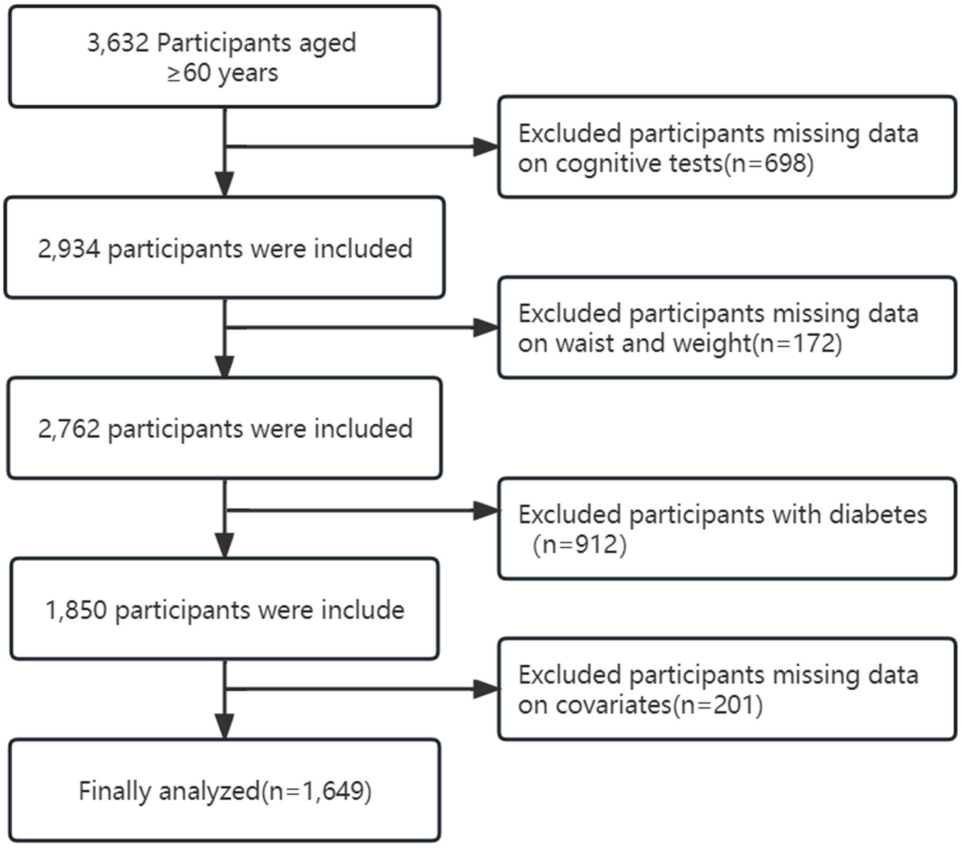

Figure 1 Flow Diagram of the Screening and Enrollment of Study Participants.

congestive heart failure and hypertension. In addition, participants had lower scores in all cognitive performance, including DSST, AFT and CERAD test.

The Association Between WWI and Cognitive Function

The univariate analysis indicated that age, gender, race and ethnicity, PIR, education level, smoking status, drinking status, stroke, angina, heart attack, congestive heart failure and hypertension were correlated with cognitive function (Table 2).

Table 1 Baseline Characteristics of Participants in NHANES, 2011–2014

Characteristics	Weight-Adjusted-Waist Index (cm/√kg)						
	Total	Q1 (<10.79)	Q2 (10.79–11.18)	Q3 (11.18–11.54)	Q4 (11.54–11.93)	Q5 (>11.93)	*p*-value
NO.	1649	330	330	329	330	330	
Age (year), Mean ± SD	69.2 ± 6.8	67.3 ± 6.2	68.5 ± 6.7	69.3 ± 6.6	70.2 ± 7.0	70.8 ± 6.8	< 0.001
Gender, n (%)							< 0.001
Male	781 (47.4)	185 (56.1)	172 (52.1)	178 (54.1)	147 (44.5)	99 (30)	
Female	868 (52.6)	145 (43.9)	158 (47.9)	151 (45.9)	183 (55.5)	231 (70)	
Race/ethnicity, n (%)							< 0.001
Non-Hispanic White	875 (53.1)	148 (44.8)	159 (48.2)	173 (52.6)	196 (59.4)	199 (60.3)	
Non-Hispanic Black	345 (20.9)	110 (33.3)	87 (26.4)	65 (19.8)	46 (13.9)	37 (11.2)	
Mexican American	128 (7.8)	19 (5.8)	20 (6.1)	24 (7.3)	36 (10.9)	29 (8.8)	
Other Hispanic	147 (8.9)	12 (3.6)	31 (9.4)	37 (11.2)	24 (7.3)	43 (13)	
Other Race	154 (9.3)	41 (12.4)	33 (10)	30 (9.1)	28 (8.5)	22 (6.7)	

(*Continued*)

Table 1 (Continued).

Characteristics	Weight-Adjusted-Waist Index (cm/√kg)						
	Total	Q1 (<10.79)	Q2 (10.79–11.18)	Q3 (11.18–11.54)	Q4 (11.54–11.93)	Q5 (>11.93)	*p*-value
Marital status, n (%)							< 0.001
Married	928 (56.3)	203 (61.5)	191 (57.9)	205 (62.3)	175 (53)	154 (46.7)	
Never married	89 (5.4)	25 (7.6)	17 (5.2)	11 (3.3)	17 (5.2)	19 (5.8)	
Living with partner	49 (3.0)	9 (2.7)	9 (2.7)	16 (4.9)	7 (2.1)	8 (2.4)	
Other	583 (35.4)	93 (28.2)	113 (34.2)	97 (29.5)	131 (39.7)	149 (45.2)	
Poverty income ratio, n%							< 0.001
≤1.30	429 (26.0)	71 (21.5)	75 (22.7)	75 (22.8)	95 (28.8)	113 (34.2)	
1.31–3.50	616 (37.4)	109 (33)	131 (39.7)	120 (36.5)	117 (35.5)	139 (42.1)	
>3.50	604 (36.6)	150 (45.5)	124 (37.6)	134 (40.7)	118 (35.8)	78 (23.6)	
Educational Level, n (%)							< 0.001
<9	708 (42.9)	117 (35.5)	143 (43.3)	136 (41.3)	141 (42.7)	171 (51.8)	
9–12	493 (29.9)	91 (27.6)	98 (29.7)	106 (32.2)	107 (32.4)	91 (27.6)	
>12	448 (27.2)	122 (37)	89 (27)	87 (26.4)	82 (24.8)	68 (20.6)	
Body mass index, n%							< 0.001
<25 kg/m^2	517 (31.4)	179 (54.2)	117 (35.5)	90 (27.4)	78 (23.6)	53 (16.1)	
25–30 kg/m^2	617 (37.4)	106 (32.1)	133 (40.3)	150 (45.6)	121 (36.7)	107 (32.4)	
≥30 kg/m^2	515 (31.2)	45 (13.6)	80 (24.2)	89 (27.1)	131 (39.7)	170 (51.5)	
Smoking status, n (%)							0.134
Never	827 (50.2)	165 (50)	164 (49.7)	148 (45)	172 (52.1)	178 (53.9)	
Former	614 (37.2)	114 (34.5)	121 (36.7)	142 (43.2)	116 (35.2)	121 (36.7)	
Current	208 (12.6)	51 (15.5)	45 (13.6)	39 (11.9)	42 (12.7)	31 (9.4)	
Drinking status, n (%)							< 0.001
Never	228 (13.8)	42 (12.7)	47 (14.2)	40 (12.2)	37 (11.2)	62 (18.8)	
Former	412 (25.0)	80 (24.2)	81 (24.5)	66 (20.1)	80 (24.2)	105 (31.8)	
Current	1009 (61.2)	208 (63)	202 (61.2)	223 (67.8)	213 (64.5)	163 (49.4)	
Coronary heart disease, n (%)	109 (6.6)	15 (4.5)	19 (5.8)	25 (7.6)	23 (7)	27 (8.2)	0.333
Stroke, n (%)	92 (5.6)	18 (5.5)	18 (5.5)	20 (6.1)	15 (4.5)	21 (6.4)	0.873
Angina, n (%)	54 (3.3)	5 (1.5)	11 (3.3)	11 (3.3)	13 (3.9)	14 (4.2)	0.323
Heart attack, n (%)	101 (6.1)	15 (4.5)	19 (5.8)	22 (6.7)	17 (5.2)	28 (8.5)	0.246
Congestive heart failure, n (%)	75 (4.5)	13 (3.9)	8 (2.4)	13 (4)	13 (3.9)	28 (8.5)	0.003
Hypertension, n (%)	1084 (65.7)	183 (55.5)	215 (65.2)	210 (63.8)	232 (70.3)	244 (73.9)	< 0.001
AFT, Mean ± SD	17.2 ± 5.6	17.8 ± 6.0	17.1 ± 5.6	17.3 ± 5.3	17.3 ± 5.4	16.4 ± 5.3	0.019
DSST, Mean ± SD	49.0 ± 17.0	52.0 ± 17.1	48.4 ± 17.2	49.3 ±16.1	50.1 ±16.2	45.1 ±17.6	< 0.001
CERAD Test, Mean ± SD	25.5 ± 6.6	26.7 ± 6.2	25.2 ± 6.7	25.4 ± 6.6	25.3 ± 6.3	24.7 ± 6.7	0.003
WWI, Mean ± SD	11.4 ± 0.7	10.4 ± 0.3	11.0 ± 0.1	11.4 ± 0.1	11.7 ± 0.1	12.4 ± 0.4	< 0.001

Note: Continuous variables were shown in mean (standard deviation, SD) and categorical variables were shown in percentages.
Abbreviations: CERAD, The Consortium to Establish a Registry for Alzheimer's Disease; DSST, Digit Symbol Substitution Test; AFT, Animal Fluency test; WWI, weight-adjusted-waist index.

Table 2 Association of Covariates and Cognitive Function

	CERAD Test		CFDAST		CFDDS	
	β (95% CI)	*p*-value	β (95% CI)	*p*-value	β (95% CI)	*p*-value
Age (year), Mean ± SD	−0.29 (−0.33,-0.24)	< 0.001	−0.17 (−0.21,-0.13)	< 0.001	−0.67 (−0.79,-0.56)	< 0.001
Gender, n (%)	2.72 (2.1, 3.34)	< 0.001	−0.06 (−0.6, 0.48)	0.818	5.51 (3.89, 7.14)	< 0.001
female vs male						
Race/ethnicity, n (%)						
Non-Hispanic White	0 (Ref)		0 (Ref)		0 (Ref)	
Non-Hispanic Black	−0.74 (−1.56, 0.07)	0.074	−3.08 (−3.75,-2.4)	< 0.001	−11.13 (−13.14,-9.13)	< 0.001

(*Continued*)

https://doi.org/10.2147/CIA.S499221

Table 2 (Continued).

	CERAD Test		CFDAST		CFDDS	
	β (95% CI)	***p*-value**	**β (95% CI)**	***p*-value**	**β (95% CI)**	***p*-value**
Mexican American	−1.36 (−2.57,-0.14)	0.028	−1.23 (−2.23,-0.22)	0.016	−10.48 (−13.46,-7.49)	< 0.001
Other Hispanic	−1.83 (−2.97,-0.68)	0.002	−2.64 (−3.58,-1.7)	< 0.001	−12.91 (−15.72,-10.09)	< 0.001
Other Race	0.06 (−1.06, 1.18)	0.923	−3.06 (−3.99,-2.14)	< 0.001	−0.44 (−3.2, 2.31)	0.752
Marital status, n (%)						
Married	0 (Ref)		0 (Ref)		0 (Ref)	
Never married	0.01 (−1.41, 1.44)	0.987	−0.39 (−1.6, 0.82)	0.527	−1.35 (−5.03, 2.33)	0.473
Living with partner	−0.11 (−1.99, 1.77)	0.91	1.99 (0.39, 3.58)	0.015	−0.72 (−5.57, 4.14)	0.773
Other	−0.78 (−1.46,-0.11)	0.024	−0.72 (−1.3,-0.14)	0.014	−3.97 (−5.72,-2.22)	< 0.001
Poverty income ratio, n%						
≤1.30	0 (Ref)		0 (Ref)		0 (Ref)	
1.31–3.50	1.4 (0.61, 2.19)	< 0.001	1.34 (0.68, 2.01)	< 0.001	7.41 (5.47, 9.34)	< 0.001
>3.50	3.3 (2.5, 4.09)	< 0.001	3.51 (2.85, 4.18)	< 0.001	16.5 (14.56, 18.45)	< 0.001
Educational Level, n (%)						
<9	0 (Ref)		0 (Ref)		0 (Ref)	
9–12	2.71 (1.97, 3.44)	< 0.001	2.5 (1.89, 3.1)	< 0.001	13.01 (11.27, 14.74)	< 0.001
>12	3.51 (2.76, 4.27)	< 0.001	4.28 (3.65, 4.9)	< 0.001	17.78 (15.99, 19.57)	< 0.001
Body mass index, n%						
<25 kg/m^2	0 (Ref)		0 (Ref)		0 (Ref)	
25–30 kg/m^2	−0.14 (−0.9, 0.63)	0.722	0.51 (−0.14, 1.16)	0.123	1.79 (−0.19, 3.78)	0.077
≥30 kg/m^2	0.73 (−0.07, 1.53)	0.075	0.6 (−0.08, 1.28)	0.086	1.53 (−0.54, 3.6)	0.148
Smoking status, n (%)						
Never	0 (Ref)		0 (Ref)		0 (Ref)	
Former	−0.8 (−1.49,-0.12)	0.022	−0.03 (−0.61, 0.55)	0.92	−1.02 (−2.79, 0.75)	0.257
Current	−1 (−2,-0.01)	0.049	−0.67 (−1.52, 0.17)	0.118	−5.37 (−7.94,-2.79)	< 0.001
Drinking status, n (%)						
Never	0 (Ref)		0 (Ref)		0 (Ref)	
Former	−0.67 (−1.72, 0.39)	0.216	0.47 (−0.41, 1.35)	0.299	−0.22 (−2.89, 2.46)	0.872
Current	0.96 (0.02, 1.9)	0.045	2.7 (1.91, 3.48)	< 0.001	8 (5.63, 10.38)	< 0.001
Coronary Heart Disease, n (%)						
NO	0 (Ref)		0 (Ref)		0 (Ref)	
YES	−1.73 (−3,-0.46)	0.008	−0.63 (−1.71, 0.45)	0.254	−3.89 (−7.19,-0.59)	0.021
Stroke, n (%)						
NO	0 (Ref)		0 (Ref)		0 (Ref)	
YES	−2.48 (−3.86,-1.11)	< 0.001	−2.11 (−3.27,-0.94)	< 0.001	−7.49 (−11.05,-3.93)	< 0.001
Angina, n (%)						
NO	0 (Ref)		0 (Ref)		0 (Ref)	
YES	−1.82 (−3.59,-0.04)	0.045	−0.99 (−2.51, 0.52)	0.197	−6.52 (−11.12,-1.92)	0.005
Heart attack, n (%)						
NO	0 (Ref)		0 (Ref)		0 (Ref)	
YES	−1.61 (−2.93,-0.29)	0.017	−0.9 (−2.02, 0.22)	0.114	−6.75 (−10.16,-3.35)	< 0.001
Congestive heart failure, n (%)						
NO	0 (Ref)		0 (Ref)		0 (Ref)	
YES	−2.76 (−4.27,-1.25)	< 0.001	−2.2 (−3.49,-0.92)	< 0.001	−8.55 (−12.47,-4.63)	< 0.001
Hypertension, n (%)						
NO	0 (Ref)		0 (Ref)		0 (Ref)	
YES	−1.47 (−2.14,-0.81)	< 0.001	−1.79 (−2.35,-1.23)	< 0.001	−5.79 (−7.49,-4.08)	< 0.001
Weight-adjusted-waist index	−0.94 (−1.39,-0.49)	< 0.001	−0.64 (−1.02,-0.26)	0.001	−2.74 (−3.9,-1.57)	< 0.001

Abbreviations: CERAD, The Consortium to Establish a Registry for Alzheimer's Disease;DSST, Digit Symbol Substitution Test; AFT, Animal Fluency test; WWI, weight-adjusted-waist index.

Table 3 The Association Between Weight-Adjusted-Waist Index and Three Cognitive Test Scores Among Non-Diabetic Older Adults

Variable	Model 1		Model 2		Model 3	
	β (95% CI)	*p*-value	β (95% CI)	*p*-value	β (95% CI)	*p*-value
CERAD Test score	−0.94 (−1.39~ −0.49)	<0.001	−0.51 (−0.94~-0.08)	0.021	−0.48 (−0.92~ −0.05)	0.03
AFT score	−0.64 (−1.02~ −0.26)	0.001	−0.3 (−0.66~0.06)	0.102	−0.23 (−0.59~0.13)	0.215
DSST score	−2.74 (−3.9~ −1.58)	<0.001	−1.3 (−2.25~-0.36)	0.007	−1.15 (−2.09~ −0.21)	0.017

Notes: Model 1 adjusted for None. Model 2 adjusted for age, gender, ethnicity, marital status, poverty income ratio and educational level. Model 3 adjusted for age, gender, ethnicity, marital status, poverty income ratio, educational level, smoking status, drinking status, coronary heart disease, stroke, angina, heart attack, congestive heart failure and hypertension.
Abbreviations: CERAD, The Consortium to Establish a Registry for Alzheimer's Disease; DSST, Digit Symbol Substitution Test; AFT, Animal Fluency test.

After fully adjusting confounding factors, WWI expressed as a continuous variable was strongly correlated with the CERAD test score [β: −0.48; 95% CI (−0.92, −0.05); P =0.03] and DSST score [β= −1.15; 95% CI: (−2.09, −0.21); P=0.017]. No significant correlations were found between the WWI and the AFT test score (Table 3).

Analysis of the Non-Linear Relationship Between WWI and Cognition Function

The relationship between WWI and DSST was found to be nonlinear rather than linear (P for non-linearity=0.022, Figure 2A). Additionally, the association between WWI and CERAD was also observed (P for non-linearity = 0.042, Figure 2B). However, linear relationships were observed between WWI and AFT (P for non-linearity = 0.418, Figure 2C).

Stratified Analysis

We further performed stratified analyses of the relationship between WWI and CERAD test, AFT and DSST (Figure 3). The effect (β) of CERAD test, AFT, and DSST, in subgroups was stable overall.

Discussion

This study included a cohort of non-diabetic older adults and explored the association between the weight-adjusted-waist index (WWI) and cognitive function evaluated through three cognitive tests. Our findings revealed after adjusting for confounding factors, significant negative correlations were found between WWI and both CERAD and DSST scores, suggesting a link to cognitive decline. No association was found with AFT scores. The relationship between WWI both CERAD and DSST scores was found to be nonlinear. However, linear relationships were observed between WWI and AFT. The subgroup analysis was overall stable.

Multiple studies have delved into the connection between Weight-Adjusted Waist Index (WWI) and cognitive function. Notably, Zhou et al research identified an independent association between WWI and dementia, with both negative and positive linear correlations observed between WWI and MMSE scores and dementia, respectively.[19] Li et al reported a significant J-shaped nonlinear relationship between WWI and DSST performance, particularly above a WWI threshold of 12.21 cm/√kg.[8] Additionally, Wang et al found that higher WWI values were positively linked to lower cognitive function across CERAD, AFT, and DSST assessments, with nonlinear associations for CERAD W-L and AFT.[9] However, our findings, potentially due to population differences, did not reveal a correlation between WWI and AFT and showed nonlinear relationships with CERAD and DSST, contrasting with the linear relationship found for AFT.

Numerous factors, including excessive body fat accumulation leading to weight gain and obesity, can impact cognitive function. The link between obesity and cognitive dysfunction may involve insulin resistance[22] and chronic inflammatory processes.[23] Obesity can lead to insulin resistance through various complex mechanisms, including changes in adipokines and cytokines, inflammatory responses, mitochondrial dysfunction, production of reactive oxygen species (ROS), endoplasmic reticulum (ER) stress, imbalance in gut microbiota, and remodeling of the extracellular matrix (ECM) in adipose tissue.[22] Excessive fat deposition can alter the secretion of important adipokines and cytokines, such as increasing levels of leptin and plasminogen activator inhibitor-1 (PAI-1), and decreasing levels of adiponectin.[24]

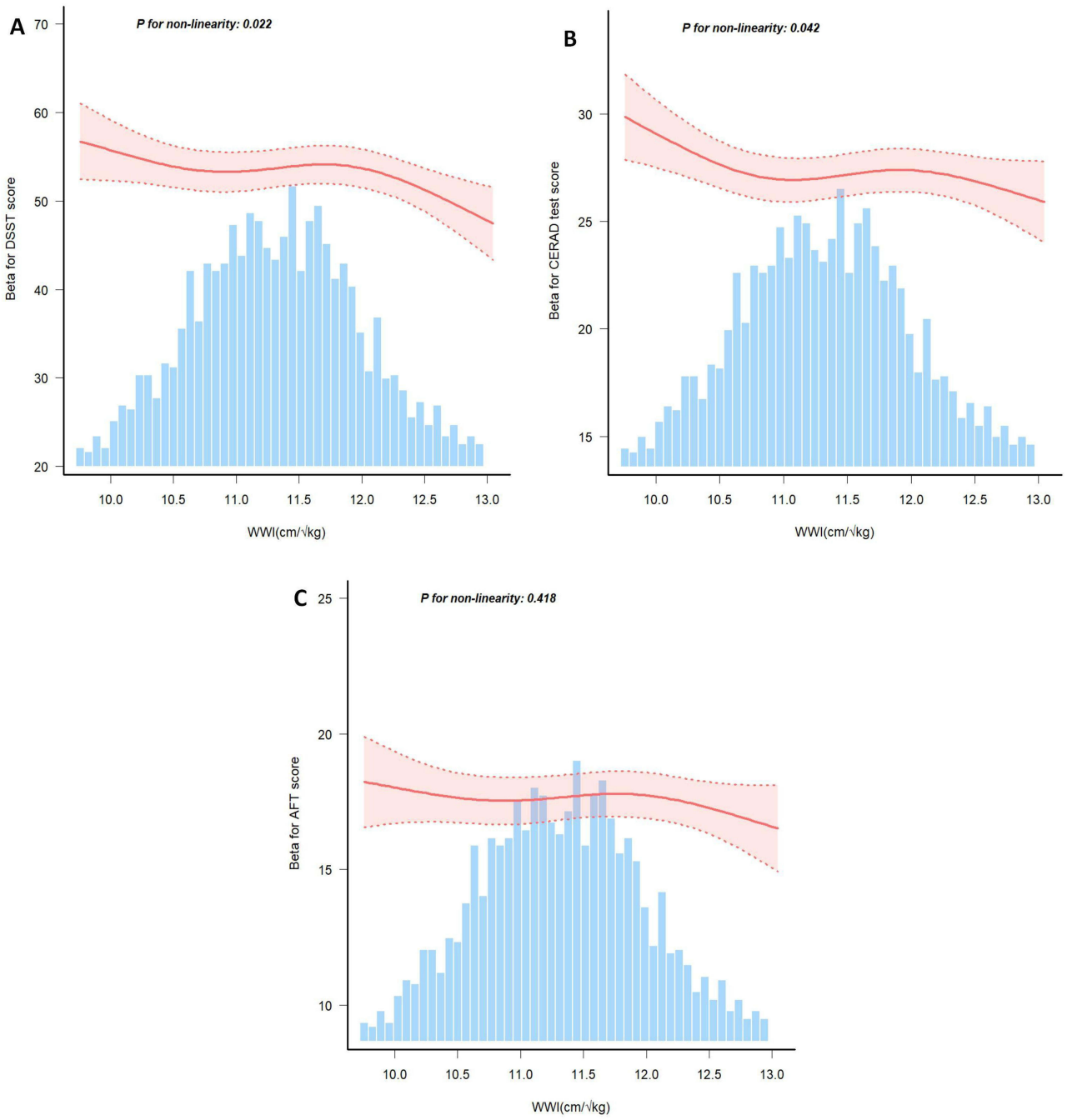

Figure 2 (**A**) Relationship between WWI and DSST score; (**B**) relationship between WWI and CERAD test score; (**C**) relationship between WWI and AFT score. Solid and dashed lines represent the predicted value and 95% confidence intervals. They were adjusted for age, gender, race/ethnicity, marital status, poverty income ratio, educational level, smoking status, drinking status, coronary heart disease, stroke, angina, heart attack, congestive heart failure and hypertension. Only 99% of the data is shown.

Abbreviations: CERAD, The Consortium to Establish a Registry for Alzheimer's Disease; DSST, Digit Symbol Substitution Test; AFT, Animal Fluency test; WWI, weight-adjusted-waist index.

These changes may trigger a systemic low-grade inflammatory response,[25] potentially accelerating the decline in cognitive function and increasing the risk of Alzheimer's disease.[26]

Our study is examine the potential correlation between Weight-Adjusted Waist Index (WWI) and cognitive function in non-diabetic individuals. We deliberately chose a non-diabetic population as the subject of our study, Previous studies have shown a significant correlation between obesity and diabetes. By excluding patients with diabetes, we can more accurately assess the relationship between WWI and cognitive function, without the potential confounding effects of diabetes itself. Non-

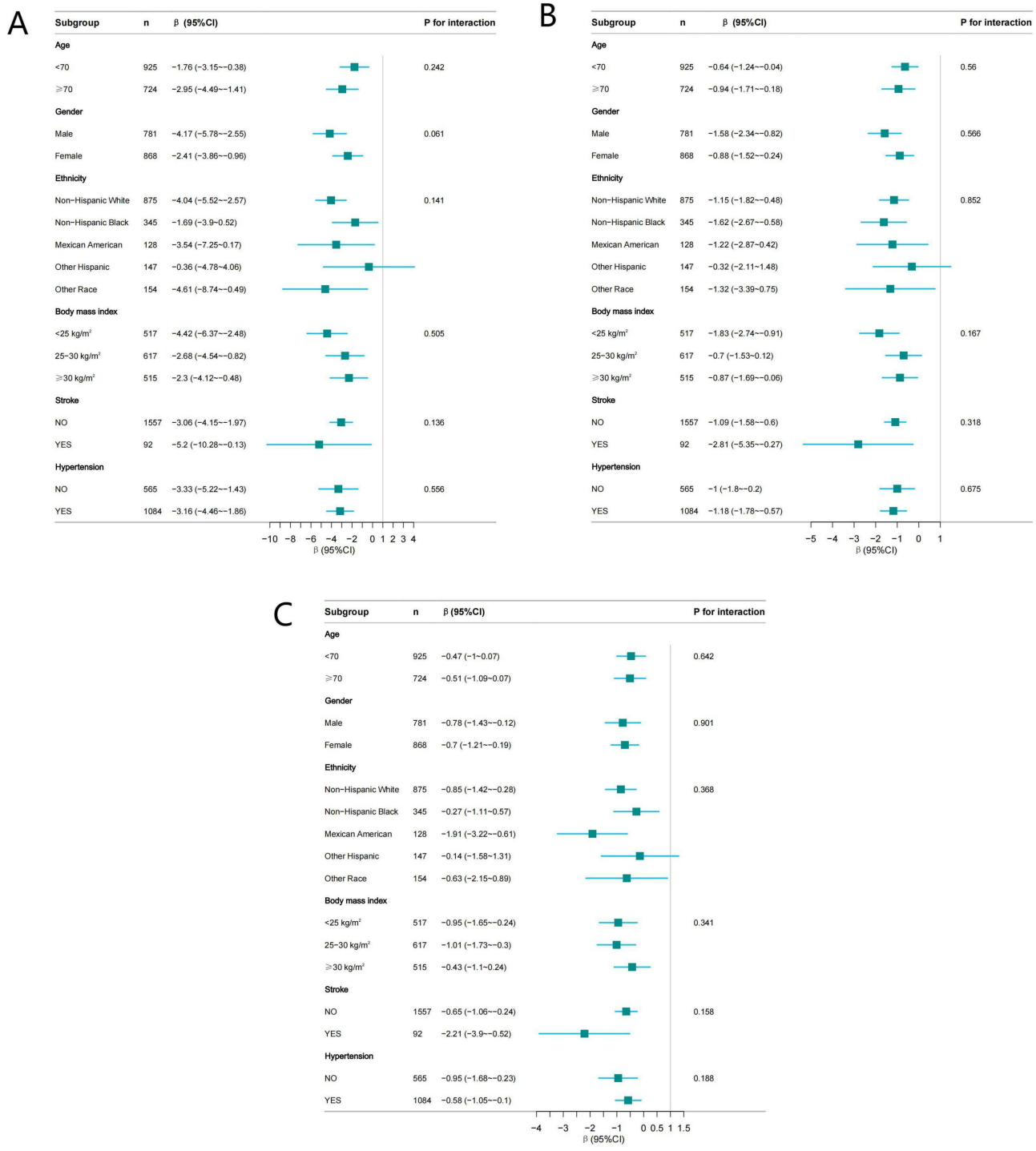

Figure 3 Effect size of WWI on CERAD test, AFT, DSST in subgroups (n = 1649). (**A**) Effect size of WWI on DSST; (**B**) effect size of WWI on CERAD test; (**C**) effect size of WWI on AFT. Adjusted for gender, race/ethnicity, marital status, poverty income ratio, educational level, smoking status, drinking status, coronary heart disease, stroke, angina, heart attack, congestive heart failure and hypertension. The *P* value for interaction represents the likelihood of interaction between the variable and WWI.
Abbreviations: CERAD, The Consortium to Establish a Registry for Alzheimer's Disease; DSST, Digit Symbol Substitution Test; AFT, Animal Fluency test; CI, confidence interval; WWI, weight-adjusted-waist index.

diabetic individuals make up a large proportion of the general population. Therefore, studying this group can better reflect the general impact of obesity on cognitive function. We took into account the impact of novel covariates such as hypertension, coronary heart disease, stroke, Angina, Heart attack and congestive heart failure on cognitive function. However, There are several limitations to our study that warrant consideration. Firstly, our sample comprised exclusively of non-diabetic

https://doi.org/10.2147/CIA.S499221

individuals, which may restrict the generalizability of our results. Secondly, the association between WWI and cognitive function, as observed in this cross-sectional study, should be further explored through prospective cohort studies to enhance the clarity of our findings. While we accounted for several potential confounders, we acknowledge that unmeasured factors associated with cognitive decline could still exert an influence. Thirdly, given that our study concentrated on US adults aged 60 and older, the broader applicability of these results to the overall elderly population necessitates additional research. Fourthly, The high WWI values among participants, potentially indicating a predominance of obesity, along with reliance on self-reported data and the presence of cognitive impairments in some participants, including those who may have undiagnosed diabetes, could introduce biases into our analysis.

Conclusion

Our cross-sectional study indicates a strong link between a high WWI and reduced cognitive function in non-diabetic older Americans, as shown by CERAD and DSST scores. Attaining an optimal WWI may be vital for preventing cognitive decline, highlighting its role in a potential preventative approach. In the future, we intend to seek multi-center studies, employ larger sample sizes, or explore alternative study designs to further validate this relationship.

Abbreviations

WWI, weight-adjusted waist index; NHANES, National Health and Nutrition Examination Surveys; CERAD, Establish a Registry for Alzheimer's disease; AFT, Animal Fluency test; DSST, Digit Symbol Substitution test; AD, Alzheimer's disease; BMI, body mass index; MEC, Mobile Examination Center; CI, confidence interval.

Data Sharing Statement

These survey data are free and publicly available, and can be downloaded directly from the NHANES website (http://www.cdc.gov/nchs/nhanes.htm) by users and researchers worldwide.

Ethics Approval and Consent to Participate

The NHANES protocol underwent rigorous evaluation and received approval from the NCHS Research Ethics Committee. Prior to taking part in the survey, all participants provided written informed consent, demonstrating their voluntary agreement to participate.

Acknowledgments

We gratefully thank Jie Liu of the Department of Vascular and Endovascular Surgery, Chinese PLA General Hospital for his contribution to the statistical support, study design consultations, and comments regarding the manuscript. We thank all the patients who took part in the study.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare that they have no competing interests in this work.

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