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Association between the weight-adjusted waist index and age-related macular degeneration

Results from NHANES 2005-2008

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Abstract

The present study aimed to explore the association between weight-adjusted waist index (WWI) levels, a newly proposed indicator for assessing obesity, and the risk of age-related macular degeneration (AMD). A cross-sectional analysis of 20,497 participants was conducted using the National Health and Nutrition Examination Survey (NHANES) 2005-2008 dataset. Trend tests, multivariable logistic regression, and smoothing curve fitting were performed to examine the association between WWI and the risk of AMD. In addition, subgroup analysis and interaction tests were used to test this association in different groups. A total of 5476 participants were included in the study, of whom 420 (7.7%) had AMD. The risk of age-related macular degeneration increased with increasing WWI in all models. In the fully adjusted model, a 55% increase in the prevalence of AMD was observed in the highest tertile (tertile 3: >11.52) of WWI (OR 1.55, 95% CI 1.09, 2.21) compared to the lowest tertile (tertile 1: <10.85). The interaction tests revealed that age, chronic kidney disease, and cardiovascular disease had significant interactions with WWI on AMD risk (*P* for interaction < .05). This study revealed that higher WWI levels were associated with increased risk of AMD, suggesting that managing obesity according to WWI may reduce AMD risk. However, additional research is warranted to corroborate our results.

Abbreviations: AMD = age-related macular degeneration, BMI = body mass index, CKD = chronic kidney disease, CRP = c-reactive protein level, CVD = cardiovascular disease, MEC = Mobile Examination Center, NCHS = National Center for Health Statistics, NHANES = National Health and Nutrition Examination Survey, PIR = family income to poverty, WC = waist circumference, WHR = waist–hip ratio, WHtR = waist-to-height ratio, WWI = weight-adjusted waist index.

Keywords: age-related macular degeneration, cross-sectional study, NHANES, obesity, weight-adjusted waist index

1. Introduction

In developed nations, age-related macular degeneration (AMD) is recognized as the primary cause of permanent visual impairment, characterized by lesions of the macular region of the retina, leading to a progressive decline in central vision. This condition significantly impacts daily activities such as driving, reading, and facial recognition, imposing a substantial public health burden due to its association with diminished quality of life, restricted mobility and independence, and heightened vulnerability to falls and depression.[1,2] AMD primarily impacts individuals aged 55 and older, and the prevalence of the disease is projected to increase with the aging global population. Estimations state that by the year 2040, 288 million individuals will be affected by AMD, representing a significant global burden.[3,4] Therefore, the identification of modifiable and preventable risk factors is essential for mitigating the prevalence of AMD.

Obesity is characterized by an accumulation of adipose tissue and is a significant public health issue linked to various comorbidities, including diabetes, hypertension, metabolic disorders, and dyslipidemia.[5] However, the relationship between obesity and AMD remains unclear. Some studies have reported a positive association between indicators of obesity and AMD risk,[6,7] whereas others have not shown such a relationship.[8,9] These conflicting findings may be attributed to the inadequacy

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

NHANES protocol approved by NCHS Research Ethics Review Board, and obtained informed consent from all participants.

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of conventional metrics including the body mass index (BMI), waist circumference (WC) in distinguishing fat from muscle mass.[10–12]

Park et al proposed the introduction of weight-adjusted waist index (WWI) as a novel anthropometric measure, which is defined as dividing the WC by the square root of the weight. This measure reserves the benefits of WC while diminishing the association with BMI,[13] thus can reflects weight-independent centripetal obesity. Additionally, WWI can indicate the composition of fat and muscle mass.[14] Furthermore, the measure can be applied to multiethnic groups,[15] and involves a simple calculation. WWI has been extensively researched in various fields, particularly in cardiovascular disease, and has shown strong predictive capabilities for numerous obesity-related conditions.[16–19] Studying the relationship between WWI and AMD can provide us with a more profound insight into the influence of obesity on the risk of AMD. Therefore, this study analyzed data from the 2005-2008 National Health and Nutrition Examination Survey (NHANES) to explore this relationship.

2. Methods

2.1. Study population

The data were obtained from 2 cycles of the NHANES 2005-2008, a research project conducted by the Centers for Disease Control and Prevention's National Center for Health Statistics (NCHS), using complicated, multistage, and probabilistic sampling methods. The NHANES provides a wealth of nutritional and healthy data from the United States, including demographic, dietary, physical examination, laboratory, and questionnaire information. The research was approved by the NCHS Research Ethics Review Board. All participants were required to provide written consent before participating in the study.[20] For more information about NHANES, visit https://www.cdc.gov/nhanes.

A total of 20,497 participants' data were extracted from NHANES. Subsequently, 13,416 individuals under the age of 40 were excluded, along with 1477 participants with missing information on AMD and 128 with missing information on weight and WC date. Ultimately, 5476 individuals were included in this study (Fig. 1).

2.2. Exposure variable

The present study utilized WWI (cm/√kg) as the exposure variable for estimating obesity. In the Mobile Examination Center (MEC), trained health technicians performed body measurements. The WWI was calculated by dividing the WC (cm) by the square root of the weight (kg),[13] and then rounding the outcome to 2 decimal points.

2.3. Outcome variable

According to the University of Wisconsin Age-Related Maculopathy Grading System,[21] the retinal images obtained from participants aged 40 years and older were graded and staged by examiners. Early AMD was characterized by the presence or absence of drusen and/or pigmentary abnormalities, whereas late AMD was characterized by exudative AMD signs and/or geographic atrophy. Discrepancies between the initial 2 assessors were settled by a third assessor of higher seniority. If both eyes' retinal photographs were deemed suitable for grading, the eye showing poorer staging was employed in the analysis.

2.4. Covariates

Other factors were also considered in our study, such as age (<60 years/≥60 years), gender (male/female), race/ethnicity (non-Hispanic White/non-Hispanic Black/Mex-American/other race), marital status (married or living with partner/never married/widowed or divorced/separated/not recorded), education level (less than high school/high school/more than high school/not recorded), BMI (<18.5 kg/m^2/18.5 kg/m^2–30.0 kg/m^2/>30.0 kg/m^2/not recorded), PIR (<1.3/1.3–3.5/>3.5/not recorded), smoking habit (never/former/current/not recorded), alcohol consumption (never/former/current/not recorded), c-reactive protein (CRP) level (≥1 mg/dL/<1 mg/dL/not recorded),

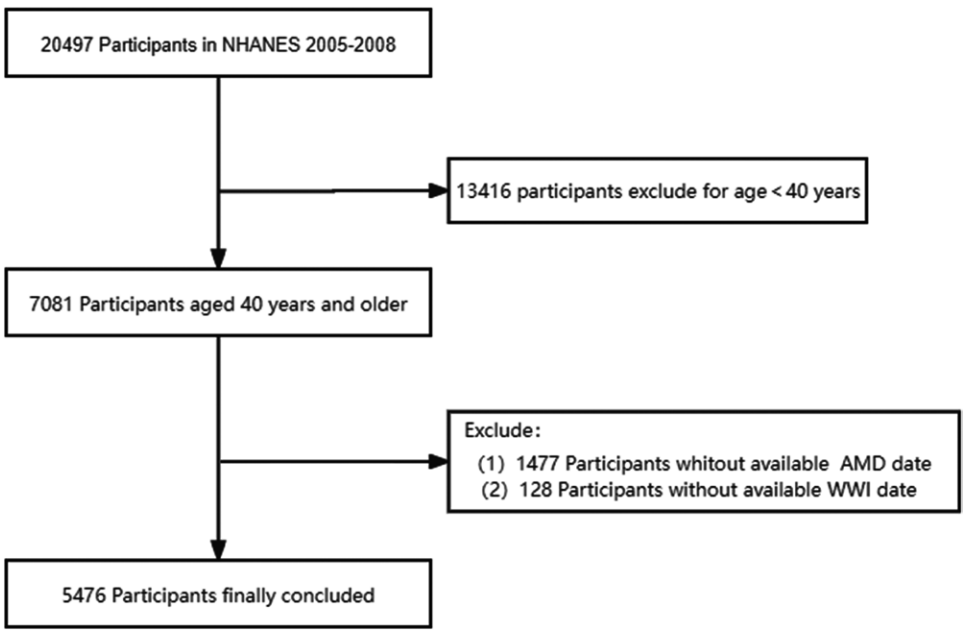

Figure 1. A flowchart showing the selection of study participants. NHANES = National Health and Nutrition Examination Survey, WWI = weight-adjusted waist index.

and current health status (poor or fair/good or excellent/not recorded).

Diabetes, hypertension, glaucoma, and cataract operation were defined as self-reported physician diagnoses. Cholesterol levels >240 mg/dL or the use of cholesterol-lowering medications were considered high cholesterol levels; sedentary behavior was defined as being absent from any vigorous or moderate recreational activities. In addition, chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate < 60 mL/min/1.73m^2; previous physician diagnoses of congestive heart failure, coronary heart disease, angina, heart attack, or stroke were defined as cardiovascular disease (CVD). Participants' dietary intake (vitamin E, beta-carotene, dietary lutein + zeaxanthin, zinc, omega-3 fatty acids) were gathered from two 24-hour dietary recall interviews and averaged, then grouped into tertiles. Samples with missing data for each covariate were assigned to a separate group named "not recorded".

2.5. Statistical analysis

In accordance with the NHANES guidelines, all analyses included sample weights derived from a stratified multistage probability sampling design. New sample weights were calculated by WTMEC2YR × 2/4. In the baseline data table, categorical variables were presented as proportions and 95% confidence intervals, while continuous variables were presented as the means and standard deviations. Weighted chi-square or weighted linear regression was performed to assess differences among individuals with and without AMD. Furthermore, the association between WWI levels and the risk of AMD was analyzed using multivariable logistic regression. The study included 4 different models: Model 1 was not adjusted for any covariates; Model 2 was adjusted for age, race/ethnicity, and gender; Model 3 was adjusted for age, gender, race/ethnicity, education, marital status, family income to poverty (PIR), BMI, alcohol consumption, smoking habits, high cholesterol level, diabetes, hypertension, cataract operation, and glaucoma; Model 4 was adjusted for all covariates, including age, gender, race/ethnicity, education, marital status, PIR, BMI, alcohol consumption, smoking habits, high cholesterol level, current health status, diabetes, hypertension, cataract operation, glaucoma, CKD, cardiovascular disease history, high c-reactive protein, physical activity, dietary vitamin E intake, dietary beta-carotene intake, dietary lutein + zeaxanthin intake, dietary vitamin C intake, dietary zinc intake, and dietary omega-3 fatty acids intake. Trend analysis was performed to explore the relationship between WWI and AMD by categorizing WWI scores into tertiles. Subgroup analysis was performed using a fully adjusted model with stratified factors to determine whether the associations were consistent across different groups. Interaction tests were used to examine the effect of covariates and WWI on the occurrence of AMD. Smooth curves were fitted to illustrate the association between WWI and AMD. The statistical analysis was conducted with R (version 4.2), Stata (version 17.0), Empower (version 5.0) software. In this study, statistically significant differences were indicated by a 2-sided P-value < .05.

3. Results

3.1. Baseline characteristics

This study included 5476 participants with an average age of 56.24 ± 11.62 years, consisting of 47.4% males and 52.6% females. Among the participants, 420 individuals (7.7%) were found to have AMD. The mean WWI level in the whole population was 11.08 ± 0.76; moreover, AMD individuals exhibited a significantly greater WWI compared to non-AMD individuals (11.39 ± 0.72 vs 11.06 ± 0.75, P < .001). There were no statistical differences in gender, BMI, education, current health status, diabetes, high cholesterol level, high c-reactive protein, dietary beta-carotene intake, dietary lutein + zeaxanthin intake, dietary vitamin C intake, dietary zinc intake between patients with and without AMD. Compared with participants without AMD, participants with AMD tended to be older, non-Hispanic White, lower economic status, former smoker, and never drinker. Participants with AMD were more likely to have hypertension, CKD, CVD, less physical activity, cataract surgery, glaucoma, and lower dietary vitamin E and omega-3 fatty acids intake (Table S1, Supplemental Digital Content, https://links.lww.com/MD/O840).

3.2. Association between the WWI and AMD

Table S2, Supplemental Digital Content (https://links.lww.com/MD/O841), shows the risk of age-related macular degeneration increased with increasing WWI in all models. In the completely adjusted model, the prevalence of AMD increased by 22% for each unit increase in WWI (OR 1.22, 95% CI 1.02–1.46). When WWI was categorized into tertiles, a 55% increase in the prevalence of AMD was observed in the highest tertile (>11.52) of WWI (OR 1.55, 95% CI 1.09, 2.21) compared to that of the lowest tertile (<10.85). The smoothed curve fitting results showed that the prevalence of AMD increased with increasing levels of WWI (Fig. 2).

3.3. Subgroup analyses

Subgroup analysis revealed statistically significant correlations between WWI and AMD among aged < 60 years, females, non-Hispanic White, individuals with hypertension, CKD, sedentary behavior, no diabetes, no CVD, no cataract operation, and no glaucoma (P < .05). Further analysis revealed that age, CKD, and CVD had significant interactions with WWI on AMD risk (P for interaction < .05) (Table 1).

4. Discussion

The analysis included 5476 adults, and revealed that individuals with higher levels of WWI were at increased risk of developing AMD.

BMI is a frequently employed metric for evaluating obesity, and previous studies have extensively explored the association between obesity and AMD using BMI. Jonasson et al reported a statistically significant association between BMI and the prevalence of AMD in their multivariate model analysis.[6] Additionally, Schaumberg et al revealed a J-shaped relationship between BMI and dry AMD, indicating that underweight individuals may also face an increased AMD risk.[7] Moreover, Zhang et al performed a dose–response meta-analysis. Their findings indicated that increased BMI was linked to a linear dose–response association with the AMD risk.[22] In contrast, several other studies did not corroborate this relationship.[8,9,23] These conflicting results may be attributed to the limitations of BMI as a measure of obesity, which does not differentiate between body fat and muscle mass and is impacted by many factors, such as age, gender, and ethnicity.[24,25] Several scholars have observed the presence of an obesity paradox in the current literature regarding BMI.[26] The obesity paradox suggests that having excess weight may actually improve clinical outcomes for certain diseases, such as CVD, CKD, chronic obstructive pulmonary disease, and stroke.[27–29] This phenomenon has also been identified in WC in a comparative analysis of heart failure,[12] indicating that WC has a strong correlation with BMI, thereby reducing its effectiveness as an independent indicator of obesity.

Furthermore, several studies have examined the correlation between abdominal obesity indicators such as the waist-to-height ratio (WHtR), waist-to-hip ratio (WHR) and AMD

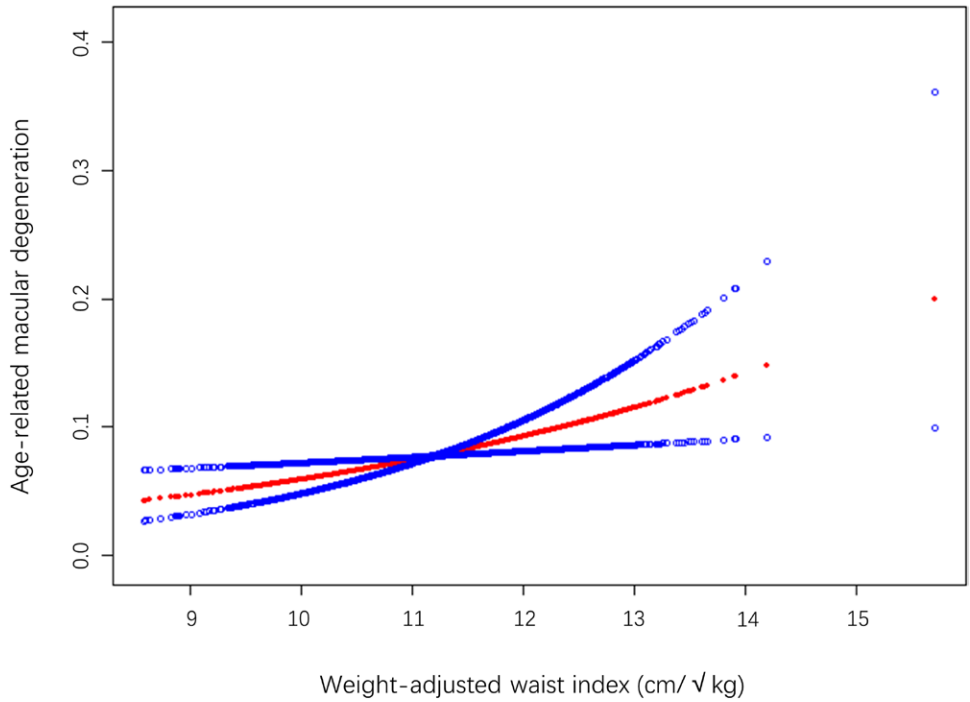

Figure 2. The association between the WWI and age-related macular degeneration. The solid red line represents the smooth curve fit between variables. Blue bands represent the 95% confidence interval from the fit. WWI = weight-adjusted waist index.

risk.[30–32] These indicators have been found to be more effective predictors of cardiovascular risk compared to BMI and WC.[33,34] Nevertheless, these measures also fail to differentiate between subcutaneous and visceral fat.[35] In addition, studies determining the WC and WHR cutoffs have primarily been carried out on European populations, and their applicability to other ethnic groups remains uncertain.[36] Hence, further studies are required to assess the effectiveness of these metrics in accurately assessing levels of obesity.

The novel obesity measure WWI, which incorporates weight and WC, aids in the detection of central obesity. WWI has been studied in various disciplines and is regarded as a more simplistic and direct approach for assessing fat distribution compared to metrics such as WHtR and WHR.[16–19] WWI can distinguish between fat and muscle mass. Previous study has reported that in people over 65, WWI was positively correlated with total abdominal fat area, visceral fat area, and total tissue fat percentage, but negatively correlated with appendicular skeletal muscle mass.[14] Furthermore, there are racial differences in the relationship between BMI and body fat distribution, thus, distinct and useable cutoff points based on race should be considered.[37,38] In contrast, WWI is suitable for different races and populations, potentially providing enhanced stability and reliability.[14]

A recent study investigating the relationship between WWI and AMD demonstrated a positive nonlinear association between them. Compared to BMI, WC, and weight, the WWI exhibited superior predictive capability for AMD, as evidenced by Receiver Operating Characteristic analysis.[39] Nonetheless, it is important to acknowledge the multitude of risk factors influencing the development of AMD. Previous research has indicated that nutrients like antioxidant vitamins C and E, zinc, beta-carotene, lutein and zeaxanthin (carotenoids), and omega-3 fatty acids may lower the risk of AMD.[40,41] Individuals with smoking, hypertension, hyperlipidemia, and high CRP, lower physical activity levels are more likely to develop AMD.[42,43] In order to more accurately observe the relationship between AMD and WWI, our study included the above factors as covariates to improve statistical accuracy. The study showed that in the fully adjusted model, a 55% increase in the prevalence of AMD was observed in the highest tertile (Tertile 3: >11.52) of WWI (OR 1.55, 95% CI 1.09, 2.21) compared to the lowest tertile (Tertile 1: <10.85). Our study also further indicated that obesity is associated with the risk of AMD.

The underlying mechanisms for the observed increased risk of AMD with elevated WWI have not been well elucidated. Potential mechanisms include the following: Lutein and zeaxanthin are carotenoids that can reduce oxidative stress, absorb blue light, and stabilize cell membranes, exerting protective effects against AMD.[44] Obesity is linked to a range of physiological alterations, including heightened inflammation, increased oxidative stress, and changes in the profile of lipoproteins,[45] which may lead to increased degradation of lutein and zeaxanthin, as well as decreased transport to the macula, thereby indirectly increasing the risk of AMD. Obese patients have increased levels of pro-inflammatory molecules, including monocyte chemotactic protein-1,[46] tumor necrosis factor-alpha,[47] and CRP,[48] which may disrupt the physiological function of the retinal pigment epithelium cells, leading to the development of AMD. Hypertension,[49] hyperlipidemia,[50] and diabetes[51] are other proposed risk factors for AMD, which are also well-known obesity-related conditions, raising the possibility that obesity may cause AMD indirectly. Obesity may lead to secondary hyperlipidemia, increasing the systemic oxidative stress response, and oxidative stress plays a significant role in AMD pathogenesis.[52]

This study offers several advantages. Primarily, this research was based on a cross-sectional analysis using a nationally representative sample and took into account sample weights, with the findings being applicable to most Americans. Furthermore, the research utilized a complex multistage probability sampling research design and thorough adjustment for covariates, enhancing its statistical precision.

However, it is important to acknowledge that this study has some limitations. First, the cross-sectional design of this study did not allow for the establishment of a causal relationship between AMD and WWI. Second, although many variables were considered, the influence of other potential confounders, such as genetic predisposition for AMD, could not be completely eliminated. Genetic predisposition was not included as

Table 1

Subgroup analysis for the association between weight-adjusted waist index and age-related macular degeneration.

Subgroup	OR(95% CI)	*P*-value	*P* for interaction
Age (yr)			
<60	1.46 (1.00, 2.13)	.05	<.001
≥60	1.17 (0.96, 1.42)	.12	
Gender			
Male	1.14 (0.83, 1.56)	.434	.636
Female	1.28 (1.01, 1.62)	.04	
Race/ethnicity			
Non-Hispanic White	1.23 (1.01, 1.51)	.042	.063
Non-Hispanic Black	1.61 (0.78, 3.30)	.196	
Mexican American	–	–	
Other race	–	–	
Hypertension			
No	1.21 (0.93, 1.57)	.154	.989
Yes	1.35 (1.05, 1.75)	.021	
Diabetes			
No	1.27 (1.04, 1.55)	.017	.481
Yes	1.02 (0.60, 1.73)	.945	
Chronic kidney disease			
No	1.17 (0.95, 1.45)	.147	.031
Yes	1.44 (1.03, 2.02)	.035	
Cardiovascular disease history			
No	1.27 (1.03, 1.56)	.025	<.001
Yes	1.15 (0.79, 1.66)	.474	
High cholesterol level			
No	1.16 (0.92, 1.47)	.204	.316
Yes	1.35 (0.99, 1.85)	.060	
Physical activity			
sedentary behavior	1.40 (1.11, 1.78)	.005	.869
No sedentary behavior	1.20 (0.91, 1.60)	.202	
Alcohol consumption			
Never	0.96 (0.59, 1.57)	.833	.258
Former	1.64 (0.72, 3.74)	.235	
Current	–	–	
Smoking habit			
Never	1.18 (0.91, 1.52)	.209	.533
Former	1.18 (0.84, 1.68)	.344	
Current	–	–	
Cataract operation			
No	1.29 (1.04, 1.60)	.020	.830
Yes	1.13 (0.80, 1.59)	.487	
Glaucoma			
No	1.27 (1.05, 1.54)	.013	.325
Yes	0.73 (0.30, 1.77)	.485	

Note: age, gender, race/ethnicity, education, marital status, PIR, BMI, alcohol consumption, smoking habits, high cholesterol, current health status, diabetes, hypertension, cataract operation, glaucoma, chronic kidney disease, cardiovascular disease history, high c-reactive protein, physical activity, dietary vitamin E intake, dietary beta-carotene intake, dietary lutein + zeaxanthin intake, dietary vitamin C intake, dietary zinc intake, dietary omega-3 fatty acids intake were adjusted.
Abbreviation: BMI = body mass index, PIR = ratio of family income to poverty.

a covariate due to the absence of genetic data in NHANES. Although many dietary nutrients were included as covariates, the potential effects of dietary supplements, interactions between various nutrients, and dietary patterns may have influenced the results. Third, in this research, we only utilized the 2005-2008 NHANES dataset because AMD data were only recorded from 2005-2008 in NHANES. Finally, our study was based on the population of the United States, and whether these results can be extrapolated to other races or countries remains uncertain. Further studies may be needed to validate our results.

5. Conclusion

This study demonstrated that higher WWI levels were associated with an increased risk of AMD, suggesting that managing obesity according to WWI may reduce AMD risk. However, additional research is warranted to corroborate our results.

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Writing – review & editing: Zhou Yang.

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