Correlation of Age-adjusted Visceral Adiposity Index with Osteoarthritis Risk: A Cross-sectional Study from NHANES 1999–2018

Keywords
Osteoarthritis, Obesity, Visceral adiposity index, Visceral adipose tissue

Abstract

Introduction
Obesity and aging are established independent risk factors for osteoarthritis (OA). This study aims to evaluate the correlation between the age-adjusted visceral adiposity index (AVAI) and OA.

Material and methods
This study was a cross-sectional study on the data from the NHANES during the period from 1999 to 2018. The correlation between AVAI and the prevalence of OA was explored through receiver operating characteristic (ROC) regression, multivariate logistic regression, restricted cubic spline regression, and subgroup analysis.

Results
The study cohort comprised 20,628 participants, of whom 2,297 (11.1%) were diagnosed as OA. An increase in the quartile range of AVAI was correlated with a significant rise in the prevalence of OA (1.5%vs.5.1% vs.14.4% vs.23.6%, p<0.001). Logistic regression analysis demonstrated a significantly positive correlation between AVAI and the risk of OA (OR=1.14, 95%CI: 1.06, 1.23). Subgroup analyses indicated that this correlation was more pronounced in individuals aged over 60 years old and those with diabetes. RCS regression analysis further identified a non-linear positive correlation, with an inflection point at -6.03. Finally, the area under the ROC curve (AUC) for AVAI was notably greater (AUC=0.757, 95% CI: 0.747, 0.766) compared to traditional obesity indices.

Conclusions
This study is the first to demonstrate a significantly positive correlation between the prevalence of OA and AVAI, with AVAI exhibiting superior diagnostic performance over traditional obesity indices in identifying OA.

Correlation of Age-adjusted Visceral Adiposity Index with Osteoarthritis Risk: A Cross-sectional Study from NHANES 1999–2018

Running Head: Age-adjusted VAI and OA Risk

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Keywords: Visceral adiposity index; Osteoarthritis; Visceral adipose tissue; Obesity

Introduction

Osteoarthritis (OA) is a chronic condition impacting joint cartilage, leading to the damage of meniscus, subchondral bones, and ligaments, which will frequently affect hips, knees, feet, and hands[1]. Clinically, OA is characterized by progressive joint swelling, stiffness, pain, and functional impairment. The incidence and prevalence of disability correlated with OA are rising each year, positioning it as the second most common and disabling condition at heart disease[2]. As reported by Cross M, the number of disability cases attributed to OA increased from 10.5 million in 1990 to 17.1 million in 2010[3]. Globally, the prevalence of OA is approximately 18% among females and 10% among males aged 60 years old and older. Approximately 80% of these individuals experience restricted mobility, and the conditions significantly impact daily life of one in four affected individuals[4, 5].

Recent research has described OA as a multifaceted disease influenced by various causative factors. Aging, obesity, disruptions in metabolic homeostasis disorders, genetic predisposition and have been identified as potential risk factors for the development of OA[6-8]. Presently, the aging population and increasing prevalence of obesity contribute to an elevated risk of obesity-related conditions, including T2DM, OA, hypertension, sleep disorders, cardiovascular disease, and premature mortality[9]. Globally, BMI is extensively utilized to evaluate health risks and weight status correlated with obesity in individuals. Nevertheless, despite BMI being widely used as a simple clinical indicator, it has several limitations and may not be able to comprehensively or accurately assess an individual's overall health status[10]. Several studies have indicated that there may be considerable variations in the quantity of muscular tissue, visceral adipose tissue (VAT), and metabolic profiles among individuals with identical BMI values[11, 12]. Presently, waist-to-height

ratio (WHtR), hip circumference, and waist circumference (WC) are increasingly being utilized as predictors for obesity in OA[13]. However, akin to BMI, these measures are not without limitations. Meanwhile, MRI is widely recognized as the gold standard for evaluating VAT, but its high cost limits researchers' exploration of the correlation between OA and visceral adiposity[8]. Consequently, it is imperative to identify more accessible indicators that can accurately reflect visceral adiposity levels for predicting OA.

The visceral adiposity index (VAI) emerges as a viable indicator for assessing VAT, calculated from triglycerides (TG), WC, HDL-C, and BMI levels[14-16]. Clinical investigations have demonstrated that VAI is an effective tool for identifying individuals at elevated risk for metabolic disorders, such as lipid abnormalities, insulin resistance, and cardiovascular risk factors[17-19]. Considering the substantial impact of age on the prevalence of various diseases, VAI has been refined through the incorporation of age-related adjustments, resulting in the development of the age-adjusted VAI (AVAI), and is particularly noteworthy for its efficacy in accurately predicting the risk of all-cause and cardiovascular mortality[20].

Similarly affected by age, OA may have a unique correlation with AVAI. However, the precision of utilizing AVAI as a predictor for OA has not been previously explored. To examine the correlation between AVAI and OA, this cross-sectional study was conducted on data from NHANES.

Methods

Research population

NHANES, administered by NCHS[21, 22], is an extensive research initiative aimed at evaluating the correlation among health promotion, disease prevention, and nutrition. This biennial survey is conducted by physical examinations, taking interviews, and a range of sections that include

demographic, dietary, laboratory and examination data.

In the present study, data were collected from NHANES during the period from 1999 to 2018. Subjects aged 20 years old or above were included (n = 46235). And the subjects missing data on AVAI (n=32396) and OA (n=2057) were excluded by exclusion criteria. Finally, the samples in this study consisted of 20628 subjects (as shown in Fig. 1).

Calculation formula of VAT surrogate markers

The calculation formulas for VAT surrogate markers have been developed with simple anthropometric measurements. These markers include AVAI, VAI, lipid accumulation product (LAP), and WHtR.

LAP (male)= TG∗(WC− 65)[23]

LAP (female)= TG∗(WC− 58)[23]

VAI (male)= [WC/[(TG/1.03)×(1.88 × BMI)])×(1.31/ HDL) +39.68][24];

VAI (female) = [WC/[(TG/0.81)×(1.89 × BMI)])×(1.52/HDL)+36.58][24].

AVAI (female)= −16.186+0.144×age−0.013×BMI+0.038×WC−1.369×HDl−C−0.151×TG

AVAI (males)= −10.727+0.101×age−0.108×BMI−0.043×WC−1.157×HDL−C+0.075×TG[20];

WHtR=WC/height

where both HDL-C and TG levels were expressed in mmol/L, WC and height were expressed in cm.

Measurement of covariates

Building upon previous studies[25-27], the final analysis incorporated potential confounding factors correlated with AVAI and OA. These factors included demographic variables such as height, race, age, WC, gender, educational attainment, physical activities, and weight, alongside questionnaire data on smoking status, diabetes, alcohol consumption, hyperlipidemia and hypertension. Blood samples were analyzed for various biomarkers, including TC, ALT, LDL-C, GGT, UA, total calcium, ALP,

AST, TG, 25(OH)D, creatinine, HDL-C, and albumin. Detailed methodologies for measurement and data acquisition for each variable are available at www.cdc.gov/nchs/nhanes.

Statistical analysis

AVAI was stratified into quartiles as follows: Q1 (≤-10.25), Q2 (-10.25 to -8.13), Q3 (-8.13 to -5.81), and Q4 (≥-5.81). The correlation between OA and AVAI was examined through multiple logistic regression models, yielding ORs and 95% CIs. Variables deemed significant in the univariate analysis were subsequently incorporated into the multivariate analysis. Three different models were used for this analysis: Model 1 (unadjusted), Model 2 (adjusted solely for gender and age), and Model 3 (comprehensively adjusted for a range of factors including alcohol consumption, gender, smoking status, age, educational attainment, moderate physical activities, race, albumin, diabetes, ALT, hyperlipidemia, hypertension, 25(OH)D, total calcium, AST, creatinine, uric acid, and ALP). The potential influence of covariates on this correlation was further examined through subgroup and interaction analyses. Additionally, the non-linear correlation between OA and AVAI was examined through RCS curves, with particular attention to potential non-linearity. Subsequently, the diagnostic efficacy of AVAI, VAI, LAP, BMI, WC, and WHtR was evaluated through ROC analyses. Data analyses were performed with Free Statistics software and R software.

Results

Characteristics of research subjects

The study encompassed a total of 20,628 subjects aged between 20 and 80 years old, with a prevalence of OA of 11.1%. Demographic characteristics categorized by AVAI quartiles are detailed in Table1. Subjects in the highest AVAI quartile demonstrated a greater prevalence of OA, hypertension, hyperlipidemia, and diabetes mellitus, alongside elevated levels of uric acid, age, BMI, triglycerides,

creatinine, WC, 25(OH)D, and ALP, compared to those in the lowest quartile. Conversely, subjects in the highest quartile exhibited reduced levels of albumin and HDL-C (p<0.01).

Correlation between AVAI and OA

To examine the correlation between AVAI and OA, three multiple regression models were developed, as presented in Table2. The unadjusted Model 1 revealed a statistically significant positive correlation between AVAI and OA, which was significant even after controlling for all covariates in Model 3 (OR=1.14, 95% CI: 1.06, 1.23, p<0.001).

Non-linearity analysis between AVAI and OA

Through RCS analyses on Model 3, the correlation between AVAI and OA was further explored. The findings illustrated in Fig. 2 indicated a non-linear correlation between AVAI and OA. Additionally, a subsequent threshold effect analysis as shown in Table 3 identified an inflection point for AVAI at -6.03, with a log-risk ratio of less than 0.001.

Subgroup analysis

The robustness of the correlation between AVAI and OA was assessed through extensive interaction tests and subgroup analyses to identify potential variations among diverse populations (Fig. 3). The results consistently demonstrated a significant correlation between AVAI and OA among the majority of subgroups. Importantly, this correlation was more pronounced among older individuals and those with diabetes.

Predictive value of AVAI for OA

The ROC curve illustrated in Fig. 4 evaluated the diagnostic efficacy of AVAI, VAI, LAP, BMI, WC, and WHtR in the identification of OA. According to the data presented in Table 4, AVAI demonstrated the highest diagnostic accuracy for OA, achieving an AUC of 0.757 (95%CI: 0.747-0.766), and

significantly outperformed other VAT surrogate markers (p<0.001).

Discussion

In this cross-sectional study comprising a representative sample of 20,628 subjects, a significant positive correlation was identified between AVAI and OA, which was especially pronounced among older adults and those with diabetes. Importantly, a non-linear correlation between AVAI and OA was observed, with a saturation point at a value of -6.03. Furthermore, among the six VAT surrogate indices evaluated AVAI, VAI, LAP, BMI, WC, and WHtR, AVAI exhibited the largest AUC in predicting the risk of OA.

OA is a pathological condition marked by degenerative alterations in joints, typically resulting in the deterioration of articular cartilage. Despite substantial advancements in medical technologies enhanced our understanding of etiology and treatment modalities for OA, its prevalence and correlated global health burden persist in escalating annually[28]. Obesity, a significant public health concern worldwide, is considered as a critical risk factor for the onset and progression of OA. On an international scale, BMI is frequently utilized as a metric for evaluating the risk of obesity and OA. Although, an increasing number of researchers has begun to critically evaluate the reliability of BMI as a measure for assessing the risk of OA and its limitations in accurately determining individuals' true obesity status[19]. This skepticism arises from the fact that BMI fails to accurately represent the proportions of muscles and adipose tissues and does not account for variations in fat distribution across different gender and age[29].

VAI has the potential to assess adipose tissue dysfunction and VAT[30]. A few studies have identified a significant correlation between VAI and conditions such as hypertension, diabetes, and cardiovascular diseases[31-34]. Furthermore, existing research indicates that aging plays a crucial

role in influencing OA and body fat distribution[35]. AVAI, a novel metric for evaluating visceral obesity, has been shown to potentially surpass BMI and VAI in predicting cardiovascular and all-cause mortality in American adults[20]. This correlation is attributed to the inclusion of age in its calculation, allowing AVAI to offer a more nuanced evaluation of the impact of visceral fat on health compared to the traditional VAI, which does not consider age-related variations in fat function and distribution. The findings in this study are consistent with previous research on AVAI (as shown in Fig. 4). To date, this study is the first to explore the correlation between AVAI and OA. AUC for AVAI was significantly greater than that of other surrogate markers for VAT.

Subgroup analysis revealed that the correlation between AVAI and OA was significantly more pronounced in older adults and those with diabetes (p for interaction < 0.001). This finding aligns with results from prior research. For example, Lv et al. reported in a cross-sectional study involving 5620 subjects that the association between VAI and type 2 diabetes was more significant in individuals over the age of 60[36]. These results may be explained by differences in body fat distribution and metabolic factors between younger and older groups[37]. Furthermore, a substantial body of research has confirmed the contribution to obesity and diabetes mellitus to the initiation and progression of OA[35]. Consequently, AVAI should be taken as a critical determinant in the identification of OA, particularly within the aforementioned population.

Furthermore, a noteworthy discovery regarding the non-linear correlation between AVAI and OA has been made. It can be found that a saturating effect of OA can occur when AVAI reaches -6.03. Previous studies have identified a curvilinear positive correlation between LAP and OA[19], which aligns with the findings in this study. This phenomenon can be attributed to the elevated prevalence of OA in those with high AVAI, resulting in a plateau in its changes. These findings have the potential

to offer new insights into the prevention and treatment of OA.

While the exact mechanisms conn ting AVAI to the onset of OA have not been fully understood yet, they are likely to be categorized into three primary areas: Inflammatory, mechanical, and metabolic factors. The accumulation of VAT leads to increased mechanical loading, especially on weight-bearing joints, which exacerbates stress on articular cartilage, which can accelerate cartilage degradation and wear and stimulate sub-chondral bone sclerosis and proliferation[38]. Moreover, excessive mechanical loading has been shown to elevate the levels of inflammatory mediators such as TNF-α and IL-1β, and activate related pathways[39]. which can be further corroborated by biomechanical evidence. Additionally, research has demonstrated that VAT is metabolically active and can influence the progression of metabolic disorders, including T2DM, thereby affecting OA. This phenomenon is attributed to the elevation of blood glucose levels, which can increase oxidative stress in chondrocytes and facilitate the formation of advanced AGEs within cartilage tissues[40]. Furthermore, VAT demonstrates a higher susceptibility to infiltration by inflammatory cells and can exhibit an augmented ability to produce proteins such as CRP, TNF-α, and IL-6[41, 42]. Additionally, the reactive adipokines generated by abnormal VAT may influence OA by impairing insulin sensitivity, exacerbating inflammation, and activating cartilage degradation mechanisms[43, 44].

This study exhibits notable strengths and limitations. Firstly, the selection of the NHANES database, known for its representative and adequate sample size, enhances the statistical validity and reliability of the findings in this study. Secondly, the identification of a nonlinear correlation between AVAI and the risk of OA offers further evidence supporting a threshold effect. However, certain limitations persist within the study. Firstly, the cross-sectional design of the study precluded the establishment of causality and limited its ability to fully account for potential bias arising from

confounding factors, representing a significant limitation of the study. Consequently, future cohort studies are necessary to validate these findings. Secondly, while the study incorporated a comprehensive range of relevant covariates, the influence of additional potential covariates could not be entirely ruled out. Furthermore, several key variables, including OA, were assessed through questionnaires, which may introduce recall bias into the results. Moreover, there is a paucity of imaging materials facilitating the assessment of visceral fat and OA. Consequently, additional validation of the findings through imaging modalities such as MRI and CT are necessary.

Based on the above discussion, we can conclude that AVAI has certain guiding significance, especially for geriatric patients. Firstly, geriatric patients often have insufficient awareness of changes in their body composition, making it difficult for them to adhere to the detection of such changes, especially with time-consuming and laborious examinations like CT scans. AVAI, as a simple indicator, can be calculated using routine biochemical and physical examination data. This is very helpful for geriatric patients to understand the changes in their body composition, particularly abdominal fat, and to manage it by changing dietary habits and increasing physical exercise. AVAI can serve as an indicator for assessing the metabolic health status of geriatric patients. Secondly, our study found that AVAI outperforms other indicators in predicting OA risk, which helps doctors assess the risk of OA and take appropriate intervention measures in a timely manner.

Conclusion

The present study demonstrates a significant correlation between elevated AVAI and the increased prevalence of OA. Compared to other VAT indices, AVAI emerges as a more effective and convenient surrogate marker for assessing VAT. This finding may facilitate healthcare providers in identifying individuals at a higher risk for developing OA, thereby enabling the earlier implementation of

preventive strategies and potentially mitigating the progression of diseases.

Declarations

Ethics approval and consent to participate

The study was approved by the National Centre for Health Statistics Research Ethics Review Board, and every participant signed informed consent. The written informed consent of all subjects was obtained following the Declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analysis during the current study are available in the NHANES, www.cdc.gov/nchs/NHANEs/

Competing interests

The authors declare that they have no conflict of interest

Clinical trial

Not applicable

Funding

Not applicable

Authors' contributions

Feng Chen, Yu Zhang and Lingling Chen designed the study; Feng Chen, Hao Lin and Yuansi Zhang wrote the manuscript. Feng Chen, Yuansi Zhang, and Jing Xu collected, analyzed and interpreted the data. Yu Zhang, Jing Xu and Lingling Chen critically reviewed, edited and approved the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of

the work.

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[44] C. Tu, J. He, B. Wu, W. Wang, Z. Li, An extensive review regarding the adipokines in the pathogenesis and progression of osteoarthritis, Cytokine 113 (2019) 1-12.

381 Table1. Characteristics of the study population based on AVAI quartiles

Characteristic	Q1	Q2	Q3	Q4	P value
Number	5157	5157	5157	5157	
Age, year	27.3±5.6	39.9±7.0	54.5±7.3	71.3±7.6	<0.001
PIR, %	2.37±1.61	2.60±1.65	2.82±1.68	2.54±1.52	<0.001
Race, n%					<0.001
Mexican American	1078 (20.9)	1030 (20)	915 (17.7)	741 (14.4)	
Other Hispanic	422 (8.2)	439 (8.5)	497 (9.6)	400 (7.8)	
Non-Hispanic White	1981 (38.4)	2105 (40.8)	2137 (41.4)	2888 (56)	
Non-Hispanic Black	1067 (20.7)	1038 (20.1)	1111 (21.5)	823 (16)	
Other Race	609 (11.8)	545 (10.6)	497 (9.6)	305 (5.9)	
Moderate activities, n%					<0.001
Yes	2408 (46.7)	2269 (44)	2006 (38.9)	1768 (34.3)	
No	2749 (53.3)	2888 (56)	3151 (61.1)	3389 (65.7)	
Diabetes, n%					<0.001
Yes	65 (1.3)	302 (5.9)	851 (16.5)	1421 (27.6)	
No	5087 (98.7)	4855 (94.1)	4303 (83.5)	3732 (72.4)	
Hypertension					
Yes	388 (7.6)	1057 (20.6)	2114 (41.1)	3151 (61.2)	
No	4725 (92.4)	4083 (79.4)	3028 (58.9)	1998 (38.8)	
Hyperlipidemia					
Yes	2627 (50.9)	3745 (72.6)	4194 (81.3)	4294 (83.3)	
No	2530 (49.1)	1412 (27.4)	963 (18.7)	863 (16.7)	
Education level, n%					<0.001
Less than high school	1091 (21.2)	1215 (23.6)	1355 (26.3)	1684 (32.7)	
High school or above	4061 (78.8)	3939 (76.4)	3799 (73.7)	3463 (67.3)	
Drinking, n%					<0.001
Current or ever	3252 (74.7)	3223 (75.4)	3070 (70.8)	2793 (63.9)	
Never	1102 (25.3)	1053 (24.6)	1268 (29.2)	1575 (36.1)	
Smoking, n%					
Current or ever	1855 (36)	2210 (42.9)	2537 (49.3)	2717 (52.7)	
Never	3297 (64)	2946 (57.1)	2614 (50.7)	2435 (47.3)	
Male, n%	2129 (41.3)	2479 (48.1)	2559 (49.6)	2877 (55.8)	<0.001
Osteoarthritis, n%	75 (1.5)	262 (5.1)	742 (14.4)	1218 (23.6)	<0.001
Body mass index, Kg/m2	25.8±5.3	29.3±6.6	29.9±6.9	29.9±6.4	<0.001
Waist circumference, cm	88.2±13.0	98.0±15.2	101.5±15.2	105.3±14.8	<0.001
ALT, U/L	23.4±21.8	28.2±36.3	27.8±33.5	22.6±12.6	<0.001
AST, U/L	24.1±22.1	26.0±25.0	26.6±27.9	24.7±10.3	<0.001
ALP, U/L	66.4±25.6	68.4±23.4	75.2±27.4	75.6±34.2	<0.001
Albumin, g/dl	42.7±4.4	42.4±3.5	41.9±3.2	41.4±3.2	<0.001
Creatinine, umol/L	69.0 (56.6,	70.7 (60.1,	72.5 (61.9,	81.3 (69.8,	<0.001

	79.6)	82.2)	86.6)	97.2)	
Uric acid, umol/L	294.3 ± 79.5	315.5 ± 82.9	329.5 ± 83.1	353.0 ± 86.9	<0.001
25(OH)D, nmol/L	60.1 ± 25.4	59.2 ± 23.9	63.4 ± 27.2	68.5 ± 28.9	<0.001
Total calcium, mg/dl	9.38 ± 0.36	9.32 ± 0.35	9.36 ± 0.36	9.38 ± 0.38	<0.001
Total cholesterol, mmol/L	4.63 (4.03, 5.35)	5.07 (4.42, 5.77)	5.28 (4.60, 5.92)	4.86 (4.19, 5.61)	<0.001
Triglycerides, mmol/L	0.96 (0.67, 1.45)	1.17 (0.81, 1.78)	1.30 (0.93, 1.92)	1.39 (0.99, 1.94)	<0.001
HDL-cholesterol, mmol/L	1.45 (1.19, 1.76)	1.29 (1.06, 1.58)	1.32 (1.09, 1.63)	1.24 (1.06, 1.53)	<0.001
LDL-cholesterol, mmol/L	2.61 (2.12, 3.21)	3.05 (2.48, 3.67)	3.15 (2.61, 3.78)	2.85 (2.22, 3.49)	<0.001
AVAI	-11.4 (-12.1, -10.8)	-9.2 (-9.7, -8.7)	-7.0 (-7.6, -6.4)	-4.5 (-5.2, -3.7)	<0.001

Values are mean±SD or number (%). P<0.05 was deemed significant. BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL-c, High density lipoprotein cholesterol; LDL-c, Low density lipoprotein cholesterol; AVAI, age-adjusted visceral adiposity index

Table2. Logistic regression analysis between AVAI with osteoarthritis

subgroups	Model1		Model2		Model3	
	OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value
AVAI	1.43 (1.40, 1.46)	<0.001	1.30 (1.22, 1.37)	<0.001	1.14 (1.06, 1.23)	<0.001
AVAI (category)						
Q1	1(Ref)		1(Ref)		1(Ref)	
Q2	3.63 (2.8, 4.7)	<0.001	2.42 (1.84, 3.18)	<0.001	2.02 (1.47, 2.78)	<0.001
Q3	11.39 (8.95, 14.49)	<0.001	4.72 (3.51, 6.36)	<0.001	3.43 (2.41, 4.89)	<0.001
Q4	20.95 (16.54, 26.55)	<0.001	5.16 (3.58, 7.45)	<0.001	3.21 (2.06, 5.01)	<0.001
P for trend	2.47 (2.35, 2.6)	<0.001	1.58 (1.42, 1.76)	<0.001	1.37 (1.20, 1.56)	<0.001

Model I: None covariates were adjusted; Model II: gender and age were adjusted; Model III: drinking, smoking, gender, educational level, age, race, moderate physical activities, diabetes mellitus, albumin, material hyperlipidemia, hypertension, ALT, 25(OH)D, total calcium, AST, creatinine, ALP, and uric acid were adjusted

Table 3. Threshold effect analysis of AVAI on osteoarthritis: using the two-piecewise linear regression model

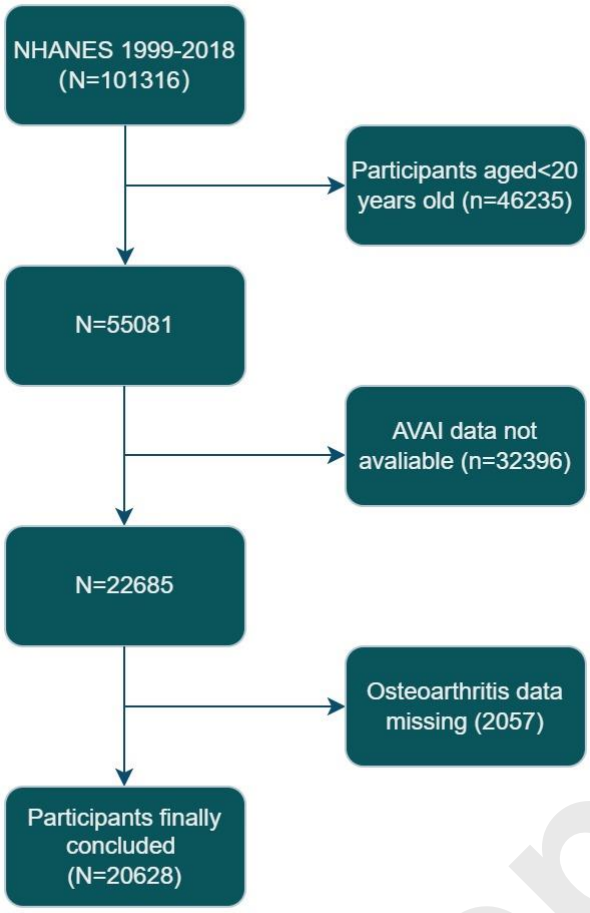
VAI	Adjusted OR (95% CI)	P value
Fitting by the standard linear model	1.14 (1.06, 1.23)	<0.001
Fitting by the two-piecewise linear model		
Inflection point	-6.03	
AVAI<6.03	1.18 (1.06, 1.32)	<0.001
AVAI>6.03	1.15 (1.01, 1.30)	<0.001
Log likelihood ratio		<0.001

AVAI, age-adjusted visceral adiposity index

Table 4. The AUC for each index to discriminate osteoarthritis.

	AUC	95%CI	Cutoff value	Sensitivity	Specificity
AVAI	0.757	0.747-0.766	-7.64	0.809	0.601
VAI	0.574	0.562-0.586	1.46	0.606	0.501
LAP	0.608	0.597-0.620	31.65	0.793	0.380
BMI	0.572	0.560-0.584	27.43	0.613	0.495
WC	0.596	0.584-0.608	97.45	0.626	0.530
WHtR	0.618	0.607-0.630	0.590	0.617	0.567

AVAI, age-adjusted visceral adiposity index; VAI: visceral adiposity index; LAP, lipid accumulation product; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio



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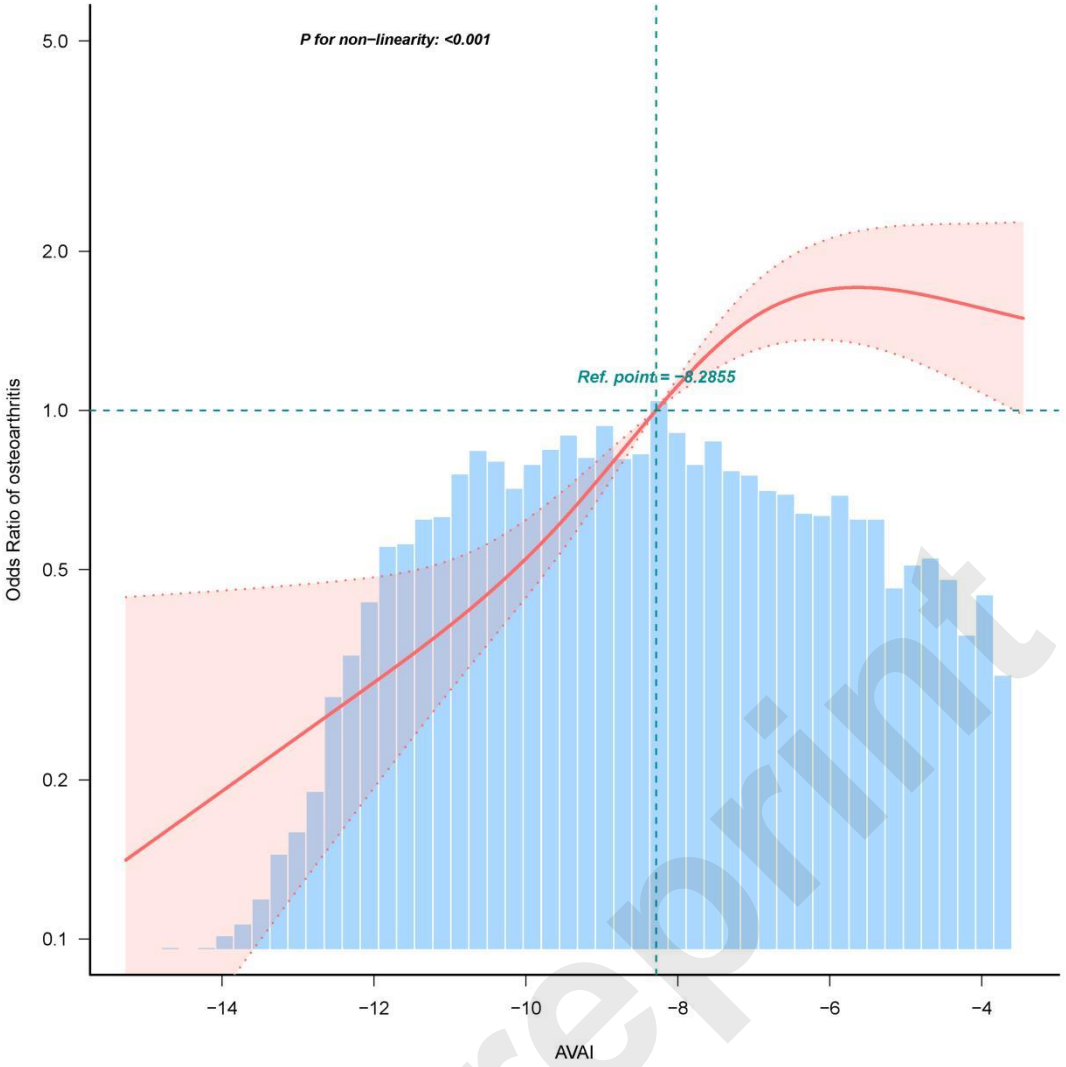
490 Figure1. Flowchart of the sample selection from the 1999-2018 NHANES.



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492 Figure2. Restricted cubic spline fitting for the association between AVAI levels and OA

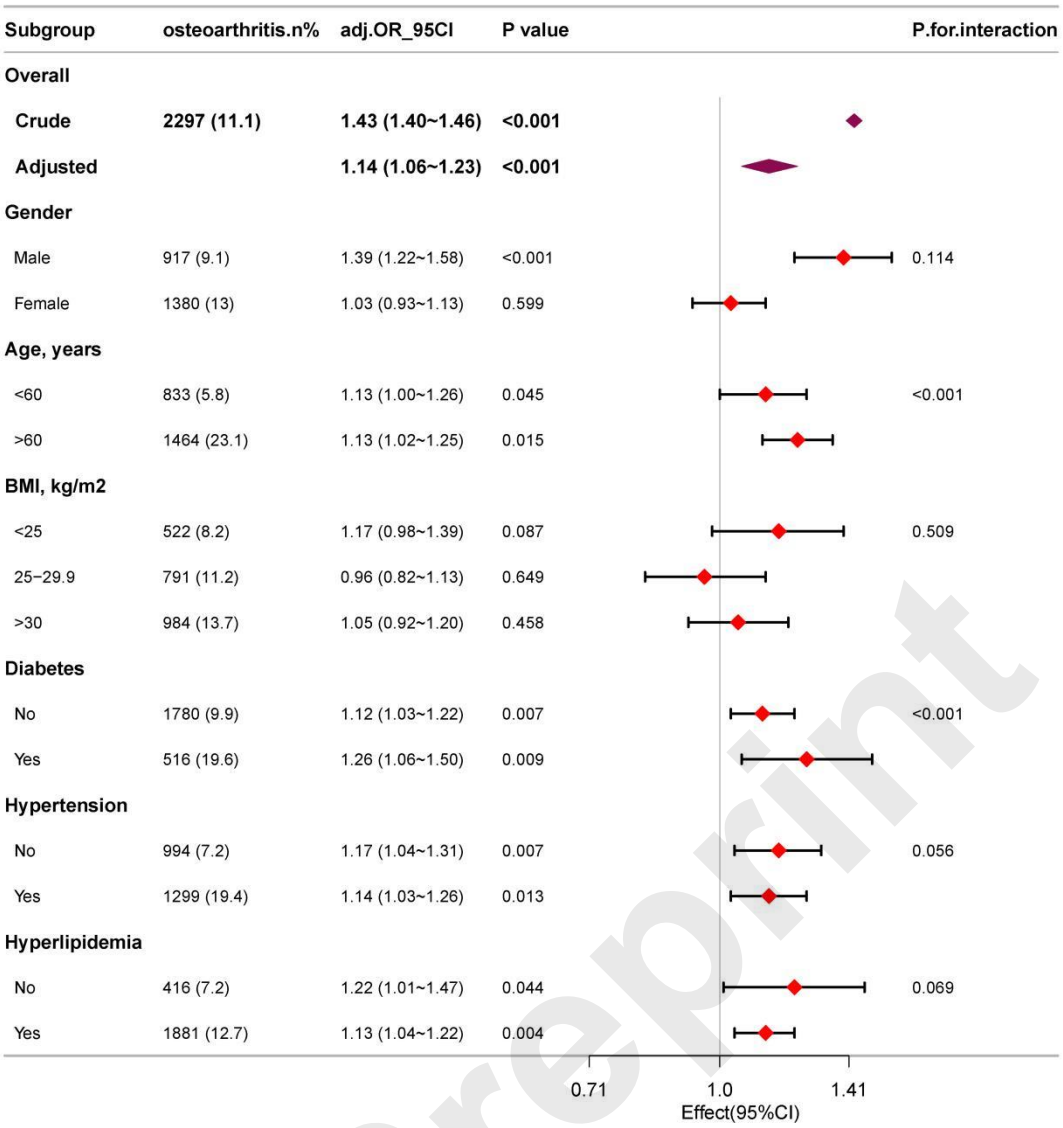


Figure3. Association between AVAI and the risk of OA in various subgroups

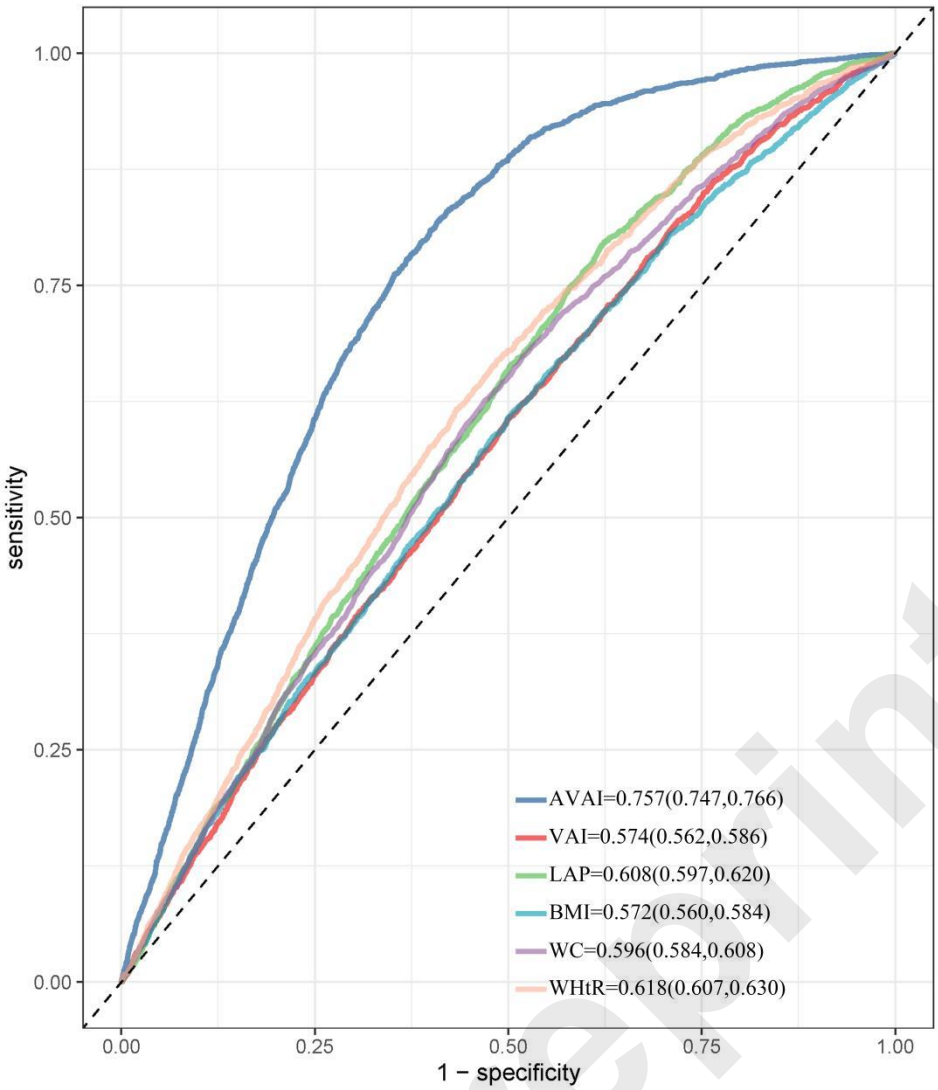
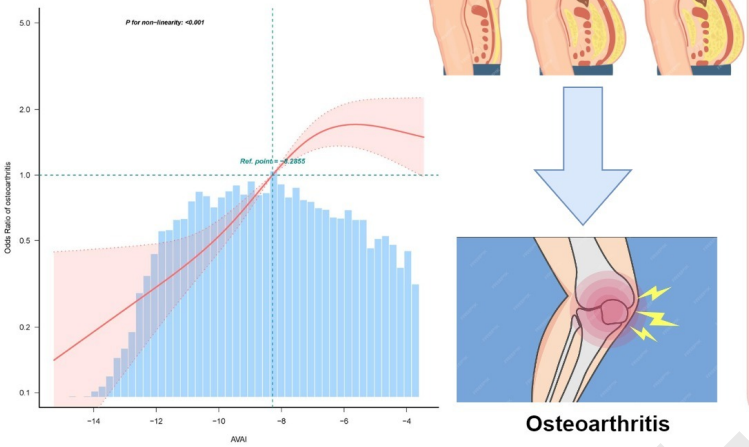


Figure4. ROC analysis of AVAI, VAI, LAP, BMI, WC, and WHtR to OA among American adults.

Correlation of Age-adjusted Visceral Adiposity Index with Osteoarthritis Risk



AVAI	OR (95%CI)
Q1	Reference
Q2	2.02 (1.47, 2.78)
Q3	3.43 (2.41, 4.89)
Q4	3.21 (2.06, 5.01)

Elevated AVAI levels are associated with an increased risk of osteoarthritis

Table1. Characteristics of the study population based on AVAI quartiles

Characteristic	Q1	Q2	Q3	Q4	P value
Number	5157	5157	5157	5157	
Age, year	27.3±5.6	39.9±7.0	54.5±7.3	71.3±7.6	<0.001
PIR, %	2.37±1.61	2.60±1.65	2.82±1.68	2.54±1.52	<0.001
Race, n%					<0.001
Mexican American	1078 (20.9)	1030 (20)	915 (17.7)	741 (14.4)	
Other Hispanic	422 (8.2)	439 (8.5)	497 (9.6)	400 (7.8)	
Non-Hispanic White	1981 (38.4)	2105 (40.8)	2137 (41.4)	2888 (56)	
Non-Hispanic Black	1067 (20.7)	1038 (20.1)	1111 (21.5)	823 (16)	
Other Race	609 (11.8)	545 (10.6)	497 (9.6)	305 (5.9)	
Moderate activities, n%					<0.001
Yes	2408 (46.7)	2269 (44)	2006 (38.9)	1768 (34.3)	
No	2749 (53.3)	2888 (56)	3151 (61.1)	3389 (65.7)	
Diabetes, n%					<0.001
Yes	65 (1.3)	302 (5.9)	851 (16.5)	1421 (27.6)	
No	5087 (98.7)	4855 (94.1)	4303 (83.5)	3732 (72.4)	
Hypertension					
Yes	388 (7.6)	1057 (20.6)	2114 (41.1)	3151 (61.2)	
No	4725 (92.4)	4083 (79.4)	3028 (58.9)	1998 (38.8)	
Hyperlipidemia					
Yes	2627 (50.9)	3745 (72.6)	4194 (81.3)	4294 (83.3)	
No	2530 (49.1)	1412 (27.4)	963 (18.7)	863 (16.7)	
Education level, n%					<0.001
Less than high school	1091 (21.2)	1215 (23.6)	1355 (26.3)	1684 (32.7)	
High school or above	4061 (78.8)	3939 (76.4)	3799 (73.7)	3463 (67.3)	
Drinking, n%					<0.001
Current or ever	3252 (74.7)	3223 (75.4)	3070 (70.8)	2793 (63.9)	
Never	1102 (25.3)	1053 (24.6)	1268 (29.2)	1575 (36.1)	
Smoking, n%					
Current or ever	1855 (36)	2210 (42.9)	2537 (49.3)	2717 (52.7)	
Never	3297 (64)	2946 (57.1)	2614 (50.7)	2435 (47.3)	
Male, n%	2129 (41.3)	2479 (48.1)	2559 (49.6)	2877 (55.8)	<0.001
Osteoarthritis, n%	75 (1.5)	262 (5.1)	742 (14.4)	1218 (23.6)	<0.001
Body mass index, Kg/m2	25.8±5.3	29.3±6.6	29.9±6.9	29.9±6.4	<0.001
Waist circumference, cm	88.2±13.0	98.0±15.2	101.5±15.2	105.3±14.8	<0.001
ALT, U/L	23.4±21.8	28.2±36.3	27.8±33.5	22.6±12.6	<0.001
AST, U/L	24.1±22.1	26.0±25.0	26.6±27.9	24.7±10.3	<0.001
ALP, U/L	66.4±25.6	68.4±23.4	75.2±27.4	75.6±34.2	<0.001
Albumin, g/dl	42.7±4.4	42.4±3.5	41.9±3.2	41.4±3.2	<0.001
Creatinine, umol/L	69.0 (56.6, 79.6)	70.7 (60.1, 82.2)	72.5 (61.9, 86.6)	81.3 (69.8, 97.2)	<0.001
Uric acid, umol/L	294.3 ± 79.5	315.5 ± 82.9	329.5 ± 83.1	353.0 ± 86.9	<0.001
25(OH)D, nmol/L	60.1 ± 25.4	59.2 ± 23.9	63.4 ± 27.2	68.5 ± 28.9	<0.001

Total calcium, mg/dl	9.38 ± 0.36	9.32 ± 0.35	9.36 ± 0.36	9.38 ± 0.38	<0.001
Total cholesterol, mmol/L	4.63 (4.03, 5.35)	5.07 (4.42, 5.77)	5.28 (4.60, 5.92)	4.86 (4.19, 5.61)	<0.001
Triglycerides, mmol/L	0.96 (0.67, 1.45)	1.17 (0.81, 1.78)	1.30 (0.93, 1.92)	1.39 (0.99, 1.94)	<0.001
HDL-cholesterol, mmol/L	1.45 (1.19, 1.76)	1.29 (1.06, 1.58)	1.32 (1.09, 1.63)	1.24 (1.06, 1.53)	<0.001
LDL-cholesterol, mmol/L	2.61 (2.12, 3.21)	3.05 (2.48, 3.67)	3.15 (2.61, 3.78)	2.85 (2.22, 3.49)	<0.001
AVAI	-11.4 (-12.1, -10.8)	-9.2 (-9.7, -8.7)	-7.0 (-7.6, -6.4)	-4.5 (-5.2, -3.7)	<0.001

Values are mean±SD or number (%). P<0.05 was deemed significant. BMI, body mass index; TC, total cholesterol; TG, triglyceride; HDL-c, High density lipoprotein cholesterol; LDL-c, Low density lipoprotein cholesterol; AVAI, age-adjusted visceral adiposity index

Table2. Logistic regression analysis between AVAI with osteoarthritis

subgroups	Model1		Model2		Model3	
	OR (95%CI)	P-value	OR (95%CI)	P-value	OR (95%CI)	P-value
AVAI	1.43 (1.40, 1.46)	<0.001	1.30 (1.22, 1.37)	<0.001	1.14 (1.06, 1.23)	<0.001
AVAI (category)						
Q1	1(Ref)		1(Ref)		1(Ref)	
Q2	3.63 (2.8, 4.7)	<0.001	2.42 (1.84, 3.18)	<0.001	2.02 (1.47, 2.78)	<0.001
Q3	11.39 (8.95, 14.49)	<0.001	4.72 (3.51, 6.36)	<0.001	3.43 (2.41, 4.89)	<0.001
Q4	20.95 (16.54, 26.55)	<0.001	5.16 (3.58, 7.45)	<0.001	3.21 (2.06, 5.01)	<0.001
P for trend	2.47 (2.35, 2.6)	<0.001	1.58 (1.42, 1.76)	<0.001	1.37 (1.20, 1.56)	<0.001

Model I: None covariates were adjusted; Model II: gender and age were adjusted; Model III: drinking, smoking, gender, educational level, age, race, moderate physical activities, diabetes mellitus, albumin, material hyperlipidemia, hypertension, ALT, 25(OH)D, total calcium, AST, creatinine, ALP, and uric acid were adjusted

Table 3. Threshold effect analysis of AVAI on osteoarthritis: using the two-piecewise linear regression model

VAI	Adjusted OR (95% CI)	P value
Fitting by the standard linear model	1.14 (1.06, 1.23)	<0.001
Fitting by the two-piecewise linear model		
Inflection point	-6.03	
AVAI<6.03	1.18 (1.06, 1.32)	<0.001
AVAI>6.03	1.15 (1.01, 1.30)	<0.001
Log likelihood ratio		<0.001

AVAI, age-adjusted visceral adiposity index

Table 4. The AUC for each index to discriminate osteoarthritis.

	AUC	95%CI	Cutoff value	Sensitivity	Specificity
AVAI	0.757	0.747-0.766	-7.64	0.809	0.601
VAI	0.574	0.562-0.586	1.46	0.606	0.501
LAP	0.608	0.597-0.620	31.65	0.793	0.380
BMI	0.572	0.560-0.584	27.43	0.613	0.495
WC	0.596	0.584-0.608	97.45	0.626	0.530
WHtR	0.618	0.607-0.630	0.590	0.617	0.567

AVAI, age-adjusted visceral adiposity index; VAI: visceral adiposity index; LAP, lipid accumulation product; BMI, body mass index; WC, waist circumference; WHtR, waist-to-height ratio

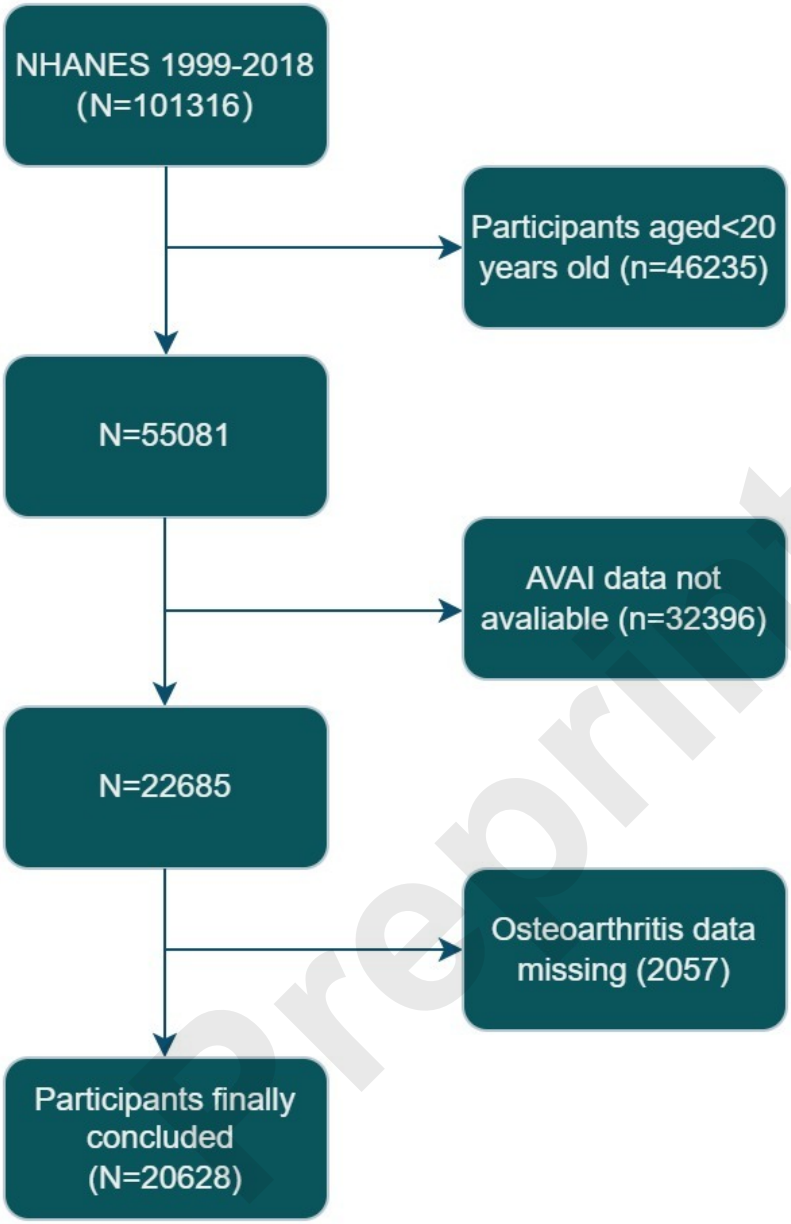


Figure1. Flowchart of the sample selection from the 1999-2018 NHANES.

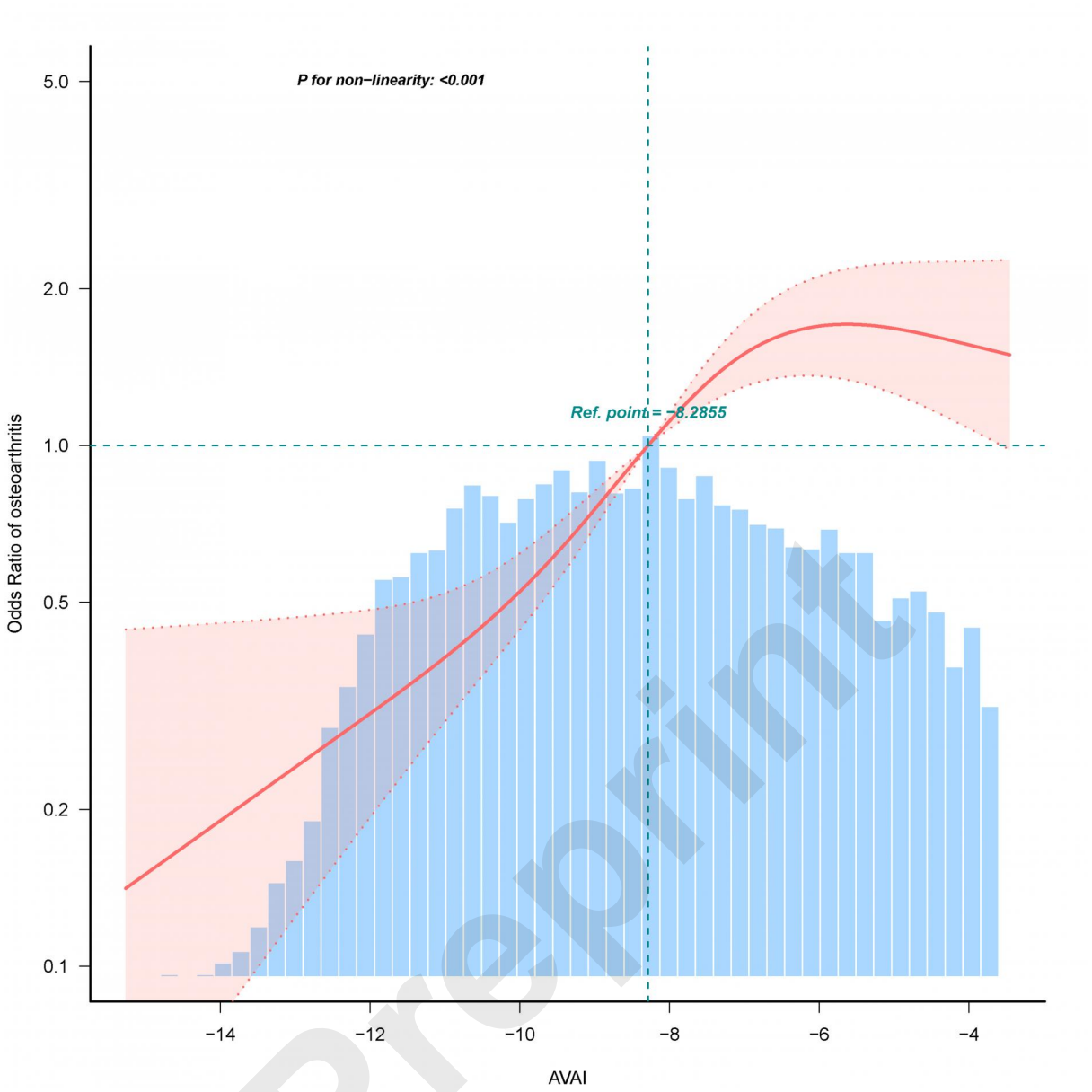


Figure2. Restricted cubic spline fitting for the association between AVAI levels and OA

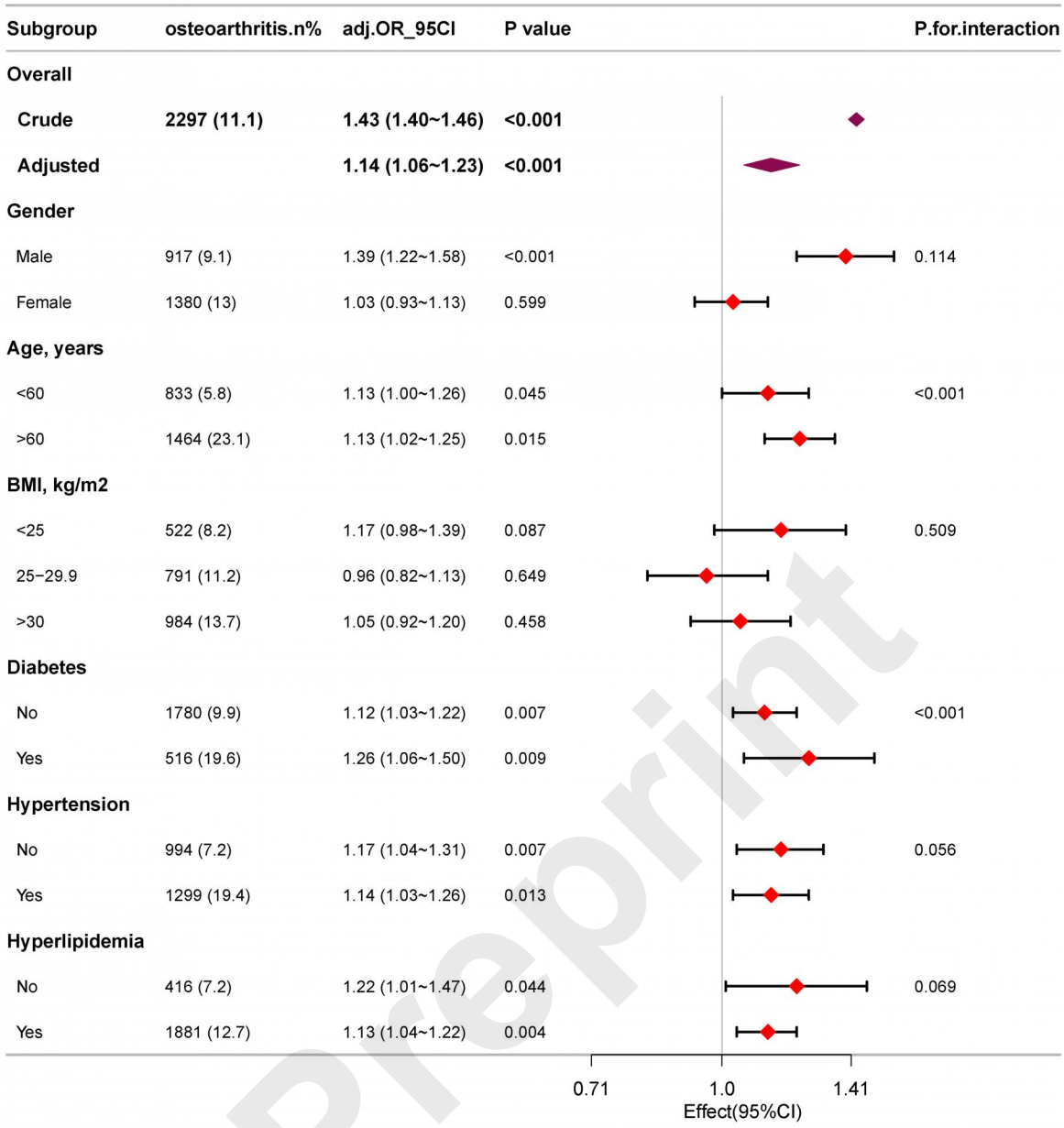


Figure3. Association between AVAI and the risk of OA in various subgroups

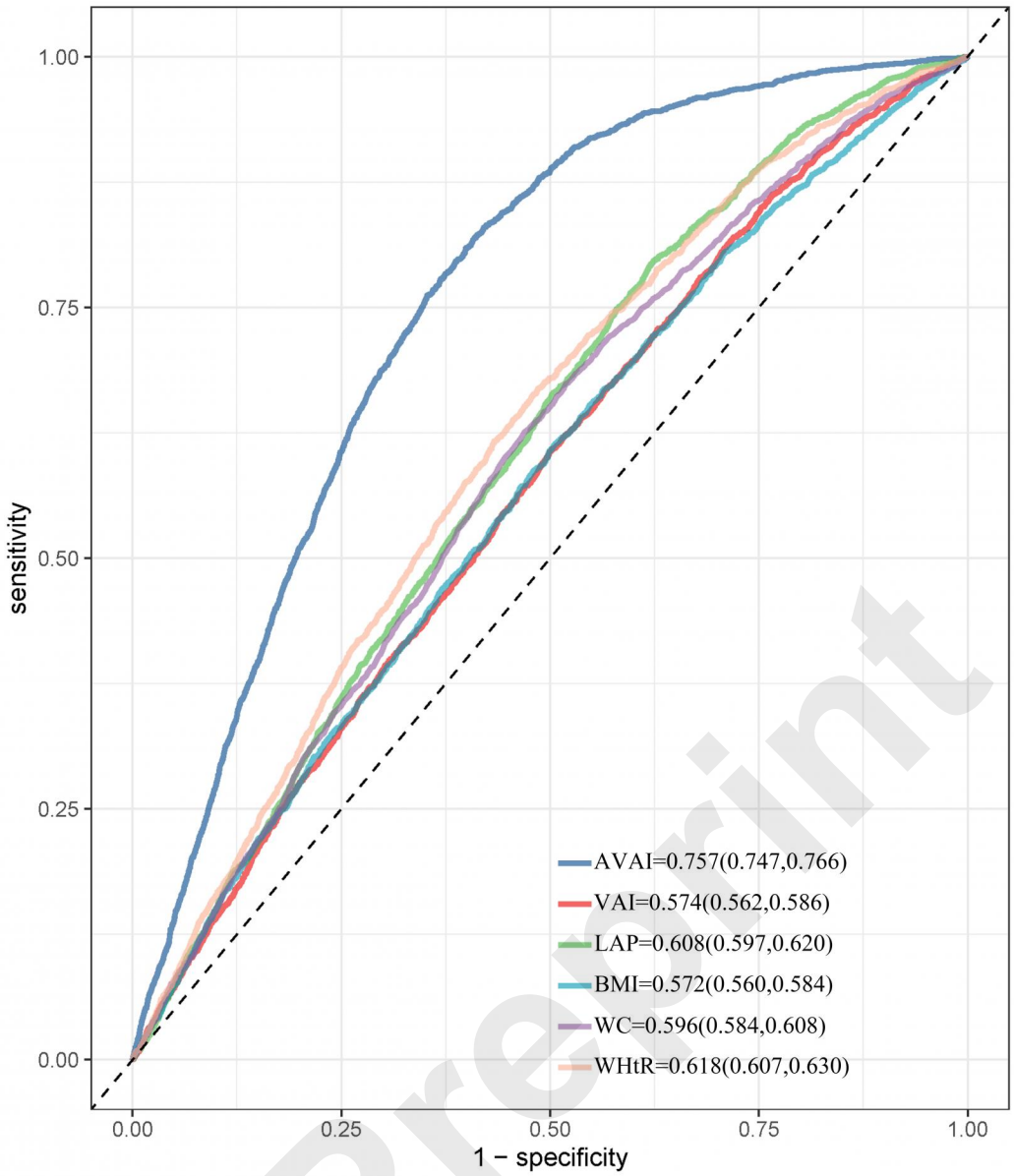


Figure4. ROC analysis of AVAI, VAI, LAP, BMI, WC, and WHtR to OA among American adults.