Original Article

Association between the age-adjusted visceral adiposity index (AVAI) and gynecologic malignancies: a cross-sectional study based on NHANES data

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Background: Gynecologic cancers pose a significant threat to women's health worldwide, with obesity and related metabolic dysfunction recognized as key risk factors. Traditional measures, such as body mass index (BMI), fail to adequately capture visceral fat, which plays a crucial role in tumorigenesis through metabolic and inflammatory pathways. This study aims to assess the association between the age-adjusted visceral adiposity index (AVAI) and the risk of gynecologic cancers using data from the National Health and Nutrition Examination Survey (NHANES).

Methods: This study analyzed a cross-sectional dataset from the NHANES [2007–2018], comprising 7,855 women, including 237 with gynecologic cancers (ovarian, endometrial, and cervical cancers) and 7,618 control participants without cancer. The AVAI was the main exposure variable. To control for potential confounders, such as age, race, educational level, the poverty-to-income ratio (PIR), smoking status, alcohol intake, hypertension, diabetes, and the BMI, multivariable logistic regression and generalized additive models were employed. The independent link between the AVAI and the risk of gynecologic cancers was examined. Additionally, subgroup analyses and restricted cubic spline functions were used to assess dose-response trends, while receiver operating characteristic (ROC) curves were generated to evaluate the discriminative performance of the AVAI.

Results: Women with gynecologic cancers were older (P=0.02) and had higher waist circumference (WC), BMI, triglyceride (TG), and AVAI levels (P<0.001) than those in the control group. In the fully adjusted model I, each unit increase in the AVAI was associated with a 28.0% higher risk of gynecologic malignancies [odds ratio (OR) =1.280, 95% confidence interval (CI): 1.089–1.504, P=0.003]. Subgroup analysis showed a significant association with cervical cancer: each unit increase in AVAI resulting in a 30.9% higher risk in model I (P=0.02) and a 45.6% higher risk in model II (P=0.03), revealing a dose-response trend [Q2 (−8.7292 to −6.3966) *vs.* Q1 (<−8.7292): OR =2.085, P=0.007; Q3 (>−6.3966) *vs.* Q1: OR =2.974, P=0.02]. No statistically significant correlation was found between the AVAI and the risk of ovarian or endometrial cancers (P>0.05). ROC analysis showed that the area under the curve (AUC) of the AVAI for distinguishing women with and without gynecologic cancers was 0.807 (95% CI: 0.790–0.825, P<0.001).

Conclusions: The AVAI, a composite index that integrates visceral fat distribution and metabolic function,

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was shown for the first time to be significantly associated with the risk of gynecologic malignancies, particularly cervical cancer, for which it demonstrated strong discriminative value. The study shows the superiority of the AVAI over traditional BMI in metabolic-inflammatory risk stratification, offering a new target for early identification and targeted interventions in gynecologic cancers. Future prospective cohort studies need to be conducted to verify causality and explore metabolic regulation strategies targeting the AVAI to reduce the risk of cancers.

Keywords: Age-adjusted visceral adiposity index (AVAI); gynecologic malignancies; cervical cancer; National Health and Nutrition Examination Survey database (NHANES database); cross-sectional study

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Introduction

Gynecologic malignancies, including endometrial, ovarian, and cervical cancers, represent a major global health burden, with over 1.2 million new cases projected annually by 2025 (1-3). Despite advances in human papillomavirus (HPV) vaccination and cervical cancer screening (4), the incidence of endometrial cancer, which has been associated with obesity-related metabolic disorders, continues to rise at an annual rate of 3.2% (5), and the 5-year survival rate for ovarian cancer remains below 40% (6). These challenges highlight the need for improved risk assessment tools to support prevention and early detection strategies (7,8).

Visceral adipose tissue (VAT) has recently gained attention for its involvement in the initiation and progression of cancer, as it is a core pathological hub in metabolic syndrome (9). Unlike subcutaneous fat, VAT is closely related to metabolic dysfunction (10,11). Clinical studies have confirmed that individuals with visceral obesity have a 2.3–3.7-fold increased risk of developing endometrial cancer compared to those with a normal body weight, and for ovarian cancer patients, every 10 cm^2 increase in the VAT area increases the risk of recurrence by 15% (12,13). Similarly, obesity-related metabolic disturbances, including elevated insulin and triglyceride (TG) levels, have been linked to an increased risk of cervical cancer, and adipokines such as adiponectin may contribute to cervical carcinogenesis through endocrine and inflammatory pathways (14). However, the traditional body mass index (BMI) only reflects total fat mass and does not distinguish between fat distribution patterns, leading to a misclassification of approximately 30% of metabolically healthy obese individuals as low risk. This limitation is particularly pronounced in the field of gynecologic cancers, as the risk of estrogen-dependent tumors such as endometrial cancer is more strongly associated with VAT than total fat mass (15).

The introduction of the age-adjusted visceral adiposity index (AVAI) offers a new paradigm for accurately assessing visceral fat-related risks. This index integrates waist circumference (WC), TG levels, the BMI, and age to construct a multidimensional model for evaluating visceral fat accumulation (16). Previous studies based on National

Highlight box

Key findings

- This study found a significant association between the age-adjusted visceral adiposity index (AVAI) and the risk of gynecologic malignancies, particularly cervical cancer. Each unit increase in the AVAI was associated with a 28% higher risk of gynecologic cancers overall, and an up to 45.6% increased risk of cervical cancer. The AVAI showed strong discriminative performance with an area under the curve of 0.807.

What is known, and what is new?

- Visceral fat plays a key role in gynecologic cancer development through inflammation and metabolic dysfunction. However, traditional measures like the body mass index (BMI) poorly reflect visceral fat distribution, limiting accurate risk assessment.
- This study revealed a strong association between the AVAI and the risk of gynecologic cancers, especially cervical cancer. The AVAI outperformed the BMI in distinguishing the risk of gynecologic cancers and could serve as a novel marker for early screening and prevention.

What is the implication, and what should change now?

- The findings suggest that the AVAI is a valuable tool for identifying women at higher risk of gynecologic cancers, particularly cervical cancer. Clinical screening strategies should consider incorporating the AVAI to improve early identification and risk stratification.

Health and Nutrition Examination Survey (NHANES) data have shown that for each standard deviation (SD) increase in the AVAI, the risk of prediabetes increases 1.8-fold, and the incidence of cardiovascular events increases by 22% (17,18).

This study aimed to further analyze the association between the AVAI and gynecologic malignancies using NHANES data, providing scientific evidence for the development of personalized intervention strategies based on visceral fat regulation. We present this article in accordance with the TRIPOD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2025-1865/rc).

Methods

Study population

This study was an observational, cross-sectional analysis using data from the NHANES, a nationally representative survey conducted by the National Center for Health Statistics (NCHS). The NHANES employs a complex, multi-stage probability sampling framework to evaluate the health and nutritional conditions of non-institutionalized individuals, both adults and children, across the United States. The study adhered to protocols approved by the NCHS Institutional Review Board, and written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments.

To ensure the integrity of the analytical variables, the study used NHANES data from the 2007–2018 survey cycles, as this period includes detailed demographic information, health indicators, and biomarker data, which provide a reliable basis for exploring the connection between the AVAI and gynecologic malignancies. The original dataset comprised 30,203 female participants. According to the study objectives, the following strict exclusion criteria were applied to select the participants who met the analysis requirements:

(I) Age: participants under the age of 30 years (n=15,219) were excluded, as the incidence of gynecologic malignancies is relatively low in this age group and may be influenced by factors such as HPV vaccination, which could hinder an accurate assessment of the association between the AVAI and gynecologic malignancies.

(II) Data completeness: participants missing key data required to calculate the AVAI, including WC (n=1,589), TG level (n=68), high-density lipoprotein (HDL) cholesterol (n=649), and BMI (n=18), were excluded.

(III) Tumor status: participants whose gynecologic cancer status could not be confirmed (n=8) were excluded to ensure the accuracy of the results.

(IV) Socioeconomic status: participants missing poverty-to-income ratio (PIR) information (n=1,203) were excluded, as the PIR is an important indicator of socioeconomic status that may influence health behaviors and outcomes.

(V) Lifestyle factors: participants missing information on marital status (n=2), smoking status (n=6), and alcohol consumption history (n=2,552) were excluded, as these factors are closely related to the risk of gynecologic malignancies.

(VI) Chronic diseases: participants missing information on hypertension (n=8) and diabetes (n=236) were excluded, as these chronic conditions may affect the association between the AVAI and gynecologic malignancies.

(VII) Other important variables: participants missing information on education level (n=8) and age at menarche (which is not directly used in the AVAI calculation but could have affected the analysis, n=718) were excluded.

(VIII) Serological data: although this study did not directly analyze the association between serological data [e.g., white blood cell (WBC) count and neutrophil count (NC)] and the AVAI, participants missing these data (n=42) were excluded to ensure data completeness.

(IX) Oral contraceptive use status: participants who did not provide information on oral contraceptive use (n=22) were excluded.

After these multiple screening steps, 7,855 female participants were included in the analysis, consisting of 237 gynecologic malignancy patients and 7,618 non-cancer controls. This sample size had sufficient statistical power to provide a reliable data foundation for further in-depth analysis of the association between the AVAI and gynecologic malignancies (including ovarian cancer, endometrial cancer, and cervical cancer) (see the flowchart in *Figure 1*).

Definition and measurement of independent variables

The core independent variable in this study was the AVAI,

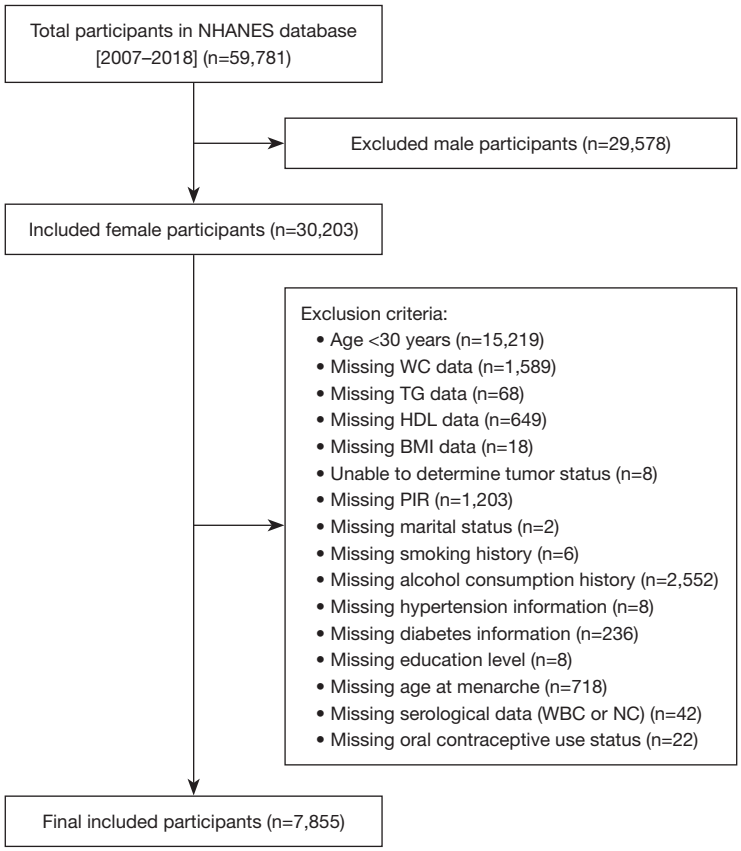

Figure 1 Participant selection flowchart for cohort study. BMI, body mass index; HDL, high-density lipoprotein; NC, neutrophil count; NHANES, National Health and Nutrition Examination Survey; PIR, poverty-income ratio; TG, triglyceride; WBC, white blood cell; WC, waist circumference.

a composite index reflecting visceral fat distribution and metabolic function. It was calculated using WC, BMI, TG, HDL cholesterol, and age. The AVAI was calculated using the following formula: AVAI = −16.186 − 1.369 × HDL + 0.038 × WC + 0.144 × age − 0.013 × BMI − 0.151 × TG (15). All anthropometric and laboratory measurements were obtained following standardized NHANES procedures with regular quality control calibration to minimize measurement bias.

Cancer diagnosis

The cancer diagnosis data were obtained through a structured questionnaire. The participants were asked whether they had ever been diagnosed with any form of cancer or malignant neoplasm by a physician or other healthcare professional (NHANES questionnaire item MCQ-220). Participants who responded affirmatively were classified as cancer cases and were subsequently directed to complete the MCQ-230A module, which captures site-specific cancer diagnoses. In this module, cervical cancer was coded as 15, ovarian cancer as 28, and endometrial cancer as 38.

Covariate adjustment

To more accurately assess the association between the AVAI and gynecologic malignancies, multiple potential confounding factors were adjusted for during the statistical analysis. These covariates included age, race, education level, the PIR, marital status, smoking status, alcohol consumption, hypertension, diabetes, the BMI, and other potential metabolic and inflammatory markers. Using multivariable logistic regression analysis, the association between the AVAI and the risk of gynecologic malignancies was evaluated across different levels of covariate adjustment.

Study outcomes

Primary outcome: The association between the AVAI and the risk of overall gynecologic malignancies (ovarian, endometrial, and cervical cancers).

Secondary outcomes: (I) subgroup associations between AVAI and each type of gynecologic malignancy (ovarian, endometrial, and cervical cancers separately); (II) the dose-response relationship between AVAI and gynecologic cancer risk; and (III) the discriminative performance of AVAI compared with BMI, assessed by receiver operating characteristic (ROC) curve analysis.

Statistical analysis

A comprehensive statistical analysis was conducted to explore the connection between the AVAI and gynecologic malignancies. All the statistical analyses were conducted using SPSS 27.0 (IBM Corp., Armonk, NY, USA) and EmpowerStat statistical software (X&Y Solutions, Inc., Boston, MA, USA), with careful consideration of the complex sampling design of the NHANES data to ensure the accuracy and reliability of the results. A descriptive statistical analysis was used to summarize the baseline characteristics of the participants. Continuous variables, such as age, the BMI, WC, TG, HDL cholesterol, the AVAI, and various blood cell counts are presented as the mean ± SD or median [interquartile range (IQR)], and group comparisons were made based on the cancer status of the participants using the weighted *t*-test or Mann-Whitney *U* test (for the non-normally distributed data). Categorical variables, such as race, marital status, the PIR, education level, smoking status, alcohol consumption, hypertension, and diabetes, are expressed as percentage, and group comparisons were made using the weighted Chi-squared test. A multivariable logistic regression model was employed to analyze the association between the AVAI and the risk of gynecologic malignancies. Given the complex, multistage probability sampling design of NHANES, all logistic regression analyses incorporated survey weights, strata, and primary sampling units. The reported odds ratios (ORs) and 95% confidence intervals (CIs) were survey-adjusted to provide nationally representative estimates. In the model, an unadjusted model was first constructed, in which the AVAI was the only included independent variable, to initially assess the strength of its association. Subsequently, covariates, such as race, marital status, education level, age, the PIR, alcohol consumption, smoking status, hypertension, diabetes, and the BMI, were progressively included for adjustment, controlling for potential confounding factors. By comparing the OR and their 95% CI across different adjustment models, the study assessed the changes in the strength of the association between the AVAI and the risk of gynecologic malignancies, and determined the independent association between the AVAI and the risk of gynecologic malignancies after fully adjusting for potential confounders. To further explore the dose-response relationship between the AVAI and the risk of gynecologic malignancies, a restricted cubic spline model was used. This model allowed the nonlinear relationship between the AVAI and the risk of gynecologic malignancies to be more flexibly captured, and the trend in the risk of gynecologic malignancies across different levels of the AVAI to be assessed. A ROC curve analysis was performed to evaluate the effectiveness of the AVAI in distinguishing the risk of gynecologic malignancies. By calculating the area under the curve (AUC), specificity, sensitivity, and other metrics, the study evaluated the ability of the AVAI to distinguish between the gynecologic malignancy patients and non-cancer controls, and further verified its clinical discriminative value. All statistical tests were two-sided, and a $P<0.05$ was considered statistically significant.

Results

Baseline characteristics

The study population was stratified into the following two groups according to the presence or absence of gynecologic malignancies: the gynecologic malignancy group (n=237), and the non-gynecologic malignancy group (n=7,618).

Statistically significant differences were observed in several baseline characteristics between the two groups ($P<0.05$). The participants in the gynecologic malignancy group were older (median age: 56.0 years, IQR: 44.0–66.0 years) than those in the non-gynecologic malignancy group (median age: 52.0 years, IQR: 41.0–64.0 years). There were also significant differences between the two groups in terms of racial distribution. Specifically, non-Hispanic white women accounted for a higher proportion in the gynecologic malignancy group (59.1%) than the non-gynecologic malignancy group (42.5%), while the distribution of other races, such as Mexican American and non-Hispanic Black, was balanced across the two groups. In terms of education level and the PIR, the women in the gynecologic malignancy group had a higher proportion of

lower educational levels and lower PIR (lower income).

In terms of lifestyle factors, the smoking rate of the gynecologic malignancy group (55.7%) was significantly higher than that of the non-gynecologic malignancy group (37.2%), but no significant differences were observed between the two groups in terms of alcohol consumption. Additionally, the prevalence of hypertension and diabetes was higher in the gynecologic malignancy group, which might be associated with the increased risk of gynecologic malignancies. In terms of the anthropometric measures, the women in the gynecologic malignancy group had a significantly higher WC, BMI, and TG level than those in the non-gynecologic malignancy group, while the HDL cholesterol levels were similar between the two groups.

There were also significant differences in the AVAI between the two groups. The median AVAI of the gynecologic malignancy group was −6.8 (IQR: −8.7 to −5.3), which was significantly higher than the median AVAI of −7.6 (IQR: −9.3 to −5.8) of the non-gynecologic malignancy group.

In conclusion, there were significant differences in various baseline characteristics between the women with and without gynecologic malignancies in this study. These differences provided important background information for the subsequent analysis of the relationship between the AVAI and the risk of gynecologic malignancies (*Table 1*).

Association between the AVAI and the risk of gynecologic cancer

To further explore the potential relationship between the AVAI and the risk of gynecologic cancers, a stratified multivariable logistic regression analysis was performed on the data of the 7,855 female participants. A statistically significant association was found between the AVAI and the risk of gynecologic malignancies when comparing the participants with and without such diagnoses. In model I, which was fully adjusted for potential confounders, including age, race, educational level, and the PIR, each one-unit increase in the AVAI was associated with a 28.0% higher risk of gynecologic cancer (OR =1.280, 95% CI: 1.089–1.504, P=0.003) (*Table 2*, *Figure 2*).

Subgroup analysis

A further subgroup analysis by gynecologic cancer type revealed that the AVAI was particularly associated with an increased risk of cervical cancer. In model I for cervical cancer, each unit increase in the AVAI significantly increased the risk of developing the disease (OR =1.309, 95% CI: 1.050–1.632, P=0.02). Similarly, in model II for cervical cancer, each unit increase in the AVAI significantly increased the risk of developing the disease (OR =1.456, 95% CI: 1.032–2.055, P=0.03). However, the association between the AVAI and the risk of ovarian cancer and endometrial cancer did not reach the level of statistical significance (P>0.05).

Additionally, an analysis of the relationship between the AVAI tertiles and gynecologic cancer risk revealed a dose-response relationship for cervical cancer in model I. Compared to the lowest tertile (Q1, <−8.7292), the risk of cervical cancer in the second (Q2, −8.7292 to −6.3966) and third (Q3, >−6.3966) tertiles was significantly increased (Q2 in model I: OR =2.085, 95% CI: 1.221–3.558, P=0.007; Q3 in model I: OR =2.974, 95% CI: 1.192–7.419, P=0.02). However, no such dose-response relationship was found for ovarian cancer and endometrial cancer; this trend supports the reliability of the AVAI as a discriminative indicator for cervical cancer (*Tables 3-5*, *Figure 3*). The AUC of the ROC curve was 0.807, indicating that the AVAI has good discriminative ability for gynecologic cancers (*Figure 4*).

Discussion

Using NHANES data, this study conducted the first in-depth analysis to reveal a connection between the AVAI and the risk of gynecologic malignancies. It also established the AVAI as a core link between visceral fat metabolism disorders and the onset of cervical cancer. This finding suggests that AVAI overcomes some limitations of traditional obesity indices and may be useful in metabolomics-based assessment of gynecologic cancer risk.

The AVAI integrates key parameters, such as WC, TG level, BMI, and age, and uses multivariate regression models to adjust for the effect of age on visceral fat distribution. It constructs a quantifiable index that comprehensively reflects the core pathological features of metabolic syndrome. Compared to the traditional BMI, the AVAI has the advantage of more precisely capturing the synergistic effects of visceral fat accumulation and metabolic abnormalities (19).

In this study, the AVAI of the gynecologic cancer group was significantly higher than that of the control group, and in the fully adjusted model I, each unit increase in the AVAI significantly increased the risk of gynecologic cancers. This result aligns with the "visceral fat-chronic inflammation-tumor progression" axis theory revealed by previous metabolomics research (20). Cowen *et al.* (21) showed that

Table 1 Baseline characteristics of the study participants

Characteristics	Control group (n=7,618)	Gynecologic cancer group (n=237)	Total (n=7,855)	P
Age (years)				0.005
<53	3,976 (52.2)	101 (42.6)	4,077 (51.9)	
≥53	3,642 (47.8)	136 (57.4)	3,778 (48.1)	
Race				<0.001
Mexican American	1,200 (15.8)	35 (14.8)	1,235 (15.7)	
Other Hispanic	877 (11.5)	25 (10.5)	902 (11.5)	
Non-Hispanic White	3,234 (42.5)	140 (59.1)	3,374 (43.0)	
Non-Hispanic Black	1,569 (20.6)	24 (10.1)	1,593 (20.3)	
Other race	738 (9.7)	13 (5.5)	751 (9.6)	
Education level				0.002
Less than high school	1,896 (24.9)	78 (32.9)	1,974 (25.1)	
High school	1,639 (21.5)	59 (24.9)	1,698 (21.6)	
More than high school	4,083 (53.6)	100 (42.2)	4,183 (53.3)	
PIR				0.005
Low-income	2,456 (32.2)	97 (40.9)	2,553 (32.5)	
Middle-income	2,851 (37.4)	88 (37.1)	2,939 (37.4)	
High-income	2,311 (30.3)	52 (21.9)	2,363 (30.1)	
Marital status				0.02
Married/living with partner	4,369 (57.4)	118 (49.8)	4,487 (57.1)	
Single	3,249 (42.6)	119 (50.2)	3,368 (42.9)	
Smoking				<0.001
No	4,786 (62.8)	105 (44.3)	4,891 (62.3)	
Yes	2,832 (37.2)	132 (55.7)	2,964 (37.7)	
Drinking				0.27
No	3,084 (40.5)	105 (44.3)	3,189 (40.6)	
Yes	4,534 (59.5)	132 (55.7)	4,666 (59.4)	
Hypertension				0.003
No	4,581 (60.1)	119 (50.2)	4,700 (59.8)	
Yes	3,037 (39.9)	118 (49.8)	3,155 (40.2)	
Diabetes				0.12
No	6,558 (86.1)	195 (82.3)	6,753 (86.0)	
Yes	1,060 (13.9)	42 (17.7)	1,102 (14.0)	
Age (years)	52.0 (41.0 to 64.0)	56.0 (44.0 to 66.0)	52.0 (41.0 to 64.0)	0.02
BMI (kg/m^2)	28.8 (24.6 to 33.8)	30.0 (25.5 to 35.1)	28.8 (24.6 to 33.8)	0.02

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Control group (n=7,618)	Gynecologic cancer group (n=237)	Total (n=7,855)	P
Waist (cm)	97.1 (87.0 to 108.1)	101.0 (90.2 to 111.3)	97.2 (87.0 to 108.2)	0.001
TG level (mmol/L)	1.3 (0.9 to 2.0)	1.6 (1.1 to 2.4)	1.4 (0.9 to 2.0)	<0.001
HDL (mmol/L)	1.4 (1.2 to 1.7)	1.4 (1.1 to 1.6)	1.4 (1.2 to 1.7)	0.002
VAI	1.3 (0.7 to 2.2)	1.7 (1.0 to 2.7)	1.3 (0.7 to 2.2)	<0.001
AVAI	−7.6 (−9.3 to −5.8)	−6.8 (−8.7 to −5.3)	−7.6 (−9.3 to −5.8)	<0.001
WBC (1,000 cells/μL)	6.9 (5.7 to 8.4)	7.7 (6.1 to 8.9)	6.9 (5.7 to 8.4)	<0.001
RBC (million cells/μL)	4.4 (4.2 to 4.7)	4.4 (4.2 to 4.7)	4.4 (4.2 to 4.7)	0.59
NC (1,000 cell/μL)	4.0 (3.1 to 5.1)	4.4 (3.4 to 5.6)	4.0 (3.1 to 5.1)	<0.001
LC (1,000 cells/μL)	2.1 (1.7 to 2.6)	2.2 (1.8 to 2.9)	2.1 (1.7 to 2.6)	<0.001
MC (1,000 cells/μL)	0.5 (0.4 to 0.6)	0.5 (0.4 to 0.6)	0.5 (0.4 to 0.6)	0.13
PLT (1,000 cells/μL)	251.0 (213.0 to 297.0)	256.0 (219.0 to 298.0)	251.0 (214.0 to 297.0)	0.30
RDW (%)	13.1 (12.5 to 13.9)	13.2 (12.5 to 13.9)	13.1 (12.5 to 13.9)	0.56
LMR	4.2 (3.3 to 5.3)	4.4 (3.5 to 5.5)	4.2 (3.3 to 5.3)	0.12
MLR	0.2 (0.2 to 0.3)	0.2 (0.2 to 0.3)	0.2 (0.2 to 0.3)	0.12
PLR	120.0 (95.7 to 151.2)	112.3 (85.4 to 147.2)	120.0 (95.3 to 151.1)	0.01

Data are presented as n (%) or median (IQR). AVAI, age-adjusted visceral adiposity index; BMI, body mass index; HDL, high-density lipoprotein; IQR, interquartile range; LC, lymphocyte count; LMR, lymphocyte-to-monocyte ratio; MC, monocyte count; MLR, monocyte-to-lymphocyte ratio; NC, neutrophil count; PIR, poverty-to-income ratio; PLR, platelet-to-lymphocyte ratio; PLT, platelet; RBC, red blood cell; RDW, red blood cell distribution width; TG, triglyceride; VAI, visceral adiposity index; WBC, white blood cell.

Table 2 Association between the AVAI and the risk of gynecologic cancer

Exposure	Non-adjusted model		Adjusted model I		Adjusted model II	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
AVAI (continuous)	1.110 (1.047, 1.177)	<0.001	1.280 (1.089, 1.504)	0.003	1.141 (0.901, 1.445)	0.27
AVAI (categorical)						
Q1 (<−8.7292)	1		1		1	
Q2 (−8.7292 to −6.3966)	1.319 (0.933, 1.865)	0.12	1.722 (1.133, 2.618)	0.01	1.409 (0.886, 2.243)	0.15
Q3 (>−6.3966)	1.808 (1.304, 2.505)	<0.001	2.933 (1.532, 5.615)	0.001	2.071 (0.976, 4.392)	0.06

Adjusted model I: model adjusted for age, race, education level, and PIR. Adjusted model II: model adjusted for age, BMI, race, education level, PIR, marital status, smoking, drinking, hypertension, and diabetes. AVAI, age-adjusted visceral adiposity index; BMI, body mass index; CI, confidence interval; OR, odds ratio; PIR, poverty-to-income ratio.

a high-fat diet induces the expansion of visceral fat tissue, activates chronic low-grade inflammation, and promotes the remodeling of the breast cancer tumor microenvironment and the expression of angiogenesis factors. Chang *et al.* (22) also suggested that inflammation caused by obesity is a key promoter of pancreatic ductal adenocarcinoma. These findings suggest that the AVAI may not just be an indicator of visceral fat accumulation, but may also link metabolic abnormalities and gynecologic cancer risk.

Our study further discovered significant subtype

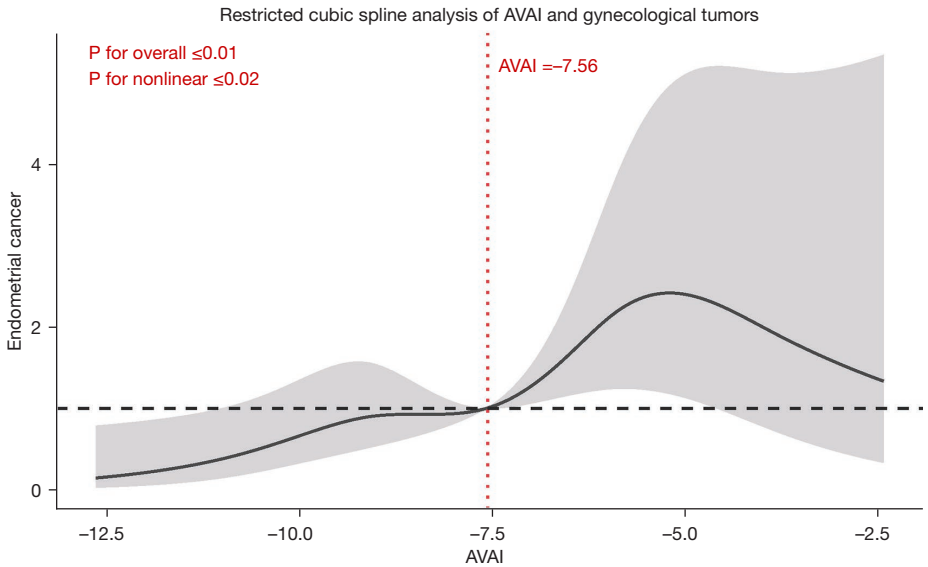

Figure 2 Restricted cubic spline analysis of the AVAI and risk of gynecologic cancers. Adjusted for age, race, PIR, education level, smoking status, alcohol consumption, BMI, platelet count, NC, and lymphocyte count. The black dotted line indicates the null reference line at OR =1.0. AVAI, age-adjusted visceral adiposity index; BMI, body mass index; NC, neutrophil count; OR, odds ratio; PIR, poverty-to-income ratio.

Table 3 Association between the AVAI and the risk of cervical cancer

Exposure	Non-adjusted model		Adjusted model I		Adjusted model II	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
AVAI (continuous)	0.966 (0.891, 1.048)	0.40	1.309 (1.050, 1.632)	0.02	1.456 (1.032, 2.055)	0.03
AVAI (categorical)						
Q1 (<−8.7292)	1		1		1	
Q2 (−8.7292 to −6.3966)	1.152 (0.752, 1.766)	0.52	2.085 (1.221, 3.558)	0.007	1.998 (1.081, 3.694)	0.03
Q3 (>−6.3966)	0.873 (0.553, 1.379)	0.56	2.974 (1.192, 7.419)	0.02	2.918 (0.998, 8.526)	0.05

Adjusted model I: model adjusted for age, race, education level, and PIR. Adjusted model II: model adjusted for age, BMI, race, education level, PIR, marital status, smoking, drinking, hypertension, and diabetes. Sample sizes: cervical cancer (n=121). AVAI, age-adjusted visceral adiposity index; BMI, body mass index; CI, confidence interval; OR, odds ratio; PIR, poverty-to-income ratio.

Table 4 Association between the AVAI and the risk of ovarian cancer

Exposure	Non-adjusted model		Adjusted model I		Adjusted model II	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
AVAI (continuous)	1.304 (1.132, 1.501)	<0.001	1.240 (0.847, 1.815)	0.27	0.930 (0.556, 1.554)	0.78
AVAI (categorical)						
Q1 (<−8.7292)	1		1		1	
Q2 (−8.7292 to −6.3966)	1.430 (0.543, 3.761)	0.47	1.046 (0.338, 3.232)	0.94	0.664 (0.198, 2.228)	0.51
Q3 (>−6.3966)	3.742 (1.621, 8.635)	0.002	1.944 (0.421, 8.981)	0.39	0.847 (0.150, 4.770)	0.85

Adjusted model I: model adjusted for age, race, education level, and PIR. Adjusted model II: model adjusted for age, BMI, race, education level, PIR, marital status, smoking, drinking, hypertension, and diabetes. Sample sizes: ovarian cancer (n=43). AVAI, age-adjusted visceral adiposity index; BMI, body mass index; CI, confidence interval; OR, odds ratio; PIR, poverty-to-income ratio.

Table 5 Association between the AVAI and the risk of endometrial cancer

Exposure	Non-adjusted model		Adjusted model I		Adjusted model II	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
AVAI (continuous)	1.270 (1.141, 1.413)	<0.001	1.244 (0.926, 1.671)	0.15	0.895 (0.596, 1.345)	0.59
AVAI (categorical)						
Q1 (<−8.7292)	1		1		1	
Q2 (−8.7292 to −6.3966)	1.824 (0.872, 3.814)	0.11	1.825 (0.778, 4.281)	0.17	1.373 (0.551, 3.424)	0.50
Q3 (>−6.3966)	3.864 (1.985, 7.522)	<0.001	3.412 (1.028, 11.328)	0.04	1.991 (0.507, 7.821)	0.32

Adjusted model I: model adjusted for age, race, education level, and PIR. Adjusted model II: model adjusted for age, BMI, race, education level, PIR, marital status, smoking, drinking, hypertension, and diabetes. Sample sizes: ovarian cancer (n=73). AVAI, age-adjusted visceral adiposity index; BMI, body mass index; CI, confidence interval; OR, odds ratio; PIR, poverty-to-income ratio.

specificity in the association between the AVAI and risk of gynecologic malignancies, notably including a prominent relationship between the AVAI and risk of cervical cancer. However, it is important to emphasize that this study is observational, and therefore, causality cannot be inferred from these findings. The pathological basis for this association may lie in the metabolic activity of VAT and its anatomical proximity to gynecologic organs. Visceral fat is not only an energy reservoir but also an active endocrine organ. The adipokines it secretes, such as adiponectin, resistin, and free fatty acids (FFAs), can influence the tumor microenvironment of gynecologic cancers through both paracrine and endocrine mechanisms (23). Soumya *et al.* (14) emphasized that fluctuations in insulin and TG levels, as well as increased adiponectin activity, may contribute to the risk of cervical cancer. Using preclinical models, Muhammad *et al.* (24) found that monounsaturated and saturated FFAs enhance the sensitivity of cervical cancer to radiotherapy through a novel p53-dependent mechanism. Additionally, our previous analysis of NHANES participants' serum metabolomics data showed that women with an AVAI ≥−6.4 had a 32% higher serum FFA concentration compared to those with an AVAI <−6.4. Further, the FFA levels were found to be independently associated with cervical cancer risk, suggesting that FFAs may be a key metabolic mediator of the AVAI-induced carcinogenesis (25). Despite these findings highlighting the association between AVAI and the risk of cervical cancer, further prospective cohort studies are still needed to confirm any causal relationship. The ROC curve analysis of this study showed that the AVAI had an AUC of 0.807, which shows the high accuracy of the AVAI in distinguishing between gynecologic cancer patients and non-gynecologic cancer patients. An AUC greater than 0.8 indicates that the AVAI performs well in accurately identifying patients, while reducing the risks of misdiagnosis (i.e., classifying non-patients as patients) and missed diagnosis (i.e., classifying patients as non-patients).

However, the association between AVAI and the risk of endometrial cancer was inconsistent across different models. In the unadjusted analysis and model I, AVAI was significantly associated with a higher risk of endometrial cancer, but there was no significant association in model II. We believe that the possible reason for this result is closely related to the complex pathological mechanism of endometrial cancer and the metabolic assessment role of the AVAI index itself. Firstly, endometrial cancer is widely recognized as an estrogen-dependent cancer. VAT is not only a site for energy storage but can also convert androgens into estrogens through aromatization, thereby influencing endometrial hyperplasia and carcinogenesis (26,27). Therefore, although AVAI can reflect the accumulation of visceral fat and its metabolic characteristics, its metabolic indicators (such as TG levels and BMI) may not fully capture the impact of hormones on the occurrence of endometrial cancer. Especially in model II, after further adjustment for more potential confounding factors (such as metabolic diseases like BMI, diabetes, and hypertension), the hormonal effect may have been over-controlled, thus weakening the association between AVAI and endometrial cancer. Secondly, although AVAI, as a composite index, reflects the accumulation of visceral fat and related metabolic functions, it may capture more of the risks associated with metabolic disorders rather than directly influencing the estrogen-related risk pathways (16). Therefore, AVAI shows a more significant association with cancers such as cervical cancer, which are more strongly affected by metabolic dysregulation, while its impact on endometrial cancer, a disease mainly related to hormone

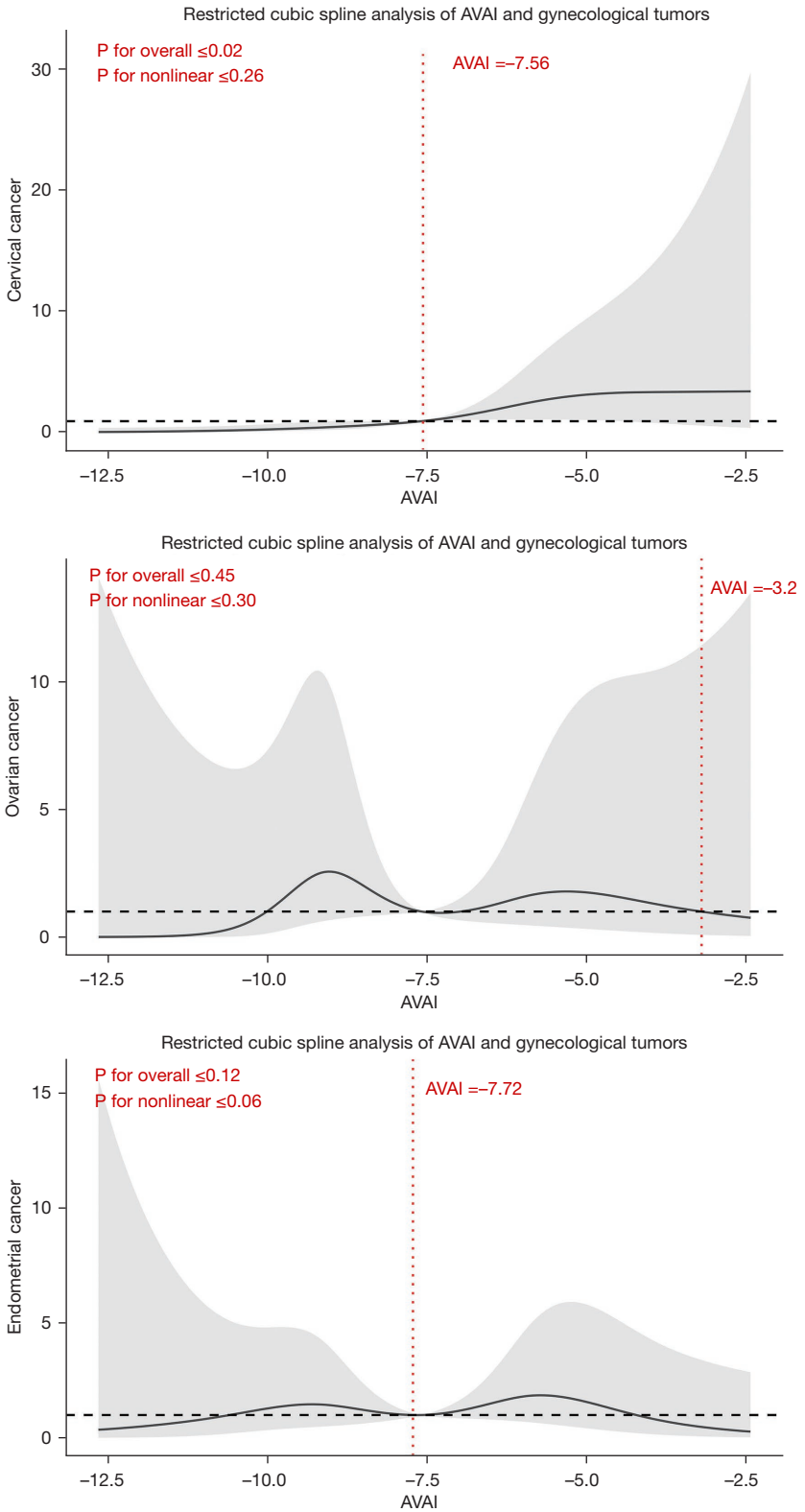

Figure 3 Restricted cubic spline analysis of the AVAI and cervical cancer, endometrial cancer, and ovarian cancer. The black dotted line indicates the null reference line at OR =1.0. AVAI, age-adjusted visceral adiposity index; OR, odds ratio.

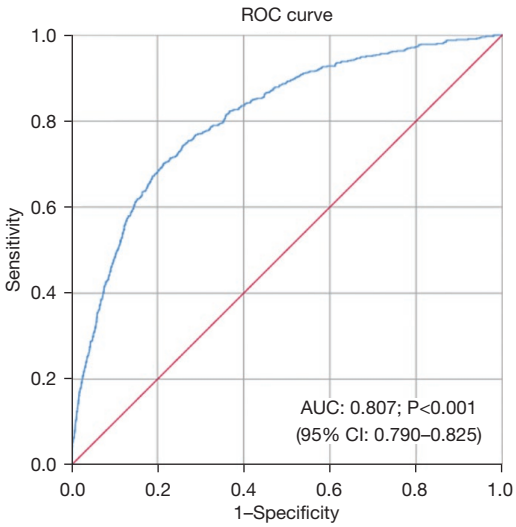

Figure 4 ROC curve of the AVAI in distinguishing gynecologic cancers. AUC, area under the curve; AVAI, age-adjusted visceral adiposity index; CI, confidence interval; ROC, receiver operating characteristic.

levels, is relatively weak. Finally, the differences in statistical analysis models may also have a certain impact on the results. Especially after adjusting for more variables, the association between AVAI and endometrial cancer may be significantly weakened due to the control of confounding factors. We believe that future research can further clarify the potential role of AVAI in different types of gynecological cancers by exploring the more refined interaction between hormone levels and metabolic disorders.

For ovarian cancer, the association with AVAI was weaker and did not reach statistical significance in the fully adjusted models. This may be attributed to the heterogeneous etiology of ovarian cancer, where genetic predispositions (e.g., *BRCA* mutations) and reproductive factors often play a larger role than metabolic abnormalities. Previous studies have suggested that visceral adiposity is more strongly associated with ovarian cancer prognosis and recurrence rather than initial incidence (28-30).

Although our findings suggest that the AVAI has potential utility in assessing the risk of gynecologic malignancies, several limitations of this index should be acknowledged. First, the AVAI is a composite measure derived from anthropometric and biochemical parameters (WC, BMI, TG, HDL, and age), and thus may still be influenced by measurement errors in these variables Second, the AVAI does not fully capture body fat distribution or ectopic fat deposition, such as hepatic or perivisceral fat, which may also play a role in cancer risk. Third, since the AVAI was developed using population-based regression models, its applicability to specific subgroups (e.g., different ethnicities, younger women, or patients with metabolic disorders) may be limited (17). Therefore, although AVAI provides an improved measure compared to BMI, it should be interpreted with caution and complemented by other clinical and imaging-based assessments of adiposity.

Several limitations inherent to this study should be acknowledged and warrant further investigation and refinement: (I) the causal inference limitation: the cross-sectional design of this study precluded the establishment of causal relationships between the AVAI and gynecologic malignancies. Future prospective cohort studies (using follow-up data from the NHANES) are required to verify the temporal association between dynamic changes in the AVAI and cancer development. (II) Although the ROC curve in this study indicated that the AVAI has good performance in distinguishing gynecologic malignancies, this finding is based solely on retrospective associations, and its clinical screening value needs to be further confirmed in prospective, multi-center studies. (III) A lack of mechanistic validation: this study was limited by the absence of metabolomic and transcriptomic data from tumor tissue samples. Future studies should explore the metabolic reprogramming mechanisms underlying the AVAI through the use of animal models or clinical specimens. (IV) Subgroup heterogeneity: this study did not differentiate between gynecologic cancer subtypes (such as the molecular subtypes of cervical cancer). Future analyses should refine the investigation to clarify the relationship between the AVAI and different cancer subtypes. For example, the AVAI risk difference between HPV-positive and HPV-negative cervical cancers may vary. (V) Additionally, participants with missing information for key variables, including socioeconomic and lifestyle factors (e.g., PIR, marital status, alcohol use), were excluded to ensure analytical completeness and allow for full covariate adjustment. Although this ensured analytical completeness, it may have introduced exclusion bias. Future studies incorporating imputation methods or sensitivity analyses are warranted to confirm robustness.

Conclusions

This study was the first to confirm a significant positive

correlation between the AVAI and the risk of gynecologic malignancies, including a particularly pronounced association with cervical cancer. As a potential biomarker, the AVAI serves as a metabolic-inflammatory composite indicator that surpasses the traditional BMI in gynecologic cancer risk assessment, showing great potential for clinical application. Future research should be conducted to further explore personalized prevention strategies guided by the AVAI to address the rising global incidence of gynecologic malignancies.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments.

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