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Correlation between the metabolic score for visceral fat and chronic obstructive pulmonary disease among middle-aged and elderly American population

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Abstract. – OBJECTIVE: A metabolism score for visceral fat (METS-VF) is an innovative method to access abdominal fat and visceral fat. So far, the relationship between the METS-VF index and chronic obstructive pulmonary disease (COPD) has remained unclear. We investigated the relationship between the METS-VF index and COPD prevalence utilizing data from the National Health and Nutrition Examination Survey (NHANES) 2007-2018.

PATIENTS AND METHODS: A binary logistic regression analysis was performed using NHANES 2007-2018 data to assess the relationship between the METS-VF index and COPD prevalence. The relationship was verified by fitted smooth curves, generalized additive models, threshold effect analyses, subgroup analyses, and sensitivity analyses.

RESULTS: In total, 7,680 subjects were recruited for the study, including 772 self-reported having COPD. The METS-VF index was positively related to COPD prevalence when adjusted for all covariates. The METS-VF index was classified by quartiles, and participants who scored highest on METS-VF were at a greater risk of COPD than those who scored lowest. According to a threshold effect analysis, the METS-VF index was negatively correlated with COPD prevalence with a METS-VF index <7.00, without statistical significance. Once the METS-VF index exceeded 7.00, there was a robust positive correlation between the METS-VF index and COPD prevalence. In the analysis of subgroups, the METS-VF index was positively correlated with COPD prevalence among subjects who were male, aged 40-59, and without asthma or hypertension. The results were robust in sensitivity analyses. METS-VF showed a significantly better diagnostic value for COPD than Body Mass Index (BMI).

CONCLUSIONS: The METS-VF index has a non-linear and positive correlation with COPD prevalence in the middle-aged and elderly American population.

Key Words:
COPD, Visceral fat, METS-VF, NHANES.

Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogeneous condition characterized by persistent airflow obstruction and airway or alveolar abnormalities. As a major cause of death globally, COPD poses a heavy burden on public economies and healthcare. A spirometry test that shows reversible airflow obstruction (defined as Forced Expiratory Volume in one second (FEV1)/Forced Vital Capacity (FVC) <0.7 post-bronchodilation) confirms the diagnosis of COPD. Many COPD patients usually show signs of cough, expectoration, dyspnea, wheezing, and activity limitation and may present with structural lung damage or abnormal physiological conditions[1].

Multiple observational research has observed that obesity is prevalent among COPD patients, accounting for 18-24.6% in different studies[2-5]. Obesity is related to poor COPD outcomes, including life quality, 6-minute walk distance (6MWD), and acute exacerbations[6]. Visceral fat can provide support and protection for organs. However, excessive visceral fat has been found to aggravate airway obstruction by reducing pulmonary compliance and restricting the movement of the chest wall or diaphragm in COPD patients[7]. Visceral fat deposition has been associated with metabolic syndrome, which has been found to worsen inflammatory status, increase exacerbations, and damage pulmonary function in COPD patients[8-10].

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Currently, magnetic resonance imaging (MRI) is the most reliable method of measuring visceral fat; however, MRI is expensive and requires professional operation and interpretation, which limits its application in clinical practice. In literature, there are no studies exploring how visceral fat influences the prevalence of COPD.

The metabolic score for visceral fat (METS-VF) index is an innovative method to estimate visceral fat and intra-abdominal fat[11]. It combines the metabolic score for insulin resistance (METS-IR), age, waist-height ratio (WHtr), and sex. Our study examined the relationship between the METS-VF index and COPD prevalence using the National Health and Nutrition Examination Survey (NHANES) 2007-2018 data.

Materials and Methods

Sources of Data

The NHANES is a national survey operated by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC), monitoring individuals' health and nutritional conditions across the United States. The survey combines interview sessions, medical examinations, laboratory testing, and health-related questionnaires. The ethical approval to conduct the NHANES 2007-2018 was granted by the National Center for Health Statistics Research Ethics Review Board (Protocol #2021-05). Each participant signed an informed consent form. Information regarding the METS-VF index was extracted from the 2007-2018 NHANES cycles, accessible on the official website (https://www.cdc.gov/nchs/nhanes).

Study Population

We enrolled 59,843 participants in six cycles (2007-2018) of the NHANES, and 36,616 participants aged <40 years were excluded. We then removed participants who did not have the following data, including COPD (n=5), METS-VF index (n=13,534), education level (n=12), situation of marriage (n=4), household income-to-poverty ratio (n=935), alcohol drinking (n=660), diabetes (n=3), hypertension (n=7), asthma (n=6), coronary heart disease (CHD, n=36), cancer (n=6), physical activity (n=1), smoking (n=7) and dietary information (n=331). Finally, 7,680 participants were included. Figure 1 shows a flow diagram of the participant enrollment process.

Definition of COPD

Diagnoses of COPD were based on self-reports from physicians, consistent with previously published research[12]. The diagnosis was confirmed using three self-reported questionnaire items in medical conditions: (1) "Has a doctor or other health professional ever told you that you had chronic bronchitis?"; (2) "Has a doctor or other health professional ever told you that you had emphysema?"; (3) "Has a doctor or other health professional ever told you that you had COPD?". The COPD group was composed of participants who answered "yes" to one or more of the three questions and excluded those who did not.

METS-VF Index

The METS-VF is an innovative method to estimate visceral fat and intra-abdominal fat, combining METS-IR, WHtR, age, and sex. In the laboratory, plasma triglycerides (TG), fasting blood glucose (GLU), and high-density lipoprotein cholesterol (HDL-C) were measured. WHtR= waist circumference (cm)/height (cm). We calculated METS-IR using the formula: (Ln ((2 × GLU) + TG) × Body Mass Index (BMI)/(Ln (HDL-C)). METS-VF was defined as: $4.466 + 0.011 \times (\text{Ln}(\text{METS-IR}))^3 + 3.239 \times (\text{Ln}(\text{WHtr}))^3 + 0.319 \times (\text{Sex}) + 0.594 \times (\text{Ln}(\text{Age}))$[11]. As defined, GLU was calculated in mg/dL, BMI in kg/m^2, TG in mg/dL, HDL-C in mg/dL, Age in years, and ex was calculated using a binary response variable (male=1, female=0).

Covariates

The potential confounding covariates were based on previous studies[13,14], including ethnicity, household income-to-poverty ratio, the situation of marriage, educational level, cigarette smoking, drinking alcohol, history of diseases (including asthma, hypertension, diabetes, CHD, and cancer), physical activity (PA), serum cholesterol, serum uric acid and dietary factors (total intake of water, energy, sugar, and fat) were obtained through questionnaires and laboratory measurements. Ethnicity was divided into Mexican Americans, Hispanics, Whites, Blacks, and others. Household income-to-poverty ratios were categorized into low incomes (≤1.3), medium incomes (>1.3 to 3.5), and high incomes (>3.5)[15]. Situations of marriage were classified into 5 categories: married, widowed, divorced, separated, unmarried, and cohabiting with someone. Levels of education were classi-

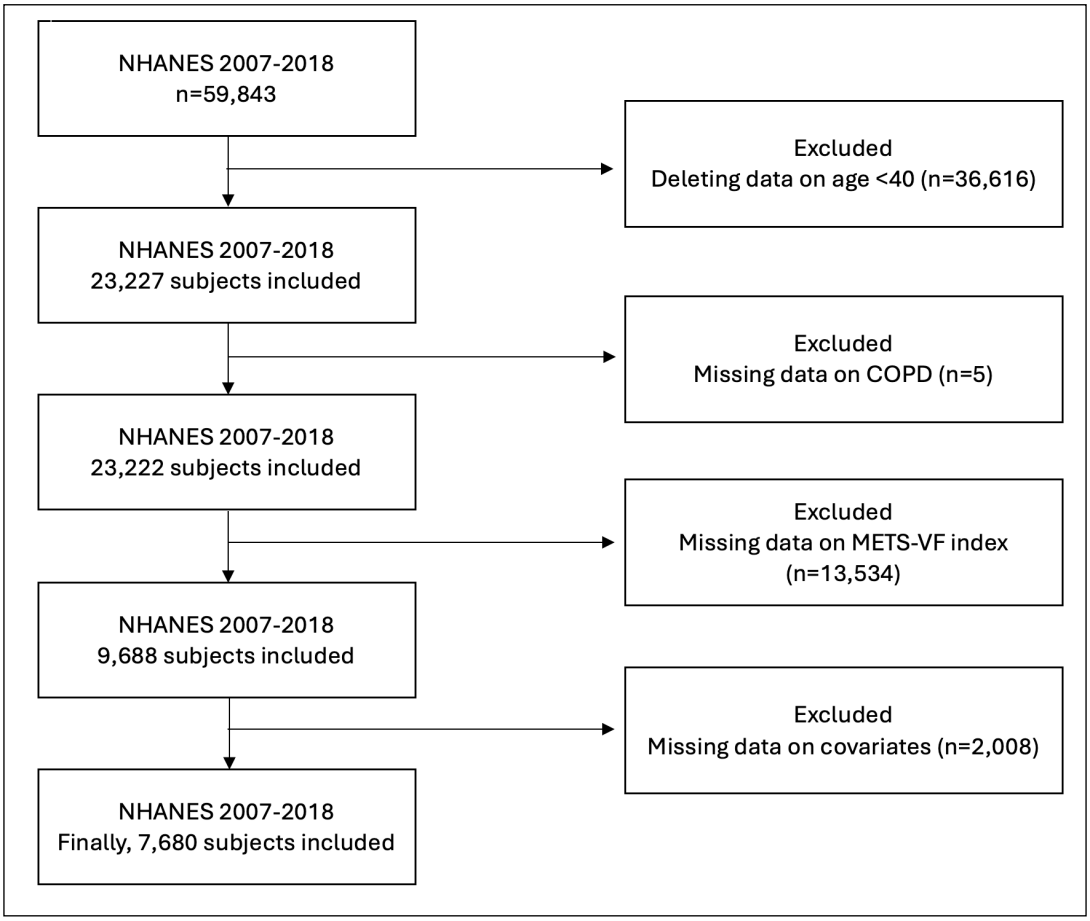

Figure 1. Flow chart for participants. COPD, chronic obstructive pulmonary disease; METS-VF, metabolism score for visceral fat.

fied into high school, high school, and higher education. Smokers and non-smokers were classified based on their smoking status. An alcohol drinker was defined by the survey questionnaire, "In any one year, have you had at least 12 drinks of any type of alcoholic beverage?". Self-reported diagnoses from a physician define a person's disease history. PA was measured through the Global Physical Activity Questionnaire. Calculating the total PA in MET-minutes per week involved adding up work-related PA, transportation-related PA, and recreation-related PA. Active PA was regarded as ≥600 MET-min per week, while inactive PA was considered as <600 MET-min per week[16]. Blood samples were tested in the laboratory for levels of cholesterol and uric acid. Dietary information was extracted from two dietary recalls of 24-hour periods. Our study used the average consumption from the two recalls.

Statistical Analysis

Using the METS-VF index quartiles, subjects were classified into four groups. For continuous variables, means ± standard deviations (SD) or medians (interquartile ranges, IQR) were analyzed, and for categorical variables, numbers (percentages). For testing differences in METS-VF groups, continuous variables were analyzed with ANOVA or non-parametric tests, while analyses of categorical variables were conducted with Chi-square tests.

An analysis of a binary logistic generalized linear model was conducted to explore the relationship between METS-VF index and COPD prevalence. The potential confounding factors were adjusted gradually for each regression model (Models 1 to 3). In Model 1, no adjustment was made. Racial, educational, and marital status were adjusted in Model 2. Besides those in Model 2, Model 3 was adjusted for ad-

ditional confounders, including household poverty-to-income ratio, diabetes, hypertension, asthma, CHD, cancer, PA, drinking, smoking, serum cholesterol, serum uric acid, and total intake of water, energy, sugar, and fat. The variance inflation factor (VIF) was used to test for multicollinearity between variables. Continuous variables (including serum cholesterol, serum uric acid, and total intake of water, energy, sugar, and fat) were categorized into 2 groups by medians in logistic models. We calculated adjusted odds ratios (ORs) and 95% confidence intervals (CIs) in the results. The generalized additive model (GAM) and fitted smooth curves were applied to explore the potential nonlinear correlation between the METS-VF index and COPD. An analysis of threshold effects between the METS-VF index and COPD was conducted by two-piecewise linear regressions. An analysis of subgroups stratified by age, gender, smoking, asthma, diabetes, and hypertension was carried out to explore the correlation between the METS-VF index and COPD. Sensitivity analyses were performed to test the robustness of the results. First, we adjusted the COPD definition: those who self-reported a physician's diagnosis of COPD were included in the COPD group. Second, both asthma and smoking were closely associated with COPD. To eliminate their co-effect on the outcome, we exclude smoking participants with asthma to verify the association between METS-VF and COPD prevalence. The receiver operating characteristic (ROC) curve was analyzed to assess the diagnostic value of METS-VF, BMI, and waist circumference. Statistics and figures were conducted using SPSS 26.0 (IBM Corp., Armonk, NY, USA), R 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria), and MedCalc 20.0 (MedCalc Software, Acacialaan, Ostend, Belgium). Statistical significance was defined as a two-sided *p*-value of less than 0.05.

Results

Participant Baseline Characteristics

In total, 7,680 participants participated in the study, whose median age was 60. Men accounted for 49.9% of the participants, and women accounted for 50.1% of the participants. We divided subjects into 4 groups based on the METS-VF index quartiles (Q1, 3.60-6.80; Q2, 6.80-7.19; Q3, 7.19-7.49; Q4, 7.49-8.38). Table I shows participant characteristics at baseline grouped by METS-VF quartiles. As a result of our study, the prevalence of COPD was 10.1%, with morbidities of 7.7%, 6.8%, 10.8%, and 14.9% in the METS-VF quartiles, respectively ($p<0.05$). Participants who scored highest on the METS-VF were mostly elderly, male, Mexican Americans, widowed and smoked, less likely to drink and exercise, prone to have poor education levels, less income-to-poverty ratios, lower total sugar intake, lower cholesterol levels, higher total fat intake, and higher uric acid levels, inclined to have diabetes, hypertension, asthma, CHD and cancer (all *p*-value <0.05).

Relationship Between the METS-VF Index and COPD

An analysis of the relationship between the METS-VF index and COPD prevalence is presented in Table II. The METS-VF index had a positive correlation with COPD prevalence in all three regression models. After fully adjusting for all covariates, the positive correlation remained stable (OR=1.216, 95% CI: 1.021, 1.448, p =0.028). Moreover, when the METS-VF index was grouped by quartiles, participants who scored highest on METS-VF were at a higher risk of COPD than those who scored lowest (reference). The ORs with 95% CIs for COPD among quartiles 1-4 were 0.897 (0.686, 1.174), 1.136 (0.879, 1.468), and 1.396 (1.073, 1.816), respectively, in model 3 (p for trend = 0.005). Multicollinearity was not present for all variables (all VIF values <5, **Supplementary Table I**).

Using fitted smooth curve analysis, the METS-VF index had a non-linear association with COPD prevalence (Figure 2). A threshold effect analysis indicated that the METS-VF index was negatively correlated with COPD prevalence with a METS-VF index <7.00 (OR=0.83, 95% CI: 0.58, 1.18), without statistical significance. Once the METS-VF index exceeded 7.00, the METS-VF index had a significantly positive correlation with COPD prevalence (OR=2.05, 95% CI: 1.40, 3.00, $p<0.001$, Table III).

Subgroup Analyses and Sensitivity Analyses

Table IV shows the results of subgroup analyses based on age, gender, smoking status, asthma, diabetes, and hypertension. METS-VF showed a stronger association with COPD prevalence among participants who were aged 40-59 (OR=1.628, 95% CI: 1.069, 2.480), male (OR=1.671, 95% CI: 1.089,

Table I. Characteristics of participants by the METS-VF index quartiles.

	Numbers, n (%)	Q1 (3.60-6.80)	Q2 (6.80-7.19)	Q3 (7.19-7.49)	Q4 (7.49-8.38)	*p*-value
Total	7,680 (100)	1,920 (25)	1,920 (25)	1,921 (25)	1,919 (25)	
Age (year), median (IQR)	60.0 (49.0, 69.0)	53.0 (45.0, 62.0)	57.0 (48.0, 66.0)	61.0 (52.0, 70.0)	65.0 (57.0, 73.0)	**<0.001**
Sex (%)						**<0.001**
Male	3,835 (49.9)	692 (36.0)	888 (46.3)	937 (48.8)	1,318 (68.7)	
Female	3,845 (50.1)	1,228 (64.0)	1,032 (53.8)	984 (51.2)	601 (31.3)	
Ethnicity n (%)						**<0.001**
Mexican Americans	1,039 (13.5)	150 (7.8)	292 (15.2)	308 (16.0)	289 (15.1)	
Hispanics	784 (10.2)	161 (8.4)	210 (10.9)	212 (11.0)	201 (10.5)	
Whites	3,659 (47.6)	934 (48.6)	832 (43.3)	875 (45.5)	1,018 (53.0)	
Blacks	1,517 (19.8)	381 (19.8)	391 (20.4)	408 (21.2)	337 (17.6)	
Others	681 (8.9)	294 (15.3)	195 (10.2)	118 (6.1)	74 (3.9)	
Education level, n (%)						**<0.001**
Below high school	1,919 (25.0)	367 (19.1)	450 (23.4)	545 (28.4)	557 (29.0)	
High school	1,765 (23.0)	404 (21.0)	452 (23.5)	450 (23.4)	459 (23.9)	
Higher education	3,996 (52.0)	1,149 (59.8)	1,018 (53.0)	926 (48.2)	903 (47.1)	
Marital status, n (%)						**<0.001**
Married	4,467 (58.2)	1,100 (57.3)	1,110 (57.8)	1,101 (57.3)	1,156 (60.2)	
Widowed	827 (10.8)	151 (7.9)	190 (9.9)	240 (12.5)	246 (12.8)	
Divorced	1,141 (14.9)	321 (16.7)	280 (14.6)	281 (14.6)	259 (13.5)	
Separated	264 (3.4)	74 (3.9)	76 (4.0)	69 (3.6)	45 (2.3)	
Never married	621 (8.1)	173 (9.0)	160 (8.3)	148 (7.7)	140 (7.3)	
Living with partner	360 (4.7)	101 (5.3)	104 (5.4)	82 (4.3)	73 (3.8)	
Household income-to-poverty ratio, n (%)						**<0.001**
≤1.30	2,187 (28.5)	491 (25.6)	530 (27.6)	583 (30.3)	583 (30.4)	
1.31-1.85	2,950 (38.4)	670 (34.9)	720 (37.5)	773 (40.2)	787 (41.0)	
>1.85	2,543 (33.1)	759 (39.5)	670 (34.9)	565 (29.4)	549 (28.6)	
Smoking, n (%)						**<0.001**
Yes	3,816 (49.7)	890 (46.4)	885 (46.1)	935 (48.7)	1,106 (57.6)	
No	3,864 (50.3)	1,030 (53.6)	1,035 (53.9)	986 (51.3)	813 (42.4)	
Drinking, n (%)						**<0.001**
Yes	5,132 (66.8)	1,359 (70.8)	1,269 (66.1)	1,227 (63.9)	1,277 (66.5)	
No	2,548 (33.2)	561 (29.2)	651 (33.9)	694 (36.1)	642 (33.5)	
Diabetes, n (%)						**<0.001**
Yes	1,403 (18.3)	100 (5.2)	247 (12.9)	390 (20.3)	666 (34.7)	
No	6,027 (78.5)	1,788 (93.1)	1,621 (84.4)	1,455 (75.7)	1,163 (60.6)	
Borderline	250 (3.3)	32 (1.7)	52 (2.7)	76 (4.0)	90 (4.7)	
Hypertension, n (%)						**<0.001**
Yes	3,717 (48.4)	526 (27.4)	831 (43.3)	1,086 (56.5)	1,274 (66.4)	
No	3,963 (51.6)	1,394 (72.6)	1,089 (56.7)	835 (43.5)	645 (33.6)	
Asthma, n (%)						**<0.001**
Yes	1,054 (13.7)	239 (12.4)	217 (11.3)	298 (15.5)	300 (15.6)	
No	6,626 (86.3)	1,681 (87.6)	1,703 (88.7)	1,623 (84.5)	1,619 (84.4)	
Coronary heart disease, n (%)						**<0.001**
Yes	480 (6.3)	62 (3.2)	73 (3.8)	134 (7.0)	211 (11.0)	
No	7,200 (93.8)	1,858 (96.8)	1,847 (96.2)	1,787 (93.0)	1,708 (89.0)	

Continued

Table I *(Continued)*. Characteristics of participants by the METS-VF index quartiles.

	Numbers, n (%)	Q1 (3.60-6.80)	Q2 (6.80-7.19)	Q3 (7.19-7.49)	Q4 (7.49-8.38)	*p*-value
Cancer, n (%)						**<0.001**
Yes	1,010 (13.2)	201 (10.5)	232 (12.1)	232 (12.1)	345 (18.0)	
No	6,670 (86.8)	1,719 (89.5)	1,688 (87.9)	1,689 (87.9)	1,574 (82.0)	
Physical activity, n (%)						**<0.001**
≥600	4,252 (55.4)	1,229 (64.0)	1,07 (57.7)	1,028 (53.5)	888 (46.3)	
<600	3,428 (44.6)	691 (36.0)	813 (42.3)	893 (46.5)	1,031 (53.7)	
Total water, n (%)						0.220
Lower	3,846 (50.1)	933 (48.6)	946 (49.3)	977 (50.9)	990 (51.6)	
Higher	3,834 (49.9)	987 (51.4)	974 (50.7)	944 (49.1)	929 (48.4)	
Total energy, n (%)						0.176
Lower	3,840 (50.0)	969 (50.5)	967 (50.4)	985 (51.3)	919 (47.9)	
Higher	3,840 (50.0)	951 (49.5)	953 (49.6)	936 (48.7)	1,000 (52.1)	
Total sugar, n (%)						**0.050**
Lower	3,841 (50.0)	930 (48.4)	930 (48.4)	998 (52.0)	983 (51.2)	
Higher	3,839 (50.0)	990 (51.6)	990 (51.6)	923 (48.0)	936 (48.8)	
Total fat, n (%)						**<0.001**
Lower	3,841 (50.0)	1,015 (52.9)	961 (50.1)	1,006 (52.4)	859 (44.8)	
Higher	3,839 (50.0)	905 (47.1)	959 (49.9)	915 (47.6)	1,060 (55.2)	
Serum cholesterol, n (%)						**<0.001**
Lower	3,894 (50.7)	864 (45.0)	860 (44.8)	961 (50.0)	1,209 (63.0)	
Higher	3,786 (49.3)	1,056 (55.0)	1,060 (55.2)	960 (50.0)	710 (37.0)	
Serum uric acid, n (%)						**<0.001**
Lower	3,889 (50.6)	1,376 (71.7)	1,065 (55.5)	877 (45.7)	571 (29.8)	
Higher	3,791 (49.4)	544 (28.3)	855 (44.5)	1,044 (54.3)	1,348 (70.2)	
COPD, n (%)						**<0.001**
Yes	772 (10.1)	148 (7.7)	131 (6.8)	208 (10.8)	285 (14.9)	
No	6,908 (89.9)	1,772 (92.3)	1,789 (93.2)	1,713 (89.2)	1,634 (85.1)	

Data are shown as median (IQR) or n (%). METS-VF index was divided to four groups by quartile Q1≤6.80; 6.80<Q2≤7.19; 7.19<Q3≤7.49; Q4>7.49. METS-VF, metabolism score for visceral fat.

Table II. Association between METS-VF index and COPD prevalence in the database from NHANES 2007-2018.

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
METS-VF	**1.721 (1.483, 1.998)**	**1.653 (1.423, 1.921)**	**1.216 (1.021, 1.448)**
p-value	<0.001	<0.001	0.028
METS-VF (IQR)			
Q1	Reference	Reference	Reference
Q2	0.877 (0.687, 1.119)	0.908 (0.709, 1.162)	0.897 (0.686, 1.174)
p-value	0.291	0.444	0.430
Q3	**1.454 (1.166, 1.813)**	**1.454 (1.161, 1.822)**	1.136 (0.879, 1.468)
p-value	0.001	0.001	0.331
Q4	**2.088 (1.693, 2.575)**	**2.011 (1.621, 2.494)**	**1.396 (1.073, 1.816)**
p-value	<0.001	<0.001	0.013
p for trend	<0.001	<0.001	0.005

Model 1 was an unadjusted model. Model 2 was adjusted for ethnicity, education level, and marital status. Model 3 was adjusted for Model 2 + household income-to-poverty ratio, diabetes, hypertension, asthma, coronary heart disease, cancer, physical activity, drinking, smoking, serum cholesterol, serum uric acid, total water intake, total energy intake, total sugar intake, and total fat intake were adjusted. METS-VF, metabolism score for visceral fat; COPD, chronic obstructive pulmonary disease.

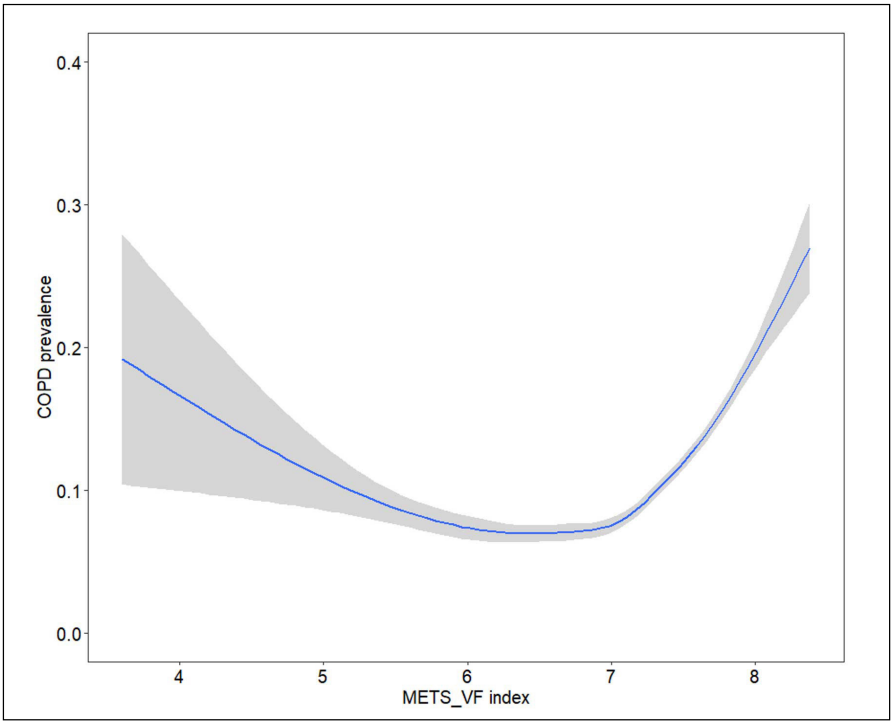

Figure 2. Density dose-response relationship between METS-VF index and COPD prevalence. The area between the upper and lower dashed lines is represented as 95% CI. The association was adjusted for ethnicity, education level and marital status, household income-to-poverty ratio, diabetes, hypertension, asthma, coronary heart disease, cancer, physical activity, drinking, smoking, serum cholesterol, serum uric acid, total water intake, total energy intake, total sugar intake and total fat intake. METS-VF, metabolism score for visceral fat; COPD, chronic obstructive pulmonary disease.

2.563), without asthma (OR=1.530, 95% CI: 1.105, 2.118) or hypertension (OR=1.983, 95% CI: 1.321, 2.975) (all *p*-value <0.05).

In the sensitivity analyses, when using more stringent COPD inclusion criteria, participants who scored highest on METS-VF were at a higher risk of COPD than those who scored lowest (reference) after fully adjusting for all covariates (**Supplementary Table II**). METS-VF was still positively associated with COPD prevalence after excluding smoking participants with asthma (**Supplementary Table III**).

Comparison of Diagnostic Value

We used ROC curve analysis to assess the diagnostic potential of METS-VF, waist circumference, and BMI for COPD and found that the area under curve (AUC) value of METS-VF was the largest, which was statistically significant compared to the AUC of BMI (METS-VF *vs.* BMI, 0.593 *vs.* 0.556, $p<0.001$), but there was no significant difference compared to the AUC of waist circumference (METS-VF *vs.* waist circumference, 0.593 *vs.* 0.588, $p=0.237$, Figure 3). The result indicated a better diagnostic ability of METS-VF for COPD.

Table III. Two-piecewise linear regression and logarithmic likelihood ratio test explained the threshold effect analysis of the METS-VF index with COPD prevalence.

METS-VF index	Adjusted OR (95% CI)	*p*-value
Fitting by the standard linear model	1.22 (1.02-1.45)	0.028
Fitting by the two-piecewise linear model		
Turning point (k)	7.00	
<7.00	0.83 (0.58-1.18)	0.295
≥7.00	2.05 (1.40-3.00)	<0.001
Log likelihood ratio test		<0.001

The model was adjusted for all covariates. METS-VF, metabolism score for visceral fat; COPD, chronic obstructive pulmonary disease.

Table IV. Subgroup analyses for the association between METS-VF and COPD prevalence.

Characteristics	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Stratified by age (year)			
40-59			
Q1	Reference	Reference	Reference
Q2	0.722 (0.512, 1.017)	0.784 (0.553, 1.111)	0.834 (0.568, 1.224)
Q3	**1.338 (0.976, 1.835)**	**1.393 (1.008, 1.924)**	1.067 (0.730, 1.561)
Q4	**1.986 (1.443, 2.733)**	**2.107 (1.515, 2.930)**	**1.628 (1.069, 2.480)**
60-80			
Q1	Reference	Reference	Reference
Q2	0.978 (0.682, 1.404)	1.010 (0.702, 1.455)	0.972 (0.625, 1.376)
Q3	1.371 (0.987, 1.904)	**1.412 (1.012, 1.972)**	1.124 (0.777, 1.628)
Q4	**1.844 (1.352, 2.514)**	**1.835 (1.337, 2.518)**	1.230 (0.850, 1.779)
Stratified by sex			
Male			
Q1	Reference	Reference	Reference
Q2	0.712 (0.457, 1.108)	0.740 (0.472, 1.158)	0.788 (0.486, 1.280)
Q3	1.275 (0.863, 1.884)	1.339 (0.898, 1.996)	1.166 (0.748, 1.819)
Q4	**2.280 (1.611, 3.228)**	**2.209 (1.540, 3.169)**	**1.671 (1.089, 2.563)**
Female			
Q1	Reference	Reference	Reference
Q2	1.034 (0.771, 1.387)	1.075 (0.797, 1.449)	1.021 (0.736, 1.415)
Q3	**1.701 (1.298, 2.228)**	**1.687 (1.278, 2.228)**	1.199 (0.867, 1.658)
Q4	**2.450 (1.839, 3.263)**	**2.296 (1.707, 3.090)**	1.367 (0.948, 1.971)
Stratified by smoking			
Yes			
Q1	Reference	Reference	Reference
Q2	0.837 (0.626, 1.118)	0.905 (0.674, 1.214)	0.932 (0.679, 1.281)
Q3	1.262 (0.968, 1.645)	**1.371 (1.046, 1.797)**	1.130 (0.834, 1.531)
Q4	**1.650 (1.288, 2.113)**	**1.741 (1.350, 2.246)**	1.351 (0.992, 1.838)
No			
Q1	Reference	Reference	Reference
Q2	0.995 (0.618, 1.603)	0.952 (0.588, 1.541)	0.836 (0.501, 1.395)
Q3	**1.940 (1.271, 2.961)**	**1.699 (1.103, 2.617)**	1.158 (0.712, 1.884)
Q4	**2.720 (1.795, 4.123)**	**2.315 (1.513, 3.542)**	1.499 (0.899, 2.499)
Stratified by asthma			
Yes			
Q1	Reference	Reference	Reference
Q2	0.742 (0.488, 1.128)	0.821 (0.532, 1.266)	0.784 (0.492, 1.248)
Q3	1.433 (0.995, 2.063)	1.439 (0.987, 2.099)	1.257 (0.823, 1.921)
Q4	**1.480 (1.029, 2.128)**	**1.479 (1.014, 2.157)**	1.163 (0.737, 1.834)
No			
Q1	Reference	Reference	Reference
Q2	1.013 (0.736, 1.394)	1.031 (0.746, 1.424)	0.947 (0.679, 1.321)
Q3	1.306 (0.962, 1.774)	1.278 (0.936, 1.746)	1.048 (0.753, 1.459)
Q4	**2.427 (1.840, 3.202)**	**2.260 (1.700, 3.004)**	**1.530 (1.105, 2.118)**

Continued

Table IV *(Continued)*. Subgroup analyses for the association between METS-VF and COPD prevalence.

Characteristics	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Stratified by diabetes			
Yes			
Q1	Reference	Reference	Reference
Q2	0.654 (0.276, 1.547)	0.751 (0.313, 1.802)	0.781 (0.295, 2.068)
Q3	1.556 (0.739, 3.275)	1.636 (0.765, 3.497)	1.295 (0.550, 3.048)
Q4	**2.429 (1.193, 4.947)**	**2.454 (1.184, 5.085)**	1.948 (0.849, 4.471)
No			
Q1	Reference	Reference	Reference
Q2	0.918 (0.708, 1.189)	0.938 (0.720, 1.220)	0.958 (0.718, 1.278)
Q3	**1.397 (1.095, 1.783)**	**1.359 (1.059, 1.744)**	1.185 (0.893, 1.573)
Q4	**1.703 (1.329, 2.183)**	**1.577 (1.221, 2.037)**	1.310 (0.969, 1.771)
Stratified by hypertension			
Yes			
Q1	Reference	Reference	Reference
Q2	**0.673 (0.479, 0.947)**	0.715 (0.506, 1.011)	0.801 (0.547, 1.173)
Q3	0.925 (0.680, 1.258)	0.956 (0.699, 1.307)	0.902 (0.633, 1.287)
Q4	1.250 (0.935, 1.673)	1.254 (0.931, 1.689)	1.042 (0.731, 1.487)
No			
Q1	Reference	Reference	Reference
Q2	0.858 (0.598, 1.231)	0.869 (0.602, 1.254)	0.916 (0.619, 1.354)
Q3	**1.589 (1.138, 2.221)**	**1.603 (1.137, 2.260)**	1.409 (0.957, 2.074)
Q4	**2.319 (1.666, 3.228)**	**2.199 (1.560, 3.098)**	**1.983 (1.321, 2.975)**

Model 1 was an unadjusted model. Model 2 was adjusted for ethnicity, education level and marital status. Model 3 was adjusted for all covariates except the stratification variable itself. METS-VF, metabolism score for visceral fat; COPD, chronic obstructive pulmonary disease.

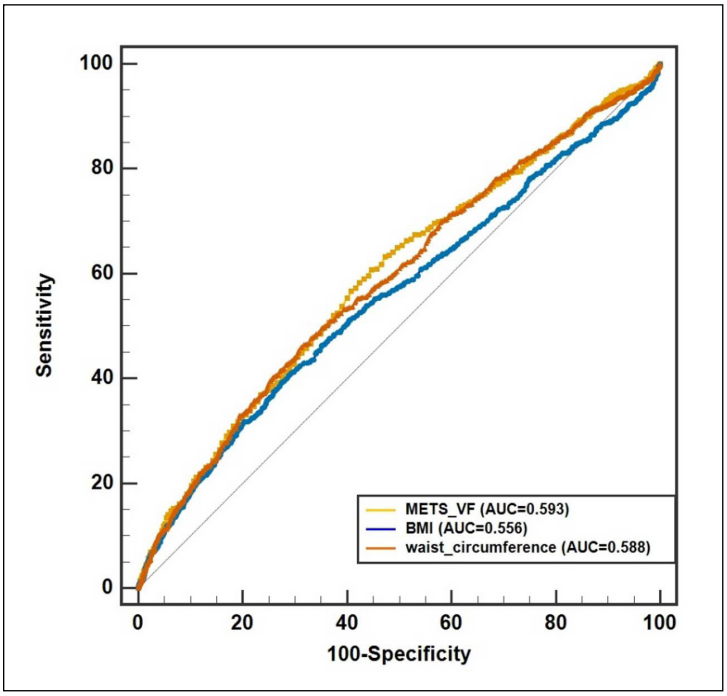

Figure 3. Comparison of receiver operating characteristic (ROC) curve analysis for predicting COPD prevalence between METS-VF, BMI, and Waist circumference. METS-VF, metabolism score for visceral fat; COPD, chronic obstructive pulmonary disease; BMI, body mass index.

Discussion

It is the first study to explore how the METS-VF index correlates with COPD prevalence, using a typical cohort of middle-aged and elderly US adults. The METS-VF index had a nonlinear and positive correlation with COPD prevalence. When the METS-VF index exceeded 7.00, the positive associations were stable. When the METS-VF index was below 7.00, the METS-VF index was negatively correlated with COPD prevalence, but this trend was not statistically significant, and METS-VF showed a significantly better diagnostic ability of COPD than BMI.

Malnutrition has been supposed to be a risk factor for many respiratory diseases, including COPD, for a long time. Otherwise, with the process of industrialization, changes in lifestyle, and the improvement of nutrition levels, increasing studies have shown that obesity is a global issue that affects a variety of respiratory diseases, including asthma, obstructive sleep apnea, pulmonary embolism, and pneumonia[17]. Previous studies found that obesity had a harmful effect on COPD-related outcomes, including poor living quality, dyspnea, declined exercise capacity, and increased risk of acute exacerbation[6,18]. Obesity might have different effects on COPD mortality based on disease severity. In patients with mild-to-moderate COPD, obese patients had an increased risk of all-cause mortality than those with normal-weight. However, obesity exerted a protective effect on mortality in patients with severe COPD compared to those with normal weight[19]. The respiratory pump consists of the respiratory center, chest wall, and diaphragm, intercostal, accessory, and abdominal muscles[20]. An obese population usually has reduced lung compliance and increased work of breathing. Fat tissue around the chest and abdomen and in the visceral cavity could limit the chest wall movement and decrease functional residual capacity (FRC). A low FRC increases the risk of abnormal ventilation distribution and airway closure, resulting in abnormal gas exchange related to ventilation-perfusion mismatch[21]. The major effect of obesity is on lung volumes, with no direct effect on airway obstruction and diffusion function.

Studies showed that COPD patients had excess visceral fat, and their adiposity increased with dyspnea severity[22]. This might be ascribed to physical inactivity due to dyspnea and impaired skeletal muscle mass in COPD patients[23,24]. Visceral fat could be involved in the pathophysiology of COPD in a variety of ways. Visceral fat could squeeze the organs, limit lung expansion, and decrease lung compliance when breathing, which might worsen airway obstruction[25]. Fat accumulation could produce various pro-inflammatory factors, including leptin, tumor necrosis factor-α (TNF-α), adiponectin, and interleukin-6 (IL-6), which elevated local and systemic inflammation levels, therefore leading to the progression of COPD[26,27]. Leptin is encoded by the obese gene, whose levels are increased with obesity[28]. Leptin also exerts pro-inflammatory effects[29]. Elevated leptin levels might induce a robust pro-inflammatory response[30]. Conversely, adiponectin exerts anti-inflammatory effects[31,32], but its expression is significantly decreased with obesity and insulin resistance[33]. Fatty tissue-related inflammation in COPD patients was found to be correlated with insulin resistance[34], as increased concentrations of IL-6 and TNF-α impaired insulin's biological effects[35,36]. Metabolic syndrome was found to be positively correlated with impaired pulmonary function, mainly due to abdominal obesity[37]. This might be caused by the mechanical and metabolic effects of fatty tissue. Abdominal fat might impede diaphragmatic position and flattening during breath, and thoracic fat might affect chest wall movement, both reducing lung volumes by limiting lung expansion when breathing[17]. Adipose tissue exerted pro-inflammatory effects by releasing pro-inflammatory factors (as described above). Our study found METS-VF showed a significantly better diagnostic ability for COPD than BMI but was comparable to waist circumference. This might be because BMI could not reflect fat distribution, whereas waist circumference is an indicator of abdominal obesity, simultaneously reflecting subcutaneous fat and visceral fat[25].

The METS-VF index had a negative correlation with COPD prevalence when the METS-VF index was below 7.00, although this trend had no statistical significance. A meta-analysis[38] integrated 22 studies reported that underweight participants had a higher mortality rate than normal-weight ones, while overweight patients had a lower death rate, indicating a protective role of adipose tissue to a certain extent. In current studies, there are several explanations for the phenomenon, including the fact that healthy obese patients with higher muscle mass have a higher chance of recovering than non-obese patients[39], brown adipose tissue reduces pro-in-

flammatory cytokines and systemic inflammation in overweight individuals[40], and overweight individuals are more likely to tolerate weight loss and fatigue[41]. Additionally, low body fat might be associated with malnutrition in COPD patients, which leads to weak respiratory muscle, compromised immunity, and impaired gas exchange[19]. Nutritional status differed among subjects enrolled in our study, although we adjusted for dietary intake as a covariate. However, as METS-VF is a novel index and has no reference range, we cannot determine which weight or nutritional status individuals with METS-VF <7.00 belong to.

In subgroup analyses, a positive correlation was more likely to be seen in men than women, possibly because body fat distribution differed. Men and postmenopausal women lacking estrogen commonly store abdominal and visceral fat, whereas premenopausal women accumulate more fat in their hips and thighs[42]. Obese men tend to have decreasing levels of testosterone with increasing body weight. Low testosterone levels in men are associated with excess visceral fat, abdominal obesity, and metabolic syndrome[43]. In addition, adults younger than 60 years tended to show a positive association. Studies suggest that body weight increases with age during early and middle adulthood before weight loss at the elderly stage[44]. Several longitudinal studies observed that White men and women aged 40-66 gained 0.30 and 0.55 kg per year, respectively[45]; and then, body weight loss was observed in the elderly White population after 60 years old[46-48]. Moreover, age-related sarcopenia is more evident after 70 years old[49], which might affect the function of respiratory muscles and physical activity. Inadequate nutrition might be another reason, as well as reduced appetite, malabsorption, and social factors in older adults. We speculate that several factors might be involved in the development of COPD in adults over 60 years old, and visceral adipose tissue may not be the main cause.

Strengths and Limitations

This is the first study to explore the relationship between the METS-VF index and COPD prevalence by using a large and typical cohort of American adults. All data was collected through standardized interviews, health screenings, laboratory testing, and health-related questionnaires, ensuring data accuracy and minimizing potential measurement bias. However, our study also has a few drawbacks. Firstly, there is no causal relationship to be established because the study is cross-sectional. Secondly, in spite of adjusting for potential confounding, residual unknown confounding cannot be excluded. Thirdly, the definitions of COPD and other diseases were confirmed by a self-reported physician diagnosis during interviews, which might cause some errors. Lastly, the participants included in this study were middle-aged and older US individuals, which limited the generalization of our results to some extent. The results do not apply to other countries; as we know, malnutrition in the COPD population is more common in developing countries. We need to explore the relationship between visceral adipose tissue and COPD in developing countries with malnourished COPD patients.

Obesity has become a serious health and social problem in the United States, and the relationship between obesity and COPD, as shown in this study, is unquestionable. Although the obesity rate in China and many other developing countries is lower than that in the United States, with the rapid economic growth, the obese population has increased rapidly in recent decades. Consequently, greater attention must be given to the potential adverse effects of obesity on COPD. Early intervention should be implemented to modify the disease and reduce the prevalence of COPD.

Conclusions

To conclude, our study demonstrates that the METS-VF index has a nonlinear and positive correlation with COPD prevalence among the middle-aged and elderly American population. The causality of the association needs to be clarified by future prospective researches.

Authors' Contribution

Tingxuan Huang analyzed the data. Tingxuan Huang and Liangliang Zhang wrote the manuscript. Jianwei Wang provided suggestions for manuscript modification. Chuntao Liu designed the study and revised the manuscript. All authors read and approved the final version of the manuscript.

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Ethics Approval
The ethical approval to conduct the NHANES 2007-2018 was granted by the National Center for Health Statistics Research Ethics Review Board. The ethics approval is public, accessed on website: https://www.cdc.gov/nchs/nhanes/irba98.htm#.

Informed Consent
All study data are from a public database. Informed consent was not applicable. The participants' information was non-identifiable.

Data Availability
The data that support the findings of this study are available in public database (https://www.cdc.gov/nchs/nhanes/index.htm).

Conflict of Interest
The authors declare no competing interests.

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AI Disclosure
The authors did not use artificial intelligence or assisted technologies in the production of the study (including figures).

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