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ORIGINAL RESEARCH

Association of Weight-Adjusted Waist Index with All-Cause and Cardiovascular Mortality in Patients with Chronic Obstructive Pulmonary Disease: A Retrospective Cohort Study

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Purpose: This study aims to evaluate potential associations between the weight-adjusted waist index (WWI) and all-cause and cardiovascular mortality in patients with chronic obstructive pulmonary disease (COPD).

Methods: Our investigation analyzed data from the National Health and Nutrition Examination Survey (NHANES, 1999–2018). From an initial cohort of 101,316 participants, we incorporated 1,396 qualified individuals with COPD. To investigate the relationship between WWI and mortality, we employed multiple analytical methods, including multivariate Cox proportional hazards regression, Kaplan-Meier survival analysis, subgroup stratification and restricted cubic spline (RCS) modeling. Additionally, the prognostic utility of WWI in predicting mortality risk was further assessed through time-dependent receiver operating characteristic (ROC) curve analysis.

Results: In fully adjusted models, the highest WWI tertile (T3) revealed higher risks for both all-cause mortality (HR: 1.82, 95% CI: 1.19–2.77, p=0.006) and CVD mortality (HR: 2.79, 95% CI: 1.48–5.26, p=0.002) compared to the lowest tertile (T1). RCS analyses revealed a strong and statistically significant linear association between WWI and mortality risk. These findings suggest that WWI may be a meaningful predictor of adverse outcomes in COPD.

Conclusion: Our study demonstrates that higher WWI significantly predicts increased mortality risk in COPD patients, highlighting its prognostic value and suggesting potential utility for risk stratification in clinical practice.

Keywords: chronic obstructive pulmonary disease, weight-adjusted waist index, mortality, NHANES

Introduction

Clinical Burden and Metabolic Complexity of COPD

Chronic obstructive pulmonary disease (COPD) is a common disease characterized by persistent airflow limitation and associated with chronic respiratory symptoms such as dyspnea, persistent cough, and sputum production.[1] Globally, it poses a substantial and growing threat to population health and imposes substantial healthcare economic burdens.[2] Patients with COPD often have varying degrees of coexisting conditions, including cardiovascular diseases (CVD) such as hypertension and atherosclerosis, metabolic syndrome, and concurrent asthma-COPD overlap,[3] further leading to increased hospitalization rates and decreased survival. Despite advances in management, the long-term prognosis for patients with COPD remains poor, and further exploration is needed to identify the factors associated with long-term mortality in this patient population.

The link between chronic respiratory diseases and impaired nutritional status is well-established. In COPD, while muscle wasting and weight loss have long been recognized as major concerns, the rising prevalence of obesity has

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introduced new complexities in nutritional management.[4] This metabolic disorder is related to cardiometabolic conditions including hypertension, diabetes, stroke, and dyslipidemia.[5,6] And obesity may increase susceptibility to respiratory diseases including COPD, asthma, and sleep apnea.[7] Growing evidence suggests that central obesity may be a more potent risk factor for cardiovascular morbidity and mortality across diverse populations.[8,9] This connection matters especially for COPD patients, since cardiovascular complications cause about 25% of their deaths.[10]

The Weight-Adjusted Waist Index as a Novel Prognostic Indicator

The adverse health effects of obesity are largely attributable to visceral adipose tissue, which exacerbates systemic inflammation and insulin resistance.[11–13] Higher visceral fat levels have been negatively correlated with pulmonary function parameters, including FEV_1 and FVC.[14] These findings indicate that body composition assessment is essential for risk classification and treatment guidance in COPD management. Although magnetic resonance imaging (MRI) remains the gold standard for visceral adiposity assessment. However, its clinical utility is limited by high costs and the need for specialized interpretation.[15]

To address these limitations, the weight-adjusted waist index (WWI) has been proposed as a novel anthropometric tool. Calculated as waist circumference divided by the square root of body weight, WWI provides a more accurate estimate of visceral adiposity compared to conventional indices.[16–18] While previous studies have explored WWI primarily in metabolic and cardiovascular contexts, its prognostic utility in COPD remains insufficiently investigated.

Therefore, the primary objective of our study was to investigate the association between WWI and both all-cause and cardiovascular mortality in COPD patients, and to evaluate its prognostic value for risk stratification.

Methods

Study Population and Design

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative, cross-sectional surveillance program conducted by the Centers for Disease Control and Prevention (CDC) that assesses the health status of the non-institutionalized US population.[19,20] Data are collected through interviews, medical examinations, and laboratory tests, following STROBE guidelines for observational studies. The NHANES study protocol received formal approval from the National Center for Health Statistics (NCHS) Institutional Review Board, with written informed consent obtained from all participants prior to data collection. In this study, the datasets analyzed were publicly accessible at https://www.cdc.gov/nchs/nhanes/.

This study analyzed cross-sectional NHANES data (1999–2018), including 101,316 participants initially. Exclusions comprised individuals aged <20 and pregnant women (n=47,451), those without COPD (n=49,719), and participants missing WWI, death data, or other covariates (n=2,750), resulting in 1,396 eligible participants for analysis. Figure 1 illustrates the process of selecting patient samples.

Definitions of COPD and WWI

COPD status was primarily determined through NHANES survey questions. To identify physician-diagnosed COPD, we included participants who answered "yes" to any of the following questions: "Has a doctor or healthcare professional ever told you that you have COPD, emphysema, or chronic bronchitis?"[21,22]

The weight-adjusted waist index (WWI) represents an emerging metric to assess visceral adiposity. Its calculation formula is expressed as waist circumference (cm) /√weight (kg). Specifically, we used the NHANES body measurement variables BMXWAIST (waist circumference, cm) and BMXWT (weight, kg) for this calculation. All measurements were performed by trained health technicians following standardized NHANES protocols. The square root transformation of weight reduces the influence of overall body size, making the index a more specific marker of central adiposity rather than general largeness. A growing body of literature has indicated that the weight-adjusted waist index (WWI) demonstrates significant advantages in predicting cardiometabolic risk and mortality across diverse populations.[16–18]

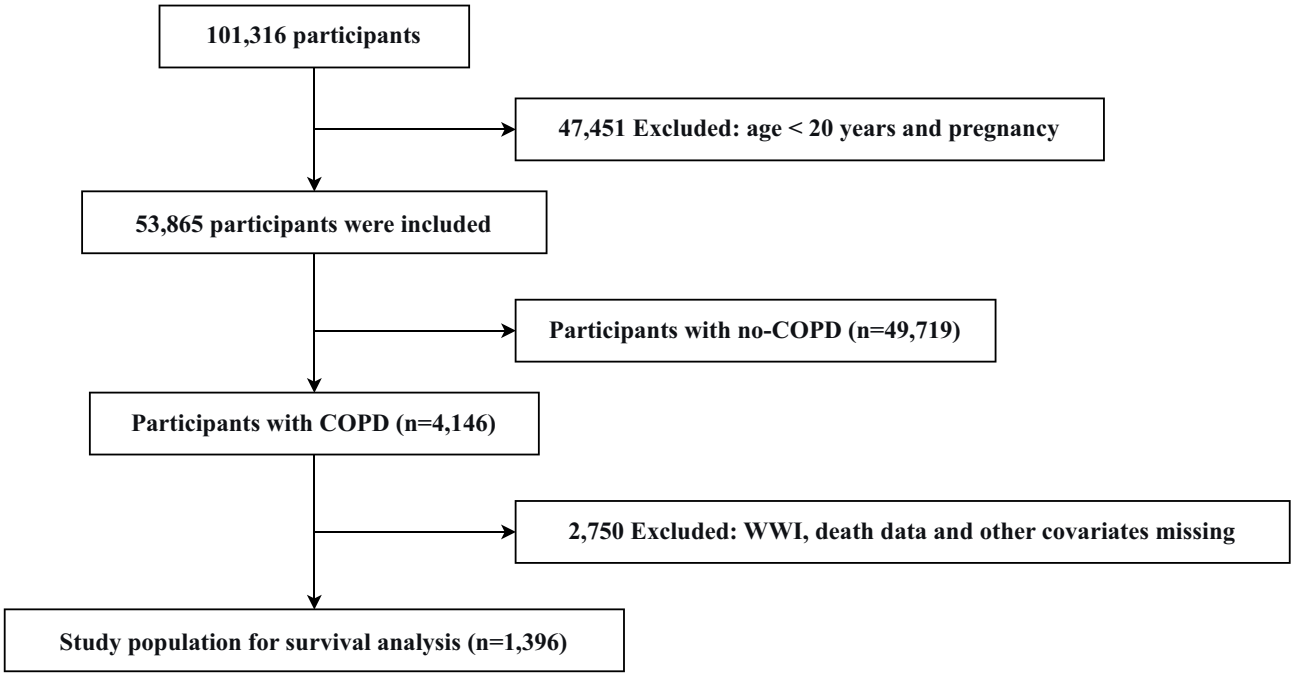

Figure 1 Flowchart of participants selection.
Abbreviations: COPD, chronic obstructive pulmonary disease; WWI, weight-adjusted waist index.

Determination of Outcomes

Mortality information came from the National Death Index (NDI) linkage to NHANES participants, as provided in the Public-Use Linked Mortality File. This linkage employs a probabilistic matching algorithm that combines Social Security Number, name, birthdate, and other identifiers to assign death records with high accuracy. In outcome definition, all-cause mortality refers to deaths from any cause. And cardiovascular mortality specifically includes deaths attributed to rheumatic heart diseases, hypertensive heart and renal diseases, ischemic heart disease, heart failure, and cerebrovascular events, as defined by ICD-10 codes I00–I09, I11, I13, I20–I51, and I60–I69.[23]

Covariates

Most data were collected via standardized household interviews using validated questionnaires in the NHANES protocol, including age, gender, race, marital status, education level, poverty income ratio (PIR), total energy intake, drinking and smoking status. Specifically, race was categorized into Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race. Marital status was divided into three groups: married/living with partners, separated/divorced/widowed, and never married. Educational level was classified into three categories with high school as the demarcation point. The poverty-income ratio (PIR) was calculated by dividing household income by federal poverty thresholds, with participants stratified into low (<1.3), middle (1.3–3.5), and high (>3.5) socioeconomic groups. Regarding drinking habits, they were classified as heavy drinking, mild to moderate drinking, and never drinking. Smoking history was categorized as current, former, or never-smokers. Body mass index, derived from weight and height measurements, was classified as underweight (18.5 kg/m^2), normal (≥18.5 and <24.9), or overweight (≥24.9). The comorbidities included in this study were hypertension, diabetes mellitus, CVD, and cancer. These conditions were identified based on laboratory measurements and self-reported physician-diagnosed status.[24,25] And we also included biochemical indicators such as uric acid, creatinine, fasting plasma glucose, HbA1c, total and HDL cholesterol.

Statistical Analyses

Given that NHANES employs a complex, multistage, probability sampling design, we incorporated the recommended sample weights, accounting for clustering via the primary sampling unit variable (SDMVPSU) and stratification via the

stratum variable (SDMVSTRA) in all analyses to produce nationally representative estimates. All weighted analyses were conducted using the survey package in R. This approach ensured the generalizability of our findings to the non-institutionalized US population while providing accurate standard errors that account for the complex survey design. Normally distributed continuous variables were reported as weighted mean ± SD, while categorical variables were expressed as unweighted counts and weighted percentages. Between-group comparisons were performed using weighted *t*-tests or Mann–Whitney *U*-tests for continuous variables, and chi-square tests for categorical variables. The statistical significance was defined as a two-sided p level less than 0.05.

We constructed three progressively adjusted multivariate Cox proportional hazards models to examine the association between WWI and mortality risk in COPD populations. Variables clinically relevant to the prognosis were incorporated into the analysis. Our primary model (Model 1) was specified without any covariate adjustments, serving as a baseline for comparison with subsequent adjusted models. Model 2 was adjusted for age group, gender, race, education level, marital status, BMI and PIR group. Model 3 was additionally adjusted for smoking status (current, former, never), drinking status (heavy, mild to moderate, never), uric acid, creatinine, total energy intake, diabetes, hypertension, cardiovascular disease and cancer. We used Kaplan-Meier (K-M) survival analysis curves to investigate variations in survival rates among distinct WWI groups. And restricted cubic splines (RCS) were applied in this study to explore whether nonlinear relationships existed.[26] Additionally, we further assessed the predictive capability of WWI for mortality risk by employing time-dependent receiver operating characteristic (ROC) curve analysis. Subgroup analyses were carried out to investigate the potential impact of confounding factors on the observed association, with stratification by nine key variables: age, gender, PIR, marital status, BMI, smoking, drinking, diabetes and hypertension. All statistical analyses in our study were performed using R software (version 4.4.2).

Results

Baseline Characteristics of Patients with COPD

The study population comprised 1,396 individuals and their baseline characteristics are detailed in Table 1. Study participants were categorized by survival status into two groups: alive (n = 1025) and deceased (n = 371). Deceased individuals exhibited significantly higher mean WWI (11.56 ± 0.79) compared to survivors (11.24 ± 0.81), with a clear

Table 1 Baseline Characteristics of Patients with COPD

Characteristic	Overall N = 1,396	Alive N = 1,025	Deceased N = 371	p-value
WWI	11.31 ± (0.82)	11.24 ± (0.81)	11.56 ± (0.79)	<0.001
WWI groups				<0.001
T1 (9.09, 11.03)	465 (37.72%)	382 (41.39%)	83 (24.96%)	
T2 (11.03, 11.78)	465 (32.12%)	349 (31.95%)	116 (32.71%)	
T3 (11.78, 13.85)	466 (30.16%)	294 (26.66%)	172 (42.33%)	
Age				<0.001
20 ≤ Age ≤ 39	242 (20.44%)	228 (24.30%)	14 (6.96%)	
40 ≤ Age ≤ 59	471 (39.38%)	406 (44.76%)	65 (20.61%)	
Age ≥ 60	683 (40.19%)	391 (30.93%)	292 (72.43%)	
Gender				<0.001
Male	593 (38.68%)	380 (35.34%)	213 (50.33%)	
Female	803 (61.32%)	645 (64.66%)	158 (49.67%)	
Race				0.045
Mexican American	119 (3.03%)	93 (3.39%)	26 (1.76%)	
Other Hispanic	95 (4.01%)	82 (4.43%)	13 (2.55%)	
Non-Hispanic White	894 (80.70%)	617 (78.81%)	277 (87.31%)	
Non-Hispanic Black	223 (7.77%)	178 (8.32%)	45 (5.85%)	
Other Race	65 (4.49%)	55 (5.05%)	10 (2.53%)	

(*Continued*)

Table 1 (Continued).

Characteristic	Overall N = 1,396	Alive N = 1,025	Deceased N = 371	p-value
Marital status				<0.001
Married/Living with partners	758 (59.51%)	568 (61.09%)	190 (54.02%)	
Separated/Divorced/Widowed	479 (29.65%)	316 (26.31%)	163 (41.28%)	
Never married	159 (10.84%)	141 (12.60%)	18 (4.71%)	
Education level				0.001
< High school	413 (22.90%)	269 (20.17%)	144 (32.41%)	
High school	364 (29.36%)	272 (30.11%)	92 (26.73%)	
> High school	619 (47.74%)	484 (49.72%)	135 (40.86%)	
PIR				0.002
<1.3	530 (29.07%)	374 (26.73%)	156 (37.23%)	
≥1.3, ≤3.5	584 (43.10%)	431 (43.24%)	153 (42.61%)	
>3.5	282 (27.83%)	220 (30.03%)	62 (20.16%)	
BMI, kg/m^2				0.010
<18.5	42 (3.51%)	24 (2.99%)	18 (5.31%)	
≥18.5, <24.9	294 (21.44%)	191 (19.81%)	103 (27.15%)	
≥24.9	1,060 (75.05%)	810 (77.20%)	250 (67.54%)	
Drinking				0.8
Heavy drinking	132 (9.79%)	97 (9.66%)	35 (10.23%)	
Mild to moderate drinking	878 (65.38%)	648 (65.85%)	230 (63.72%)	
Never drinking	386 (24.84%)	280 (24.49%)	106 (26.04%)	
Smoking				<0.001
Current smoker	499 (38.11%)	369 (38.41%)	130 (37.06%)	
Former smoker	494 (33.56%)	322 (30.80%)	172 (43.17%)	
Never smoker	403 (28.33%)	334 (30.79%)	69 (19.77%)	
Hypertension				<0.001
Yes	757 (48.32%)	515 (44.86%)	242 (60.38%)	
No	639 (51.68%)	510 (55.14%)	129 (39.62%)	
Diabetes				0.006
Yes	279 (15.37%)	189 (13.78%)	90 (20.91%)	
No	1,117 (84.63%)	836 (86.22%)	281 (79.09%)	
CVD				<0.001
Yes	400 (24.03%)	236 (19.27%)	164 (40.63%)	
No	996 (75.97%)	789 (80.73%)	207 (59.37%)	
Ever told you had cancer				<0.001
Yes	233 (17.21%)	142 (14.64%)	91 (26.16%)	
No	1,163 (82.79%)	883 (85.36%)	280 (73.84%)	
Uric acid, mg/dL	5.52 ± (1.49)	5.47 ± (1.43)	5.69 ± (1.68)	0.2
Creatinine, mg/dL	0.87 ± (0.28)	0.85 ± (0.23)	0.97 ± (0.41)	<0.001
Total energy intake, (kcal)	2,094.64 ± (994.28)	2,158.17 ± (1,012.37)	1,873.28 ± (895.28)	<0.001
Plasma fasting glucose, mg/dL	111.08 ± (38.19)	109.17 ± (33.35)	117.75 ± (51.13)	0.009
TG, mg/dL	151.80 ± (143.66)	152.26 ± (153.18)	150.24 ± (104.05)	0.6
HDL-C, mg/dL	53.16 ± (18.17)	52.43 ± (15.59)	55.72 ± (25.06)	0.3
HbA1c, %	5.79 ± (1.03)	5.74 ± (0.97)	5.98 ± (1.21)	<0.001

Notes: Data are presented as the weighted mean±SD for skewed variables or as unweighted numbers and weighted frequencies for categorical variables.

Abbreviations: WWI, weight-adjusted waist index; PIR, poverty income ratio; BMI, body mass index; CVD, cardiovascular diseases; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol.

trend of increased mortality across higher WWI groups ($p < 0.001$). Adults ≥ 60 years and males had higher mortality than younger groups and females. Notably, comorbidities including hypertension, diabetes, cardiovascular disease, and cancer history showed significantly higher prevalence among deceased participants compared to survivors. And deceased

patients had higher levels of creatinine (0.97 ± 0.41 mg/dL), fasting glucose (117.75 ± 51.13 mg/dL), and HbA1c (5.98 ± 1.21%), along with lower total energy intake (1,873.28 ± 895.28 kcal, p < 0.001).

Association Between WWI and Mortality

This study constructed three progressively adjusted multivariate Cox proportional hazards models to examine the association between WWI and all-cause and cardiovascular mortality in COPD populations (Table 2). All participants were categorized by WWI tertile distribution (T1: 9.09–11.03; T2: 11.03–11.78; T3: 11.78–13.85). Finally, we found that the highest WWI tertile (T3) revealed higher risks for both all-cause mortality (HR: 1.82, 95% CI: 1.19–2.77, p=0.006) and CVD mortality (HR: 2.79, 95% CI: 1.48–5.26, p=0.002) compared to the lowest tertile (T1) in the fully adjusted model. Trend tests across tertiles confirmed a significant dose-response relationship for both outcomes (p-trend < 0.01).

The Kaplan-Meier survival curves further validated these findings (Figure 2). It showed significantly higher risks of both all-cause and cardiovascular mortality in higher WWI groups (both p < 0.0001), and the survival disparity gradually widened over time. To assess the predictive performance of WWI, we plotted the ROC curve (Figure 3). For all-cause mortality, the area under the curve (AUC) were 0.810 (95% CI: 0.778–0.841) at 5 years, 0.848 (95% CI: 0.821–0.875) at 10 years, and reaching 0.904 (95% CI: 0.878–0.929) at 15 years. Similar strong discrimination was observed for cardiovascular mortality, with AUCs of 0.832 (95% CI: 0.783–0.882), 0.873 (95% CI: 0.841–0.906), and 0.929 (95% CI: 0.898–0.960) at 5, 10, and 15 years respectively.

Furthermore, restricted cubic spline (RCS) regression analysis (Figure 4) confirmed a linear relationship between WWI and mortality risks after full covariate adjustment (nonlinear p = 0.937 and 0.424 for all-cause and cardiovascular mortality, respectively).

Table 2 Multivariate Cox Regression Analysis of the Association Between WWI and Mortality of COPD

	Events (incidence)	Model 1		Model 2		Model 3	
		HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
All-cause mortality							
WWI							
per 1 unit increment	371	1.86 (1.58, 2.19)	<0.0001	1.36 (1.10, 1.69)	0.005	1.36 (1.07, 1.72)	0.01
WWI groups							
Q1 (9.09, 11.03)	83	Reference		Reference		Reference	
Q2 (11.03, 11.78)	116	1.86 (1.27, 2.74)	0.0016	1.36 (0.89, 2.09)	0.16	1.29 (0.84, 1.98)	0.23
Q3 (11.78, 13.85)	172	3.39 (2.41, 4.78)	<0.0001	1.89 (1.27, 2.82)	0.002	1.82 (1.19, 2.77)	0.006
p_{trend}		<0.0001		0.001		0.004	
CVD mortality							
WWI							
per 1 unit increment	109	2.48 (1.88, 3.28)	<0.0001	1.62 (1.15, 2.30)	0.006	1.69 (1.19, 2.40)	0.003
WWI groups							
Q1 (9.09, 11.03)	16	Reference		Reference		Reference	
Q2 (11.03, 11.78)	38	2.70 (1.32, 5.52)	0.006	1.54 (0.77, 3.11)	0.23	1.71 (0.85, 3.44)	0.13
Q3 (11.78, 13.85)	55	6.29 (3.38, 11.71)	<0.0001	2.60 (1.39, 4.85)	0.003	2.79 (1.48, 5.26)	0.002
p_{trend}		<0.0001		0.0005		0.0003	

Notes: Model 1 adjusted for none. Model 2 adjusted for age group (20 ≤ Age ≤ 39, 40 ≤ Age ≤ 59, Age ≥ 60); gender, race, education level and marital status; BMI group (BMI < 18.5, 18.5 ≤ BMI < 24.9, BMI ≥ 24.9); PIR group (PIR < 1.3, 1.3 ≤ PIR ≤ 3.5, PIR > 3.5). Model 3 further adjusted for smoking group (current smoker, former smoker, never smoker), drinking group (heavy drinking, mild to moderate drinking, never drinking), creatinine (mg/dl), uric acid (mg/dl), total energy intake (kcal), diabetes, hypertension, cardiovascular disease and cancer.

Abbreviations: WWI, weight-adjusted waist index; PIR, poverty income ratio; BMI, body mass index.

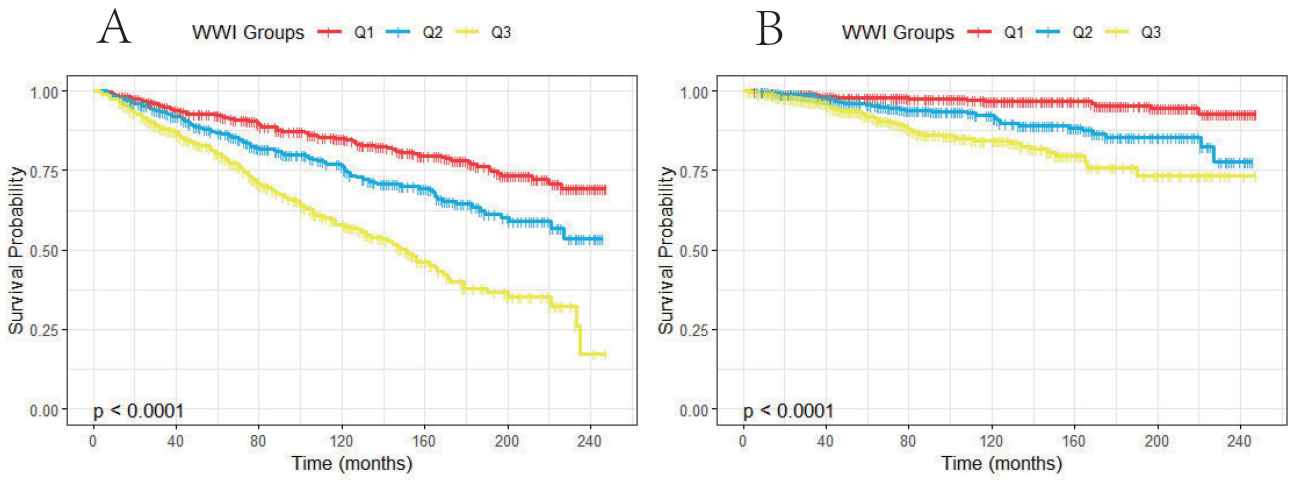

Figure 2 Kaplan-Meier survival curve of WWI with all-cause mortality (**A**), CVD mortality (**B**).
Abbreviations: WWI, weight-adjusted waist index; CVD, cardiovascular diseases.

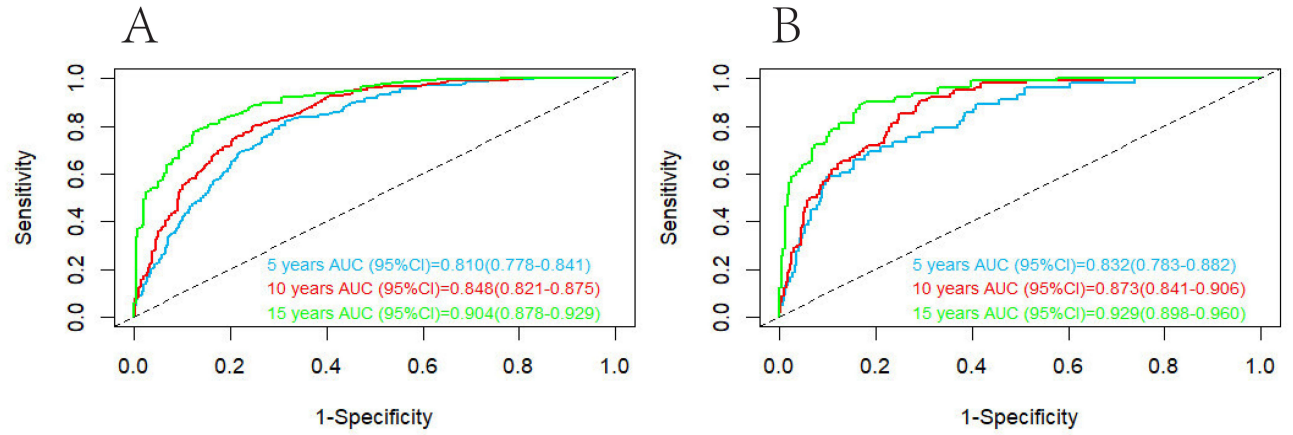

Figure 3 The ROC curve of WWI for predicting all-cause mortality (**A**), CVD mortality (**B**).
Abbreviations: AUC, area under the curve; ROC, receiver operating characteristic; WWI, weight-adjusted waist index; CVD, cardiovascular diseases.

Subgroup Analysis and Interaction Analysis

Subgroup analyses were carried out to investigate the potential impact of confounding factors on the observed association, with stratification by nine key variables (Figure 5). For all-cause mortality risk, no significant interaction effects were observed across all included patient subgroups (all $p > 0.05$). When evaluating cardiovascular mortality risk, we detected no statistically significant interactions for age, sex, poverty-income ratio (PIR), matrimonial status, smoking status, drinking status, diabetes and hypertension (all p-for-interaction > 0.05). However, we found a statistically significant interaction with body mass index (BMI, p-for-interaction=0.004). In COPD patients with BMI ≥24.9, the risk of cardiovascular death was elevated by approximately 1.5- to 4.4-fold for each one-unit increase in WWI (HR: 2.52, 95% CI: 1.45–4.37). In contrast, WWI was not significantly associated with risk in patients with a BMI <24.9 (HR: 0.58, 95% CI: 0.29–1.14).

Discussion

This nationwide retrospective cohort study examines the association between the weight-adjusted waist index (WWI) and all-cause and cardiovascular mortality among 1,396 clinically diagnosed COPD patients. After a series of analyses, we identified the significantly linear positive correlations between them. Our findings underscore the potential value of WWI as an important biomarker for prognostic assessment in COPD patients, providing new theoretical foundations for clinical intervention and risk management.

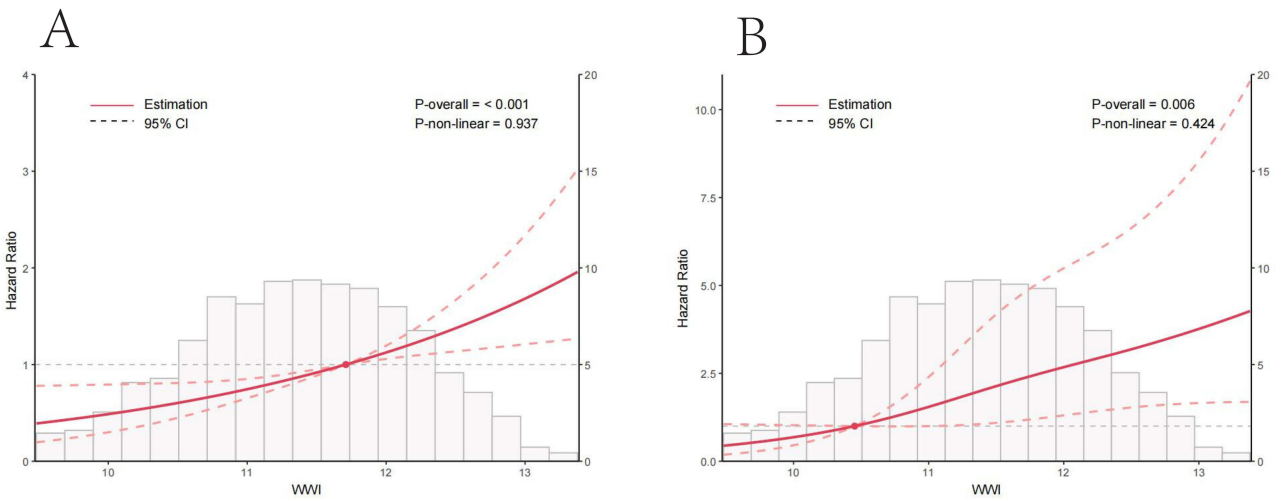

Figure 4 Restricted cubic spline (RCS) analysis of WWI with all-cause mortality (**A**), CVD mortality (**B**).
Abbreviations: WWI, weight-adjusted waist index; CVD, cardiovascular diseases.

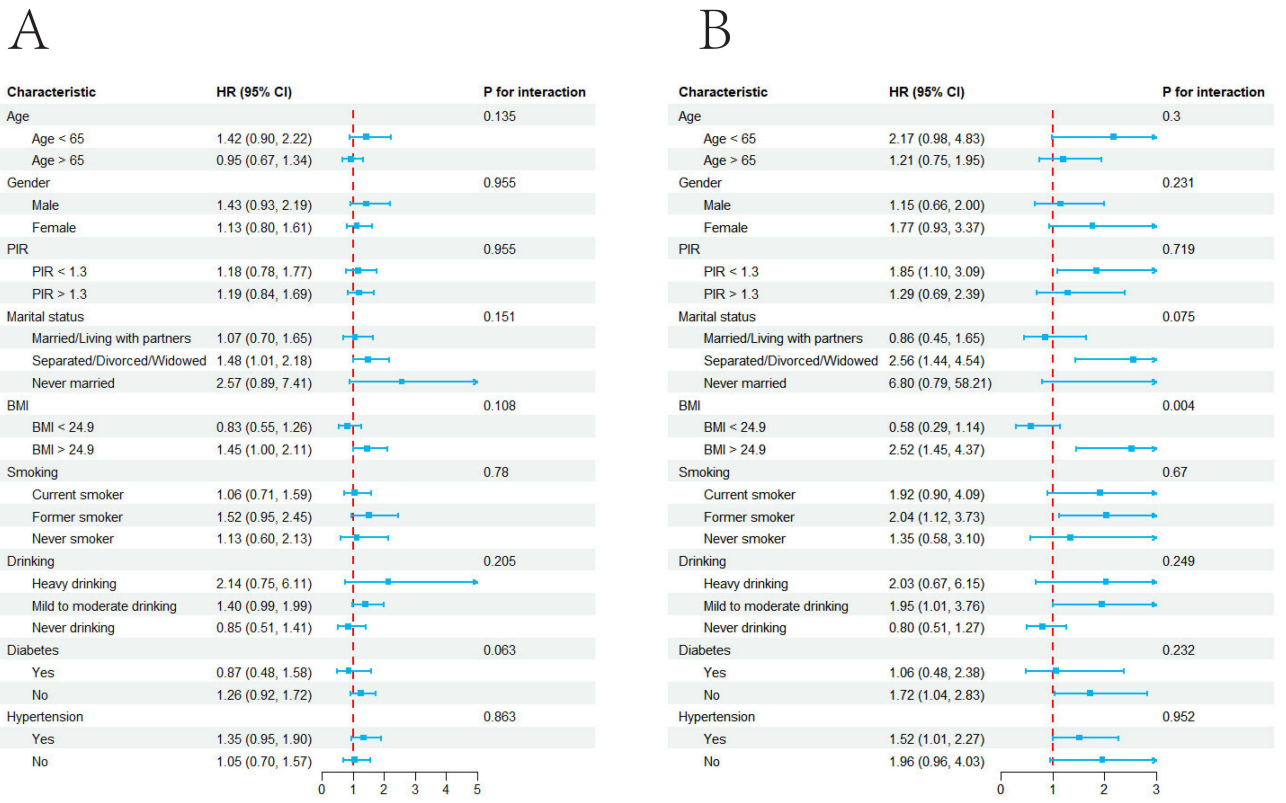

Figure 5 Subgroup analyses of WWI with all-cause mortality (**A**), CVD mortality (**B**).
Abbreviations: WWI, weight-adjusted waist index; PIR, poverty income ratio; BMI, body mass index; CVD, cardiovascular diseases.

Among obesity assessment metrics, central obesity indicators exhibit prominent predictive efficacy for adverse clinical outcomes.[27,28] Previous research findings have shown that conventional anthropometric indices including waist-to-hip ratio and waist circumference have established associations with cardiovascular disease severity.[29] The weight-adjusted waist index (WWI) is an emerging metric that enables more precise assessment of abdominal fat distribution and associated health risks, demonstrating robust prognostic value across diverse disease states. A US adult cohort study confirmed its

consistent predictive capacity for cardiovascular and all-cause mortality.[30] Additional research has validated WWI as a clinically meaningful predictor of adverse outcomes in type 2 diabetes, asthma, and hypertension.[31–33] While prior studies have primarily focused on other populations, our study extends these findings to COPD survival outcomes.

Growing evidence demonstrates that obesity significantly contributes to respiratory disease progression through multiple pathways.[34] In a large population-based cross-sectional study (n=121,965), abdominal obesity emerged as the strongest predictor of accelerated lung function decline.[35] Notably, the chronic metabolic consequences of obesity not only worsen respiratory outcomes but also substantially increase cardiovascular and all-cause mortality during early-stage COPD.[4] However, previous observations have identified an "obesity paradox" in COPD patients and this unexpected phenomenon has generated significant controversy in the medical community. A meta-analysis examining the relationship between BMI and mortality in this population revealed that underweight patients face significantly heightened risks of all-cause, respiratory, and cardiovascular mortality, whereas overweight and mildly obese individuals exhibit protective effects.[36] But our findings appear to contradict BMI-driven conclusions, showing that elevated WWI correlates strongly with increased all-cause and cardiovascular mortality among patients diagnosed with COPD. This contradiction likely stems from fundamental differences in the metabolic implications of these indices. BMI serves as a global measure of adiposity without distinguishing fat from lean mass, whereas WWI specifically quantifies central obesity and visceral fat accumulation.[37] This discrepancy suggests that central obesity assessed via WWI may offset the survival benefits associated with overall adiposity measured by BMI, particularly in individuals with sarcopenic obesity or metabolic syndrome. In addition to the above, heterogeneity in study populations and residual confounding factors in prior analyses may contribute to divergent findings.[38–40] These observations underscore the critical need to consider fat distribution patterns, rather than relying solely on global weight metrics, when evaluating obesity-related risks in COPD patients.

This study identified a positive association between WWI and adverse COPD outcomes, and this relationship may be explained by several pathophysiologic mechanisms as follows. Firstly, inflammatory mechanisms likely mediate the association between visceral fat and COPD. Chronic inflammation is a hallmark of COPD, characterized by persistent infiltration of neutrophils, macrophages, and CD8+ T lymphocytes in the lungs, along with elevated production of pro-inflammatory chemokines and cytokines.[41,42] Visceral fat significantly amplifies this inflammatory cycle, as dysfunctional adipose tissue not only secretes excess proinflammatory mediators but also suppresses protective adiponectin, generating a systemic proinflammatory state.[43] Secondly, visceral obesity impairs diaphragmatic excursion, aggravating ventilation-perfusion mismatch and hypoxemia, while increasing overlap risks with obstructive sleep apnea (OSA), further elevating cardiovascular burdens.[44–46] Furthermore, metabolic disturbances including insulin resistance and dyslipidemia compound these effects by promoting vascular damage and cardiac remodeling.[47–49] This vicious cycle of metabolic dysfunction and chronic inflammation accelerates lung function decline and tissue remodeling, ultimately increasing cardiovascular complications and mortality in COPD. And there is still an urgent need for more in-depth research in the future to further elucidate the underlying mechanisms.

In this study, we accounted for potential confounding factors that could impact survival outcomes in individuals with COPD and implemented Cox models to investigate whether WWI is strongly associated with both mortality risk. We finally found even after adjusting for a wide range of demographic, socioeconomic, lifestyle, and clinical factors, increased WWI remained an independent risk factor for both cardiovascular and all-cause mortality among individuals with COPD. To further investigate potential covariates influencing the relationship, we conducted subgroup analyses, which showed that WWI remained independently correlated with all-cause mortality across subgroups. However, WWI had different effects on CVD mortality in different BMI groups: higher WWI may increase CVD mortality in overweight or obese patients, while there is no significant association in normal or lean patients. It is noteworthy that the confidence interval crossing 1 in the BMI <24.9 group suggests uncertainty, necessitating further validation in larger cohorts. The prognostic performance of WWI in predicting risk of death was also quantified using ROC curves, further validating its excellent long-term prognostic ability. To further analyze the correlation, we conducted a restricted cubic spline (RCS) analysis and the linear curves indicate a monotonically increasing risk association without significant nonlinear thresholds, suggesting that central adiposity exerts a cumulative detrimental effect on prognosis. These findings establish WWI as a clinically robust central adiposity metric for risk stratification in COPD prognosis and underscore the importance of integrating weight management strategies into the clinical care of COPD patients, particularly those with abdominal obesity. Weight management

interventions, including dietary modifications and supervised exercise programs, may not only mitigate metabolic risks but also potentially improve respiratory symptoms and overall quality of life. However, further research is needed to establish the optimal approaches and long-term benefits of weight management in this population.

While our study demonstrates the prognostic value of the weight-adjusted waist index (WWI), its integration into clinical practice will require further validation and implementation efforts. Future large-scale studies are needed to establish clinically meaningful threshold values for WWI that correspond to different mortality risk levels in COPD patients, which may vary based on factors such as age, gender, and disease severity. Furthermore, incorporating WWI into existing COPD prognostic tools, such as by adding it to the BODE index to create a modified "BODEW" index, represents a promising approach to enhance risk stratification by better capturing visceral adiposity and metabolic risk not fully reflected by BMI alone. The integration of WWI calculation into electronic health systems could facilitate automatic risk assessment during routine clinical measurements, though future implementation studies should evaluate the feasibility, patient acceptance, and cost-effectiveness of such applications across diverse healthcare settings.

The research exhibits several significant advantages. Our study utilized a sample of 1,396 individuals from the NHANES database, combined with standardized data collection procedures, making the results more representative and generalizable. We rigorously adjusted for key confounding factors and finally confirmed WWI as a novel prognostic indicator in COPD management, thereby advocating its use as a practical tool to guide clinical decision-making. However, our study also has limitations. The research relied on baseline WWI levels without longitudinal follow-up, making it difficult to clarify the temporal association between changes in WWI and the development of COPD outcomes. Additionally, due to the constraints of the NHANES database, we lacked data on COPD-specific factors such as disease severity (eg, GOLD stage) and history of exacerbations. The inability to adjust for these important prognostic factors represents a limitation and should be addressed in future studies with more detailed clinical data.

Conclusion

Our findings reveal WWI as a graded, dose-dependent indicator of mortality risk in COPD populations, showing consistent relationships across both all-cause and cardiovascular-specific outcomes. These results underscore the clinical relevance of central adiposity assessment through WWI measurements, suggesting its potential integration into routine risk stratification protocols for COPD management.

Data Sharing Statement

In this study, the datasets analyzed were publicly accessible at the website https://www.cdc.gov/nchs/nhanes/.

Ethics Statement

The NHANES study protocol received formal approval from the National Center for Health Statistics (NCHS) Institutional Review Board, with written informed consent obtained from all participants prior to data collection. This study utilized publicly available, de-identified data from NHANES, which qualifies for exemption from ethical review according to Article 32 of the Measures for Ethical Review of Life Science and Medical Research Involving Human Subjects (National Health Commission, China, 2023).

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Author Contributions

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

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Disclosure

The authors state that there are no competing interests present.

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