THE ANATOLIAN JOURNAL OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Weight-Adjusted Waist Index Outperforms Conventional Adiposity Indices in Predicting All-Cause Mortality: A Population-Based Cohort Study

ABSTRACT

Background: Body mass index (BMI), the most widely used adiposity metric, cannot differentiate fat distribution from lean mass, limiting its prognostic utility. This study compared the weight-adjusted waist index (WWI) with BMI, waist-to-height ratio, and relative fat mass (RFM) as predictors of all-cause and cardiovascular mortality using a z-standardized framework.

Methods: Data from 18 496 adults aged ≥20 years from the National Health and Nutrition Examination Survey 2011-2018 were linked to the National Death Index through December 31, 2019. Four adiposity indices were z-standardized and analyzed using survey-weighted Cox models with sequential adjustment. Dose–response relationships were assessed using restricted cubic splines, and subgroup analyses examined the effect modification by sex, multimorbidity, and estimated glomerular filtration rate (eGFR).

Results: Over a median follow-up of 4.83 years, 976 all-cause and 291 cardiovascular deaths occurred. Weight-adjusted waist index demonstrated the strongest association with all-cause mortality (hazard ratio [HR] 1.34; 95% CI 1.23-1.46; $P < .001$); BMI and RFM did not reach significance. After mutual adjustment, WWI retained its association (HR 1.40; $P < .001$) while BMI did not reach statistical significance in the adjusted model. Weight-adjusted waist index showed a linear dose–response relationship, contrasting the J-shaped curve of BMI. The association was consistent across subgroups but attenuated in participants with eGFR < 60 (interaction $P = .034$).

Conclusion: Weight-adjusted waist index was the strongest independent predictor of all-cause and cardiovascular mortality among 4 adiposity indices. Its linear dose–response relationship, consistency across subgroups, and calculability from waist circumference and body weight alone support its use as a practical alternative to BMI for mortality risk stratification.

Keywords: Cardiovascular mortality, cardiovascular risk factors, central adiposity, obesity paradox, weight-adjusted waist index

ORIGINAL INVESTIGATION

INTRODUCTION

Obesity is a global health concern whose prevalence has been rising rapidly, directly increasing cardiovascular disease risk and mortality. An analysis by the Non-Communicable Disease (NCD) Risk Factor Collaboration spanning 200 countries demonstrated a notable increase in the global burden of obesity among both adults and children between 1990 and 2022.[1] An individual-participant-data meta-analysis of 239 prospective studies across 4 continents showed that each 5 kg/m^2 increment in body mass index (BMI) above 25 kg/m^2 significantly increases all-cause mortality.[2]Body mass index remains the most widely adopted metric for quantifying this risk; however, it fails to differentiate between muscle mass and adiposity, nor does it account for regional fat distribution. Consequently, highly muscular individuals may be erroneously stratified as high-risk, while cachectic or sarcopenic patients might be misclassified as low-risk. This limitation gives rise to counter-intuitive clinical observations widely termed the "obesity paradox"

Ercan Kahraman[1]
Şirin Çetin[2]
Özkan Özler[3]

[1]*Department of Cardiovascular Surgery, Amasya University Faculty of Medicine, Amasya, Türkiye*
[2]*Department of Biostatistics, Amasya University Faculty of Medicine, Amasya, Türkiye*
[3]*Department of Cardiovascular Surgery, İstanbul Atlas University Faculty of Medicine, İstanbul, Türkiye*

Corresponding author:
Ercan Kahraman,
✉ ercan.kahraman@amasya.edu.tr

Received: June 11, 2026
Accepted: August 31, 2026
Available Online Date: September 21, 2026

Cite this article as: Kahraman E, Çetin Ş, Özler Ö. Weight-adjusted waist index outperforms conventional adiposity indices in predicting all-cause mortality: a population-based cohort study. *Anatol J Cardiol.* 2026;30(11):805-816.

DOI: 10.14744/AnatolJCardiol.2026.6756

Copyright@Author(s) - Available online at anatoljcardiol.com.
Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

wherein a higher BMI is paradoxically associated with an improved prognosis in certain patient populations.[3]

Accumulating evidence indicates that central adiposity, rather than total adiposity, plays a decisive role in cardiovascular risk assessment. A scientific statement from the American Heart Association emphasized that waist circumference is a cardiovascular risk marker independent of BMI and that visceral adiposity is independently associated with adverse cardiovascular outcomes.[4] Because waist circumference alone does not provide normalization independent of height and weight, composite indices have been developed to more accurately capture central adiposity: the waist-to-height ratio (WHtR) normalizes waist circumference to height and was significantly associated with both all-cause and cardiovascular mortality in a meta-analysis;[5] relative fat mass (RFM) provides a sex-adjusted estimate of body fat percentage derived from the height-to-waist circumference ratio.[6] Each of these indices employs a different normalization strategy, yet their comparison as mortality predictors within a common analytical framework has been limited.

In 2018, Park et al[7] developed the weight-adjusted waist index (WWI = waist circumference [cm]/$\sqrt{}$weight [kg]) in a South Korean national cohort of 465 629 individuals and reported that WWI was the only adiposity measure showing a linear positive association with cardiovascular mortality. Subsequent studies supported a consistent link between WWI and both all-cause and cardiovascular mortality in general populations[8] and in specific patient groups such as those with type 2 diabetes.[9] The current literature, however, has notable gaps. Most studies compared WWI with only a limited number of indices, and because comparisons were conducted on different scales, direct comparison of effect sizes was not possible. The shape of the dose–response relationship remains contested, with some studies reporting a linear association and others a U-shaped curve. Interactions within clinically relevant subgroups such as kidney function and cardiometabolic multimorbidity have not been adequately explored.

The study addresses these gaps using National Health and Nutrition Examination Survey (NHANES) 2011-2018 data through 4 specific aims: (1) compare WWI, BMI, WHtR, and RFM head-to-head within the same modeling framework using z-standardization, (2) evaluate the dose–response relationship of each index with all-cause and cardiovascular mortality through restricted cubic spline analysis, (3) test the independent prognostic value of WWI beyond BMI using a mutual adjustment model, and (4) examine interactions across kidney function, cardiometabolic multimorbidity, and sex subgroups.

HIGHLIGHTS

- Weight-adjusted waist index (WWI) was the strongest independent predictor of all-cause and cardiovascular mortality among 4 z-standardized adiposity indices.
- Body mass index (BMI) lost its independent prognostic contribution after mutual adjustment with WWI.
- Weight-adjusted waist index showed a linear dose–response relationship with mortality, contrasting the J-shaped curve of BMI.
- Weight-adjusted waist index's prognostic capacity was attenuated in participants with estimated glomerular filtration rate < 60 mL/min/1.73 m^2, a finding unique to WWI.

METHODS

Study Design and Population

This study used data from the NHANES 2011-2018 cycles. National Health and Nutrition Examination Survey NHANES is a cross-sectional survey program conducted using a multistage, stratified probability sampling design to assess the health status of the non-institutionalized civilian population in the United States. Demographic and health information was collected from participants during household interviews, followed by anthropometric measurements and laboratory examinations at mobile examination centers (MEC). The study protocol was approved by the NCHS) Research Ethics Review Board (Protocol No: 2011-2017), and written informed consent was obtained from all participants. Because this study is a secondary analysis of publicly available, de-identified data, additional ethics approval was not required. The study was conducted in accordance with the Declaration of Helsinki.

Individuals aged ≥ 20 years who completed the MEC examination were considered eligible (Figure 1). From an initial pool of 39 156 participants, exclusions were applied for age criteria, missing anthropometric data, ineligibility for mortality follow-up, and missing follow-up duration, yielding an eligible cohort of 20 196 individuals. For the primary analyses, participants with missing key covariates (estimated glomerular filtration rate [eGFR], HbA1c, systolic blood pressure [SBP], or smoking status) were further excluded, resulting in a complete-case analytic sample of 18 496 individuals (976 all-cause deaths). Details of the exclusion process are presented in Figure 1. The attrition rate between the eligible cohort (n = 20 196) and the analytic sample (n = 18 496) was 8.4%. Demographic and clinical baseline characteristics did not differ meaningfully between the 2 groups (Supplementary Table 1), supporting that the complete-case approach did not introduce substantial selection bias.

Variables

The WWI = waist circumference (cm)/$\sqrt{}$weight (kg) served as the primary exposure variable. Waist circumference was measured at the level of the iliac crest. Comparator indices included BMI (weight/height^2), WHtR (waist circumference/height), and RFM (64 − 20 × height/waist circumference + 12 × sex; male = 0, female = 1). All 4 indices were z-standardized before entry into the models to allow direct comparison of effect sizes.

The primary endpoint was all-cause mortality; cardiovascular mortality served as the secondary endpoint. Mortality data were obtained from the National Death Index through

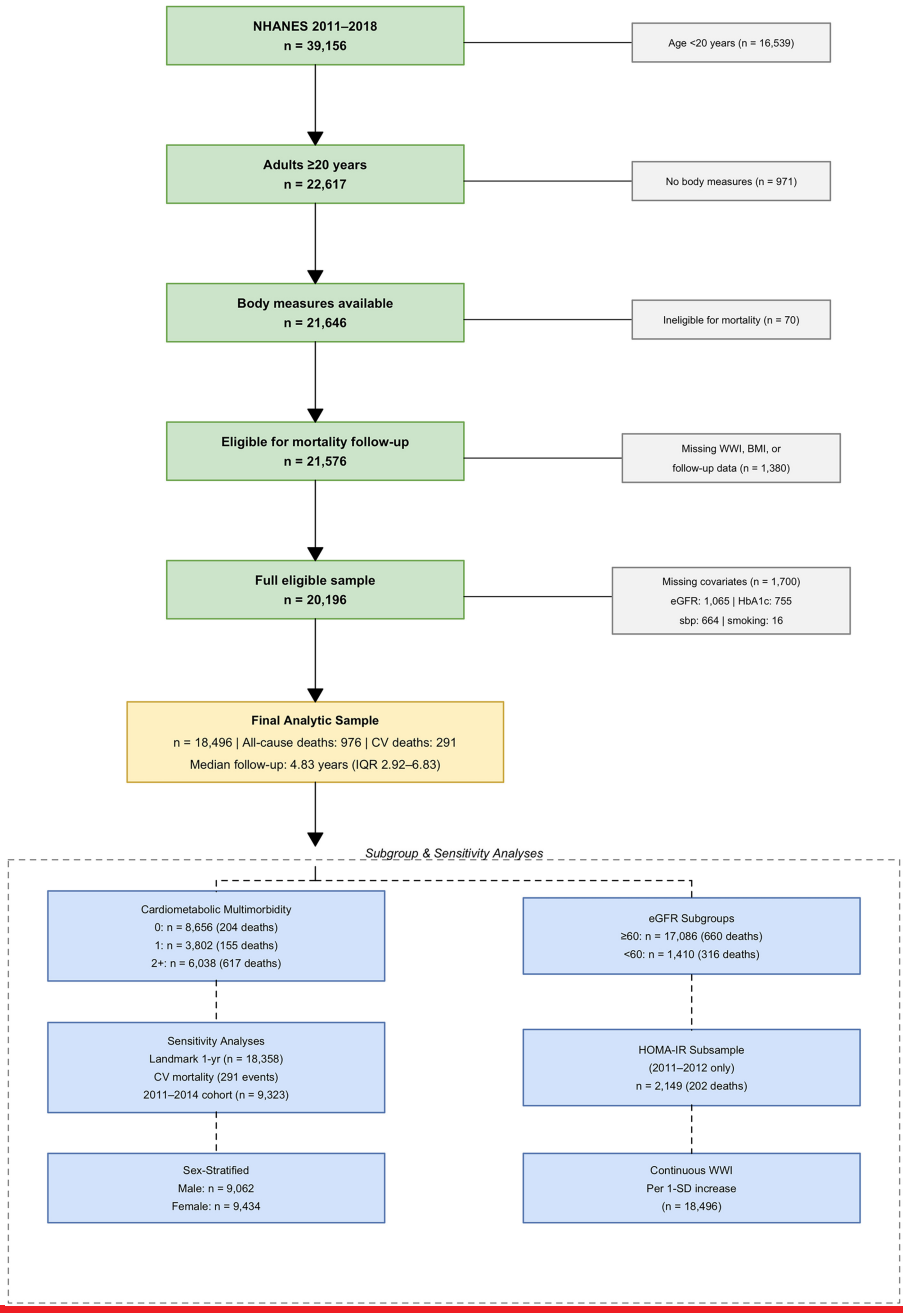


Figure 1. Flow diagram of participant selection from NHANES 2011-2018. NHANES, National Health and Nutrition Examination Survey.

the NCHS Public-Use Linked Mortality Files (2019 release); person-time was calculated from the interview date to death or December 31, 2019. Cardiovascular mortality was defined using the UCOD_LEADING variable as heart disease International Classification of Diseases, Tenth Revision [(ICD-10: I00-I09, I11, I13, I20-I51) and cerebrovascular disease (ICD-10: I60-I69). Because cerebrovascular deaths were not separately coded in the 2015-2018 cycles, the definition for those cycles predominantly reflects cardiac mortality; to address this limitation, a separate sensitivity analysis was conducted in the 2011-2014 subcohort where complete coding was available.

Diabetes (physician diagnosis or HbA1c ≥6.5%), hypertension (physician diagnosis or SBP ≥ 130 or diastolic blood pressure [DBP] ≥ 80 mm Hg),[10] and dyslipidemia (use of lipid-lowering medication, triglycerides ≥ 150, or Low-Density Lipoprotein (LDL ≥ 130 mg/dL) were included as individual covariates in the regression models. A cardiometabolic multimorbidity score (0, 1, ≥2) derived from the co-presence of these 3 conditions was used as a classification variable in subgroup analyses. Other covariates were sex, ethnicity, smoking status (never/former/current), eGFR (Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] 2021 creatinine equation),[11] SBP (mean of consecutive measurements), and

HbA1c. Homeostatic model assessment of insulin resistance (HOMA-IR) was available only in the 2011-2012 fasting subsample and was used in a dedicated sensitivity analysis.

Statistical Analysis

All analyses accounted for the complex sampling design of NHANES (survey weights, stratification, primary sampling units); 2-year examination weights were scaled by 1/4 for combining 4 cycles. Baseline characteristics were reported as unweighted counts and percentages. Group comparisons used Analysis of Variance (ANOVA) for normally distributed continuous variables, the Kruskal–Wallis test for others, and the chi-square test for categorical variables.

The association between adiposity indices and all-cause mortality was assessed using survey-weighted Cox proportional hazards models (svycoxph). Because age violated the proportional hazards assumption at the individual level, it was used as a stratification variable rather than a covariate in all models (age groups: 20-39, 40-59, 60-79, ≥80 years). Four nested models were constructed: Model 1 was stratified by age and adjusted for sex; Model 2 additionally included ethnicity and smoking status; Model 3a further incorporated diabetes, hypertension, dyslipidemia, eGFR, SBP, and HbA1c. Body mass index was not included in Model 3a to ensure an equal comparison among indices. To test whether WWI provides prognostic value independent of overall adiposity, Model 3b (Model 3a + BMI, mutual adjustment) was constructed for WWI only.

The proportional hazards assumption was evaluated using scaled Schoenfeld residuals. Because the cox.zph() function does not support svycoxph objects, testing was performed on standard Cox models with normalized survey weights applied as case weights; the global test was nonsignificant for all 4 models ($P > .05$). The dose–response relationship between WWI and mortality was examined using restricted cubic spline (RCS) analysis with 4 knots placed at the 5th, 35th, 65th, and 95th percentiles; the median WWI value was taken as the reference. Spline curves were plotted from normalized-weight Cox models, while the *P*-value for departure from linearity was obtained from survey-weighted models using the Rao–Scott test.

Prespecified subgroup analyses examined the WWI–mortality association according to multimorbidity score (0, 1, ≥2), eGFR level (<60 vs. ≥60), and sex. Model 3a covariates were applied in each subgroup; age stratification was retained across all subgroup models, but the subgroup variable itself was removed from its corresponding model (e.g., sex was not included as a covariate in the sex-stratified model). Effect modification was assessed using the likelihood ratio test (LRT) with multiplicative interaction terms. These analyses were exploratory in nature, and no correction for multiple comparisons was applied.

Sensitivity analyses included: (i) cardiovascular mortality analyzed within the same modeling framework, (ii) a landmark analysis excluding deaths within the first year, (iii) additional adjustment for HOMA-IR in the fasting subsample (n = 2149), (iv) restriction to the 2011-2014 subcohort (n = 9323), and (v) sex-stratified models (male n = 9062, female n = 9434). The discriminative capacity of each index for mortality was evaluated using unadjusted, single-predictor area under the receiver operating characteristic curve (AUC); these values should be interpreted as a descriptive measure that does not account for covariates or the time-to-event structure. In addition, Harrell's C-index was calculated from the fully adjusted Cox models (Model 3a) for each adiposity index. No formal pairwise comparison of C-indices was performed; differences between indices should therefore be interpreted descriptively. Time-dependent discriminative capacity was assessed at 1-, 3-, and 5-year time points using the linear predictors of the Cox models with inverse probability of censoring weighting (IPCW). For descriptive analyses and Kaplan–Meier curves, participants were divided into 3 groups (tertiles) based on the 33rd and 66th percentiles of the WWI distribution; these cut points are sample-specific and are not proposed as clinical decision thresholds. Survival differences between groups were assessed using the log-rank test. Inter-index correlations were evaluated using Pearson coefficients, and multicollinearity was assessed using variance inflation factors (VIFs).

Analyses were performed using R software (version 4.4.2; survey, survival, rms, pROC, and timeROC packages). Two-sided $P < .05$ was considered statistically significant.

RESULTS

Baseline Characteristic

The analytic sample comprised 18 496 adults with a median age of 49.0 years (Interquartile Range [IQR]: 34.0-63.0); 49.0% were male. Median follow-up was 4.83 years (IQR = 2.92-6.83). During follow-up, 976 (5.3%) all-cause deaths and 291 (1.6%) cardiovascular deaths were recorded.

When participants were grouped by WWI tertiles, the cut-points were 10.72 and 11.46 cm/$\sqrt{}$kg. Compared with the lowest tertile (T1 ≤ 10.72), individuals in the highest tertile (T3 > 11.46) were considerably older (median 61.0 vs. 37.0 years), had higher BMI (32.97 vs. 25.57 kg/m^2), and had larger waist circumference (111.6 vs. 87.7 cm; all $P < .001$). Prevalences of diabetes (29.8% vs. 4.8%), hypertension (60.8% vs. 23.6%), and dyslipidemia (53.0% vs. 19.0%) were also markedly higher in the upper tertile. All-cause mortality rose from 2.3% in T1 to 9.1% in T3, and cardiovascular mortality from 0.5% to 2.9% (Table 1).

Association of Adiposity Indices with All-Cause Mortality

In the survey-weighted Cox regression, all 4 indices were significantly associated with all-cause mortality in the age- and sex-adjusted model (Model 1). The strongest association was observed for WWI (hazard ratio [HR]:1.476; 95% CI: 1.364-1.597; $P < .001$). Further adjustment for ethnicity and smoking status did not materially alter these associations (Model 2; Table 2).

In Model 3a, which adjusted for all clinical covariates, WWI emerged as the most robust predictor (HR: 1.337; 95% CI: 1.227-1.458; $P < .001$). Waist-to-height ratio retained statistical significance (HR: 1.143; $P = .004$), whereas BMI (HR: 1.032; $P = .565$) and RFM (HR: 1.176; $P = .054$) did not reach significance. In Model 3b, which tested the independence of WWI from

Table 1. Baseline Characteristics of the Study Population by Tertiles of the Weight-adjusted Waist Index (WWI)

Variables	Overall (n = 18 496)	T1 (≤10.72) (n = 6166)	T2 (10.72-11.46) (n = 6165)	T3 (>11.46) (n = 6165)	*P*
Age, years, median (IQR)	49.0 (34.0-63.0)	37.0 (27.0-49.0)	51.0 (37.0-63.0)	61.0 (47.0-71.0)	<.001
Male sex, n (%)	9062 (49.0)	3693 (59.9)	3164 (51.3)	2205 (35.8)	<.001
Ethnicity, n (%)					<.001
Mexican American	2549 (13.8)	537 (8.7)	890 (14.4)	1122 (18.2)	
Non-Hispanic Asian	2320 (12.5)	958 (15.5)	832 (13.5)	530 (8.6)	
Non-Hispanic Black	4043 (21.9)	1657 (26.9)	1311 (21.3)	1075 (17.4)	
Non-Hispanic White	6958 (37.6)	2250 (36.5)	2187 (35.5)	2521 (40.9)	
Other Hispanic	1964 (10.6)	506 (8.2)	719 (11.7)	739 (12.0)	
Other/multiracial	662 (3.6)	258 (4.2)	226 (3.7)	178 (2.9)	
BMI, kg/m^2, mean (SD)	29.26 (6.69)	25.57 (4.97)	29.25 (5.93)	32.97 (7.53)	<.001
Waist circumference, cm, mean (SD)	99.73 (16.37)	87.67 (11.32)	99.89 (12.62)	111.63 (15.81)	<.001
Weight, kg, mean (SD)	81.78 (21.30)	75.32 (17.56)	82.31 (20.65)	87.71 (24.08)	<.001
Height, cm, mean (SD)	166.92 (10.07)	171.17 (9.43)	167.11 (9.51)	162.48 (9.41)	<.001
WWI, cm/$\sqrt{}$kg, mean (SD)	11.09 (0.85)	10.16 (0.44)	11.09 (0.21)	12.02 (0.45)	<.001
WHtR, mean (SD)	0.60 (0.10)	0.51 (0.06)	0.60 (0.06)	0.69 (0.09)	<.001
RFM, %, mean (SD)	35.79 (8.69)	29.24 (7.37)	36.00 (6.70)	42.14 (6.95)	<0.001
SBP, mm Hg, mean (SD)	124.18 (18.17)	118.53 (15.45)	124.39 (17.69)	129.63 (19.65)	<.001
DBP, mm Hg, mean (SD)	70.54 (12.85)	70.28 (11.55)	71.74 (12.52)	69.61 (14.28)	<.001
HbA1c, %, mean (SD)	5.79 (1.10)	5.44 (0.77)	5.79 (1.10)	6.16 (1.29)	<.001
eGFR, mL/min/1.73 m^2, mean (SD)	94.24 (22.11)	100.24 (19.41)	94.68 (21.62)	87.79 (23.92)	<.001
Creatinine, mg/dL, mean (SD)	0.90 (0.43)	0.91 (0.36)	0.89 (0.44)	0.89 (0.47)	.044
Diabetes, n (%)	3066 (16.6)	296 (4.8)	930 (15.1)	1840 (29.8)	<.001
Hypertension, n (%)	7908 (42.8)	1454 (23.6)	2703 (43.8)	3751 (60.8)	<.001
Dyslipidemia, n (%)	6745 (36.5)	1172 (19.0)	2307 (37.4)	3266 (53.0)	<.001
Smoking status, n (%)					<.001
Current	3595 (19.4)	1415 (22.9)	1156 (18.8)	1024 (16.6)	
Former	4319 (23.4)	1039 (16.9)	1541 (25.0)	1739 (28.2)	
Never	10 582 (57.2)	3712 (60.2)	3468 (56.3)	3402 (55.2)	
CKD (eGFR <60), n (%)	1410 (7.6)	167 (2.7)	426 (6.9)	817 (13.3)	<.001
Follow-up, years, median (IQR)	4.83 (2.92-6.83)	5.33 (3.25-7.17)	4.83 (2.92-6.83)	4.42 (2.75-6.50)	<.001
All-cause mortality, n (%)	976 (5.3)	139 (2.3)	278 (4.5)	559 (9.1)	<.001
CV mortality, n (%)	291 (1.6)	30 (0.5)	84 (1.4)	177 (2.9)	<.001

Data are presented as mean (SD) for normally distributed continuous variables, median (IQR) for non-normally distributed continuous variables, and n (%) for categorical variables. *P*-values were calculated using one-way ANOVA for normally distributed variables, Kruskal–Wallis test for non-normally distributed variables, and chi-square test for categorical variables. Descriptive statistics are unweighted; all regression analyses incorporated NHANES survey weights and complex sampling design.

BMI, body mass index; CV, cardiovascular; CKD, chronic kidney disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; NHANES, National Health and Nutrition Examination Survey; RFM, relative fat mass; SBP, systolic blood pressure; T, tertile; WHtR, waist-to-height ratio; WWI, weight-adjusted waist index.

Complete-case analysis; n = 18 496 after exclusion of participants with missing data for eGFR, HbA1c, SBP, or smoking status from the eligible cohort (n = 20 196). NHANES 2011-2018, adults aged ≥ 20 years.

overall adiposity through mutual adjustment with BMI, WWI remained significant (HR: 1.404; 95% CI: 1.252-1.575; *P* < .001), while BMI did not demonstrate a statistically significant independent association (HR: 0.900; 95% CI: 0.783-1.034; *P* = .135).

Dose–Response and Survival Analysis

Restricted cubic spline analysis revealed a linear dose–response relationship between WWI and all-cause mortality (nonlinearity *P* = .713). No significant departure from linearity was detected for WHtR either (*P* = .064). By contrast, nonlinear associations were observed for BMI (*P* = .003) and RFM (*P* = .028). Body mass index displayed a J-shaped curve: mortality risk was elevated at low values, reached its nadir at intermediate values, and rose again at high values (Figure 2; Supplementary Table 2). Kaplan–Meier curves constructed by WWI tertiles showed that survival probability in the highest tertile was distinctly lower than in the middle and lowest tertiles (log-rank *P* < .001; Figure 3).

Subgroup and Interaction Analyses

The association between WWI and all-cause mortality was examined across prespecified subgroups (Table 3). The

Table 2. Association of Adiposity Indices with All-cause Mortality: Survey-weighted Cox Proportional Hazards Regression Models

Index	Model	HR (95% CI)	*P*
WWI	Model 1	1.476 (1.364-1.597)	<.001
	Model 2	1.483 (1.366-1.610)	<.001
	Model 3a	1.337 (1.227-1.458)	<.001
	Model 3b	1.404 (1.252-1.575)	<.001
BMI	Model 1	1.137 (1.029-1.257)	.012
	Model 2	1.157 (1.053-1.272)	.002
	Model 3a	1.032 (0.927-1.149)	.565
WHtR	Model 1	1.271 (1.165-1.387)	<.001
	Model 2	1.283 (1.184-1.391)	<.001
	Model 3a	1.143 (1.043-1.254)	.004
RFM	Model 1	1.412 (1.205-1.656)	<.001
	Model 2	1.446 (1.249-1.672)	<.001
	Model 3a	1.176 (0.997-1.386)	.054

Hazard ratios are expressed per 1-SD increment of each z-standardized index. n = 18 496; events (all-cause mortality) = 976. Model 1: adjusted for age and sex. Model 2: Model 1 + ethnicity, smoking status. Model 3a: Model 2 + diabetes, hypertension, dyslipidemia, eGFR, SBP, and HbA1c. Model 3b (WWI only): Model 3a + BMI (mutual adjustment); BMI in Model 3b: HR 0.900 (0.783-1.034), *P* = .135.
BMI, body mass index; eGFR, estimated glomerular filtration rate; HR, hazard ratio; RFM, relative fat mass; SBP, systolic blood pressure; WHtR, waist-to-height ratio; WWI, weight-adjusted waist index.

association was significant in both males (HR: 1.453; 95% CI: 1.237-1.707; *P* < .001) and females (HR: 1.243; 95% CI: 1.065-1.450; *P* = .006), with no significant interaction between sexes (*P* = .708; Table 3; Supplementary Figure 1). For cardiometabolic multimorbidity, the association was maintained in both the <2 comorbidity group (HR: 1.432; *P* < .001) and the ≥2 comorbidity group (HR: 1.325; *P* < .001), with no significant interaction (*P* = .479).

A notable difference emerged in the analysis by kidney function: WWI showed a strong association in the eGFR ≥ 60 group (HR: 1.417; 95% CI: 1.276-1.575; *P* < .001) but was nonsignificant in the eGFR < 60 group (HR: 1.090; *P* = .291). Among the 4 indices, only WWI showed a significant interaction with eGFR group (*P* = .034); no such interaction was observed for the other 3 indices (Supplementary Table 3).

Sensitivity Analyses

The robustness of the primary finding was evaluated through several sensitivity analyses (Table 4). When cardiovascular mortality was analyzed as the secondary endpoint, WWI retained its significant association (Model 3a HR: 1.461; *P* = .008; Model 3b HR: 1.418; *P* = .026). In a landmark analysis designed to reduce the possibility of reverse causation, excluding deaths within the first year (n = 18 358; 853 events), results were consistent with the primary analysis (Model 3a HR: 1.311; *P* < .001).

In the 2011-2014 subcohort (n = 9323; 716 events), the association was similar in magnitude and remained significant (HR: 1.398; *P* < .001). In the fasting subsample (n = 2149; 202 events), the direction and magnitude of the effect were preserved regardless of HOMA-IR adjustment. However, statistical significance was not reached owing to the limited sample size (without HOMA-IR: HR 1.429, *P* = .051; with HOMA-IR: HR 1.415, *P* = .059). In sex-stratified models, the association was significant in both sexes across Models 3a and 3b; the effect size was numerically larger in males than in females (male Model 3b HR: 1.546; female Model 3b HR: 1.297; Table 4).

Discrimination Analysis and Model Diagnostics

Unadjusted AUC values calculated by subgroup showed that WWI had the highest or among the highest discriminative capacity across all subgroups. The highest AUC was observed in males (0.700; 95% CI: 0.678-0.722). In the eGFR < 60 group, BMI (0.563) was numerically higher than WWI (0.541), a finding consistent with the eGFR interaction analysis (Supplementary Table 4). The proportional hazards assumption was satisfied for all 4 index models (global *P* : WWI = 0.086; BMI = 0.101; WHtR = 0.097; RFM = 0.094). In the multicollinearity assessment, all generalized variance inflation factor [GVIF^(1/2df)] values remained below 2, indicating acceptable levels (Supplementary Tables 2, 5). Pearson correlations among indices revealed a moderate correlation between WWI and BMI (r = 0.476), a level that supports the feasibility of the mutual adjustment model (Model 3b; Supplementary Table 5).

Harrell's C-index was highest for the WWI-containing model (0.686; 95% CI: 0.653-0.719), followed by WHtR (0.676), RFM (0.675), and BMI (0.675). Time-dependent AUC analysis confirmed that WWI maintained the highest discriminative capacity at all time points (1-year: 0.711; 3-year: 0.681; 5-year: 0.678; Supplementary Table 6). As no formal statistical comparison was conducted, these differences should be considered descriptive.

DISCUSSION

Among the 4 adiposity indices evaluated in this study, WWI demonstrated the most pronounced independent association with both all-cause and cardiovascular mortality (fully adjusted model, HR per 1 SD: 1.337; 95% CI: 1.227-1.458). Unlike BMI, WHtR, and RFM, which were compared within the same modeling framework through z-standardization, WWI retained its significance after mutual adjustment with BMI, whereas BMI lost its independent contribution. This finding suggests that WWI carries a prognostic signal specific to central fat distribution beyond total adiposity, and that BMI-based risk assessment may entail a substantial loss of information.

Park et al[7] developed WWI in 2018 using a South Korean national cohort of 465 629 individuals and reported that it was the only adiposity measure displaying a linear positive association with cardiovascular mortality.[7] The present analysis confirmed this finding in a Western population and, by presenting a head-to-head comparison of 4 indices within a single analytical framework, demonstrated that WWI is distinguished from the other indices not only by its linear association but also by its effect size.

Studies examining the WWI–mortality relationship have increased rapidly in recent years. In general populations,

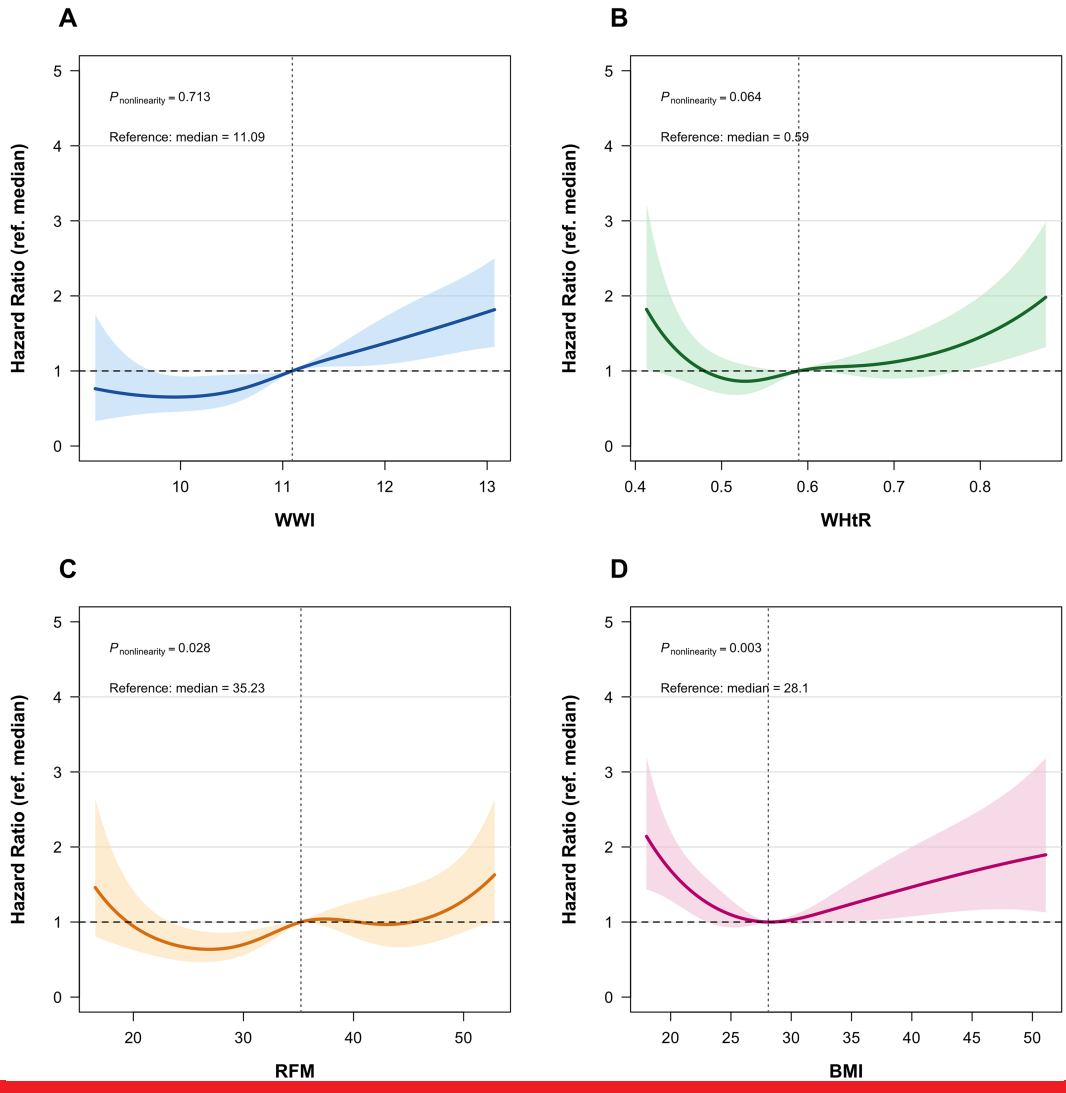


Figure 2. Restricted cubic spline curves for adiposity indices and all-cause mortality. (A) WWI, (B) WHtR, (C) RFM, and (D) BMI. Reference values were set at the median (dotted vertical line). Shaded areas represent 95% confidence intervals. *P* values for nonlinearity are shown within each panel. BMI, body mass index; RFM, relative fat mass; WHtR, waist-to-height ratio; WWI, weight-adjusted waist index.

Han et al, using NHANES 2005-2014 data and Cao et al[13], using NHANES 2011-2018 data restricted to non-Asian participants, both reported a positive association between WWI and all-cause mortality along with superior discriminative capacity compared with BMI and waist circumference.[12,13] Similarly, WWI consistently demonstrated the highest discriminative capacity across all subgroups, a pattern concordant with both of these reports. Previous studies, however, evaluated WWI against a limited number of indices on different scales. The present work is among the few to compare 4 adiposity indices using z-standardization within the same modeling framework, showing that WWI is distinguished from the others not only in statistical significance but also in effect size.

An important inconsistency exists in the literature regarding the shape of the dose–response relationship. Cao et al[13] reported a U-shaped association between WWI and all-cause mortality, identifying an inflection point at 10.46 cm/$\sqrt{}$kg below which an inverse relationship was observed. In the analysis, restricted cubic spline analysis showed no significant departure from linearity ($P = .713$), and the WWI–mortality relationship followed a monotonically increasing pattern. Several methodological factors may account for this discrepancy. First, nonlinearity was assessed using different approaches: Cao et al employed piecewise linear regression, whereas this study applied restricted cubic spline analysis with a formal linearity test that does not assume a predetermined shape; the sensitivity of these 2 methods to detecting an inflection point differs. Second, and likely most critical, the depth of covariate adjustment differed substantially: the fully adjusted model of Cao et al included self-reported disease status, whereas our model incorporated eGFR, HbA1c, and systolic blood pressure as continuous variables. This additional adjustment may have more effectively controlled for residual confounding attributable to subclinical disease and cachexia at the lower end of the

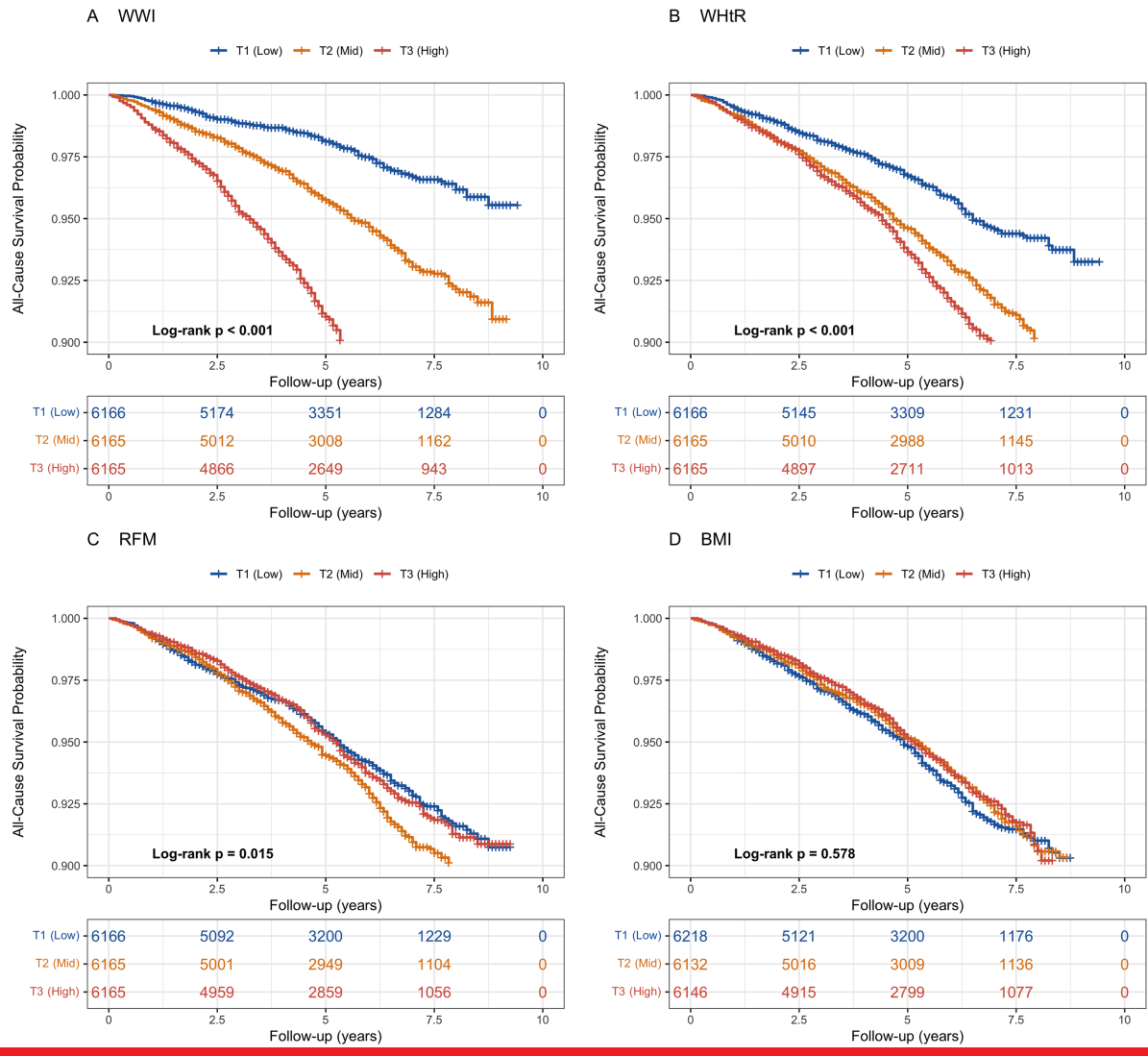


Figure 3. Kaplan–Meier survival curves for all-cause mortality by adiposity index tertiles. (A) WWI, (B) WHtR, (C) RFM, and (D) BMI. Number-at-risk tables are shown below each panel. BMI, body mass index; RFM, relative fat mass; WHtR, waist-to-height ratio; WWI, weight-adjusted waist index.

WWI distribution. Third, differences in population definition (non-Asian only vs. all ethnic groups) and missing data strategy (multiple imputation vs. complete-case analysis) may also have influenced the shape of the curve.

Regarding cardiovascular mortality, our study yielded results that maintained statistical significance in the fully adjusted model (HR: 1.461; $P = .008$) and after BMI adjustment (HR: 1.418; $P = .026$). These findings are comparable in magnitude to those of Qiu et al[14], who reported an HR of 1.45 for the combined triglyceride-glucose (TyG)-WWI index for cardiovascular mortality. Notably, WWI achieved a similar effect size on its own without the addition of metabolic parameters, which is relevant from the standpoint of clinical applicability. Notably, WWI is calculated simply as waist circumference (cm) divided by the square root of body weight (kg), making it a practical and easily applicable index in clinical settings.

A noteworthy finding also emerged from the mutual adjustment model (Model 3b): WWI maintained its significance (HR: 1.404; $P < .001$) while BMI did not demonstrate a statistically significant independent contribution in the fully adjusted model (HR: 0.900; $P = .135$). This pattern suggests that the association of BMI with mortality largely originates from its central adiposity component, and that once this component is captured by WWI, BMI did not provide additional prognostic information within the present analytical framework. The dose–response analyses further confirm the structural difference between these 2 indices. WWI displayed a monotonically increasing linear relationship, whereas BMI showed a J-shaped curve and failed to establish a clear risk gradient.

Although WHtR also measures central adiposity, it exhibited a substantially lower effect size than WWI in Model 3a (HR: 1.143 vs. 1.337). This difference has a formulaic basis: because WHtR divides waist circumference by height and height is constant in adults, the index in practice reflects waist circumference itself. WWI, by contrast, normalizes waist circumference by the square root of body weight,

Table 3. Subgroup Analyses for the Association Between the Weight-adjusted Waist Index and All-cause Mortality: Cox Proportional Hazards Regression Models

Subgroup	n	Events	HR (95% CI)	*P*	*P* Interaction
Overall	18 496	976	1.337 (1.227-1.458)	<.001	
Sex					.708
Male	9062	579	1.453 (1.237-1.707)	<.001	
Female	9434	397	1.243 (1.065-1.450)	.006	
Multimorbidity					.479
≥2 comorbidities	6038	617	1.325 (1.161-1.512)	<.001	
<2 comorbidities	12 458	359	1.432 (1.180-1.737)	<.001	
Kidney function					**.034**
eGFR ≥60 mL/min/1.73 m^2	17 086	660	1.417 (1.276-1.575)	<.001	
eGFR <60 mL/min/1.73 m^2	1410	316	1.090 (0.929-1.279)	.291	

Hazard ratios are expressed per 1-SD increment of z-standardized WWI. All models adjusted for age, sex, ethnicity, smoking status, diabetes, hypertension, dyslipidemia, eGFR, SBP, and HbA1c (Model 3a), except the stratification variable itself.
P interaction was derived from the likelihood ratio test comparing models with and without the cross-product interaction term (WWI × subgroup variable).
Multimorbidity was defined as the co-presence of ≥2 of diabetes, hypertension, and dyslipidemia. Bold values indicate statistical significance at $P < .05$.
eGFR, estimated glomerular filtration rate; HR, hazard ratio; WWI, weight-adjusted waist index.

thereby differentiating among individuals with the same waist circumference according to body weight. Individuals with a lower body weight for a given waist circumference receive a higher WWI value, pointing to a phenotype in which the central fat burden is dominant relative to total body mass or in which muscle mass is relatively reduced, both of which are metabolically higher-risk states. This mechanistic distinction explains why WWI carries a stronger prognostic signal than WHtR.

The dose–response relationship between BMI and mortality substantiated this pattern through restricted cubic spline analysis (nonlinearity $P = .003$): mortality risk was elevated at low BMI values, reached a minimum at intermediate

Table 4. Sensitivity Analyses for the Association Between the Weight-adjusted Waist Index and Mortality: Cox Proportional Hazards Regression Models

Sensitivity Analysis	n	Events	HR (95% CI)	*P*
Primary analysis (Model 3a)	18 496	976	1.337 (1.227-1.458)	<.001
Landmark analysis (excluding deaths <1 year)				
Model 3a	18 358	853	1.311 (1.185-1.450)	<.001
Model 3b (+ BMI)	18 358	853	1.360 (1.192-1.551)	<.001
Cardiovascular mortality (secondary outcome)				
Model 3a	18 496	291	1.461 (1.105-1.931)	.008
Model 3b (+ BMI)	18 496	291	1.418 (1.042-1.929)	.026
Restricted to NHANES 2011-2014 cycles				
Model 3a	9323	716	1.398 (1.267-1.543)	<.001
HOMA-IR subset (fasting subsample)				
Model 3a (without HOMA-IR)	2149	202	1.429 (0.998-2.047)	.051
Model 3a + HOMA-IR	2149	202	1.415 (0.987-2.029)	.059
Sex-stratified (Model 3a)				
Male	9062	579	1.453 (1.237-1.707)	<.001
Female	9434	397	1.243 (1.065-1.450)	.006
Sex-stratified (Model 3b, + BMI)				
Male	9062	579	1.546 (1.273-1.878)	<.001
Female	9434	397	1.297 (1.068-1.574)	.009

Hazard ratios are expressed per 1-SD increment of z-standardized WWI. Model 3a: adjusted for age, sex, ethnicity, smoking status, diabetes, hypertension, dyslipidemia, eGFR, SBP, and HbA1c. Model 3b: Model 3a + BMI (mutual adjustment).
Landmark analysis excluded participants who died within the first year of follow-up to reduce reverse causation bias. The HOMA-IR subset was restricted to the fasting subsample with available insulin measurements (NHANES morning fasting session). The 2011-2014 subcohort analysis was performed to assess temporal consistency.
BMI, body mass index; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HOMA-IR, homeostatic model assessment of insulin resistance; HR, hazard ratio; SBP, systolic blood pressure; WWI, weight-adjusted waist index.

values, and rose again at high values. This nonlinear pattern explains why BMI lost significance in the linear Cox model. The opposing risks at the low and high ends of the distribution cancel each other out, driving the net effect size toward zero. This finding aligns with the phenomenon described as the "obesity paradox," whereby BMI fails to predict mortality consistently. This paradox has been documented even in high-risk procedural settings, where elevated BMI did not confer a consistent survival advantage.[15] Lv et al[16] demonstrated a reverse-J relationship between BMI and mortality in the oldest age group (≥80 years) and reported that the optimal BMI range shifted toward the overweight-to-obese region. Liu et al[17] reported that BMI exhibited a paradoxical inverse association with mortality in patients with metabolic dysfunction-associated steatotic liver disease (MASLD), whereas WWI maintained its linear positive association. Yeo et al[18], in a study spanning 4 large cohorts, argued that the obesity paradox observed with BMI may in fact result from the use of an inappropriate metric and that waist-based indices reflect mortality more accurately.

There is a structural explanation for why WWI does not fall into this paradox. Body mass index (kg/m^2) cannot distinguish between muscle mass and fat mass; individuals with high muscle mass carry low mortality risk despite a high BMI, while those with low BMI may face increased risk due to cachexia or sarcopenia. This constitutes the left arm of the J-curve. Weight-adjusted waist index, by normalizing waist circumference by the square root of body weight, captures differences in central fat distribution even among individuals of the same weight and is therefore less susceptible to the protective effect of muscle mass or the confounding effect of cachexia. In line with this reasoning, no statistically significant departure from linearity was found in our data for WWI ($P = .713$) and a monotonically increasing relationship with mortality was observed, confirming that WWI is not affected by the structural limitations of BMI. From a clinical perspective, the linear and consistently increasing relationship between WWI and mortality offers a practical advantage: each increment in WWI corresponds to a proportional increase in risk, without the paradoxical risk reduction at lower values observed with BMI. This unidirectional association simplifies risk assessment and facilitates clinical interpretation; higher values consistently indicate higher risk.

The independent prognostic value of WWI beyond BMI points to pathophysiological mechanisms specific to central adiposity. Visceral adipose tissue is metabolically far more active than subcutaneous fat and directly elevates cardiometabolic risk through proinflammatory, prothrombotic, and insulin resistance-promoting effects.[4,19] The divergence in Model 3b, where WWI retained significance (HR: 1.404) while BMI did not retain statistical significance ($P = .135$), supports the notion that these visceral-specific mechanisms constitute a risk component independent of total adiposity.

This concordance has a structural basis: normalizing waist circumference by the square root of body weight isolates differences in central fat distribution among individuals of the same weight and thereby captures the variability in the visceral-to-subcutaneous fat ratio that BMI cannot detect. Geng et al[20], in a dual-cohort study (Chinese Changshu cohort and UK Biobank), demonstrated that the WWI–mortality association was mediated by insulin resistance (16%-38% mediation via estimated glucose disposal rate [eGDR]) and inflammation (8%-9% mediation via C-reactive protein [CRP]). In a complementary fashion, Wang et al[21] reported that inflammatory markers played a significant mediating role in the WWI–mortality association among patients with cardiometabolic syndrome. Collectively, these observations indicate that the prognostic information carried by WWI reflects not merely an anatomical measurement but an active metabolic process.

Along these lines, in the fasting subsample where insulin measurements were available (n = 2149; 202 events), the effect size of WWI was virtually unchanged after additional adjustment for HOMA-IR (unadjusted HR: 1.429; adjusted HR: 1.415). This minimal change indicates that the insulin resistance component measurable by HOMA-IR explains only a small fraction of the WWI signal. HOMA-IR, however, is a crude measure based on fasting insulin and glucose and may not fully capture tissue-level insulin resistance associated with visceral adiposity. Under either interpretation, the conclusion points in the same direction: the prognostic signal of WWI reflects a constellation of multiple metabolic processes that encompasses insulin resistance but also includes additional pathways such as inflammation, ectopic fat deposition, and endothelial dysfunction. The failure to reach statistical significance ($P = .059$) due to the limited number of events (n = 202) does not alter this interpretation; it merely constrains the precision of quantitative inference.

In the subgroup analyses, a statistically significant interaction with eGFR group was detected for WWI alone among the 4 indices ($P = .034$): WWI was a strong mortality predictor in participants with preserved kidney function (eGFR ≥ 60; HR: 1.417; $P < .001$) but lost its association in the eGFR < 60 group (HR: 1.090; $P = .291$). Similarly, Tao et al[22] reported that the association of WWI with cardiovascular disease and mortality in 12 641 individuals with metabolic syndrome was observed only in those with preserved kidney function and could not be detected in the CKD subgroup. Wu et al[23], on the other hand, reported a nonlinear rather than linear association between WWI and all-cause mortality directly in a CKD population (UK Biobank, n = 22 523). No interaction was observed for the other 3 indices (Supplementary Table 3); however, because these indices already exhibited more modest or nonsignificant effect sizes in the fully adjusted model, the lack of interaction reflects low effect sizes insufficient to generate a detectable difference between subgroups rather than consistent prognostic strength.

A possible mechanistic explanation for this interaction may lie in the formulaic structure of WWI. Because WWI normalizes waist circumference by the square root of body weight, any change in weight directly affects the index value. Protein-energy wasting, uremic sarcopenia, and fluid retention, all commonly observed in CKD, may disrupt the relationship

between waist circumference and weight in multiple ways: muscle loss reduces weight while waist circumference may be relatively preserved, and edema increases weight without reflecting visceral fat.[24] Under these conditions, WWI may no longer accurately reflect central adiposity, potentially compromising its measurement validity and contributing to the loss of its prognostic capacity. This sensitivity of WWI's formulaic structure to weight fluctuations may explain why the interaction was detected for WWI alone among the 4 indices. These mechanistic considerations are hypothesis-generating and warrant confirmation in prospective studies.

The WWI–mortality association was consistent with respect to cardiometabolic multimorbidity and sex. WWI remained significant in both the <2 comorbidity (HR: 1.432; $P < .001$) and ≥2 comorbidity (HR: 1.325; $P < .001$) groups, with no interaction by comorbidity level ($P = .479$), indicating that the prognostic value of WWI is preserved even in the presence of a high disease burden. This finding is concordant with the results of Fan et al[25], who showed that elevated WWI independently increased mortality risk in multimorbid older adults in China. With respect to sex, significant associations were observed in both males (HR: 1.453; $P < .001$) and females (HR: 1.243; $P = .006$), with no interaction between sexes ($P = .708$), demonstrating that WWI retains its prognostic value in both sexes. Ding et al[26] also reported that the WWI–mortality association remained consistent across sex subgroups in adults from southern China (n = 12 447; median follow-up 5.6 years). Although the numerically larger effect size in males is concordant with sex differences in visceral fat distribution,[27] this difference did not reach the level of a statistically significant interaction. Considered together, these findings demonstrate that the prognostic value of WWI is consistently maintained across the general population regardless of comorbidity burden and sex.

From a clinical applicability standpoint, the linear association between WWI and mortality offers a notable advantage for risk communication: as the index value increases, risk increases progressively, avoiding the "safe range" misconception created by the J-shaped curve of BMI. This property may facilitate more straightforward communication of adiposity-related risk to patients. However, no validated clinical decision thresholds were proposed in this study, as the cut-points derived from the same dataset are sample-specific and cannot be generalized without external validation. The establishment of population- and sex-specific clinical thresholds through prospective cohorts represents a necessary next step for the integration of WWI into routine risk assessment.

Limitations

This study has a design that compares 4 adiposity indices using z-standardization within a single analytical framework based on a nationally representative cohort. Comprehensive sensitivity analyses and a robust analytic sample that preserved baseline characteristics with minimal attrition of 8.4% (Supplementary Table 1) are among the study's strengths. Several limitations, however, should be acknowledged. Anthropometric measurements in NHANES were obtained at a single time point and do not capture changes in adiposity over the follow-up period; this may have attenuated the true effect size through regression dilution bias. Physical activity and dietary data, based on self-report and 24-hour recall, were not included in the models due to high measurement error, although residual confounding attributable to these variables cannot be excluded. Similarly, socioeconomic variables such as income and education level were not included in the models. Although the clinical covariates in the model may partially reflect the health effects of these factors, residual confounding from socioeconomic variables cannot be disregarded. The median follow-up of 4.83 years is relatively short for capturing long-term dynamics of adiposity–mortality associations, and longer-term relationships may differ. However, the sensitivity analysis conducted in the 2011-2014 subcohort provides a longer follow-up period (~7 years) and yielded results consistent with the primary analysis (HR: 1.398; $P < .001$). Nonetheless, validation of these associations through prospective cohorts with longer follow-up is warranted. NHANES represents the non-institutionalized civilian population of the United States, which limits the generalizability of the findings to different ethnic backgrounds. The observational design precludes causal inference; temporal ordering and the landmark analysis, however, reduce the likelihood of reverse causation. In the definition of cardiovascular mortality, cerebrovascular deaths were not separately coded in the 2015-2018 cycles. The sensitivity analysis conducted in the 2011-2014 subcohort, where complete coding was available, yielded results consistent with the primary analysis that included all cycles; however, this coding difference may have potentially affected cardiovascular mortality estimates.

CONCLUSION

WWI was identified as the most robust independent predictor of all-cause and cardiovascular mortality among the 4 adiposity indices examined. Its monotonically increasing linear association with mortality indicates that the index establishes a clear risk gradient. This association is consistent across sex and levels of cardiometabolic multimorbidity; however, the prognostic capacity of the index is notably attenuated in the eGFR < 60 subgroup. The fact that WWI can be calculated using only waist circumference and body weight renders it a practical clinical tool that does not require expensive imaging or laboratory testing. Nonetheless, the determination of population- and sex-specific clinical decision thresholds and the validation of the index through prospective cohorts with longer follow-up, particularly in patients with impaired kidney function, will clarify the role of WWI in routine risk assessment.

Ethics Committee Approval: This study used publicly available, de-identified data from the National Health and Nutrition Examination Survey (NHANES), which was approved by the NCHS Research Ethics Review Board (Protocol #2011-17 and Protocol #2018-01). Additional institutional review board approval was not required for this secondary analysis.

Informed Consent: Written informed consent was obtained from all NHANES participants by the National Center for Health Statistics during the original data collection. No additional consent was required for this secondary analysis of de-identified data.

Peer-review: Externally peer-reviewed.

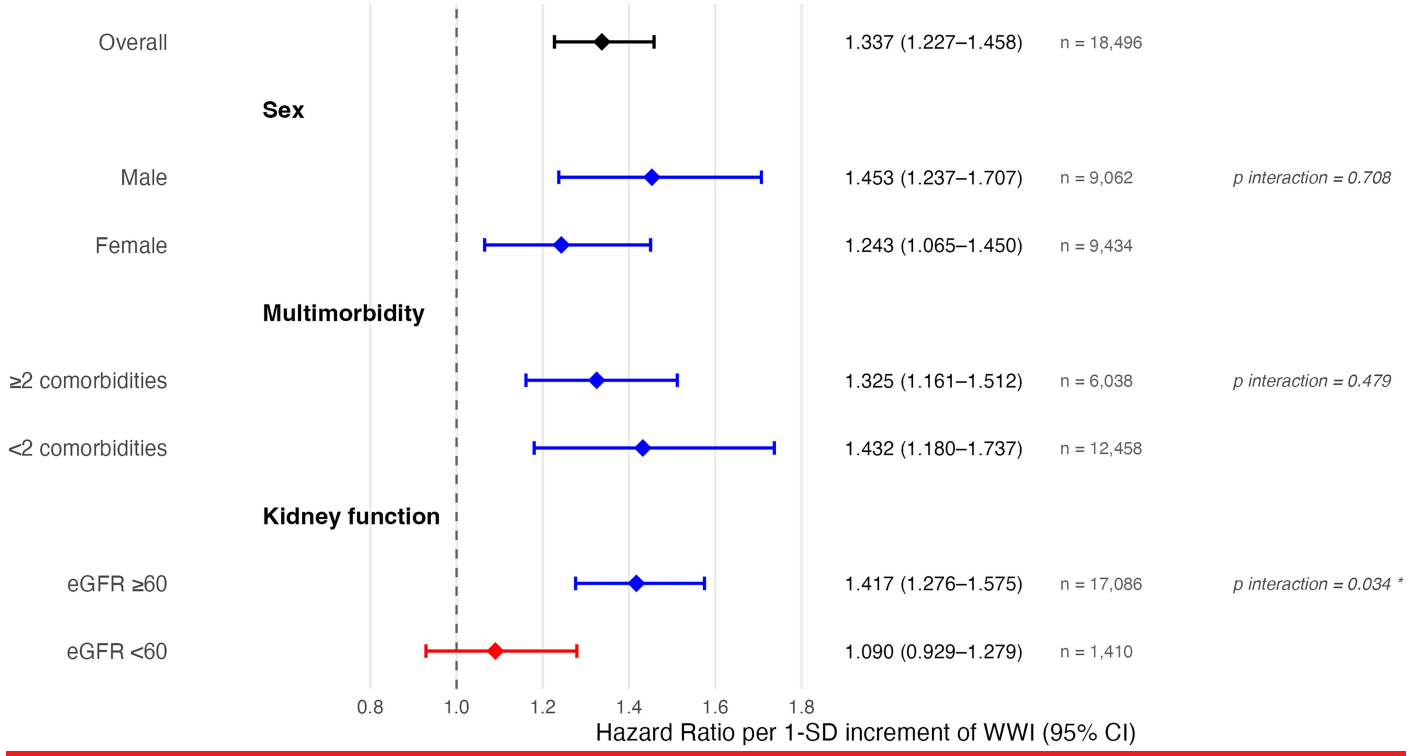
Author Contributions: Concept – E.K., Ö.Ö.; Design – E.K., Ö.Ö.; Supervision – Ş.Ç., Ö.Ö.; Analysis and/or Interpretation – E.K., Ş.Ç.; Literature Search – E.K., Ö.Ö.; Writing – E.K.; Critical Review – Ş.Ç., Ö.Ö.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in underweight and obesity from 1990 to 2022: a pooled analysis of 3663 population-representative studies with 222 million children, adolescents, and adults. *Lancet*. 2024;403(10431):1027-1050. [CrossRef]
2. Global BMI Mortality Collaboration, Di Angelantonio E, Bhupathiraju ShN, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in 4 continents. *Lancet*. 2016;388(10046):776-786. [CrossRef]
3. Tutor AW, Lavie CJ, Kachur S, et al. Updates on obesity and the obesity paradox in cardiovascular diseases. *Prog Cardiovasc Dis*. 2023;78:2-10. [CrossRef]
4. Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2021;143(21):e984-e1010. [CrossRef]
5. Abdi Dezfouli R, Mohammadian Khonsari N, Hosseinpour A, et al.. Waist to height ratio as a simple tool for predicting mortality: a systematic review and meta-analysis. *Int J Obes (Lond)*. 2023;47(12):1286-1301. [CrossRef]
6. Woolcott OO, Bergman RN. Relative fat mass (RFM) as a new estimator of whole-body fat percentage – a cross-sectional study in American adult individuals. *Sci Rep*. 2018;8(1):10980. [CrossRef]
7. Park Y, Kim NH, Kwon TY, et al. A novel adiposity index as an integrated predictor of cardiometabolic disease morbidity and mortality. *Sci Rep*. 2018;8(1):16753. [CrossRef]
8. Cai S, Zhou L, Zhang Y, et al. Association of the weight-adjusted-waist index with risk of all-cause mortality: a 10-year follow-up study. *Front Nutr*. 2022;9:894686. [CrossRef]
9. Zhang TY, Zhang ZM, Wang XN, et al. Relationship between weight-adjusted-waist index and all-cause and cardiovascular mortality in individuals with type 2 diabetes. *Diabetes Obes Metab*. 2024;26(12):5621-5629. [CrossRef]
10. Whelton PK, Carey RM, Aronow WS, et al. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice guidelines. *Hypertension*. 2017;71(6):e13-e115. [CrossRef]
11. Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med*. 2021;385(19):1737-1749. [CrossRef]
12. Han Y, Shi J, Gao P, et al. The weight-adjusted-waist index predicts all-cause and cardiovascular mortality in general US adults. *Clinics (Sao Paulo)*. 2023;78:100248. [CrossRef]
13. Cao T, Xie R, Wang J, et al. Association of weight-adjusted waist index with all-cause mortality among non-Asian individuals: a national population-based cohort study. *Nutr J*. 2024;23(1):62. [CrossRef]
14. Qiu J, Li J, Xu S, et al. Triglyceride glucose-weight-adjusted waist index as a cardiovascular mortality predictor: incremental value beyond the establishment of TyG-related indices. *Cardiovasc Diabetol*. 2025;24(1):306. [CrossRef]
15. Yamashita Y, Baudo M, Sicouri S, et al. Effect of elevated body mass index on outcomes of transcatheter aortic valve replacement for severe aortic stenosis. *Anatol J Cardiol*. 2024;28(12):565-574. [CrossRef]
16. Lv Y, Mao C, Gao X, et al. The obesity paradox is mostly driven by decreased noncardiovascular disease mortality in the oldest old in China: a 20-year prospective cohort study. *Nat Aging*. 2022;2(5):389-396. [CrossRef]
17. Liu W, Yang X, Zhan T, et al. Weight-adjusted waist index is positively and linearly associated with all-cause and cardiovascular mortality in metabolic dysfunction-associated steatotic liver disease: findings from NHANES 1999-2018. *Front Endocrinol (Lausanne)*. 2024;15:1457869. [CrossRef]
18. Yeo YH, Zhu Y, Gao J, et al. Anthropometric measures and mortality risk in individuals with metabolic dysfunction-associated steatotic liver disease (MASLD): a population-based cohort study. *Aliment Pharmacol Ther*. 2025;62(2):168-179. [CrossRef]
19. Shimabukuro M. Cardiac adiposity and global cardiometabolic risk: new concept and clinical implication. *Circ J*. 2009;73(1):27-34. [CrossRef]
20. Geng Y, Gu S, Fan Y, et al. Weight-adjusted-waist index, estimated glucose disposal rate, C-reactive protein, and mortality risks among individuals with type 2 diabetes: 2 prospective cohort studies in China and the United Kingdom. *Am J Clin Nutr*. 2025;122(5):1442-1451. [CrossRef]
21. Wang H, Cai W, Zeng H, et al. Inflammatory markers mediate the association between weight-adjusted waist circumference and mortality in patients with cardiometabolic syndrome. *Sci Rep*. 2025;15(1):8505. [CrossRef]
22. Tao Z, Zuo P, Ma G. Association of weight-adjusted waist index with cardiovascular disease and mortality among metabolic syndrome population. *Sci Rep*. 2024;14(1):18684. [CrossRef]
23. Wu C, Pan C, Liu L, et al. Association between weight-adjusted waist index and risk of mortality and disease progression in participants with chronic kidney disease: a prospective study from the UK Biobank. *Front Nutr*. 2026;13:1646414. [CrossRef]
24. Hanna RM, Ghobry L, Wassef O, et al. A practical approach to nutrition, protein-energy wasting, sarcopenia, and cachexia in patients with chronic kidney disease. *Blood Purif*. 2020;49(1-2):202-211. [CrossRef]
25. Fan B, Ren K, Li L, et al. The joint effect of weight-adjusted waist index and physical activity on all-cause mortality in Chinese elderly patients with multimorbidity: a study based on the CLHLS from 2011 to 2018. *PLOS One*. 2025;20(6):e0325886. [CrossRef]
26. Ding C, Shi Y, Li J, et al. Association of weight-adjusted-waist index with all-cause and cardiovascular mortality in China: a prospective cohort study. *Nutr Metab Cardiovasc Dis*. 2022;32(5):1210-1217. [CrossRef]
27. Palmer BF, Clegg DJ. The sexual dimorphism of obesity. *Mol Cell Endocrinol*. 2015;402:113-119. [CrossRef]



Supplementary Figure 1. Forest plot of subgroup analyses for WWI and all-cause mortality. Subgroups were stratified by sex, cardiometabolic multimorbidity, and kidney function. Hazard ratios are per 1-SD increment of WWI. P values for interaction are displayed on the right.

Supplementary Table 1. Comparison of baseline characteristics between participants included in and excluded from the analytic sample

Variables	Excluded (n = 1,700)	Included (n = 18,496)	p	SMD
Age, years, mean (SD)	48.57 (17.78)	49.26 (17.42)	0.119	0.039
Male sex, n (%)	783 (46.1)	9,062 (49.0)	0.022	0.059
Ethnicity, n (%)			<0.001	0.270
Mexican American	188 (11.1)	2,549 (13.8)		
Non-Hispanic Asian	272 (16.0)	2,320 (12.5)		
Non-Hispanic Black	528 (31.1)	4,043 (21.9)		
Non-Hispanic White	488 (28.7)	6,958 (37.6)		
Other Hispanic	162 (9.5)	1,964 (10.6)		
Other/ Multiracial	62 (3.6)	662 (3.6)		
BMI, kg/m^2, mean (SD)	28.93 (7.36)	29.26 (6.93)	0.062	0.046
Waist circumference, cm, mean (SD)	98.34 (17.34)	99.73 (16.58)	0.001	0.082
Weight, kg, mean (SD)	79.64 (22.51)	81.78 (21.54)	<0.001	0.097
WWI, cm/$\sqrt{}$kg, mean (SD)	11.09 (0.90)	11.09 (0.85)	0.869	0.004
All-cause mortality, n (%)	128 (7.5)	976 (5.3)	<0.001	0.092
CV mortality, n (%)	26 (1.5)	291 (1.6)	0.970	0.004

Data are presented as mean (SD) for continuous variables and n (%) for categorical variables. The eligible cohort (N = 20,196) comprised adults aged ≥20 years with complete anthropometric data and valid mortality follow-up from NHANES 2011–2018. The analytic sample (n = 18,496) further required non-missing values for eGFR, HbA1c, systolic blood pressure, and smoking status. Participants excluded from the analytic sample (n = 1,700) had missing data for at least one of these covariates.
p-values were calculated using the independent samples t-test for continuous variables and the chi-square test for categorical variables. SMD, standardized mean difference; values <0.1 indicate negligible between-group differences.
WWI, weight-adjusted waist index; BMI, body mass index; CV, cardiovascular; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; SMD, standardized mean difference.

Supplementary Table 2. Model diagnostics: proportional hazards assumption and restricted cubic spline nonlinearity tests

Index	Test	Statistic	df	*P*
WWI	Schoenfeld global	26.65	18	.086
	Schoenfeld (WWI term)	1.38	1	.240
BMI	Schoenfeld global	25.94	18	.101
	Schoenfeld (BMI term)	0.09	1	.769
WHtR	Schoenfeld global	26.13	18	.097
	Schoenfeld (WHtR term)	0.12	1	.730
RFM	Schoenfeld global	26.27	18	.094
	Schoenfeld (RFM term)	0.45	1	.503
WWI	RCS nonlinearity	1.35	3	.713
BMI	RCS nonlinearity	16.58	3	.003
WHtR	RCS nonlinearity	7.83	3	.064
RFM	RCS nonlinearity	10.09	3	.028

The proportional hazards assumption was assessed using Schoenfeld residuals (cox.zph). Because cox.zph() does not support survey-weighted Cox objects (svycoxph), standard Cox models with normalized survey weights as case weights were used, an approach consistent with prior NHANES mortality studies. The assumption was satisfied for all four index models (global p > 0.05) and for all exposure terms (P > 0.05).
Nonlinearity was assessed using restricted cubic splines (natural splines, df = 4) in survey-weighted Cox models. The p-value reflects the Rao-Scott likelihood ratio test comparing the nonlinear (spline) model to the linear model. A significant p-value indicates departure from linearity.
WWI, weight-adjusted waist index; BMI, body mass index; WHtR, waist-to-height ratio; RFM, relative fat mass; RCS, restricted cubic spline; PH, proportional hazards.

Supplementary Table 3. Interaction tests between adiposity indices and subgroup variables for all-cause mortality

Index	Interaction term	*P* interaction
WWI	× Sex	.708
	× Multimorbidity	.479
	× eGFR group	**.034**
BMI	× Sex	.736
	× Multimorbidity	.974
	× eGFR group	.677
WHtR	× Sex	.625
	× Multimorbidity	.720
	× eGFR group	.750
RFM	× Sex	.817
	× Multimorbidity	.521
	× eGFR group	.573

P interaction was derived from the likelihood ratio test comparing survey-weighted Cox models (Model 3a) with and without the cross-product interaction term. Bold indicates statistical significance (p < 0.05). Only the WWI × eGFR group interaction reached significance.
Multimorbidity was defined as the co-presence of ≥2 of diabetes, hypertension, and dyslipidemia. eGFR group: ≥60 vs <60 mL/min/1.73 m^2.
WWI, weight-adjusted waist index; BMI, body mass index; WHtR, waist-to-height ratio; RFM, relative fat mass; eGFR, estimated glomerular filtration rate.

Supplementary Table 4. Discriminative ability (AUC) of adiposity indices for all-cause mortality by subgroup

Subgroup	WWI	BMI	WHtR	RFM
Male (n = 9,062)	0.700 (0.678–0.722)	0.522 (0.497–0.547)	0.584 (0.560–0.608)	0.584 (0.560–0.608)
Female (n = 9,434)	0.669 (0.643–0.695)	0.511 (0.482–0.540)	0.566 (0.539–0.594)	0.566 (0.539–0.594)
MM ≥2 (n = 6,038)	0.582 (0.559–0.606)	0.587 (0.562–0.612)	0.528 (0.503–0.553)	0.548 (0.524–0.571)
MM <2 (n = 12,458)	0.655 (0.626–0.684)	0.529 (0.499–0.559)	0.556 (0.526–0.586)	0.533 (0.504–0.562)
eGFR ≥60 (n = 17,086)	0.658 (0.637–0.679)	0.521 (0.498–0.543)	0.560 (0.538–0.582)	0.516 (0.494–0.538)
eGFR <60 (n = 1,410)	0.541 (0.505–0.576)	0.563 (0.526–0.601)	0.527 (0.490–0.564)	0.541 (0.505–0.577)

Area under the receiver operating characteristic curve (AUC) with 95% confidence intervals. Higher AUC indicates better discriminative ability for all-cause mortality.
AUC values represent unadjusted, single-predictor discrimination for binary mortality status and do not account for survival time or covariate adjustment. These values are intended for relative comparison among indices within each subgroup rather than as measures of overall model performance. The relatively low AUC values reflect the limited discriminative ability of any single anthropometric index for mortality prediction in isolation.
MM, multimorbidity (≥2 of diabetes, hypertension, dyslipidemia); eGFR, estimated glomerular filtration rate (mL/min/1.73 m^2); WWI, weight-adjusted waist index; BMI, body mass index; WHtR, waist-to-height ratio; RFM, relative fat mass.

Supplementary Table 5. Multicollinearity assessment and correlation matrix of adiposity indices

	Panel A: Generalized variance inflation factors (Model 3b)		
Variables	**GVIF**	**df**	**GVIF^(1/2df)**
WWI (z-score)	1.479	1	1.216
BMI (z-score)	1.422	1	1.192
Sex	1.143	1	1.069
Ethnicity	1.261	5	1.023
Smoking status	1.126	2	1.030
Diabetes	1.776	1	1.333
Hypertension	1.656	1	1.287
Dyslipidemia	1.508	1	1.228
eGFR	1.096	1	1.047
SBP	1.185	1	1.089
HbA1c	1.709	1	1.307

	Panel B: Pearson correlation matrix					
	WWI	**BMI**	**Waist**	**WHtR**	**RFM**	**Age**
WWI	1.000	0.476	0.649	0.790	0.678	0.473
BMI	0.476	1.000	0.907	0.913	0.605	0.028
Waist circumference	0.649	0.907	1.000	0.932	0.519	0.180
WHtR	0.790	0.913	0.932	1.000	0.729	0.233
RFM	0.678	0.605	0.519	0.729	1.000	0.171
Age	0.473	0.028	0.180	0.233	0.171	1.000

GVIF, generalized variance inflation factor. GVIF^(1/2df) is the scale-adjusted metric comparable to the square root of classical VIF. Values <2 indicate acceptable collinearity. Model 3b includes both WWI and BMI as mutual adjustment.
Pearson correlation coefficients among adiposity indices, waist circumference, and age. n = 18,496.
Waist circumference and age are included to illustrate the structural relationship among indices; waist circumference is a component of WWI, and age was used as a stratification variable rather than a covariate.

Supplementary Table 6. Time-dependent discriminative ability of adiposity indices for all-cause mortality				
	WWI	**BMI**	**WHtR**	**RFM**
Harrell's C-index (95% CI)	**0.686 (0.653–0.719)**	**0.675 (0.641–0.708)**	**0.676 (0.643–0.710)**	**0.675 (0.642–0.709)**
Time-dependent AUC				
1-year	0.711	0.708	0.703	0.704
3-year	0.681	0.679	0.676	0.676
5-year	0.678	0.671	0.670	0.670

Harrell's C-index was derived from fully adjusted Cox proportional hazards models (Model 3a: age stratification + sex + ethnicity + smoking + diabetes + hypertension + dyslipidemia + eGFR + SBP + HbA1c). Time-dependent AUC was calculated using inverse probability of censoring weighting (IPCW) based on the linear predictors of the same Cox models at 1-, 3-, and 5-year time points. WWI, weight-adjusted waist index; BMI, body mass index; WHtR, waist-to-height ratio; RFM, relative fat mass; AUC, area under the receiver operating characteristic curve; CI, confidence interval; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.