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Body roundness index and mortality risk in patients with chronic kidney disease: moving beyond the obesity paradox

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ABSTRACT

Background. Body roundness index (BRI), an emerging anthropometric measure, has been shown to outperform body mass index (BMI) in predicting mortality risk in the general population. However, its prognostic value among patients with chronic kidney disease (CKD), where the obesity paradox may exist, remains unknown.

Methods. This observational study utilized data from the National Health and Nutrition Examination Survey. BRI was calculated using waist circumference (WC) and height, whereas BMI was calculated using body weight and height. Restricted cubic splines (RCSs) were applied to determine optimal cut-off points of BRI for all-cause and cardiovascular mortality in patients with CKD. Associations were examined using Cox proportional hazards models adjusted for potential confounders.

Results. Over a median follow-up of 6.6 years, 6240 patients with CKD (mean age 63 years, 43% men) were included, with 1922 all-cause and 715 cardiovascular deaths recorded. RCSs demonstrated J-shaped associations between BRI with mortality. A BRI >10 was associated with a significantly increased risk of all-cause {adjusted hazard ratio [aHR] 1.82 [95% confidence interval (CI) 1.34–2.47]} and cardiovascular mortality [aHR 2.15 (95% CI 1.27–3.62)] compared with the reference of 5.9–6.8 and 5.9–6.5, respectively, with dose-response trends (P for trend < .05). A BMI >30 was paradoxically associated with 44% and 40% lower risks of all-cause and cardiovascular mortality compared with the reference of 18.5–25, respectively. A WC >125 was associated with an increased risk of all-cause mortality [aHR 2.17 (95% CI 1.47–3.18)] but not with cardiovascular mortality [aHR 1.83 (95% CI 0.97–3.45)] compared with the reference of 95–105 cm. The associations between BRI >10 and mortality risks were particularly pronounced among younger adults <65 years of age or individuals with elevated albuminuria (P for interaction < .05).

Conclusions. Higher BRI was independently associated with increased all-cause and cardiovascular mortality risk among patients with CKD, offering greater prognostic value for risk stratification than BMI or WC.

Keywords: body mass index, body roundness index, cardiovascular event, obesity, waist circumference

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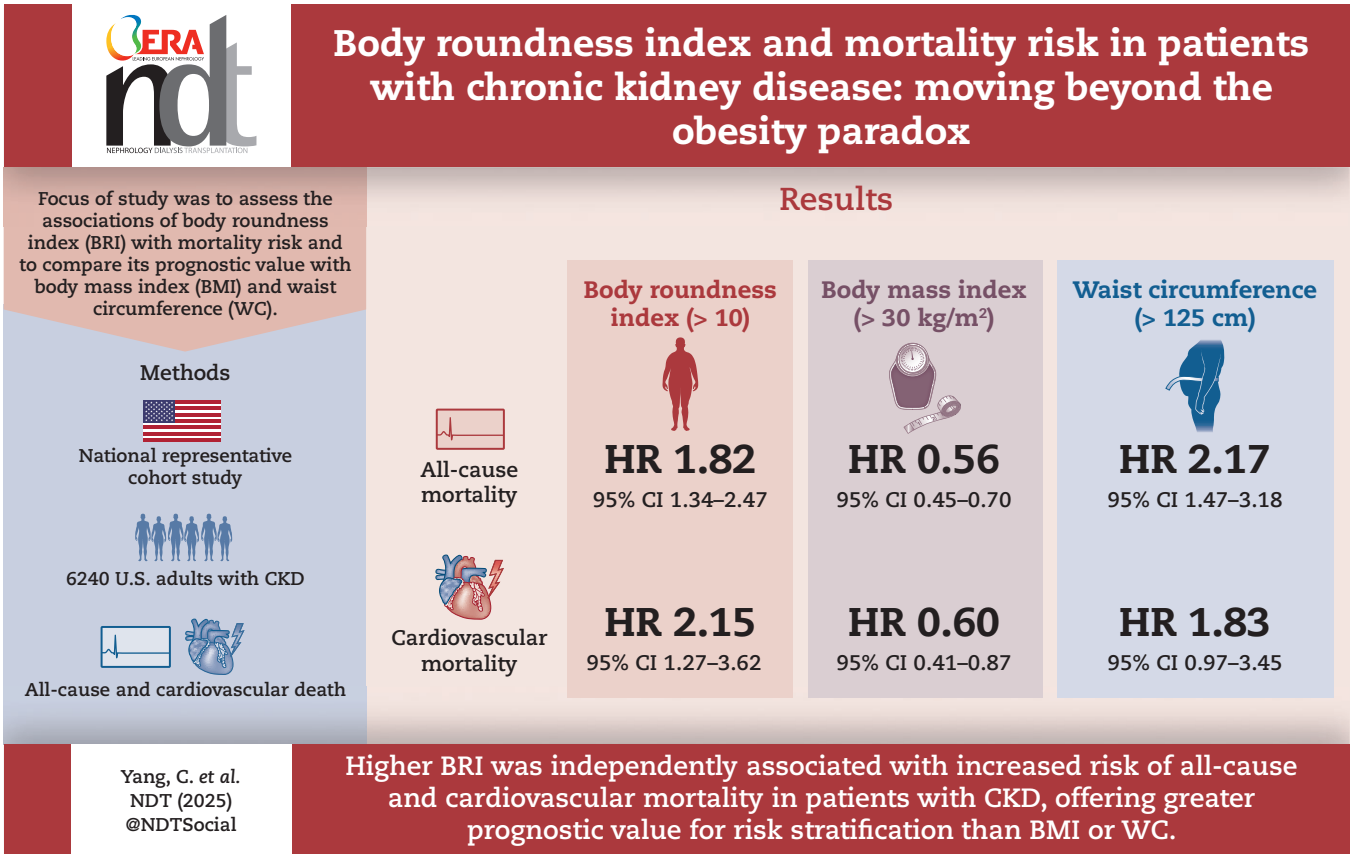
GRAPHICAL ABSTRACT



KEY LEARNING POINTS

What was known:

- Body roundness index (BRI), an emerging anthropometric measure, has been shown to outperform body mass index (BMI) in predicting mortality risk in the general population.
- In chronic kidney disease (CKD), the prognostic value of BRI remains unclear, particularly given the presence of the 'obesity paradox', where higher BMI may appear protective.

This study adds:

- In this prospective cohort study of 6240 adults with CKD, a J-shaped association was observed between BRI and mortality.
- Higher BRI and waist circumference (WC) were associated with an increased risk of all-cause mortality in this population, whereas higher BMI was paradoxically associated with lower all-cause mortality risk.
- Only a higher BRI was associated with an increased risk of cardiovascular mortality, while BMI and WC were not.
- Additional adjustment for body weight (in BRI and WC models) and WC (in BMI models) further strengthened the observed associations.

Potential impact:

- These findings underscore the clinical importance of recognizing central obesity as a critical risk factor in patients with CKD.
- BRI may offer greater value for mortality risk stratification than BMI and WC in patients with CKD, particularly in younger adults or those with albuminuria. This suggests the potential utility of early BRI-based screening and intervention strategies.

INTRODUCTION

Obesity, a chronic complex disease defined by excessive fat deposits that can impair health, has become a global epidemic, affecting approximately one in eight adults worldwide [1]. Traditionally, obesity is assessed by body mass index (BMI), calculated as weight (in kg) divided by height (in m^2) [2, 3]. Higher BMI has been significantly associated with an increased risk of all-cause mortality in the general population [4]. Obesity, defined by BMI, is also prevalent among patients with chronic kidney disease (CKD) [5, 6]. However, higher BMI has been paradoxically associated with better survival observed in patients with both pre-dialysis and dialysis-dependent CKD [7–9]. This obesity paradox in CKD may be attributed to BMI's inability to differentiate between fat distribution, lean muscle mass and fat mass [10]. A recent Lancet Commission also

highlighted concerns that the current BMI-based measures of obesity can both underestimate and overestimate adiposity and provide inadequate information [11]. These reports underscore the need for alternative anthropometric indices that better capture the relationship between body composition and health risks.

Body roundness index (BRI) was developed as a novel anthropometric measure. It models the human body as an ellipse, where height represents the major axis and waist circumference (WC) represents the minor axis [12, 13]. BRI is calculated based on the eccentricity of this ellipse, providing a geometric approximation of body roundness and central adiposity through human body modelling. Unlike BMI, BRI specifically reflects central adiposity, which is more strongly associated with metabolic disturbances and cardiovascular risk—key determinants of mortality [12]. WC is also widely used to capture central adiposity, but it cannot fully account for body shape and proportionality [14]. Emerging evidence suggests that BRI outperforms other anthropometric indicators, such as BMI and waist:hip ratio, in estimating the risk of incident cardiometabolic disease [15, 16] and mortality [12, 17] in the general population. Furthermore, longitudinal studies have shown that BRI trajectories are significantly associated with increased risks of all-cause mortality and cardiovascular mortality [18, 19]. Nevertheless, despite its potential advantages, the prognostic value and optimal cut-off of BRI in patients with CKD remain unexplored.

Therefore, this study aims to determine the optimal cut-off of BRI in association with all-cause and cardiovascular mortality risks and to assess the associations of BRI, BMI and WC with mortality risk in patients with CKD using data from a nationally representative US population.

MATERIALS AND METHODS

Study design and population

This observational study analysed the data from the National Health and Nutrition Examination Survey (NHANES; 2003–2018). NHANES is a complex, multistage and probabilistic sampling design survey conducted annually and released biannually by the National Center for Health Statistics (NCHS) [20]. More details about NHANES survey procedures are available at https://www.cdc.gov/nchs/index.htm. The NHANES protocol was approved by the NCHS ethics review board and written informed consent was obtained from all participants. This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline [21].

We included individuals if they met the following criteria: age ≥20 years and diagnosed as CKD [defined as an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 and/or a urinary albumin:creatinine ratio (UACR) ≥30 mg/g] [22–25]. eGFR was calculated based on the 2021 Chronic Kidney Disease Epidemiology Collaboration equation [26]. We used the NHANES-recommended calibrations for serum creatinine correction across time periods if needed. We classified CKD stages using the cut-offs of eGFR recommended by the Kidney Disease: Improving Global Outcomes (KDIGO) initiative (Supplementary Table S1) [27].

Participants were excluded if they met any of the following criteria: an eGFR <15 ml/min/1.73 m^2 (stage 5 CKD) due to a small sample size and the inability to confirm whether they were on maintenance dialysis and incomplete data for assessing CKD, BRI, BMI, WC and outcome.

Data collection

Exposure

The primary exposure of interest was BRI, whereas BMI and WC were assessed as secondary exposures. BRI was calculated as $364.2 - 365.5 \times \sqrt{(1 - [\text{WC (in cm)}/2\pi]^2/[0.5 \times \text{height (in cm)}]^2)}$ [12, 13]. BMI was calculated as body weight (in kg)/height (in m^2) [2]. WC, body weight and height were measured using standard anthropometric procedures at baseline at mobile examination centres by trained health professionals. Height and WC were measured to the nearest 0.1 cm, while weight was measured to the nearest 0.1 kg, with participants in light clothes and without shoes. BMI levels were categorized into five groups according to the guideline from the Centers for Disease Control and Prevention: <18.5 kg/m^2 (underweight), 18.5–24.9 kg/m^2 (normal weight), 25.0–29.9 kg/m^2 (overweight), ≥30.0 kg/m^2 (obesity) and ≥40.0 kg/m^2 (severe obesity) [28].

Outcome of interest

The outcome of interest was all-cause and cardiovascular mortality. We used the NHANES Public-Use Linked Mortality File through 31 December 2019 (https://www.cdc.gov/nchs/data-linkage/mortality-public.htm), which linked to National Death Index (NDI) data with a probabilistic matching algorithm to determine mortality status. The NDI is an NCHS-centralized database of all deaths in the USA. The underlying cause of death was coded according to the International Classification of Diseases, Tenth Revision (ICD-10). Cardiovascular mortality was defined as death due to heart diseases (codes I00–I09, I11, I13, I20–I51) and stroke (codes I60–I69).

Covariates

Predefined clinically relevant covariates were assessed at baseline and included demographic and lifestyle details (age, sex, race/ethnicity, education level, marital status, employment status, levels of physical activity, alcohol intake and smoking status) and self-reported histories of comorbid conditions (hypertension, diabetes, coronary heart disease and cancer), collected via standardized questionnaires; and laboratory tests (eGFR, UACR, haemoglobin, serum albumin, high-density lipoprotein cholesterol (HDL-C) and total cholesterol) (Supplementary Table S1).

Statistical analysis

Given the complex sampling design of the NHANES, all analyses in the present study incorporated sample weights to provide nationally representative estimates for non-institutionalized civilian US residents. We summarized the baseline characteristics across the quarter of BRI using analysis of Kruskal–Wallis H for continuous variables and chi-squared tests for categorical variables.

Due to the lack of a reference range in patients with CKD, restricted cubic spline (RCS) curves with 4 knots set at the 5th, 35th, 65th and 95th percentiles were conducted to test non-linearity and determine optimal range for BRI and WC when estimating the risk of mortality. The crossover points (null effect points) were defined as the BRI/WC values where the hazard ratio (HR) is 1. BRI and WC were converted into categorized variables based on the crossover points identified by RCSs [12]. The association of BRI, BMI and WC, in both continuous and categorized forms, with all-cause and cardiovascular mortality was assessed using Cox

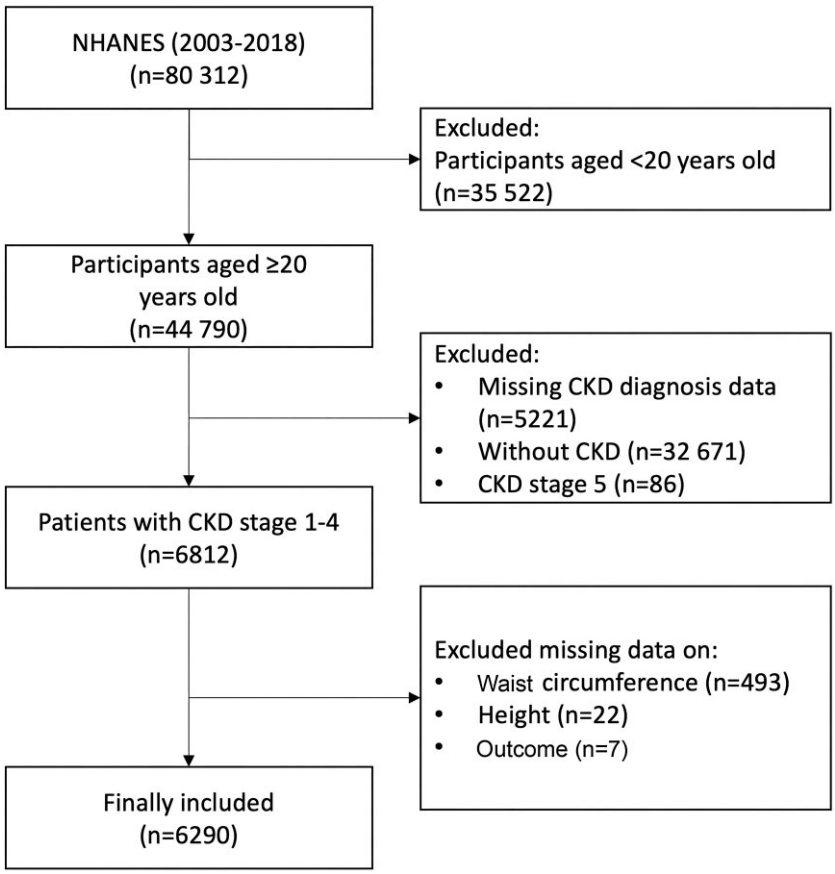


Figure 1: Flow chart of participant selection.

proportional hazards regression, presented as HRs with 95% confidence intervals (CIs). Patients were followed from examination date (baseline) until the occurrence of death or the end of follow-up (31 December 2019).

Subgroup analyses were performed to estimate the association of BRI, BMI and WC with mortality across prespecified variables, including sex (male versus female), age (<65 years versus ≥65 years), hypertension (yes/no), diabetes (yes/no), eGFR (≥45 versus 15–44 ml/min/1.73 m^2) and UACR (<30 versus ≥30 mg/g). Model 1 adjusted for age and sex. Model 2 further adjusted for race/ethnicity, education level, marital status, employment status, alcohol intake, smoking status, physical activity level, presence of hypertension, diabetes, coronary heart disease, cancer, eGFR, UACR, haemoglobin, serum albumin, total cholesterol and HDL-C. Models 1 and 2 were applied identically when assessing the associations of all indices with mortality. In model 3, body weight was further adjusted when assessing the association of BRI and WC with mortality, while WC was further adjusted when assessing the association of BMI with mortality [29]. Variance inflation factors (VIFs) were examined to evaluate potential multicollinearity in model 3. A VIF value >5 was considered indicative of moderate to high multicollinearity [30]. The pattern of data missingness was evaluated (Supplementary Fig. S1). Multiple imputations by chained equations were applied for missing data regarding covariates to avoid potential bias [31]. We also conducted a sensitivity analysis of cardiovascular mortality using a competing risk model (i.e. Fine–Gray models), with non-cardiovascular death handled as a competing outcome. A two-sided *P*-value <.05 was considered statistically significant. All statistical analyses were conducted using R (version 4.4.3; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

A total of 80 312 participants were drawn from the NHANES database (2003–2018). Among these, 6290 adult patients with stage 1–4 CKD were included (Fig. 1), representing an estimated 25.4 million individuals in the US civilian population. The median age of participants was 63 years [interquartile range (IQR) 47–75] and 43% were men. The median eGFR was 73.5 ml/min/1.73 m^2 and the median UACR was 43.9 mg/g, with proportions of 31.4%, 24.3%, 41% and 3.3% for CKD stages 1–4, respectively. The distribution of participants across GFR and albuminuria categories was shown in a KDIGO heatmap-style figure, with the majority of individuals falling into moderately increased and high-risk categories (Supplementary Fig. S2). More than two-thirds of participants were non-Hispanic white and unemployed. A total of 64% and 17% of patients were current alcohol drinkers and current smokers, respectively. Hypertension was the most prevalent comorbidity (59%), followed by diabetes mellitus (27%). The median BRI, BMI and WC of participants were 5.91 (IQR 4.56–7.46), 29.0 (IQR 24.9–34.1) and 102.4 (IQR 91.5–114.2), respectively. Compared with participants in the lowest quartile of BRI, those in the highest quartile were more likely to be older, female, unemployed, have a higher BMI, have a history of hypertension, have diabetes mellitus, have coronary heart disease, have a lower eGFR and have a higher UACR (Table 1).

Table 1: Baseline characteristics of the study population stratified by quartiles of the BRI.

Characteristics	Q1 [1.07–4.56)	Q2 [4.56–5.91)	Q3 [5.91–6.20)	Q4 (≥6.20)
Age (years), median (IQR)	57 (38–73)	67 (50–78)	66 (52–77)	62 (48–72)
Male, *n* (%)	761 (38)	856 (50)	765 (48)	612 (38)
Race/ethnicity, *n* (%)				
Mexican American	132 (4.6)	229 (8.4)	263 (8.8)	269 (8.7)
Non-Hispanic Black	433 (14)	380 (14)	361 (14)	407 (15)
Non-Hispanic White	729 (69)	694 (66)	710 (66)	700 (66)
Other Hispanic	82 (3.4)	128 (5.6)	138 (5.5)	120 (4.7)
Other Race	197 (9.7)	141 (6.6)	100 (5.6)	77 (5.8)
Education level, *n* (%)				
Less than high school	436 (19)	494 (22)	570 (27)	560 (25)
High school graduate/GED	368 (24)	408 (28)	343 (24)	398 (28)
Some college or AA degree	431 (28)	387 (27)	410 (29)	444 (34)
College graduate or above	338 (28)	283 (23)	249 (20)	171 (13)
Marital status, *n* (%)				
Never married	233 (16)	127 (8.2)	139 (8.6)	169 (11)
Married	841 (57)	906 (61)	853 (59)	815 (56)
Separated	499 (27)	539 (31)	580 (33)	589 (33)
Employed, *n* (%)	591 (45)	506 (38)	467 (37)	481 (38)
Alcohol drinking, *n* (%)	1051 (71)	976 (64)	916 (61)	880 (59)
Smoking status, *n* (%)				
Never smoker	779 (54)	806 (49)	799 (50)	736 (47)
Former smoker	409 (24)	505 (33)	558 (37)	588 (37)
Current smoker	385 (22)	261 (17)	215 (14)	249 (16)
BMI (kg/m^2), median (IQR)	22.7 (20.8–24.8)	27.5 (25.8–29.4)	31.1 (29.1–33.4)	38.2 (35.0–42.2)
<18.5	109 (6.8)	0 (0)	0 (0)	0 (0)
18.5–24.9	1104 (70)	298 (16)	22 (1.2)	0 (0)
25–29.9	346 (22)	1013 (64)	577 (34)	53 (2.5)
≥30	14 (1.0)	261 (20)	973 (65)	1520 (98)
Waist circumference (cm), median (IQR)	84.1 (77.8–90.2)	98.5 (94.0–103.3)	107.6 (103.0–113.0)	122.6 (115.5–131.8)
Hypertension, *n* (%)	732 (40)	978 (59)	1068 (65)	1165 (74)
Diabetes mellitus, *n* (%)	252 (11)	419 (23)	526 (29)	760 (46)
Coronary heart disease, *n* (%)	118 (6.8)	191 (12)	163 (9.8)	197 (13)
Cancer, *n* (%)	251 (16)	284 (19)	274 (19)	214 (14)
eGFR (ml/min/1.73 m^2), median (IQR)	82.9 (56.6–106.2)	66.3 (53.3–95.5)	67.1 (52.5–97.4)	75.6 (53.5–100.5)
≥90	599 (43)	410 (30)	447 (31)	519 (38)
60–89	374 (22)	386 (23)	399 (24)	369 (24)
45–59	443 (28)	521 (33)	479 (31)	417 (25)
15–44	157 (7.2)	255 (13)	247 (14)	268 (14)
UACR (mg/g), median (IQR)	42.6 (20.0–80.6)	41.9 (13.8–96.9)	43.9 (14.0–91.0)	47.4 (29.2–127.4)
<30	440 (28)	498 (32)	486 (31)	414 (25)
30–300	985 (64)	902 (59)	906 (58)	933 (61)
>300	148 (7.9)	172 (8.7)	180 (10)	226 (13)

GED: general educational development, AA: associate of arts degree.

BRI and all-cause and cardiovascular mortality

During a median follow-up period of 6.6 years (IQR 3.5–10.4), a total of 1922 deaths (30.6% of patients) occurred, including 715 (37.2% of all-cause deaths) from cardiovascular diseases. The RCS analysis revealed a U-shaped risk trajectory between BRI and all-cause mortality after adjustment for potential confounders in model 2 (P for non-linearity < .001) (Fig. 2). Interestingly, this association transformed into a J-shaped relationship after further adjustment for body weight (P for non-linearity < .001) (Fig. 2). All VIFs in the fully adjustment model were <5, indicating no significant multicollinearity. A similar pattern was also observed in the relationship between BRI and cardiovascular mortality (Supplementary Fig. S3). Within the range where BRI was greater than the higher crossover point, each unit increase in BRI was associated with a higher risk of all-cause mortality [HR 1.16 (95% CI 1.07–1.26)] and cardiovascular mortality [HR 1.15 (95% CI 1.01–1.30)] in the fully adjusted model.

When BRI was treated as a categorized variable, the reference group for BRI was defined as 5.9–6.8 for all-cause mortality and 5.9–6.5 for cardiovascular mortality, based on the crossover points observed in the RCS curve. Model 2 indicated that patients with a BRI >10 had a 41% increased risk of all-cause mortality. However, after additional adjustment for weight, this risk nearly doubled, with BRI >10 associated with an 82% increased risk of all-cause mortality. A similar pattern was also observed in the relationship between BRI and cardiovascular mortality (Table 2).

This association remained robust and consistent across most subgroup analyses, including age, sex, hypertension, diabetes, eGFR and UACR (Table 3). Interactions were observed between a BRI >10 and key subgroups. Specifically, the association between higher BRI and mortality was notably stronger among younger individuals (<65 years) or those with elevated albuminuria (UACR >30 mg/g) (P for interaction < .05). In sensitivity analyses for cardiovascular death using Fine–Gray models accounting for

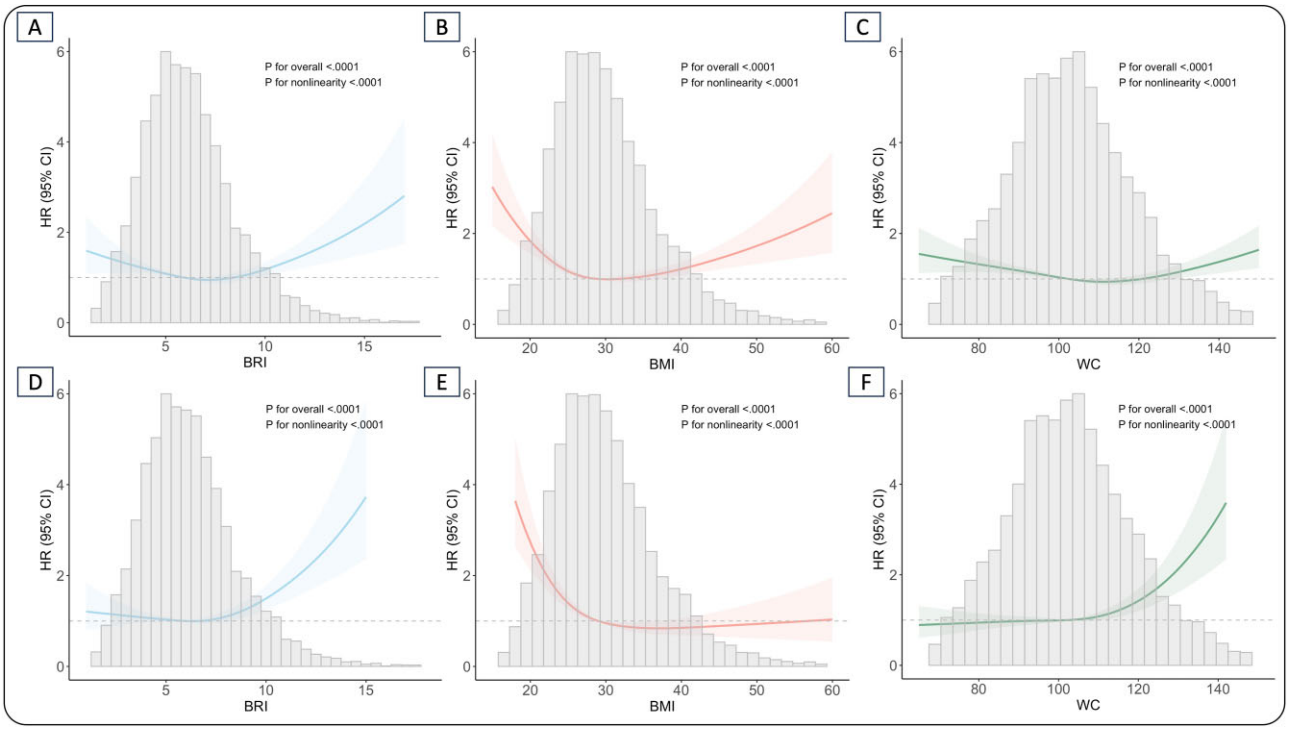


Figure 2: RCS plots depicting associations of BRI, BMI and WC with all-cause mortality in patients with CKD. All models were adjusted for age, sex, race/ethnicity, education level, marital status, employment status, alcohol intake, smoking status, physical activity level, presence of hypertension, diabetes, coronary heart disease, cancer, eGFR, UACR, haemoglobin, serum albumin, total cholesterol and HDL-C. Figures D and F were further adjusted for body weight; Figure E was further adjusted for waist circumference.

non-cardiovascular death as a competing risk, the results were consistent with the main findings (Supplementary Table S2).

BMI and WC and all-cause and cardiovascular mortality

Similarly, RCS analyses demonstrated an approximate U-shaped relationship between BMI and WC, and all-cause and cardiovascular mortality in model 2 (Fig. 2, Supplementary Fig. S3). However, after further adjustment for WC, the right arms of the BMI curves flattened and became nearly parallel to the x-axis (*P* for non-linearity < .001). In contrast, for WC, the right arms of the curves became markedly steeper after adjustment for weight (*P* for non-linearity < .001). When BMI was categorized, BMI >30 was associated with a 25% lower risk of all-cause mortality in model 2 and with a 44% lower risk of all-cause mortality after further adjustment for WC. A similar pattern was also observed for cardiovascular mortality (Table 2). In the fully adjusted model, WC >125 was associated with a significantly increased risk of all-cause mortality [HR 2.17 (95% CI 1.47–3.18)] but not with cardiovascular mortality [HR 1.83 (95% CI 0.97–3.45)] compared with the reference of 95–105.

These associations remained robust and consistent across most subgroup analyses (Table 3). Sensitivity analyses using Fine–Gray models, accounting for non-cardiovascular death as a competing risk, yielded results consistent with the main findings. However, the association between higher BMI and cardiovascular mortality was not statistically significant (Supplementary Table S2).

DISCUSSION

In this nationally representative cohort study, we demonstrated that higher BRI was independently associated with an increased risk of both all-cause and cardiovascular mortality among patients with non-dialysis CKD. Higher BMI was paradoxically associated with a lower risk of mortality, whereas WC demonstrated prognostic value only for all-cause mortality in this population. Notably, the association between higher BRI and mortality was significantly stronger among younger individuals or those with elevated albuminuria. These findings underscore the importance of prioritizing early-life clinical screening and targeted interventions for elevated BRI in this high-risk population, supporting its potential role as a valuable public health tool in CKD management.

Obesity, particularly abdominal obesity, is an established risk factor for cardiovascular events and mortality in both the general population [32] and patients with CKD [33]. Growing evidence supports the notion that visceral fat poses a greater threat to health than subcutaneous fat [34]. For practical reasons, there remains a need for an effective anthropometric proxy that can reliably reflect visceral adiposity in the clinical setting. Prior findings demonstrated that higher BRI was associated with elevated risks of all-cause and cardiovascular mortality in the general population [12, 17, 35] as well as in patients with metabolic syndrome [36]. Our findings extend the evidence to patients with CKD—a population already at high baseline risk for adverse outcomes. This association became even stronger after further adjustment for body weight. This observation highlights the importance of considering both WC and weight simultaneously

Table 2: Association of BRI, BMI and WC with all-cause and cardiovascular mortality in patients with CKD.

Variable	Hazard ratio (95% CI)					*P* for trend
BRI						
All-cause mortality	**≤5.9**	**(5.9–6.8]**	**(6.8–8.5]**	**(8.5–10.0]**	**>10.0**	
Events/cases, *n*/*N*	988/3136	299/972	375/1231	146/526	114/425	
Model 1	1.07 (0.92–1.24)	Ref	1.09 (0.91–1.30)	**1.41 (1.12–1.78)**	**1.85 (1.39–2.45)**	
Model 2	1.13 (0.96–1.33)	Ref	0.96 (0.80–1.14)	1.03 (0.80–1.32)	**1.41 (1.05–1.88)**	
Model 3	1.05 (0.88–1.24)	Ref	1.02 (0.85–1.22)	1.21 (0.93–1.57)	**1.82 (1.34–2.47)**	**0.02**
Cardiovascular mortality	**≤5.9**	**(5.9–6.5]**	**(6.5–8.5]**	**(8.5, 10.0]**	**>10.0**	
Events/cases, *n*/*N*	365/3136	77/661	163/1542	58/526	52/425	
Model 1	1.02 (0.78–1.34)	Ref	1.01 (0.73–1.41)	**1.59 (1.04–2.43)**	**2.23 (1.41–3.51)**	
Model 2	1.10 (0.83–1.47)	Ref	0.92 (0.66–1.28)	1.16 (0.75–1.79)	**1.66 (1.03–2.70)**	
Model 3	1.03 (0.77–1.38)	Ref	0.97 (0.69–1.37)	1.36 (0.82–2.25)	**2.15 (1.27–3.62)**	**0.04**
BMI						
All-cause mortality	**<18.5**	**[18.5–25)**	**[25–30)**	**≥30**	**≥40**	
Events/cases, *n*/*N*	41/109	525/1424	640/1989	716/2768	114/553	
Model 1	**1.75 (1.14–2.70)**	Ref	**0.77 (0.67–0.90)**	0.95 (0.83–1.10)	0.77 (0.47, 1.26)	
Model 2	**1.72 (1.06–2.79)**	Ref	**0.74 (0.64–0.87)**	**0.75 (0.65–0.86)**	**0.52 (0.30–0.92)**	
Model 3	**2.01 (1.24–3.26)**	Ref	**0.66 (0.55–0.79)**	**0.56 (0.45–0.70)**	**0.37 (0.19–0.72)**	**<0.001**
Cardiovascular mortality	**<18.5**	**[18.5–25)**	**[25–30)**	**≥30**	**≥40**	
Events/cases, *n*/*N*	11/109	191/1424	231/1989	282/2768	49/553	
Model 1	1.28 (0.63–2.59)	Ref	**0.69 (0.52–0.91)**	1.00 (0.80–1.25)	**1.71 (1.13–2.59)**	
Model 2	1.31 (0.63–2.72)	Ref	**0.66 (0.49–0.88)**	**0.77 (0.59–0.99)**	1.11 (0.70–1.76)	
Model 3	1.51 (0.71–3.21)	Ref	**0.59 (0.43–0.81)**	**0.60 (0.41–0.87)**	0.93 (0.49–1.79)	0.35
Waist circumference						
All-cause mortality	**≤95**	**(95–105]**	**(105–115]**	**(115–125]**	**>125**	
Events/cases, *n*/*N*	596/1990	509/1579	421/1337	227/784	169/600	
Model 1	1.12 (0.96–1.32)	Ref	1.07 (0.92–1.25)	1.08 (0.89–1.30)	**1.93 (1.53–2.44)**	
Model 2	1.22 (1.06–1.41)	Ref	0.97 (0.84–1.12)	0.96 (0.80–1.15)	**1.32 (1.02–1.71)**	
Model 3	1.06 (0.90–1.24)	Ref	1.10 (0.92–1.30)	1.24 (0.95–1.60)	**2.17 (1.47–3.18)**	**0.002**
Cardiovascular mortality	**≤95**	**(95–105]**	**(105–115]**	**(115–125]**	**>125**	
Events/cases, *n*/*N*	220/1990	195/1579	151/1337	86/784	63/600	
Model 1	1.13 (0.90–1.41)	Ref	1.02 (0.79–1.32)	1.12 (0.82–1.55)	**2.05 (1.43–2.92)**	
Model 2	1.26 (1.00–1.59)	Ref	0.93 (0.72–1.19)	1.00 (0.73–1.35)	1.41 (0.95–2.08)	
Model 3	1.16 (0.88–1.54)	Ref	0.99 (0.75–1.30)	1.14 (0.76–1.71)	1.83 (0.97–3.45)	0.21

P-values <.05 are in bold.
Model 1 adjusted for age and sex. Model 2: model 1 + race/ethnicity, education level, marital status, employment status, alcohol intake, smoking status, physical activity level, presence of hypertension, diabetes, coronary heart disease, cancer, eGFR, UACR, haemoglobin, serum albumin, total cholesterol and HDL-C. Model 3: model 2 + body weight when assessing the association of BRI with mortality; model 2 + WC when assessing the association of BMI with mortality.
We selected the point at which the HR was 1 as the crossover point (null effect point) and BRI and WC were converted into a categorized variable based on the crossover points identified by the RCS curve. BMI levels were categorized into five groups: <18.5 kg/m^2 (underweight), 18.5–24.9 kg/m^2 (normal weight), 25.0–29.9 kg/m^2 (overweight), ≥30.0 kg/m^2 (obesity) and ≥40.0 kg/m^2 (severe obesity) according to the guideline from the Centers for Disease Control and Prevention.

when evaluating mortality risk in patients with CKD, aligning with the recent Lancet Commission [11].

Several mechanisms might explain the observed association. First, BRI may serve as a surrogate marker of visceral adiposity, which has been strongly linked to systemic inflammation, insulin resistance and dyslipidaemia—even among individuals with body weight within the normal range [37, 38]. In patients with CKD, these pathophysiological disturbances are particularly detrimental, compounding the already elevated baseline risk of cardiovascular morbidity and mortality [39]. In our study, cardiovascular mortality accounted for a substantial proportion of deaths, suggesting that cardiovascular causes may represent one of the major pathways linking elevated BRI to mortality among patients with CKD. Furthermore, excess visceral fat may accelerate CKD progression through the secretion of adipokines and oxidative stress mediators [40, 41]. Second, obesity, as captured by BRI, may lead to structural and functional changes in the kidney, including increased kidney weight, glomerular and tubular hypertrophy and activation of the intrarenal renin–angiotensin–aldosterone system, all of which can contribute to accelerated kidney function decline and increased mortality risk [42].

We demonstrated that elevated BRI may confer a significantly greater relative risk of mortality in younger patients with CKD, aligning with prior findings in the general population [18]. This may be partly explained by the fact that younger individuals with higher levels of visceral fat may experience accelerated atherosclerotic progression, thereby increasing their risks of cardiovascular disease and premature mortality [43]. In contrast, among older patients with CKD, the prognostic impact of BRI may be diminished due to competing age-related factors such as frailty, sarcopenia and multimorbidity [44, 45]. These results highlight the importance of early identification and targeted intervention for central obesity in younger patients with CKD, for whom effective risk modification may yield more substantial long-term benefits. In addition, the observed interaction between BRI and elevated albuminuria suggests a possible synergistic effect between central adiposity and kidney damage on mortality. Albuminuria is a well-established marker of endothelial dysfunction [46] and renal injury [47] and may amplify the harmful metabolic and cardiovascular consequences of excess visceral fat. Elevated BRI may exacerbate inflammation, insulin resistance and atherogenesis—pathways already activated in patients with albuminuria [37–39].

Table 3: Subgroup analysis of the association of BRI, BMI and WC with all-cause and cardiovascular mortality in patients with CKD.

	All-cause mortality			Cardiovascular mortality		
Variable	**Events/cases, *n/N***	**HR (95% CI)**	***P* for interaction**	**Events/cases, *n/N***	**HR (95% CI)**	***P* for interaction**
BRI (>10)						
Sex			0.13			0.05
Male	43/143	2.46 (1.53–3.95)		20/143	2.69 (1.25–5.79)	
Female	71/282	1.35 (0.89–2.04)		32/282	1.69 (0.82–3.50)	
Age (years)			**0.003**			**0.02**
<65	56/277	2.16 (1.03–4.52)		21/277	3.61 (0.98–13.3)	
≥65	58/148	1.58 (1.06–2.34)		31/148	2.08 (1.11–3.86)	
Hypertension			0.8			0.2
Yes	100/327	1.73 (1.28–2.33)		46/327	1.82 (1.05–3.14)	
No	14/98	2.86 (1.04–7.91)		6/98	5.81 (1.55–21.8)	
Diabetes			0.8			0.8
Yes	72/232	1.64 (1.03–2.61)		30/232	2.97 (1.21–7.32)	
No	42/193	1.78 (1.10–2.90)		22/193	2.12 (1.13–3.98)	
eGFR (ml/min/1.73 m^2)			0.2			0.2
≥45	85/351	2.02 (1.39–2.93)		40/351	2.48 (1.47–4.18)	
15–44	29/74	1.29 (0.61–2.73)		12/74	1.27 (0.37–4.28)	
UACR (mg/g)			0.05			**0.03**
<30	29/97	1.13 (0.59–2.14)		16/97	1.21 (0.41–3.62)	
≥30	85/328	1.90 (1.32–2.73)		36/328	2.42 (1.35–4.35)	
BMI (>30 kg/m^2)						
Sex			0.9			0.9
Male	377/1247	0.61 (0.42–0.88)		135/1247	0.55 (0.32–0.94)	
Female	339/1521	0.54 (0.41–0.70)		147/1521	0.67 (0.41–1.12)	
Age (years)			0.9			0.9
<65	218/1567	0.42 (0.23–0.76)		74/1567	0.29 (0.10–0.81)	
≥65	498/1201	0.63 (0.49–0.81)		208/1201	0.77 (0.52–1.15)	
Hypertension			**0.028**			**0.028**
Yes	583/1939	0.49 (0.37–0.64)		234/1939	0.50 (0.33–0.77)	
No	133/829	0.82 (0.50–1.36)		48/829	0.95 (0.42–2.16)	
Diabetes			0.5			0.5
Yes	366/1148	0.52 (0.36–0.75)		140/1148	0.76 (0.41–1.41)	
No	350/1620	0.56 (0.41–0.77)		142/1620	0.46 (0.27–0.79)	
eGFR (ml/min/1.73 m^2)			0.9			0.7
≥45	529/2356	0.49 (0.37–0.65)		203/2356	0.49 (0.31–0.76)	
15–44	187/412	0.83 (0.55–1.26)		79/412	1.13 (0.56–2.31)	
UACR (mg/g)			0.3			0.3
<30	243/764	0.75 (0.51–1.09)		101/764	0.99 (0.52–1.90)	
≥30	473/2004	0.49 (0.37–0.64)		181/2004	0.50 (0.32–0.77)	
Waist circumference (>125 cm)						
Sex			0.3			0.6
Male	112/355	1.85 (1.01–3.40)		40/355	0.96 (0.38–2.46)	
Female	57/245	2.71 (1.66–4.41)		23/245	3.99 (1.72–9.23)	
Age (years)			**0.003**			0.09
<65	77/389	2.64 (1.16–6.03)		28/389	1.43 (0.41–4.95)	
≥65	92/211	2.33 (1.54–3.53)		35/211	2.41 (1.27–4.57)	
Hypertension			0.9			0.7
Yes	145/460	2.14 (1.44–3.18)		56/460	2.00 (0.97–4.15)	
No	24/140	2.85 (1.19–6.80)		7/140	1.47 (0.34–6.38)	
Diabetes			0.8			0.8
Yes	107/326	2.18 (1.33–3.56)		38/326	2.54 (1.04–6.22)	
No	62/274	2.25 (1.38–3.66)		25/274	1.69 (0.84–3.39)	
eGFR (ml/min/1.73 m^2)			0.4			0.7
≥45	130/508	2.25 (1.44–3.51)		48/508	1.80 (0.89–3.65)	
15–44	39/92	1.97 (0.89–4.37)		15/92	2.13 (0.57–8.00)	
UACR (mg/g)			0.7			0.8
<30	45/125	2.32 (1.24–4.36)		18/125	2.32 (0.62–8.69)	
≥30	124/475	1.73 (1.07–2.81)		45/475	1.27 (0.59–2.76)	

P-values <.05 are in bold.
All analyses were adjusted for age, sex, race/ethnicity, education level, marital status, employment status, alcohol intake, smoking status, physical activity level, presence of hypertension, diabetes, coronary heart disease, cancer, eGFR, UACR, haemoglobin, serum albumin, total cholesterol, HDL-C and body weight when assessing the associations of BRI/WC with mortality or WC when assessing the association of BMI with mortality.
The reference groups were BRI of 5.9–6.8 for all-cause mortality and 5.9–6.5 for cardiovascular mortality. For BMI and WC, the reference group (18.5–25 kg/m^2 and 95–105 cm, respectively) was used for both all-cause and cardiovascular mortality.

These results suggest that clinical risk assessment in CKD should account not only for kidney function and albuminuria but also for body fat distribution, particularly central adiposity.

We observed higher BMI was associated with lower risks of both all-cause and cardiovascular mortality, consistent with the so-called obesity paradox, previously reported in haemodialysis CKD populations [48]. One possible explanation is that BMI fails to differentiate between fat and lean mass and does not account for fat distribution—factors particularly relevant in CKD, where muscle wasting and sarcopenia are common [49]. These limitations can lead to misclassification of risk when BMI is used in isolation. Moreover, another study reported that higher BMI was associated with increased composite cardiovascular risk in adults with glomerular nephropathy [50]. Additionally, we found that WC was associated with all-cause but not cardiovascular mortality, suggesting that WC may partly capture general health status but lacks specificity for cardiovascular risk. In contrast, by incorporating both body shape and fat distribution, BRI offers a more accurate estimation of central obesity and incremental prognostic value beyond WC alone, particularly for cardiovascular mortality. Although the relatively low number of cardiovascular deaths could raise concerns about statistical power, BRI demonstrated a significant association even with fewer events than WC. This highlights the added value of BRI in the CKD population, where traditional anthropometric measures like BMI and WC may be confounded and less reflective of true cardiometabolic risk.

Our study has several notable strengths. To our knowledge, this is the first study to evaluate the predictive value of BRI, BMI and WC for both all-cause and cardiovascular mortality in patients with CKD, using a large, nationally representative sample of the US population. The extended duration of follow-up, along with comprehensive adjustment for a wide range of confounders, strengthens the validity of our findings. However, several limitations should be acknowledged when interpreting these results. First, although NHANES offers standardized and high-quality data, only single measurements of serum creatinine and albuminuria were available for each participant. Both eGFR and UACR are subject to biological variability and may fluctuate over time [51, 52]. Nevertheless, NHANES remains the cornerstone of epidemiologic research on CKD in the US population [22–25]. Second, anthropometric measures were assessed at a single time point, which does not account for longitudinal changes in body composition that may influence outcomes. Third, the majority of participants in this study had early-stage CKD characterized by preserved eGFR but elevated UACR, which may limit the generalizability of our findings to patients with more advanced CKD. Moreover, as the study was based on a US population, caution should be exercised when generalizing the findings to other populations with different ethnic, lifestyle or healthcare backgrounds. Finally, factors such as dietary patterns and medication use were not assessed and could confound observed associations.

In conclusion, this study highlights that elevated BRI is independently associated with an increased risk of all-cause and cardiovascular mortality in patients with early-stage CKD, providing greater prognostic value for risk stratification than BMI or WC. These findings underscore the clinical importance of recognizing central obesity as a critical risk factor and incorporating BRI into routine clinical assessments and public health strategies to improve patient outcomes in CKD. Future research should explore longitudinal trajectories of BRI in relation to mortality risk and other clinical outcomes, particularly in patients with advanced CKD.

SUPPLEMENTARY DATA

Supplementary data are available at *Nephrology Dialysis Transplantation* online.

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AUTHORS' CONTRIBUTIONS

C.Y. and G.S. contributed to the study conception. C.Y. and B.L. contributed to data acquisition. C.Y. conducted the data analysis and was responsible for writing the first draft of the manuscript. P.V., D.W.J., R.T.G. and G.S. critically reviewed the manuscript. All authors read and approved the final version of the manuscript. Each author contributed important intellectual content during manuscript drafting or revision and agreed to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work are answered.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the National Health and Nutrition Examination Survey (https://www.cdc.gov/nchs/nhanes/).

CONFLICT OF INTEREST STATEMENT

None declared.

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